Fachbereich Erziehungswissenschaft und Psychologie
der Freien Universität Berlin

The Fidelity of Neural Representations Shapes Episodic Memory Across the Human Lifespan

Dissertation
zur Erlangung des akademischen Grades
doctor rerum naturalium (Dr. rer. nat.)

vorgelegt von
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MSc Cognitive Neuroscience

Berlin, 2020

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Tag der Disputation: 26. Oktober 2020

Eidesstattliche Erklärung

Hiermit versichere ich, dass ich die vorgelegte Arbeit selbstständig verfasst habe. Andere als die angegebenen Hilfsmittel habe ich nicht verwendet. Die Arbeit ist in keinem früheren Promotionsverfahren angenommen oder abgelehnt worden.

Berlin, den 10. Juni 2020

Verena Sommer

Acknowledgements

This dissertation was conducted within the research project Cognitive and Neural Dynamics of Memory across the Lifespan (ConMem) as well as the Minerva group Lifespan Age Differences in Memory Representations (LIME) at the Center for Lifespan Psychology of the Max Planck Institute for Human Development. During my time as a graduate student, I was a fellow of the International Max Planck Research School on the Life Course (IMPRS LIFE). I am very grateful to these institutions and the people involved for making my dissertation project possible.

I would particularly like to thank Prof. Dr. Ulman Lindenberger and Dr. Myriam Sander for their invaluable commitment in mentoring my dissertation. I deeply thank Myriam for always having time for me, for encouraging me, and for her exceptional support and guidance. Furthermore, I am very grateful to Dr. Markus Werkle-Bergner for his valuable feedback and helpful discussions that greatly improved my projects. I further thank Prof. Dr. Michael Niedeggen for his willingness to evaluate my dissertation and Prof. Dr. Thad Polk, Prof. Dr. Steffi Pohl, and Dr. Radoslaw Cichy for kindly agreeing to join my doctoral committee.

I would like to thank everyone in ConMem/LIME, at the Center for Lifespan Psychology, as well as at the IMPRS LIFE for their helpful input and discussions over the years. I am very thankful to my co-authors, without whom I could not have conducted the research presented in this dissertation: Dr. Yana Fandakova, Dr. Thomas Grandy, Dr. Attila Keresztes, Malte Kobelt, Luzie Mount, Dr. Myriam Sander, Prof. Dr. Yee Lee Shing, Prof. Dr. Sarah Weigelt, and Dr. Markus Werkle-Bergner. I thank them for their contribution to developing the studies, collecting data, discussing the results, as well as their valuable input for writing the manuscripts. I especially thank Malte for his great collaboration and work on the fMRI data analysis. I am furthermore very grateful to all student assistants and interns who were involved in the Merlin, BloSsoM, and BeBo studies, and to everyone who provided technical and organizational support, particularly Gabriele Faust. I would also like to thank Julia Delius and Claire Pauley for their editorial assistance. My special thanks go out to all $\sim$400 participants who took part in the pilot and main experiments.

Furthermore, I am immensely grateful to my doctoral colleagues who always supported me professionally and emotionally. I could not imagine this journey without your collegiality and friendship. Special thanks to Martin and Beate who taught me so much, and also Anna and Anka who never hesitated to help out – all of you and everyone else who shared our office over the years made it not only a productive, but fun time that I will always keep in good memory.

Finally, I am very lucky to have family and friends who accompanied and helped me throughout all these years. I could not be more grateful to my parents, Doris and Rolf, as well as Petra and Germano for their unconditional support and encouragement. I thank my friends who are always there for me, and especially Jannis for being the most supportive life companion I could wish for.

List of Studies

Study I

Sommer VR, Mount LK, Weigelt S, Werkle-Bergner M, Sander MC (under revision). Memory specificity is linked to repetition effects in event-related potentials across the lifespan. Preprint doi: 10.1101/2020.09.14.295972.

Study II

Sommer VR, Fandakova Y, Grandy TH, Shing YL, Werkle-Bergner M, Sander MC (2019). Neural pattern similarity differentially relates to memory performance in younger and older adults. The Journal of Neuroscience 39:8089–8099. doi: 10.1523/JNEUROSCI.0197-19.2019.

Study III

Sommer VR*, Kobelt M*, Keresztes A, Werkle-Bergner M, Sander MC (under revision). From age differences in category distinctiveness to item level specificity and stability: Bridging representational levels. Preprint doi: 10.1101/2020.07.06.187187v1

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Summary

Episodic memory is the ability to remember past experiences. How well we remember is influenced by how well the information is encoded in the brain at the time of memory formation. Given that memory performance improves across childhood and declines in old age, the question arises whether this is related to changes in the quality of neural information representation. In three empirical studies, I investigated how the neural representations during memory encoding shape memory success, explaining differences within and between individuals as well as between age groups.

In Study I, we identified age-independent neural indicators of the formation of high-fidelity memory representations in children, young adults, and older adults. Specifically, changes in the amplitudes of electroencephalography (EEG) signals in response to repeated object images were related to inter-individual differences in memory specificity, that is, the ability to distinguish highly similar items, which requires precise encoding of perceptual details. Studies II and III further looked into the specific neural representational properties associated with successful memory and how these may change across the adult lifespan. Study II found that the similarity between neural representations during memory acquisition was differentially linked to subsequent memory performance in young and older adults. Neural representations were measured as EEG time–frequency patterns while participants studied scene–word pairs that were later tested in a cued recall task. While young adults performed better in the task than older adults and their memory benefited from forming distinct neural representations, older adults' memory benefited from forming similar representations. These findings might reflect age differences in encoding strategies and accordingly a shift in the neural representational properties supporting memory performance in the course of aging. Study III further examined the distinctiveness of neural representations as well as their stability over time as assessed by activation patterns measured with functional magnetic resonance imaging (fMRI). We quantified the amount of broader category information (i.e., whether an image of a face or house was presented) and the amount of information about individual items (i.e., the particular face or house) contained in neural activity patterns, and how this representational specificity related to memory performance. While age differences coexisted across different representational levels and brain regions, particularly item specificity accounted for intra- and inter-individual differences in recognition memory performance and was reduced in older adults. Together, Studies I–III demonstrate the importance of the fidelity of neural information representation for episodic memory. The findings suggest that changes in neural representational properties relate to the development of memory abilities across the lifespan.

Overall, the goals of this dissertation were to (1) uncover the influence of how information is neurally represented at the time of encoding for later memory success, and (2) how this brain–behavior relationship may be altered during childhood and old age. The findings highlight the neural mechanisms of successful memory formation across the lifespan as well as the specific neural representational properties benefiting memory performance in young and older adults.

Zusammenfassung

Als episodisches Gedächtnis wird die Fähigkeit bezeichnet, sich an vergangene Erlebnisse zu erinnern. Wie gut wir uns erinnern können, wird davon beeinflusst, wie gut diese Informationen während der Gedächtnisbildung im Gehirn kodiert werden. Da sich die Gedächtnisleistung im Laufe der Kindheit verbessert und im hohen Alter abnimmt, stellt sich die Frage, ob dies mit Veränderungen in der Qualität der neuronalen Repräsentationen zusammenhängt. In drei empirischen Studien habe ich untersucht, wie die neuronalen Repräsentationen während der Gedächtnisformierung dessen Erfolg beeinflussen, und wie dadurch Gedächtnisunterschiede innerhalb und zwischen Individuen sowie zwischen Altersgruppen erklärt werden können.

In Studie I konnten altersunabhängige neuronale Indikatoren für die Bildung von sehr akkuraten Gedächtnisrepräsentationen in Kindern, jungen und älteren Erwachsenen bestimmt werden. Insbesondere gab es einen Zusammenhang zwischen Amplitudenunterschieden im Elektroenzephalogramm (EEG) als Reaktion auf wiederholt gezeigte Objektbilder und interindividuellen Unterschieden in der Gedächtnisspezifizität. Gedächtnisspezifizität bezeichnet die Fähigkeit, sehr ähnliche Bilder auseinanderhalten zu können, was eine präzise Enkodierung perzeptueller Details erfordert. Die Studien II und III haben darüber hinaus die spezifischen Eigenschaften von neuronalen Repräsentationen, die im Zusammenhang mit Gedächtnis stehen, und deren Veränderungen im Erwachsenenalter, untersucht. Dabei hat Studie II ergeben, dass in jungen und älteren Erwachsenen die Ähnlichkeit zwischen verschiedenen neuronalen Repräsentationen während des Gedächtniserwerbs auf unterschiedliche Weise mit der späteren Gedächtnisleistung zusammenhängt. Neuronale Repräsentationen wurden als Zeit-Frequenz-Muster im EEG gemessen, während die StudienteilnehmerInnen Bild-Wort-Assoziationen gelernt haben, die anschließend in einem Cued-Recall-Test abgefragt wurden. Während junge Erwachsene in der Aufgabe besser abschnitten als ältere Erwachsene und ihr Gedächtnis von der Bildung unterschiedlicher neuronaler Repräsentationen profitierte, profitierte das Gedächtnis älterer Erwachsener von der Bildung ähnlicher Repräsentationen. Diese Ergebnisse könnten Altersunterschiede in den Lernstrategien widerspiegeln und demensprechend eine Veränderung der Eigenschaften neuronaler Repräsentationen, die die Gedächtnisleistung im Laufe des Alterns unterstützen. In Studie III wurde des Weiteren die Unterschiedlichkeit und Stabilität neuronaler Repräsentationen als Aktivierungsmuster mittels funktioneller Magnetresonanztomographie (fMRT) bestimmt. Dafür wurde ermittelt, wie viel Information über die generelle Kategorie eines gezeigten Stimulus (d.h., ob ein Gesicht oder Haus abgebildet war) und wie viel Information über das individuelle Item (d.h., ein bestimmtes Gesicht oder Haus) in den neuronalen Aktivierungsmustern vorhanden war, und wie diese Spezifizität der Repräsentationen mit der Gedächtnisleistung einherging. Altersunterschiede bestanden auf verschiedenen Repräsentationsebenen und in unterschiedlichen Gehirnregionen, wobei vor allem Item-Spezifizität zu intra- und interindividuellen Gedächtnisunterschieden beitrug und in älteren Erwachsenen verringert war. Zusammengenommen zeigen die drei Studien, dass die Genauigkeit neuronaler Repräsentation von Informationen wichtig für das epi-

sodische Gedächtnis ist. Diese Befunde legen nahe, dass Veränderungen in den Eigenschaften neuronaler Repräsentationen mit der Entwicklung des Gedächtnisvermögens über die Lebensspanne einhergehen.

Alles in allem war es das Ziel dieser Dissertation, aufzudecken, (1) wie die neuronale Repräsentation während der Informationsaufnahme beeinflusst, wie gut die Informationen später erinnert werden und (2) wie sich dieses Verhältnis von Gehirn und Verhalten während der Kindesentwicklung und im hohen Alter verändert. Die Ergebnisse beleuchten die neuronalen Mechanismen erfolgreicher Gedächtnisbildung über die gesamte Lebensspanne sowie die spezifischen neuronalen Repräsentationseigenschaften, die die Gedächtnisleistung bei jungen und älteren Erwachsenen begünstigen.

Contents

1 Introduction

Our ability to remember our past makes us who we are. Memories form our understanding of the world, guide our behavior, and help us anticipate what is coming. Losing the ability to remember radically impairs our capability to orient ourselves, adapt to and interact with our ever-changing environments. One of the fundamental questions of cognitive neuroscience is how the brain is able to “save” our experiences such that they can be relived in the future, so called *episodic memory* (Tulving, 1983). How are memories realized in brain tissue, that is, in neurons and their communication, and what factors determine whether a certain event becomes a vivid and long-lasting episodic memory? Furthermore, how does a system that accomplishes such complex abilities develop over the course of the lifespan and what happens in old age when it (often) becomes more difficult to remember certain things? These questions are the basis of the work presented and discussed in this dissertation.

In order to remember an event, information about the event needs to be processed in the brain, which entails translating incoming sensory information into a neural code that represents said information (Dudai, Dudai, & Fitzpatrick, 2007; Tulving, 2007). Thus, a *neural representation* is encoded structured information about the world that can influence behavior (Dudai, 1989; Dudai et al., 2007). In the same way as, for instance, a picture can be described with varying specificity, from the level of color in each pixel to the depicted objects and their meaning, neural representations can vary in the specificity of the information they contain. Incoming visual information, for example, is processed in the visual cortex where the signals undergo successive transformations, from the level of representing low-level sensory features, which are integrated while the signals progress through the hierarchy of the visual processing streams to construct high-level abstract representations of, for example, the objects in one’s surrounding (cf. Gallant & Popham, 2020; Grill-Spector & Malach, 2004; Hubel & Wiesel, 1959; C. B. Martin, Douglas, Newsome, Man, & Barense, 2018; Mather, 2006). In order to maintain information about events over time, the neural signal processing needs to induce lasting cellular changes, which form the basis of long-term memory (Kandel, Dudai, & Mayford, 2014; Milner, Squire, & Kandel, 1998; Semon, 1904).

It is generally agreed upon that neural representations are realized as the patterns of neural activity elicited by what is represented (e.g., Averbeck, Latham, & Pouget, 2006). However, multiple theories abut the underlying neural code exists. Its exact form has yet to be established (Josselyn & Tonegawa, 2020; Roy, Perlovsky, Besold, Weng, & Edwards, 2018; Treves, 2007). Nevertheless, content-specific neural activation patterns can be indentified with various neuroimaging methods (Ishai, Ungerleider, Martin, & Haxby, 2000; Kuhl, Rissman, & Wagner, 2012; Michelmann, Bowman, & Hanslmayr, 2018; Xue, 2018) which allows for the investigation of the nature of memory representations and the neural factors influencing whether and how well information will be remembered. Specifically, the fidelity with which information is encoded into neural representations is thought to be directly related to the accuracy and specificity of memories (Rissman & Wagner, 2012). Here, *fidelity* denotes how faithfully and precisely neural activity represents a certain content (see definitions of frequently used terms to describe neural representations in the Glossary). In particular, the distinctiveness and stability of neural representations are considered to be crucial for memory success (e.g., Y. Lu, Wang, Chen, & Xue, 2015; Kuhl et al., 2012; Xue, 2018). Alterations in these representational properties may be underlying age-related differences in memory abilities across the lifespan (e.g., Koen, Srokova, & Rugg, 2020; D. C. Park et al., 2004), accompanying changes in the critical brain structures and functions including neocortical and medial temporal lobe (MTL) regions (Cabeza, Nyberg, & Park, 2017; Casey, Giedd, & Thomas, 2000; Ofen & Shing, 2013; Shing et al., 2010). Episodic memory abilities improve across childhood and adolescence (Keresztes, Ngo, Lindenberger, Werkle-Bergner, & Newcombe, 2018; W. Schneider, 2014; Shing et al., 2010), suggesting an enhancement of neural functioning that enables the formation of increasingly high-fidelity neural representations, which has, however, only scarcely been studied (cf. M. A. Cohen et al., 2019; Fandakova, Leckey, Driver, Bunge, & Ghetti, 2019). Old age, in turn, is associated with reduced memory competences (Naveh-Benjamin & Ohta, 2012; W.-C. Wang & Cabeza, 2017) which has been linked to a degradation of neural representational quality (S.-C. Li, Lindenberger, & Frensch, 2000; S.-C. Li, Lindenberger, & Sikström, 2001; Koen, Hauck, & Rugg, 2019; J. Park, Carp, Hebrank, Park, & Polk, 2010). Thus, further understanding of the properties of neural representations that enable successful memory encoding, and the age-specific differences therein, will enhance our comprehension of human episodic memory in general as well as its development across the lifespan.

Within this dissertation I will review the current theoretical and empirical evidence on how information is neurally represented in children, young adults, and older adults, how the properties of neural representations influence memory, and how this relationship may differ across the lifespan. In three empirical studies, I investigated the neural mechanisms of successful memory formation across the lifespan as well as the specific neural representational properties benefiting memory performance in young and older adults.

2 Theoretical, Empirical, and Methodological Foundations

Neural representations are a central concept in neurocognitive research linking brain activity and cognition, for example, how the brain encodes, maintains, and retrieves information. First, I will provide an overview of the neurocognitive basics of episodic memory, including the most relevant cognitive theories and neural mechanisms underlying memory encoding, consolidation, and retrieval (2.1.1). I will discuss the current theoretical and empirical evidence on how information is represented in neural activity (2.1.2). Most work focuses on spatial aspects of neural representations, but also the temporal dynamics of neural activity play a critical role in information representation. Different methods have been developed over the last decades that allow us to investigate these different aspects of neural representations and their relation to memory performance (2.1.3). Representational properties may already determine during encoding whether and how specific experiences will be remembered later on. Specifically, two properties of neural representations are of central interest, namely their distinctiveness from each other as well as their stability over time (2.2.1). I will review relevant findings indicating that differences in the discussed neural markers of representational quality can help us to understand intra- and inter-individual differences in memory during aging (2.2.2) and maturation (2.2.3).

2.1 Neural representations as a central concept of neural information processing and memory

2.1.1 The neurocognitive basis of episodic memory

Episodic memory is the ability to consciously remember and mentally relive past experiences which can guide future behavior (Tulving, 1983, 2002). Episodic memory is part of the declarative long-term memory system that enables explicit recollection of facts and events as opposed to implicit (unconscious) memory (N. J. Cohen & Squire, 1980; Graf & Schacter, 1985; Squire, 2004; Squire & Zola, 1996; Tulving, 1972). To achieve this, external and internal information needs to be translated into a lasting neural code that represents and retains the respective information to be retrievable at a later time (Dudai et al., 2007; Hasselmo, 2007; Josselyn, Köhler, & Frankland, 2015; Tulving, 1983, 2007). Here, I will refer to this translation as *memory encoding* and the neural code or substrate of a memory as *memory representation*[1]. One of the critical brain structures for episodic memory is the MTL, in particular the hippocampus, which has connections to temporal and frontal lobes (McClelland, McNaughton, &

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[1] Other terms with varying connotations are also used in the literature, including memory *formation* or *acquisition* (for encoding) and memory *image*, *engram*, or *trace* (for representation) (cf. Tulving, 2007). If adopted here, they will be used interchangeably.

O'Reilly, 1995). Especially the interactions of the MTL and prefrontal regions have been shown to be essential for memory encoding, consolidation, and retrieval (Eichenbaum, 2017; Moscovitch, Cabeza, Winocur, & Nadel, 2016; Simons & Spiers, 2003). During encoding, incoming information is processed in cortical areas and the associated features are bound together in the MTL, whereby regions in the prefrontal cortex provide top-down control to adapt and organize MTL representations (Simons & Spiers, 2003). Following encoding, memory consolidation strengthens the memory representations and integrates them into existing knowledge (Dudai, 2004; Dudai, Karni, & Born, 2015; McClelland, McNaughton, & Lampinen, 2020; Redondo & Morris, 2011; Takeuchi, Duszkiewicz, & Morris, 2014; Tonegawa, Pignatelli, Roy, & Ryan, 2015). This is done through fast cellular consolidation that forms and stabilizes synaptic connections by neurochemical changes as well as slower systems consolidation (Dudai, 2004; Mednick, Cai, Shuman, Anagnostaras, & Wixted, 2011). According to systems consolidation theory, memories undergo time-dependent reorganization and stabilization from the initial fast encoding in the hippocampus to a more permanent retention in distributed neocortical regions (Frankland & Bontempi, 2005; Nadel & Moscovitch, 1997; S.-H. Wang & Morris, 2009; Wiltgen, Brown, Talton, & Silva, 2004). Finally, successful memory retrieval can be achieved when representations are reactivated (Jonker, Dimsdale-Zucker, Ritchey, Clarke, & Ranganath, 2018; Josselyn & Tonegawa, 2020; Poo et al., 2016; Nyberg, Habib, McIntosh, & Tulving, 2000; Rugg et al., 1998; Rugg, Johnson, Park, & Uncapher, 2008; see also 2.2.1). Such reactivation can be triggered by cues that were available at encoding, for example, the context or (parts of) a stimulus, leading to cortical reinstatement of the respective memory representation (J. D. Johnson, McDuff, Rugg, & Norman, 2009; Marr, 1971; Staresina, Henson, Kriegeskorte, & Alink, 2012; Staudigl, Vollmar, Noachtar, & Hanslmayr, 2015; Tulving & Thomson, 1973; Wimber, Maaß, Staudigl, Richardson-Klavehn, & Hanslmayr, 2012; Yaffe et al., 2014). To sum up, experiences induce lasting changes in the brain which constitute the ability to remember those experiences (Josselyn & Tonegawa, 2020; Kandel et al., 2014; Semon, 1904; Schacter, Eich, & Tulving, 1978), which further depends on the successful memory consolidation and retrieval.

However, not all experiences become long-term memories, and not all memories "feel" the same: Memories differ in their subjective qualities, such as confidence, vividness, and specificity (Bowman, Chamberlain, & Dennis, 2019; Busey, Tunnicliff, Loftus, & Loftus, 2000; M. K. Johnson, Kuhl, Mitchell, Ankudowich, & Durbin, 2015; Richter, Cooper, Bays, & Simons, 2016). While these qualities often change over time, transforming detailed, vivid, and event-specific memories to more general knowledge (see memory transformation theory and complementary learning systems theory; McClelland et al., 1995, 2020; O'Reilly & Norman, 2002; O'Reilly, Bhattacharyya, Howard, & Ketz, 2014; Robin & Moscovitch, 2017; Wiltgen & Silva, 2007; Winocur & Moscovitch, 2011), memories can already to some extent vary in these dimensions shortly after encoding. With regard to memory specificity, it has been suggested that the amount of specific versus general information that can be remembered may already be in part determined by the fidelity of the neural representations during perception, that is, how precisely incoming information has been encoded (McClelland & Rumelhart, 1985; Trelle, Henson, & Simons, 2019; see Figure 1A). The more accurate a representation has been formed in the first place, the more details will be retrievable afterwards.

However, a lack of detail is not necessarily a failure of the memory system. The need to balance the faithful representation of specific details and allowing for sufficient overlap to detect regularities is a major tradeoff that adaptive memory systems face (Keresztes et al., 2017; Xu & Südhof, 2013). On the one hand, remembering concrete details about past events and the encountered people and objects without confusing similar information is critical in many situations (Keresztes et al., 2018). On the other hand, memories of past experiences need to be abstracted and applied to future events to guide successful behavior (McClelland & Rumelhart, 1985; Wiltgen & Silva, 2007). In general, highly specific memories can be maintained and dissociated from similar memory representations through pattern separation processes of the hippocampus, whereas generalization and integration into former representations are realized through pattern completion (Keresztes et al., 2018; McHugh et al., 2007; Nakashiba et al., 2012; Yassa & Stark, 2011). The question of what mechanisms regulate the balance of necessary and sufficient specificity and generalization is central to the study of the neurocognitive foundations of memory (e.g., Xu & Südhof, 2013). One way to address this question is to examine how information is represented in the brain, and what representational properties may be related to more specific or more general memories (see 2.2.1).

In summary, episodic memory depends on the successful encoding, maintenance, and retrieval of memory representations. The success and specificity of memory may be particularly related to the quality of neural information representation, raising the principle question of how information representation is implemented in the brain.

2.1.2 The spatial, temporal, and spectral code of information representation in the brain

Variations in memory success and specificity (see above) may be associated with differences in the quality of the underlying neural representations. However, despite the long history of theories and experiments concerned with the nature of representations, the exact code in which information is written into the neural substrate continues to be a matter of debate (cf. Josselyn & Tonegawa, 2020; Milner et al., 1998; Roy et al., 2018; Treves, 2007). In general, incoming sensory information initiates a neural activation cascade, and the elicited (pattern of) activity corresponds to what is perceived. In that way, neural representations link the physical world to how it is mentally experienced (cf. Bain, 1874; Churchland, 1986; Hofstadter, 1999; Kim, 2010; Koch, 2004), indicated by a systematic relationship between features of the world and observed neural activity (Poldrack, 2020).

Traditionally, the contents of the mind have been regarded as different from the operations that form these contents, change, or use them (Tulving & Bower, 1974). In this view, a memory itself is seen as different from the processes of learning and remembering. Although true for computers, this dichotomy is, like the computer metaphor of the brain in general, useful for cognitive theories but does not actually reflect the biology of neural systems (Besold & Kühnberger, 2013; Feldman, 2016; Searle, 1990). As will be discussed in more detail in the following, one common theory is that it is the pattern of activity of neurons, large neural populations, or circuits in which information is encoded (Averbeck et al., 2006; Roy et al., 2018). As the underlying neural units are recurrently connected in local and global networks (e.g., Bullmore & Sporns, 2009; van den Heuvel & Hulshoff Pol, 2010), any activity of a given neural assembly that represents a certain mnemonic content will also immediately lead to its transformation in the context of the ongoing network activity. This transformation can be regarded as a process or operation, emphasizing the practical inseparability of representations and processes as understood in the cognitive literature (e.g., Tulving & Bower, 1974). Hence, although one can focus more on the representational aspects of the neural basis of cognition rather than on specific neural processes, in the current thesis, neural representations are not in a strict sense understood as separate from processes such as encoding (cf. Feldman, 2016).

Currently, in cognitive neuroscience, representations are a central concept that link cognition to brain activity (Kriegeskorte & Kievit, 2013), and do not necessarily distinguish between contents and processes. Neural activity represents content and, at the same time, reflects the processes concerned with these contents. In practice, the neural representation of a specific stimulus is often defined as the pattern of brain activity elicited by that stimulus as recorded by a given brain signal measure, for example, during stimulus perception (e.g., Carp, Park, Polk, & Park, 2011; Y. Lu et al., 2015; Visser, Scholte, Beemsterboer, & Kindt, 2013; Xue, 2018; Zheng et al., 2018). Currently available tools to measure brain activity (see 2.1.3) cannot in the strict sense (practically nor theoretically) separate represented content from the associated processes. However, they are able to differentiate content-specific information (e.g., Kuhl & Chun, 2014), even at the level of individual stimuli (e.g., Yaffe et al., 2014; Zheng et al., 2018) and thus are suitable to study neural representations in a broader sense. Nonetheless, it has been postulated that different approaches to analyzing brain activation data can have different foci on rather the level of neural processes or the level of representations (see 2.1.3).

In line with the evident significance of the brain's structure and spatial organization (cf. Buzsáki, 2006; Gall, 1835; Grill-Spector & Malach, 2004; Price & Friston, 2005; Riese & Hoff, 1950), most theories focus on spatial properties of the neural code in which information is thought to be represented. A clear example of information from the environment being neurally represented in a spatial manner are topographic representations. Here, high-dimensional sensory input is projected to a lower dimensional space in the brain (Roy et al., 2018), for instance, in the form of retinotopy in the visual system (e.g., Sereno et al., 1995). In addition to such sensory representations, space has been implicated also in higher-order concept representations, namely via activity of specialized cells (localist representations) or via patterns of activity across cells and cell populations (distributed representations).

According to localist theories, any concept of interest, for example, words or objects, are coded in their individual, distinct, and non-overlapping representations (Bowers, 2009). The (theoretical) limit of this sparseness is a reduction of a representation to a single neuron (Connor, 2005), often called "Gnostic unit" or "Grandmother cell" (Bowers, 2009; Connor, 2005; Feldman, 2016; Konorski, 1967). There are indeed findings that support the notion of single-unit representations, for example, category-selective neurons (e.g., Heit, Smith, & Halgren, 1988; Kreiman, Koch, & Fried, 2000; Perrett, Rolls, & Caan, 1982; Quiroga, Kraskov, Koch, & Fried, 2009; Quiroga, Reddy, Kreiman, Koch, & Fried, 2005; Roy, 2017). However, the theory of a one-to-one mapping is often criticized as being biologically implausible (Connor, 2005; Logothetis & Sheinberg, 1996; O'Reilly, 1998; but for arguments and evidence in favour of single-unit representations, see, e.g., Bowers, 2009; Roy, 2017).

Contrasting and generally more popular theories suggest that information is coded in a parallel and distributed manner such that individual units can be involved in multiple representations (McClelland, Rumelhart, & PDP Research Group, 1987; O'Reilly, 1998; Rumelhart, McClelland, & PDP Research Group, 1986). Computationally, distributed representations benefit from a "division of labor" across many neurons (A. R. McIntosh, 2007) such that more concepts can be represented by a set of units rather than by units representing single concepts (i.e., dense or coarse population coding; Bowers, 2009; Feldman, 2016; Fotheringhame & Young, 1997; Roy, 2017). At the extreme, representations that are very distributed, that is, far from sparse, would contain little to no information about the represented content in their single units (Fotheringhame & Young, 1997). On the cellular level, evidence that information is represented in distributed patterns of neural activity was, for example, provided by Young and Yamane (1992). They showed that inferotemporal (IT) cortex neurons of macaques were systematically involved in representing several face stimuli such that stimulus identity was encoded at the population level. Although this clearly suggests a distributed coding scheme, information about specific stimulus dimensions was nevertheless available in single units, suggesting sparse distributed representation (Fotheringhame & Young, 1997). To conclude, evidence for both one-to-one and many-to-many mappings suggest a co-occurrence of localist and distributed coding schemes (Bowers, 2009) and/or a mix of the two extremes (e.g., sparse distributed representations; Fotheringhame & Young, 1997).

A similar distinction of theories concerning localist versus distributed representations can be seen on a macroscopic level. Based on findings that activation of particular brain regions reliably correlates with specific conditions, such as stimulus classes or behaviors (e.g., Eichenbaum, 2010; Friston, Jezzard, & Turner, 1994; Grill-Spector & Malach, 2004), it has been assumed that these regions are specialized for certain tasks. In the domain of visual encoding, fMRI studies indicated that there are dedicated regions in ventral visual cortex (VVC) for representing visual categories such as faces, places, and words (Aguirre, Zarahn, & D'Esposito, 1998; Epstein & Kanwisher, 1998; Kanwisher, McDermott, & Chun, 1997; Polk et al., 2002). Images of faces, for instance, maximally activate a specific area in the fusiform gyrus (therefore named "fusiform face area;" FFA) that is less activated by images of, for example, houses, whereas houses maximally activate a different area, therefore named "parahippocampal place area" (PPA) which is less activated by faces (D. C. Park et al., 2004). However, although the principles of functional localization have proven very successful for advancing cognitive neuroscience and critical for the development of theories and methods, it has also been criticized as too simplified to assume there is a dedicated region for every cognitive function and concept representation (Price & Friston, 2005). Different cognitive processes can involve the same region, and several regions can be involved in a single function (M. X. Cohen, 2011; Price & Friston, 2005). Memory, for example, has been shown to be dependent on many other regions outside the hippocampus, especially within the prefrontal cortex (see above; e.g., Schacter, Norman, & Koutstaal, 1998). In the case of visual stimulus categories, Haxby et al. (2001) showed that a particular stimulus class (for example, faces) could not only be identified from the respective brain activity in the region that responded maximally (in this example, FFA), but also based on the multivariate activation patterns within different areas excluding the seemingly specialized region (see also Ishai, Ungerleider, Martin, Schouten, & Haxby, 1999; Ishai et al., 2000; Kuhl et al., 2012; A. Martin & Chao, 2001). This suggests that these visual categories are represented highly distributed and overlapping across larger brain areas (Haxby et al., 2001; Rissman & Wagner, 2012).

By sharing neural units that represent coinciding features, distributed and overlapping neural patterns furthermore allow the representation of the similarity between different information or events. This was also part of the early propositions of engrams as the loci of memories (Semon, 1904) suggesting engram complexes of connected cells across brain regions, with different parts representing different features of a memory (Josselyn & Tonegawa, 2020; Schacter et al., 1998, 1978; Squire, 1992). While overlapping representations enable the integration and generalization across memories, keeping different memories separate is critical for remembering specific details (see below; e.g., Keresztes et al., 2018; Xu & Südhof, 2013). This is believed to be achieved by sparse coding of the hippocampus that orthogonalizes overlapping input from the cortex and can thus form distinct representations (i.e., pattern separation; Bakker, Kirwan, Miller, & Stark, 2008; Chanales et al., 2017; J. K. Leutgeb, Leutgeb, Moser, & Moser, 2007; O'Reilly & McClelland, 1994; Yassa & Stark, 2011). Overall, distributed neural representations can reflect similarities in their overlap which may vary between brain regions and characterize different levels of specificity.

In addition to representing information in the two dimensions space and activation magnitude, neural activity is continuous, recurrent, and highly dynamic. Thus, time is also an important aspect for neural information coding, allowing multiple neural networks to coexist in the same space (M. X. Cohen, 2011). Multiple observations demonstrated that the temporal firing patterns of neurons carry information (e.g., Adrian, 1926; Fotheringhame & Young, 1997; Gerstner, Kreiter, Markram, & Herz, 1997; Moore, Perkel, & Segundo, 1966; Rose, Brugge, Anderson, & Hind, 1967). For example, one of the first experimental findings of a neuronal code showed that stimulus intensity was represented in the firing rate of sensory neurons, providing support for a frequency coding scheme (Adrian, 1926; Adrian & Zotterman, 1926; see also Gelbard-Sagiv, Mukamel, Harel, Malach, & Fried, 2008; Kapoor et al., 2020; Ng, Logothetis, & Kayser, 2013). How the human brain uses time to encode information can be investigated by measuring the electromagnetic field of certain synchronized neural populations using magneto- and electroencephalography (M/EEG; see 2.1.3). For example, event-related potentials (ERPs) derived from EEG allow for the discrimination of differences in the precise timing and magnitude of population activity at different cortical regions in response to, for instance, sensory input. In this way, various signal components have been identified that predominantly occur under specific conditions and can thus be interpreted as being involved in representing the respective input, such as the processing of faces (Schweinberger & Neumann, 2016) or objects (Schendan & Kutas, 2003). Moreover, low-level stimulus features and high-level conceptual or semantic information can be decoded from spatiotemporal M/EEG signals (see 2.1.3; e.g., A. M. Chan, Halgren, Marinkovic, & Cash, 2011; Carlson, Hogendoorn, Kanai, Mesik, & Turret, 2011). This indicates that changes of activation amplitude over time constitute important aspects of the neural code in addition to the spatial distribution of activity. Importantly, focusing on temporally resolved brain activity allows for the identification of when, and for how long, specific information is represented in the brain (King & Dehaene, 2014).

Furthermore, temporal signals carry information in the frequency domain, that is, in the proportion of a signal lying within certain frequency bands, characterized by the number of events, for example, neuron firings, per time unit. The spectral power in a given frequency band can indicate the rhythmicity of the neural activity (Buzsáki, Anastassiou, & Koch, 2012; Kosciessa, Grandy, Garrett, & Werkle-Bergner, 2020). The excitability of neural populations fluctuates rhythmically, resulting in oscillatory electrophysiological activity (Buzsáki & Draguhn, 2004; Singer, 1999; Tiesinga, Fellous, & Sejnowski, 2008; X.-J. Wang, 2010), which is thought to enable communication and integration across brain networks (Fries, 2015; Varela, Lachaux, Rodriguez, & Martinerie, 2001). Thus, neural oscillations integrate information across multiple neural ensembles that involve different temporal activity patterns (Akam & Kullmann, 2010; Jacobs, Kahana, Ekstrom, & Fried, 2007). Especially concerning synaptic plasticity, the basis of long-term memory, oscillatory mechanisms have proven to be crucial (Buzsáki & Draguhn, 2004; Düzel, Penny, & Burgess, 2010; Fell & Axmacher, 2011; Hanslmayr & Staudigl, 2014; Sander, Fandakova, Grandy, Shing, & Werkle-Bergner, 2020). Both synchronization and desynchronization are suggested to play critical roles (Hanslmayr, Staresina, & Bowman, 2016; Parish, Hanslmayr, & Bowman, 2018). In line with complementary learning systems and memory transformation theory (O'Reilly et al., 2014; Robin & Moscovitch, 2017), it has been suggested that the hippocampus rapidly binds information through synchronized theta ($\sim$7 Hz) and gamma ($>$30 Hz) oscillations (Lisman & Jensen, 2013; Rutishauser, Ross, Mamelak, & Schuman, 2010; Staudigl & Hanslmayr, 2013), whereas neocortical systems form long-term representations mediated by desynchronization of alpha ($\sim$10 Hz) and beta ($\sim$15 Hz) frequencies (Griffiths, Parish, et al., 2019; Hanslmayr, Staudigl, & Fellner, 2012; Hanslmayr et al., 2016; Parish et al., 2018; Staudigl et al., 2015). Overall, theories and empirical evidence (Axmacher et al., 2010; Lisman & Jensen, 2013) as well as simulations (Akam & Kullmann, 2010; Parish, Michelmann, Hanslmayr, & Bowman, 2020) indicate that neural activity on various time scales, i.e., frequencies, is well suited for segregation and representation of diverse contents (e.g., Whittingstall & Logothetis, 2009).

With regard to content representation, a study by Ng et al. (2013) showed that individual auditory stimuli could be discriminated by the firing rates of neurons in macaque auditory cortex as well as by the oscillatory phase patterns of human scalp EEG recordings. According to the study, their correlation demonstrated that the stimulus selectivity of sensory neurons was directly reflected in the stimulus selectivity of EEG phase patterns (Ng et al., 2013). Moreover, encoding-related oscillatory activity showed to be reactivated during successful memory retrieval (see also 2.2.1), indicating context reinstatement (Staudigl et al., 2015; Wimber et al., 2012; Yaffe et al., 2014) as well as stimulus-specific reinstatement (Michelmann, Bowman, & Hanslmayr, 2016; Kerrén, Linde-Domingo, Hanslmayr, & Wimber, 2018; Zhang et al., 2015). Beyond the relevance of power in single frequency bands, scalp EEG (Kerrén et al., 2018; Michelmann et al., 2018) and intracranial EEG studies (Staresina et al., 2016; Zhang et al., 2015) have furthermore demonstrated the rich information profile carried by a wide range of frequencies. Altogether, these findings indicate a key function of a spectral code, where information can be coded in the frequency, power, and phase dimensions (M. X. Cohen, 2011; Schyns, Thut, & Gross, 2011) and their coupling (e.g., Fell & Axmacher, 2011; Lisman & Jensen, 2013; Siems & Siegel, 2020), for the formation, retention, and reactivation of memory representations.

The relationship of spectral EEG and spatial fMRI representations was investigated in a simultaneous EEG–fMRI study by Griffiths, Mayhew, et al. (2019). The study revealed that alpha/beta power was negatively correlated with the amount of stimulus-specific information within the cortex during both perception and retrieval. Rather than representing information itself, the study indicated that alpha/beta decreases provide the conditions that support high-fidelity information representation, presumably by reducing the predictability of neural firing patterns (Griffiths, Mayhew, et al., 2019; Hanslmayr et al., 2012). Accordingly, M. X. Cohen (2011) argued that spatial patterns in fMRI data and time–frequency patterns in M/EEG data may provide complementary insights.

All in all, it is suggested that the brain uses different neural codes in different regions varying between the (theoretical) extremes of sparse and dense representation, which can be studied by analyzing the spatial distribution of neural activation within and across different areas (e.g., Bowers, 2009; Haxby et al., 2001; McClelland & Rumelhart, 1985; Rissman & Wagner, 2012; Young & Yamane, 1992). Furthermore, the dynamic patterns of synchronization and desynchronization within and across brain regions demonstrate to play an important role for neural information processing (e.g., Fries, 2015) and memory (e.g, Hanslmayr et al., 2016). Specifically, oscillations showed to be directly (e.g., Zhang et al., 2015) or indirectly (e.g., Griffiths, Mayhew, et al., 2019) involved in content representation, indicating a representational coding scheme that engages spatial, temporal, and spectral properties (cf. Ghuman & Martin, 2019; King & Dehaene, 2014; Treves, 2007).

2.1.3 Methods to study neural memory representations

The brain encodes information in the spatial distribution, timing, and dynamics of its electrochemical signals (see above; M. X. Cohen, 2011; Fries, 2015; Treves, 2007). These aspects of neural activation can be differentially accounted for by different, complementary methods for recording and analyzing brain activity (Otten & Rugg, 2005). Furthermore, certain study designs and data analysis approaches are particularly suited for studying the content and properties of neural representations.

A focus on the localization of neural functions and representations favors neuroimaging techniques with high spatial resolution such as fMRI. FMRI estimates brain activity by measuring the metabolic correlates of neuronal activity, namely the blood oxygen level dependent (BOLD) signal, which varies in response to the metabolic demands of active neurons (Huettel, Song, & McCarthy, 2014). Although the spatial resolution provided by fMRI is much higher than that by, for instance, EEG, a typical voxel size still contains tens of thousands of neurons whose activities are averaged (Barron, Garvert, & Behrens, 2016). Furthermore, relative to neuronal activity, the hemodynamic response is slow, contributing to the rather low temporal resolution of fMRI. An activation pattern measured with fMRI is usually averaged over a given experimental trial, such as presentation of a stimulus, providing a static spatial neural representation of that stimulus (e.g., Carp, Park, Polk, & Park, 2011; Ghuman & Martin, 2019; Kriegeskorte & Diedrichsen, 2019; but see Schuck & Niv, 2019). Focusing instead on temporal aspects of the neural code favors brain activity measures with high temporal resolution, such as MEG or EEG, which measure the electric potential and magnetic field generated by neural activity, respectively (Kutas & Dale, 1997). Time–frequency decomposition furthermore permits studying the rhythmic nature of brain activity (Gross, 2014). Thus, in contrast to the static representations assessed with fMRI, M/EEG can reflect the neural activity elicited by an experimental trial as a temporal pattern of amplitude or spectral power changes over certain cortical locations, that is, at the dimensions time, frequency, and/or space, providing a measure of dynamic neural representations (cf. King & Dehaene, 2014; Schyns et al., 2011). Together, fMRI and M/EEG are complementary non-invasive methods to record brain activity that allow investigation of neural representations with a stronger focus on spatial or temporal aspects, respectively.

Furthermore, some techniques are particularly suitable for investigating neural representations and their properties, including repetition paradigms and multivariate analysis approaches. The former utilizes the observation that repeated stimulus input results in altered neural responses, indicating the formation of memory representations (Koen et al., 2020). Specifically, the magnitude of neural activity in response to repeated stimuli is often decreased or increased with respect to first presentations

(Doniger et al., 2001; M. E. Nagy & Rugg, 1989; Nordt, Hoehl, & Weigelt, 2016; Rugg & Doyle, 1994). These repetition suppression and/or enhancement effects have been identified in single neurons (e.g., Miller & Desimone, 1994), ERPs (e.g., Penney, Mecklinger, & Nessler, 2001; Rugg & Doyle, 1994; Schweinberger & Neumann, 2016; Stefanics, Heinzle, Czigler, Valentini, & Stephan, 2018), EEG time–frequency representations (e.g., Gruber & Müller, 2005), BOLD signal (e.g., Henson, Shallice, & Dolan, 2000; Segaert, Weber, de Lange, Petersson, & Hagoort, 2013), and positron emission tomography (PET) (e.g., Henson & Rugg, 2003). The underlying neural mechanisms that give rise to the repetition effects are still under debate (Gotts, Chow, & Martin, 2012; Grill-Spector, Henson, & Martin, 2006; Henson & Rugg, 2003; Krekelberg, Boynton, & van Wezel, 2006; Larsson, Solomon, & Kohn, 2016), for instance, with respect to the meaning of the direction of the effect, that is, suppression versus enhancement (Desimone, 1996; Müller, Strumpf, Scholz, Baier, & Melloni, 2013; Segaert et al., 2013; Turk-Browne, Yi, Leber, & Chun, 2007). However, the observation of an altered neural response to a repeated stimulus suggests that the first encounter with the stimulus has left a lasting neural trace that is re-accessed upon repetition (Koen et al., 2020; Rugg & Doyle, 1994).

Repetition effects have been linked to, for example, behavioral priming effects, i.e., implicit memory (Doniger et al., 2001; Gotts et al., 2012; A. D. Wagner, Maril, & Schacter, 2000; Wiggs & Martin, 1998) and old/new effects during retrieval (Brown & Aggleton, 2001; Gonsalves, Kahn, Curran, Norman, & Wagner, 2005; Turk-Browne, Yi, & Chun, 2006; Van Petten & Senkfor, 1996), while the association with explicit memory performance is debated (cf. M. E. Nagy & Rugg, 1989; Turk-Browne et al., 2006; A. D. Wagner et al., 2000; Ward, Chun, & Kuhl, 2013). Crucially, repetition effects also provide a useful tool to investigate the nature of neural representations (cf. Barron, Garvert, & Behrens, 2016; Grill-Spector et al., 2006). For example, the specificity of neural representations can be tested by presenting not only identical but also highly similar repetitions. If repetition effects only occur for exact repeats, highly item-specific neural representations can be assumed, whereas repetition effects for similar stimuli show that, on the neural level, they are treated as the same, and thus suggest rather general/indistinct representations (cf. Barron, Vogels, et al., 2016; Goh, Suzuki, & Park, 2010; Koolschijn et al., 2019; Schacter, Dobbins, & Schnyer, 2004). Furthermore, repetition effects may indicate representational fidelity in their association with behavior, for example, discrimination performance or memory specificity for highly similar information (e.g. Goh et al., 2010; see 2.2.1). Overall, neural repetition effects offer a great potential for elucidating the neural representational properties supporting memory.

Another approach to examine neural representations is provided by multivariate pattern analysis (MVPA). In contrast to the (mass-)univariate standard fMRI approach in which each voxel's hemodynamic response function is modeled and correlated with, for example, the experimental condition (Friston et al., 1994), MVPA considers multiple voxels, namely the pattern of BOLD activation across these voxels, at once (Pillet, Op de Beeck, & Lee Masson, 2020). This means that instead of identifying clusters of voxels that show common activity changes and thus maximal activation in a given condition, the complete "landscape" pattern of high and low activations is taken into account (Mur, Bandettini, & Kriegeskorte, 2009). From these patterns of activity, aspects of a person's current mental state can be "read out" using machine-learning classifiers (decoding models; e.g. Haynes & Rees, 2006; Mitchell et al., 2004; Rissman, Greely, & Wagner, 2010) and future, untrained activity patterns can be generatively predicted (encoding models; e.g. Kay, Naselaris, Prenger, & Gallant, 2008; Mitchell et al., 2008; van Gerven, 2016).

Moreover, patterns of activity can be compared between different conditions using representational similarity analysis (RSA; Edelman, 1998; Kriegeskorte, Mur, & Bandettini, 2008; Kriegeskorte & Kievit, 2013). In a first step, RSA assesses the similarity (or dissimilarity, if preferred[2]) between neural representations by, for example, correlations of the underlying activity patterns or decoding accuracy to distinguish between conditions. This can be used to assess the similarity between different neural representations (Davis, Xue, Love, Preston, & Poldrack, 2014) or the stability of a representation over time (e.g., Xue et al., 2010), two representational properties that are critical for cognitive performance (see 2.2.1). Indicating that neural activity indeed represents external information, RSA revealed that the representations of similar content, such as different face stimuli, are more similar to each other than relatively distinct contents, such as faces and houses (cf. Kriegeskorte et al., 2008). Comparing the similarity of several conditions, for instance, stimulus items and categories, gives a similarity structure that is often illustrated in a matrix of all pairwise comparisons (representational dissimilarity matrix; RDM), characterizing the information that a given region represents and distinguishes. In a second step, the representational similarity structure in a certain region can then be compared to other regions, modalities, computational models, behavior, or between different individuals or species (i.e., second-order isomorphism; Edelman, 1998; Kriegeskorte et al., 2008; e.g., Cichy, Pantazis, & Oliva, 2014; M. A. Cohen et al., 2019). That is, in this step the represented information is compared rather than the activity patterns themselves (Kriegeskorte et al., 2008). Originally, this second comparison (of RDMs) was the main idea behind RSA as it provides a common, modality-independent measuring unit that can be used to relate findings from different methods and disciplines. However, studies with research questions directly con-

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[2] Dissimilarity is sometimes preferred as it can be directly understood as the distance between neural representations in multidimensional space (cf. Kriegeskorte et al., 2008). Dissimilarity is often measured as the correlation distance 1 – correlation coefficient. Other dissimilarity measures include Euclidean distance (e.g., Edelman, Grill-Spector, Kushnir, & Malach, 1998) or Mahalanobis distance (e.g., Kriegeskorte, Goebel, & Bandettini, 2006).

cerned with the similarity of neural activity patterns have also addressed those by computing only the first step (see 2.2; e.g., Visser et al., 2013; Xue et al., 2010).

Multivariate approaches such as RSA are more commonly utilized in fMRI research but have become increasingly popular also for time-resolved brain recordings which allows studying the temporal dynamics of neural representations (Carlson, Grootswagers, & Robinson, 2019; Fahrenfort, van Driel, van Gaal, & Olivers, 2018; Jafarpour, Barnes, Fuentemilla, Duzel, & Penny, 2013; King & Dehaene, 2014). These methods can be applied to spatiotemporal (A. M. Chan et al., 2011; Fellner, Waldhauser, & Axmacher, 2020; Y. Lu et al., 2015; Schaefer, Farquhar, Blokland, Sadakata, & Desain, 2011) as well as spectral (time–frequency) M/EEG patterns (Duncan et al., 2010; Kerrén et al., 2018; Michelmann et al., 2018; Schyns et al., 2011) and have revealed critical insights concerning, for example, object recognition (e.g., Contini, Wardle, & Carlson, 2017), decision-making (e.g., Bode et al., 2012), and memory (e.g., Jafarpour, Horner, Fuentemilla, Penny, & Duzel, 2013; Kerrén et al., 2018; Y. Lu et al., 2015). Furthermore, the high temporal resolution enables examining the similarity between different time points of neural patterns within a trial, for example, how well a classifier trained to distinguish certain stimuli at a given time point generalizes to other time points during stimulus presentation (King & Dehaene, 2014). This allows inferences about how transient or persistent neural activity is as well as what kind of information is represented at different time points, for example, during object processing (Cichy et al., 2014). To sum up, tools for analyzing the similarity of multivariate neural activity patterns offer great potentials for studying the neural properties of spatial (e.g., fMRI), temporal and spectral (e.g., EEG) representations and their relationship to cognitive performance.

The differences between classic univariate and multivariate analyses have been interpreted as focusing on different neurocognitive aspects, namely on the *involvement* of a particular region in a function versus the representational *content* in that region (Mur et al., 2009), or that they measure neural processes versus neural representations (Davis & Poldrack, 2013; Xue, 2018). However, as discussed above, processes and representations may not be strictly separable (see 2.1.2). Nevertheless, whereas the mere localization of functions to specific regions does not explain the underlying neural mechanisms, multivariate analysis approaches are thought to be more sensitive to the brain's functional organization and subtle changes in activity that allow for the investigation of how the brain may encode information (Haxby, 2012; Yang, Fang, & Weng, 2012). This has led to remarkable findings with regard to content representation during the perception (e.g., Haxby et al., 2001; Vetter, Smith, & Muckli, 2014) and retrieval of information (e.g., Chadwick, Hassabis, Weiskopf, & Maguire, 2010; Polyn, Natu, Cohen, & Norman, 2005; Schultz, 2010). For example, Chadwick et al. (2010) showed that memories of previously viewed video clips could be discriminated based on hippocampal BOLD activity patterns while participants mentally recalled the clips. This demonstrates that multivariate patterns of activity comprise meaningful information, beyond mere involvement of a brain region in a task. Overall, methodological advances like RSA allow researchers to study the fine-grained properties, for example, the fidelity, of neural representations that enable an individual to remember relevant experiences and details (e.g., Bowman et al., 2019; Rissman & Wagner, 2012; see 2.2).

In summary, available non-invasive brain recording techniques provide differential accuracy with regard to localization, timing, and dynamics of neural activity, and thus offer various, complementary means to examine neural representational properties. Certain analysis approaches, such as repetition-related activity comparison and multivariate similarity analysis, are furthermore especially suited for investigating neural representations by aiming particular attention at the informational content in neural activation compared to standard analyses. Relating these measures with behavioral outcomes enables the investigation of the neural representations underlying episodic memory.

2.2 The neural representations underlying episodic memory across the human lifespan

Memory success depends on the quality of the underlying memory representations. As has been introduced in the previous section (2.1), understanding how information is represented in the brain and what properties of neural representations may determine whether and how well information can be remembered are major goals in neuroscientific research on memory (for related reviews, see Rissman & Wagner, 2012; Xue, 2018). In the following, I will review the theoretical and empirical foundations of the factors that reflect and may influence the formation of memory representations. First, I will discuss the two most prominent representational properties, namely the distinctiveness and stability of neural representations, and their association to memory performance. Subsequently, I will elaborate on how differences in the formation and properties of neural representations are associated to differences in memory abilities across the lifespan.

2.2.1 Two central properties of memory representations: distinctiveness and stability

In the previous section, I introduced the current theories and empirical findings concerned with how information is represented in the brain and how these neural representations can be investigated. In this section, I will discuss specific representational properties that are linked to memory performance. These properties concern the relation of neural representations to each other, that is, how similar or distinct they are, and their stability over time, that is, how precisely they are reactivated. In most studies, these properties are quantified by comparing the underlying neural activity patterns using RSA (see 2.1.3).

Representational distinctiveness. An individual memory is not independent and isolated from other memories. However, it is debated how the relation of different representations to each other influences memory, namely whether high similarity or distinctiveness[3] of the representations in memory space is beneficial for remembering their associated content. Memory space can be understood in terms of network models of long-term memory, where memory representations are organized in systems of nodes (concepts, memories) that are connected by their semantic or episodic relations (cf. J. R. Anderson, 1983; Arbib, 2002; Raaijmakers & Shiffrin, 1992; Tulving & Donaldson, 1972). For example, if you first met a friend at a particular place, your internal representations of your friend and the place are linked to each

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[3] The relationship between representations has been targeted from different angles and has been operationalized in various ways which is also reflected in the many, differentially connoted terms used to describe it, including *between-item* or *across-item representational similarity* (Poh & Chee, 2017; Ward et al., 2013), *global similarity* or *global matching* (Davis, Xue, et al., 2014; LaRocque et al., 2013; Y. Lu et al., 2015; I. C. Wagner, van Buuren, Bovy, & Fernandez, 2016), *representational* or *cortical overlap* (Tompary & Davachi, 2017; Wing et al., 2020), *neural selectivity* (D. C. Park et al., 2004), *neural specificity* (St-Laurent, Abdi, Bondad, & Buchsbaum, 2014; Zheng et al., 2018), and *neural distinctiveness* (Carp, Park, Polk, & Park, 2011; LaRocque et al., 2013). Here, I use *distinctiveness* as the opposite of similarity and as a superordinate term for the relation of neural representations of different contents (see also Glossary).

other, and if you return to this place, you may immediately remember how the two of you met. This may be accomplished through the process of spreading activation: The activation from a specific node spreads to nearby nodes that get reactivated and result in the retrieval of associated memories (J. R. Anderson, 1983; Collins & Loftus, 1975; Kintsch, 1988; Leahey & Harris, 2000; Raaijmakers & Shiffrin, 1992). Such reactivation further strengthens the memories and their connections (Raaijmakers & Shiffrin, 1992). More similar representations that share a lot of features can be conceived as nodes that are closer to each other in this memory space, for example, representing items from the same object category (within-category similarity), whereas more distinct representations have a larger distance between each other, for example, representing items from different categories (between-category similarity) (cf. Kriegeskorte & Kievit, 2013). Similar ideas have been proposed by other cognitive and computational models, for example, theories of global matching (Clark & Gronlund, 1996; Gillund & Shiffrin, 1984; Hintzman, 1984; Humphreys, Bain, & Pike, 1989; Humphreys, Pike, Bain, & Tehan, 1989; Raaijmakers & Shiffrin, 1981, 1992). Global matching postulates that the memory strength for a specific item arises from the similarity of its representation to the representations of other encoded items (Clark & Gronlund, 1996; Hintzman, 1984; Humphreys, Pike, et al., 1989; Raaijmakers & Shiffrin, 1992; Xue, 2018). Specifically, the model proposes that retrieval is achieved by matching a presented item to all items in memory space, and the amount of overlap scales with the sense of familiarity that the item creates. This familiarity is interpreted as evidence that the item corresponds to a past experience and, if exceeding a specific decision criterion, the participant will claim to remember the item (Clark & Gronlund, 1996; Hicks & Starns, 2006) which can be correct or incorrect (Arndt & Hirshman, 1998; Hintzman, 1988). In the framework of memory networks, item representations with high global similarity are located in the center of the multidimensional memory space with relatively short distances to other representations (cf. Davis, Xue, et al., 2014). Thus, high global similarity is linked to high memory performance.

The similarity with which information is neurally represented can be examined using neural repetition effects and pattern similarity analyses (see 2.1.3). Utilizing the former, Jiang et al. (2006) modulated the similarity of face images by morphing, and showed that moderately similar faces elicited smaller fMRI repetition suppression effects in FFA than identical faces but larger effects than clearly distinct faces. This result indicates that similarity of external information is reflected in the neural responses they engage, namely in their sensitivity to stimulus differences. Furthermore, Gilaie-Dotan and Malach (2007) demonstrated that the link between the level of face similarity and activation suppression was directly related to participants' face discrimination performance. These studies show that repetition effects can track the fidelity of neural representations which is associated with behavior (see also Barron, Vogels, et al., 2016; Bakker et al., 2008; Koolschijn et al., 2019). However, evidence on whether the magnitude of repetition effects reflects a representational quality that is directly linked to memory performance is mixed, with some studies showing a positive relation (Ewbank et al., 2017; Pihlajamäki, O'Keefe, O'Brien, Blacker, & Sperling, 2011; Turk-Browne et al., 2006), no relation (Rugg, 1990; Ward et al., 2013), or even a negative one (A. D. Wagner et al., 2000; Xue et al., 2011). In summary, the specificity of repetition effects can give some indication of how similarly or distinctively information is represented in the brain, but the direct influence on memory success is not yet fully established.

Using neural pattern similarity to compare the distributed activity patterns elicited by different stimuli, Davis, Xue, et al. (2014) found that higher global similarity of fMRI patterns in the MTL, including the hippocampus, was related to higher memory confidence in a recognition task as well as higher memory strength in a category learning task (see also Visser et al., 2013 for fear memory). This provides neural evidence for the benefit of similar representations as postulated, for example, by global matching (see above). Similar results in neocortical regions were obtained by I. C. Wagner et al. (2016) who demonstrated that representational similarity between encoded items (unique picture–location associations) was larger for long-lasting memories compared with weaker and not remembered items. Adding evidence for the benefit of similarity also in time-resolved representations, Y. Lu et al. (2015) found that, at around 500 ms after stimulus onset, global EEG spatiotemporal pattern similarity was higher for later remembered than for not remembered items. These effects were independent from the effects of pattern stability (see below). In line with the prediction that global matching can also result in false recognition, the fMRI study by Ye et al. (2016) showed that the similarity of both old and new item representations during recognition and all other items during encoding was associated with whether the item would be identified as old. Specifically, high representational similarity in parietal regions was linked to both correct and incorrect recognition of the items, whereas representational similarity in visual cortex was only linked to correct recognition, suggesting distinct global matching signals in different brain areas. In summary, these studies show that similarity between different representations during encoding (Davis, Xue, et al., 2014; Y. Lu et al., 2015; Visser et al., 2013; I. C. Wagner et al., 2016) and between encoding and retrieval (Ye et al., 2016) can be beneficial for memory performance, confirming cognitive models and previous behavioral results (Hintzman, 1988; see above). However, consistent with the models, high global similarity can also promote incorrect recognition (Ye et al., 2016), indicating that there may be a drawback of high similarity.

Although representational similarity benefits memory, representations that are too similar may be prone to interference. Behavioral studies showed that items that are very different from other studied items (isolation paradigm) are better remembered than similar items (Hunt & Worthen, 2006; Smith, 2011), which may indicate that high representational distinctiveness rather than similarity benefits memory. Interference from similar memories can also trigger a repulsion of memory representations in the hippocampus, making overlapping represesentations more distinct, which is suggested by activation patterns in the hippocampus becoming less similar with learning (Chanales et al., 2017; Chanales, Tremblay-McGaw, & Kuhl, 2020; Favila, Chanales, & Kuhl, 2016). Critically, these changes were only observed in hippocampal and not cortical regions (Favila et al., 2016), suggesting how pattern similarity outside the hippocampus and distinctiveness in the hippocampus (via pattern separation) may jointly benefit memory (see also Ye et al., 2016). In line with the presumed pattern separation processes in the hippocampus that form distinct representations of overlapping experiences (Chadwick, Hassabis, & Maguire, 2011; Kumaran & Maguire, 2006; Schlichting, Mumford, & Preston, 2015), LaRocque et al. (2013) found that encoding-related global (within-category) similarity in perirhinal and parahippocampal cortex was positively related to recognition memory, whereas the opposite relationship was observed in the hippocampus, where lower similarity was linked to better memory (see also Wing et al., 2020). However, these findings conflict with the results of Davis, Xue, et al. (2014) showing a benefit of global similarity also in the hippocampus (see above). These opposite effects in the hippocampus may be related to the relative contribution of different subfields that demonstrated to be involved in pattern separation versus pattern completion (Keresztes et al., 2017; S. Leutgeb, Leutgeb, Treves, Moser, & Moser, 2004; Nakashiba et al., 2012), revealing that the hippocampus can contribute to both integration and dissociation of similar memories (cf. Schlichting et al., 2015). Seemingly at odds with the benefit of representational similarity, Kuhl et al. (2012) demonstrated that the better the BOLD response to a given encoding trial could be classified as face or scene image, the higher was the probability that the corresponding item would be later remembered correctly. This suggests that more distinct face and scene representations were related to successful memory encoding. Also on the level of individual differences, the study revealed that memory performance was positively associated with distinct category representations. Confirming these decoding results as an indicator for representational distinctiveness, additional (correlation-based) pattern similarity analyses showed that between-category (faces/scenes) similarity was lower for remembered than not remembered items. However, at the same time, the representational similarity between items *within* the categories was higher for later remembered items, demonstrating that within-category similarity in temporal and prefrontal regions was beneficial for memory. That is, on the category-level, distinctiveness benefited memory, and on the item-level (within-categories), similarity benefited memory. These results highlight that the accurate representation of the similarity structure of presented information, for example, that related information is represented more similarly than unrelated information, reflects high-fidelity encoding and is thus linked to successful retrieval.

In conclusion, it is not a categorical question about neural distinctiveness versus similarity, but both, and particularly the right balance between them, are beneficial for memory. Whereas similarity is advantageous by giving rise to familiarity and thus recognition (global matching), it can also result in false recognition. Highly distinct representations may prevent false memories, but may also prevent correct recognition, for example, if an item's representation is so specific and unique that the item would not be recognized under different lighting or viewpoint conditions (cf. Andresen, Vinberg, & Grill-Spector, 2009; Verfaillie, 1992). Hence, the drawback of distinct versus similar representations is closely related to the challenges the memory system faces with regard to specific versus general memories (see 2.1.1; McClelland & Rumelhart, 1985; Schlichting et al., 2015). Different brain regions contribute to balancing these opposing requirements in one or the other direction, such as certain hippocampal subfields that orthogonalize similar inputs and thus represent specifics (e.g., LaRocque et al., 2013; Wing et al., 2020) and other subfields and neocortical areas that integrate related memories (Keresztes et al., 2017; McClelland et al., 1995; Norman & O'Reilly, 2003; Schlichting et al., 2015; I. C. Wagner et al., 2016).

All in all, the relationship between different representations is a critical property to consider when investigating the formation of memories. The discussed findings suggest that distinctiveness between representations of distinct information (e.g, different categories), but similarity between representations of related information (e.g., items of the same category), may often benefit memory, as long as they are separable by the hippocampus, indicated by dissimilar patterns in the hippocampus being related to memory success. However, the evidence is still partly conflicting and open questions regarding the right balance of similarity and distinctiveness remain. Particularly, studies examining temporal and spectral representations are lacking as most studies deployed spatial fMRI patterns (except Y. Lu et al., 2015). There may be temporal differences in the encoding of information such that the dynamic pattern of (dis)similarity influences the success of memory formation, which may be identified in M/EEG-based neural representations.

Representational stability. The retention of representations over time and the potential to retrieve them make up the ability of memory for past experiences (see 2.1.1). If an event is neurally represented by the activation pattern it elicited, then re-encountering or remembering aspects from that event should reactivate the corresponding pattern. The more precisely a representation can be reactivated the more accurately and confidently its content should be remembered (cf. Xue, 2018). Thus, in addition to representational distinctiveness, high-fidelity item-specific neural representation furthermore entails that the representations are stable over time, indicated by accurate reactivation of the underlying neural activity patterns which benefits memory. This stability[4] of representations can be quantified by the similarity of the underlying neural activity patterns (see Figure 1B).

Accordingly, studies using multivariate analysis approaches on fMRI and EEG data have demonstrated that activation patterns of subsequently remembered items showed higher stability across repetitions compared to not remembered items. In three fMRI experiments, Xue et al. (2010) showed that greater pattern similarity across repeated encoding (of faces or words) was associated with better subsequent recognition and recall. This positive relationship between representational stability and subsequent memory was identified in many brain regions, including prefrontal, parietal, occipitotemporal, and MTL areas (see also Visser et al., 2013). Reanalysis of parts of the data furthermore indicated that higher (univariate) frontoparietal activity may increase pattern similarity across the cortex, resulting in more consistent input to the MTL and thus improving memory encoding (Xue et al., 2013). In line with this, Y. Lu et al. (2015) demonstrated that beyond the positive link between spatiotemporal EEG pattern stability (approximately 500 ms after stimulus onset) and subsequent memory, transcranial direct current stimulation (tDCS) of the left lateral prefrontal cortex enhanced both pattern stability over right frontal electrodes and memory performance. This finding indicates a causal role of frontal activity for representational stability and memory (Y. Lu et al., 2015). To sum up, fMRI and EEG studies have shown that the stability of neural representations in cortical and subcortical areas, measured as pattern similarity of the underlying activity patterns, is supported by frontal activity and positively associated with memory outcomes.

Besides indicating representational stability, repetition-related neural activity also has shown to be suppressed or enhanced, posing the question of how these repetition effects and representational similarity are compatible. In an fMRI study, Ward et al. (2013) revealed that repeated scenes elicited repetition suppression effects in prefrontal, parietal, and occipitotemporal regions, which was associated with faster responses (indicating implicit memory), whereas pattern stability in occipitotemporal regions was associated with explicit scene recognition. Although co-occurring in the same region, repetition suppression was not related to explicit memory and pattern similarity was not related to implicit memory, indicating that the two measures were sensitive to different behaviourally-relevant aspects of neural representations. Other studies, in contrast, identified a positive effect of suppressed activity on explicit memory (Ewbank

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[4] Stability is also referred to as *within-item pattern similarity* (Poh & Chee, 2017; Ward et al., 2013) or *self-similarity* (Y. Lu et al., 2015; I. C. Wagner et al., 2016; Ye et al., 2016). Reactivation of encoding-related activity during retrieval is often referred to as *(cortical) reinstatement* (Staresina et al., 2016; Xue et al., 2010), *replay* (Jafarpour, Fuentemilla, Horner, Penny, & Duzel, 2014; Wimber et al., 2012), or *(hippocampal) pattern completion* (Staresina et al., 2016; Tompary, Duncan, & Davachi, 2016). For a recent consensus on definitions of terms including *reactivation*, *replay*, and *reinstatement*, see Genzel et al. (2020).

et al., 2017; Pihlajamäki et al., 2011; Turk-Browne et al., 2006), raising the question of how these findings are compatible with the beneficial effect of neural stability. Since the measures of repetition effects and pattern stability are based on different methodologies (see 2.1.3), it is conceivable to identify changes in the univariate mean activation level while the overall (multivariate) pattern of activity remains stable, which would explain how both changed and stable activity can be beneficial for memory (see also Discussion).

Connecting representational stability and distinctiveness, the similarity of neural patterns across repetitions can also be corrected for their similarity to other representations, which indicates the amount of stimulus-specific information. Hasinski and Sederberg (2016) related the stability of face representations to the representational similarity between different faces and revealed that only subsequently remembered faces showed larger stability than between-face similarity in FFA. This difference of within-item and between-item similarity can be interpreted as a measure of item specificity (see also Xue et al., 2010; Zheng et al., 2018). The findings suggests that perceived information can be best remembered if eliciting stimulus-specific representations, that is, highly stable neural patterns and, in comparison, high distinctiveness between different representations. How this is compatible with the finding that high similarity between representations can profit memory is a remaining question that has not yet been explicitly answered (see also Discussion). Given that most memory tasks require retrieving stimulus-specific information, it is plausible to assume that item specificity of neural representations is crucial for successful memory formation (cf. Xue, 2018).

As in the studies discussed above, representational stability is often measured across repeated encounters with a stimulus. Such repeated learning or exposure itself usually helps memory performance (Benjamin, 2001; Opitz, 2010; Sievers, Bird, & Renoult, 2019). In line with the suggested positive effect of representational stability on memory, one hypothesis is that the pattern reactivation during repetitions strengthens and stabilizes the memory representations (e.g., Appleton-Knapp, Bjork, & Wickens, 2005; Sievers et al., 2019; Xue et al., 2010). Note that earlier hypotheses suggested the opposite, namely that more variable rather than stable representations help memory by providing multiple traces (Hintzman, 1986; Nadel & Moscovitch, 1997) and hence a larger variety of retrieval cues (E. Martin, 1968). More recently, however, empirical evidence accumulates in favor of more stable rather than variable representations for successful memory (see above). However, other findings also show that repeated exposure can lead to an increase in false recognition of similar lures (Reagh & Yassa, 2014) and/or hinder the ability to access earlier memories, a phenomenon called retroactive interference (Postman & Underwood, 1973). Retroactive interference can, for example, occur in associative memory tasks when an item A is first encoded in association with B and then repeated with a different association (AC), leading to forgetting of the old association (AB) (Postman & Underwood, 1973; Wixted, 2004). This kind of forgetting is believed to be due to an interruption of hippocampus-dependent memory consolidation by the processes associated with the formation of new memories (Wixted, 2004). With fMRI it could be shown that the reactivation of memory representations, measured as the pattern similarity between AB and AC trials, could predict whether the memories would be affected by or resist a potential interference (Koen & Rugg, 2016). Thus, the study provided evidence that representational stability reduced the interference effects, which has been further shown to be mediated by the hippocampus (Kuhl, Shah, DuBrow, & Wagner, 2010). These findings further support the suggested benefit of representational stability, in its relation to distinctiveness, for memory.

In addition to stable neural representations during repeated encounters, it is a key element of multiple models of episodic memory (Alvarez & Squire, 1994; McClelland et al., 1995; Norman & O'Reilly, 2003; Rolls, 2000; Shastri, 2002) that the neurocognitive processes involved during event encoding are also involved when an event is retrieved (Damasio, 1989; Nyberg et al., 2000; Rugg et al., 2008). Accordingly, several studies using fMRI or MEG showed reinstatement of stimulus category information during successful retrieval (Cichy, Heinzle, & Haynes, 2012; Jafarpour et al., 2014; Kuhl, Rissman, Chun, & Wagner, 2011; Kuhl & Chun, 2014; Polyn et al., 2005). Furthermore, reinstatement of item information has been demonstrated in spatial fMRI representations (Ritchey, Wing, Labar, & Cabeza, 2013; Staresina et al., 2012; Tompary et al., 2016; Wing, Ritchey, & Cabeza, 2015) and temporal/spectral EEG and iEEG representations (Michelmann et al., 2018; Zhang et al., 2015; see also Kerrén et al., 2018; Michelmann et al., 2016; Yaffe et al., 2014.). These findings show that neural activity patterns during retrieval reflect the reinstatement of the representations of encoding, which is supported by the hippocampus (e.g., Staresina et al., 2012), and positively related to memory outcomes.

In summary, the above studies have consistently shown that reliable neural reactivation both during encoding and retrieval, in both cortical and subcortical regions, is positively related to the ability to retrieve the presented material. High representational stability indicates item-specific neural representations as well as the reactivation and thus strengthening and stabilization of the representations, related to the benefit of repetition for memory (cf. Xue, 2018). Hence, representational stability measured as the item-level similarity of neural activity patterns constitutes a representational property that benefits successful memory encoding and retrieval.

Together, the presented studies reveal that both the (dis)similarity between different representations (distinctiveness) and their similarity to themselves across repetitions and between encoding and retrieval

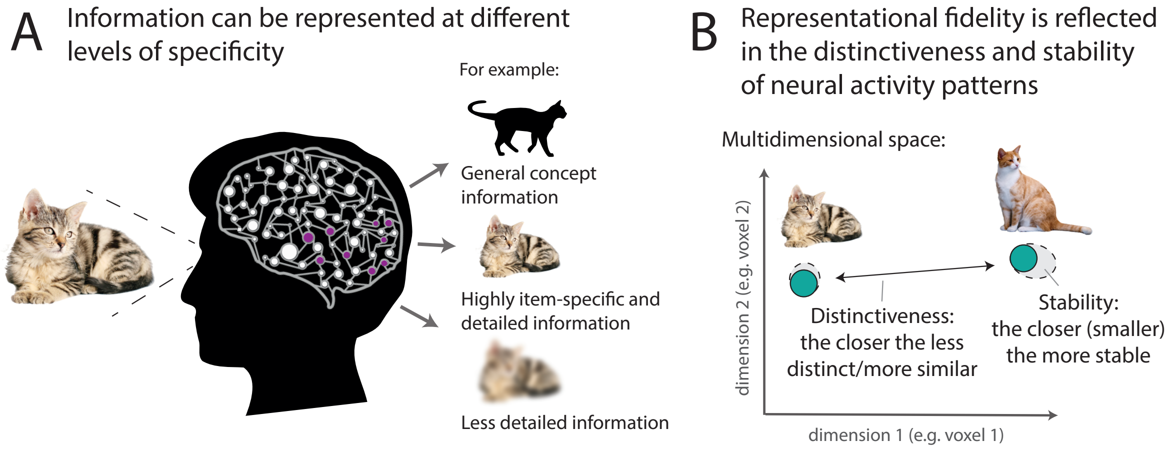

Figure 1: The fidelity of neural representations. **A.** Incoming information can be represented with varying specificity from general concept information to item-specific perceptual details (see 2.1.1). The neural activation pattern elicited by the visual input is simplified as the spatial pattern of activated (purple) and not activated (white) neural units, but information is not only represented in the spatial distribution but also in the timing and dynamics of the brain's electrochemical signals (see 2.1.2). General concept representation is illustrated as a simplified cat icon that does not share visual details with the input; lack of represented details is illustrated as a blurred version of the encoded visual information. This quality of content representation may determine whether and how detailed information will be remembered and can be investigated by examining specific representational properties. **B.** The two main representational properties discussed here are the distinctiveness of neural representations and their stability over time (see 2.2.1). The neural activity patterns that represent certain information can be illustrated as coordinates in a representational space that spans across multiple dimensions, reflecting activity at, for example, multiple voxels (see also representational geometry; Kriegeskorte & Kievit, 2013; multidimensional scaling; Cox & Cox, 2008). Pattern distinctiveness can be directly understood as the distance between the representations. Pattern stability is illustrated as the area in which the spatial coordinates of a representation vary over time (like a margin of error), for example, indicating the distance of a reactivated pattern during a repeated encounter. The smaller the area, the more stable the representation. Higher representational stability than similarity to other representations is an index of item specificity.

(stability) reflect the fidelity of neural information representation and are important for memory performance (see Figure 1). Thus, distinctiveness and stability are representational properties that provide crucial insights into the conditions under which experiences are successfully transformed into lasting memories. In the following section, I will address the question of whether differences in these representational properties may be associated with lifespan differences in memory abilities.

2.2.2 Differences in neural representations during aging

Aging is often accompanied by a decline of cognitive abilities. In general, age-related behavioral changes can be attributed to alterations in brain structure and function (Cabeza et al., 2017; Grady, 2012; Langnes et al., 2020; Persson et al., 2006; Raz et al., 2005; Reuter-Lorenz & Park, 2010; Sander et al., 2020; Shing et al., 2011) as well as neurochemical modulation (Bäckman, Lindenberger, Li, & Nyberg, 2010; Ordy & Kaack, 1975). Despite large commonalities in the observed pattern of age-related differences, there are also considerable inter-individual differences in the extent, onset, and rate of age-related cognitive and neural decline (Lindenberger & von Oertzen, 2006; Lindenberger, 2014; Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012; Nyberg & Pudas, 2019). However, reduced episodic memory performance, in particular, is one of the most evident limitations for humans when growing older (Fandakova, Werkle-Bergner, & Sander, 2020; Grady, 2008, 2012; Naveh-Benjamin & Ohta, 2012; Nyberg et al., 2012; Shing et al., 2010; Tromp, Dufour, Lithfous, Pebayle, & Després, 2015) and is in large part due to deficits in memory formation (Craik & Rose, 2012; Després, Lithfous, Tromp, Pebayle, & Dufour, 2017; Old & Naveh-Benjamin, 2008; Sander et al., 2020; Werkle-Bergner, Müller, Li, & Lindenberger, 2006). Especially the prefrontal cortex and MTL areas, which are critical for episodic memory, are affected by aging (Raz et al., 2005; Reagh et al., 2018; Tromp et al., 2015). Accordingly, a commonly observed age pattern for episodic memory is a decline in the ability to remember event-specific details (Bowman et al., 2019; Greene & Naveh-Benjamin, 2020; Koutstaal & Schacter, 1997). Instead, older adults often tend to over-generalize, and are thus prone to false memories, especially regarding highly similar information (Fandakova, Shing, & Lindenberger, 2013b; Fandakova et al., 2020; Koutstaal & Schacter, 1997; Schacter, Koutstaal, & Norman, 1997; Toner, Pirogovsky, Kirwan, & Gilbert, 2009).

This loss in memory abilities and the increase in false memories may relate to age-associated differences in neural representations, specifically in representational distinctiveness and stability. As the fidelity of information representation during encoding has been shown to be linked to memory success (see 2.2.1), degraded quality of these neural representational properties may partially explain age-related memory deficits. In line with the early idea that neural activity may become more noisy in old age (Welford & Birren, 1965), an influential model by Li and colleagues suggested that cognitive aging was linked to deficient neuromodulation, which increases neural noise and thus leads to less stable and less distinct neural representations (S.-C. Li et al., 2000, 2001; S.-C. Li & Sikström, 2002; S.-C. Li & Lindenberger, 2006). Specifically, they argued that age-related impaired dopaminergic activation reduced neurons' responsivity, thus making neural activity patterns evoked by the same input less consistent, and patterns evoked by different stimuli less differentiable. Li and colleagues provided evidence for this framework by simulation studies in which altering the dopaminergic gain function could explain performance differences between young and older adults (S.-C. Li et al., 2001). In the following, I will review the neural evidence for the predicted reduction in representational distinctiveness and stability in old age.

With regard to representational distinctiveness, the prevalent hypothesis that neural representations become less distinct with advancing age is called *neural dedifferentiation* (for recent reviews, see Koen & Rugg, 2019; Koen et al., 2020). The term originated from behavioral studies demonstrating that different abilities, for example, cognitive and perceptual, have been shown to be more intercorrelated in old age, based on which it has been suggested that behavior becomes less specialized for different tasks during aging and that this might be due to a reduction in brain integrity (Baltes & Lindenberger, 1997; de Frias, Lövdén, Lindenberger, & Nilsson, 2007; Tucker-Drob, 2009; Tucker-Drob, Brandmaier, & Lindenberger, 2019). Neural evidence for the model by Li and colleagues (see above) was provided by non-human animal studies showing aging-related reduced selectivity of the receptive fields of sensory neurons (e.g., Leventhal, Wang, Pu, Zhou, & Ma, 2003; Schmolesky, Wang, Pu, & Leventhal, 2000; Turner, Hughes, & Caspary, 2005). In humans, first fMRI studies operationalized neural distinctiveness as how selectively regions in the VVC responded to their preferred stimulus categories, for example, FFA to face images and PPA to house images (see 2.1.2). D. C. Park et al. (2004) showed that for young adults, the voxels that showed the highest BOLD response to stimuli from one category exhibited considerably less activity when stimuli from other categories were presented, but for older adults, the activation difference between these preferred and non-preferred categories was smaller. This provided evidence for age-related neural dedifferentiation in the form of reduced univariate regional selectivity and was replicated by a number of fMRI studies (e.g., Koen et al., 2019; J. Park et al., 2012; Payer et al., 2006; Voss et al., 2008). Furthermore, studies deploying multivariate analysis approaches (see 2.1.3) have also revealed reduced neural distinctiveness between the neural activation patterns elicited by different categories for older compared with younger adults (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010; Zheng et al., 2018). For example, J. Park et al. (2010) operationalized neural distinctiveness as how well a pattern classifier was able to differentiate between faces and houses based on the elicited BOLD patterns. Classification accuracy was lower in older adults compared to young adults, indicating age-related neural dedifferentiation. Other studies used the difference in similarity between representations of stimuli from the same and different categories as an indicator of neural representational category specificity, which has been shown to be reduced in older adults (e.g., Carp, Park, Polk, & Park, 2011). To sum up, these findings are in line with the observations from the general memory literature that, on the category-level, high distinctiveness is beneficial for memorizing the respective material (Kuhl et al., 2012). Thus, less category-specific neural representations may explain worse cognitive performance in older adults.

However, despite the assumed role of neural dedifferentiation as an important factor for age-related cognitive deficits, many of the earlier studies did not actually investigate the relationship between age differences in neural distinctiveness and behavior. Those studies that did examine the association of representational quality and performance during aging, did so by regarding (1) inter-individual differences in general cognitive abilities (e.g., J. Park et al., 2010), (2) inter-individual differences in memory for the respective materials used to measure neural distinctiveness (e.g., Koen et al., 2019), or (3) intra-individual differences (i.e., subsequent memory effects; Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998), contrasting neural distinctiveness for later remembered and not remembered material (e.g., Zheng et al., 2018).

Specifically, addressing neural distinctiveness on the category level, the fMRI study by J. Park et al. (2010) showed that neural category specificity (classification accuracy) in older adults was associated with fluid processing abilities (but not crystallized knowledge). More recently, Koen et al. (2019) identified a direct link between neural category selectivity in PPA during encoding of scenes and objects and recognition performance for the same stimuli, for both young and older adults. A further study showed reduced category selectivity in perirhinal and entorhinal cortex, which was associated with reduced memory specificity, that is, lure discrimination, in older adults compared with young adults (Berron et al., 2018). All in all, reduced representational distinctiveness of category-level information during aging is commonly reported and has been shown to be behaviorally significant. However, there have also been null findings with regard to age differences in neural distinctiveness for certain stimuli and brain regions (scenes in parahippocampal cortex: Berron et al., 2018; faces in FFA: Srokova, Hill, Koen, King, & Rugg, 2020; objects in lateral occipital complex (LOC): Koen et al., 2019; words in visual word form area: Voss et al., 2008), suggesting that category-level neural dedifferentiation is not ubiquitous but dependent on other factors (e.g., regional differences) that are not yet completely identified. Nevertheless, and most importantly, the results showed that in addition to reflecting a relationship to general cognitive decline (J. Park et al., 2010), distinctiveness of neural patterns was directly related to memory for the respective material (Koen et al., 2019), including mnemonic discrimination of highly similar information (Berron et al., 2018). This indicates that category distinctiveness is an important factor for the fidelity of neural information representation associated with memory success, and related to age-related memory deficits.

The proposed neural basis for reduced neural distinctiveness by Li and colleagues (see above) is a broadening of neural responses, that is, increased activity to normally non-preferred stimuli, which is supported by findings in single neurons (Leventhal et al., 2003; Schmolesky et al., 2000). The alternative would be a decreased response to preferred stimuli (attenuation). J. Park et al. (2012) examined whether a broadening of neural responses was underlying reduced category selectivity observed in fMRI. They found broadening in FFA but attenuation in the extended face network. Evidence for attenuation in PPA was also provided by Koen et al. (2019). These results suggest that different processes contribute to neural dedifferentiation depending on the level of observation (single neurons versus large neural populations) and brain region.

In addition to the model by Li and colleagues (see above) that connected reduced neural distinctiveness mainly to deficient dopaminergic modulation, the age-associated reduction in single-neuron selectivity has also been linked to a decline in inhibitory neurotransmission by gamma-aminobutyric acid (GABA; Ding et al., 2017; Hua, Kao, Sun, Li, & Zhou, 2008; Leventhal et al., 2003). This relationship has also been demonstrated in humans (Cassady et al., 2019; Chamberlain et al., 2019; Gagnon et al., 2019; Lalwani et al., 2019). Measuring neural distinctiveness with fMRI and GABA levels with magnetic resonance spectroscopy (MRS), it was found, for example, that individual differences in the neural distinctiveness of faces versus houses (Chamberlain et al., 2019) and music versus speech (Lalwani et al., 2019) were related to individual differences in GABA levels in older adults, suggesting a contribution of GABA in age-related neural dedifferentiation. Other studies showed that GABA concentrations were positively related to cognitive performance and thus reduced GABA levels in old age were linked to cognitive deficits (Hermans et al., 2018; Porges et al., 2017; Simmonite et al., 2019). In the framework of competing neural representations (O'Reilly, 1998), GABAergic interneurons might mediate the inhibition of less active representations by more strongly activated representations (Isaacson & Scanziani, 2011; Lalwani et al., 2019; O'Reilly, 1998). Thus, in line with neural broadening, decreased GABA levels would be associated with a weaker inhibition of other representations, resulting in less distinct neural representations (Lalwani et al., 2019).

In addition to the category level, fMRI-based neural dedifferentiation has also been investigated for single items. Based on the assumption that neural distinctiveness is reflected in the specificity of repetition suppression effects (e.g., Grill-Spector et al., 2006; Koen & Rugg, 2019; see 2.2.1), Goh et al. (2010) showed that, compared to young adults who exhibited suppressed FFA activity to identical faces and only minimally to similar (morphed) faces (cf. Jiang et al., 2006), older participants showed large suppression effects for both identical and similar faces. That is, for older adults, similar faces were represented identically, which was furthermore associated with poorer face discrimination ability. Although episodic memory performance was not tested, the observation that indistinct neural representations were linked to the inability to discriminate similar faces suggests that their representational similarity was beyond what has been shown to be beneficial for performance by the general memory literature (see 2.2.1). Furthermore, St-Laurent et al. (2014) investigated the similarity between representations of individual short video clips during perception and mental replay. The BOLD patterns elicited by the different videos were more similar to each other in older adults than in young adults. This age-related increase in similarity was larger during recall than during direct perception, while individual differences in the similarity of on-line representations did not explain individual differences in the similarity of off-line representations. Although older adults freely recalled fewer details about the clips, these performance differences were rather linked to the stable reinstatement of the representations than to their distinctiveness (see below). Equivalent to the assessment of category specificity, Zheng et al. (2018) furthermore assessed the level of item specificity of the neural representations in visual cortex as the difference between within-item (across repetitions) and between-item pattern similarity (see also Hasinski & Sederberg, 2016). While item specificity was related to memory performance, evidence regarding age differences were less clear (Zheng et al., 2018).

In summary, utilizing different methodologies (repetition effects and pattern similarities), these findings indicate that in addition to category-level distinctiveness also single items are represented less distinctively in old age[5] (see also Trelle et al., 2019). These results are in line with the model by Li and colleagues about age-related cognitive decline (e.g., S.-C. Li et al., 2001). However, the question how the quality of item-level representations are related to episodic memory performance is less well established than for category-level distinctiveness. Moreover, the apparent conflict with the general memory literature that indicates a beneficial effect of high representational similarity has not been directly addressed yet.

Item-level specificity, as assessed above (Zheng et al., 2018), depends on high representational stability as well as high representational distinctiveness, both of which are associated with memory performance (see 2.2.1). According to the model of Li and colleagues, increased variability in neural responses would lead to less stable and in turn less distinct neural representations (S.-C. Li et al., 2000). However, the (mainly fMRI) studies discussed so far, primarily investigated age differences in the distinctiveness

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[5] For completeness, in addition to category and item representations, age-related reduced neural distinctiveness has been shown between different tasks (Carp, Gmeindl, & Reuter-Lorenz, 2010; St-Laurent, Abdi, Burianová, & Grady, 2011) and in other modalities including the motor (Cassady, Ruitenberg, Reuter-Lorenz, Tommerdahl, & Seidler, 2020; Carp, Park, Hebrank, Park, & Polk, 2011), sensorimotor (Cassady et al., 2019), somatosensory (Cassady et al., 2020), and auditory system (Erb, Schmitt, & Obleser, 2020; Lalwani et al., 2019). Furthermore, neural dedifferentiation can be identified on the level of neural networks, namely in reduced functional segregation of resting state connectivity patterns (e.g., Cassady et al., 2019; M. Y. Chan, Park, Savalia, Petersen, & Wig, 2014; see Damoiseaux, 2017; Koen et al., 2020 for reviews), which provided first evidence that neural dedifferentiation may be related to a biomarker of Alzheimer's disease, namely tau pathology (Maass et al., 2019).

of neural representations. Thus, the question arises whether deficient representational quality in old age is mainly due to reduced neural distinctiveness or also due to reduced neural stability, which has barely been investigated yet. Zheng et al. (2018) compared item stability across repeated encoding between younger and older adults and found that, independent of their distinctiveness from other representations, the stability of item representations in the visual cortex was reduced in older adults. This was furthermore associated with lower memory performance compared with young adults. Crucially, item stability was an important contributor to memory performance as indicated by subsequent memory effects. Adding to their finding of reduced neural distinctiveness in older adults (see above), St-Laurent et al. (2014) identified less stable cortical reinstatement of item representations during mental replay of short video clips in older adults compared with young adults. Older adults freely recalled fewer details about the videos, which was linked to their less precise neural reactivation (see also Folville et al., 2019). To sum up, in line with the predictions by Li and colleagues, there is first evidence that age differences in the stability of representations across encoding repetitions and retrieval are a critical factor contributing to age-related memory decline (see also Abdulrahman, Fletcher, Bullmore, & Morcom, 2017; Thakral, Wang, & Rugg, 2016; T. H. Wang, Johnson, de Chastelaine, Donley, & Rugg, 2016 for findings on age differences in category or task context reinstatement). This reduced neural stability may lead to reduced neural distinctiveness, however, their direct relationship has rarely been investigated (cf. Hill, King, & Rugg, 2020; St-Laurent et al., 2014). In order to unravel the precise contributions of age differences in neural distinctiveness and stability to the fidelity of neural information representation and how they influence memory success, further studies are needed that carefully delineate these representational properties.

All in all, the representational properties distinctiveness and stability have been shown to be subject to age-related differences, that could explain memory performance differences. This provides further evidence that the precision with which information is encoded in neural activation patterns, determines how detailed the information can be retrieved. This fidelity of neural representations appears to change across the adult lifespan, explaining memory deficits in both healthy and possibly pathological aging (Maass et al., 2019). Open questions remain with regard to the relationship between distinctiveness and stability, which can be specifically addressed by focusing on the item specificity of neural representations, and the compatibility with beneficial effects of high between-item representational similarity for memory.

2.2.3 Differences in neural representations during maturation

Many cognitive abilities including episodic memory improve across childhood and adolescence (Graf & Ohta, 2002; S.-C. Li et al., 2004; Ngo, Newcombe, & Olson, 2018; W. Schneider, 2014), which is accompanied by the development of relevant brain regions and functions (Casey et al., 2000; Chai, Ofen, Jacobs, & Gabrieli, 2010; Keresztes et al., 2017; Ofen et al., 2007; Ofen, 2012; Tang, Shafer, & Ofen, 2018). Similarly to performance differences in old age, different aspects of memory abilities vary in their developmental trajectories during childhood (Golarai et al., 2007; Shing et al., 2010), for example, item memory matures earlier than source memory (Cycowicz, Friedman, Snodgrass, & Duff, 2001). The observation that performance in many tasks improves across childhood, particularly with regard to the formation and retention of memories, indicates increasing quality of the underlying neural representations (Bauer, 2015). For example, the ability to bind different features of an event into a unique memory representation and to keep similar memories separate are crucial competences developing during childhood (Lee, Wendelken, Bunge, & Ghetti, 2016; Ngo et al., 2018). Accordingly, maturation of the hippocampus has been associated with improving episodic memory in children (Ghetti & Bunge, 2012; Lee, Ekstrom, & Ghetti, 2014), particularly regarding pattern separation (Canada, Ngo, Newcombe, Geng, & Riggins, 2018; Keresztes et al., 2017). These findings suggest that enhanced functionality of the hippocampus helps age-related memory advancement, but the influences of the quality of the sensory input to the hippocampus, the cortical representations, have received much less attention (Fandakova et al., 2019). In this section, I review the evidence for potential age differences in neural representations, specifically regarding representational distinctiveness and stability, that may be associated with memory performance differences during childhood development.

Concerning neural category selectivity, the finding that 7–11-year-old children showed worse recognition memory for faces and houses than adolescents and young adults but not for objects indicates differential maturation of the specialized brain regions (Golarai et al., 2007). This was confirmed by age differences in FFA and PPA volumes but not object-selective regions (Golarai et al., 2007). Furthermore, as a measure of category-level representational distinctiveness, another fMRI study demonstrated adult-like univariate category selectivity in VVC, that is, larger responses to preferred than to non-preferred stimuli (see 2.1.2), for places and objects but no functional specialization for faces in 5–8-year-olds (Scherf, Behrmann, Humphreys, & Luna, 2007). However, the study did not test whether this was linked to performance, which would indicate whether category-selective processing is behaviorally relevant in children, for example, associated with memory for the respective stimuli. Together, these studies indicate different trajectories in the development of memory for different stimulus categories as well as the structural and functional development of the underlying brain regions (cf. Golarai et al., 2007; Golarai, Liberman, Yoon, & Grill-Spector, 2010; Gomez et al., 2017; Peelen, Glaser, Vuilleumier, & Eliez, 2009; Scherf et al., 2007). These findings demonstrate that differences in the quality of information representation between children and adults may be associated with age-related memory differences.

However, there is conflicting evidence with respect to whether children's neural representations develop from more general to more specific or vice versa. While studies directly assessing the amount of category- or item-specific information in neural activation patterns in children are rare (see below), behavioral findings might indicate whether children's representations are more or less specific than adults'. On the one hand, increasing representational specificity across childhood was suggested by children's improving ability to discriminate highly similar memories (Keresztes et al., 2017, 2018; Ngo et al., 2018). This is in line with the maturation of the hippocampus, especially with regard to its pattern separation processes (Canada et al., 2018; Keresztes et al., 2017). On the other hand, increasing generalization was indicated by children's stronger reliance on perceptual details before being able to form more general concept representations (Brainerd, Reyna, & Forrest, 2002; Brainerd, Reyna, & Ceci, 2008; Ofen & Shing, 2013; Sloutsky & Fisher, 2004). Studies specifically targeting the relationship of memory specificity and neural representational properties are currently lacking.

Addressing the question how distributed neural representations develop during childhood, the fMRI study by M. A. Cohen et al. (2019) compared the similarity of neural category representations in 5–7-year-olds and adults to univariate category selectivity (for faces, bodies, and scenes). They found that the similarity patterns of children who exhibited no category selectivity correlated with adults' representational similarity structures (i.e., second-order representations; see 2.1.3). The authors interpreted these findings as indicating that representational similarity patterns mature before the functional specialization assessed by univariate analyses. However, other than their correlation to adults' similarity patterns, it is not reported whether children's distributed activity patterns were actually meaningful, for instance, category-specific or related to performance. In contrast, Fandakova et al. (2019) showed that neural distinctiveness of individual scene representations, measured as classification accuracy, was positively associated with memory performance in 7–12-year-old children. However, neural distinctiveness was not different between children and adults, and the study found no evidence that improved memory performance (0.7–3 years later) was related to an increase in neural distinctiveness. This indicates that forming neural representations of scenes was relatively mature by middle childhood and age-related increases in cognitive performance appeared to be not due to changes in representational distinctiveness.

Furthermore, in line with the finding that the similarity of different neural representations was beneficial for young adults' memory performance (e.g., Davis, Xue, et al., 2014; see 2.2.1), O'Hearn, Larsen, Fedor, Luna, and Lynn (2020) found that within-category pattern similarity increased from childhood and adolescence to adulthood, and was related to recognition memory performance. Another fMRI study investigated how precisely faces were represented in 5–12-year-old children by using neural repetition suppression effects (Natu et al., 2016). Similar to the findings in older adults (Goh et al., 2010; see 2.2.2), Natu et al. (2016) found that neural representations of similar faces were less distinct in children than in young adults, which was linked to face discrimination performance. Together, these results suggest a behaviorally relevant improvement of how precisely information is encoded from childhood to adulthood and a decline during aging.

All in all, the discussed findings show differential age patterns with regard to the distinctiveness of neural representations of different contents, in particular, later maturation of face representations (see also Golarai et al., 2010). Age-related representational differences may be linked to performance differences, however, research directly targeting the properties of neural representations in children is sparse. Especially research on potential age differences in representational stability is missing. Together, insights into the representational distinctiveness and stability in children may elucidate how the fidelity of neural representations develops during childhood. Specifically, regarding the question of age differences in memory for specific details versus generalization, age-comparative studies could relate differences in neural representations to memory performance during childhood development.

3 Summary and Research Objectives

In the preceding chapter, I reviewed the theoretical and empirical evidence of how experiences are encoded into neural representations that can be maintained over time and later retrieved, which constitutes the ability of episodic memory. Information is represented in the activation of neurons and neural populations, specifically in their spatial, temporal, and oscillatory activity patterns (cf. M. X. Cohen, 2011; Fries, 2015; Griffiths, Mayhew, et al., 2019; Haxby et al., 2001; Treves, 2007). Critically, the precision in which specific contents and details are neurally represented at the time of encoding may determine whether and how accurately the respective information will be remembered (McClelland & Rumelhart, 1985; Rissman & Wagner, 2012; Robin & Moscovitch, 2017; Xue, 2018). Thus, the fidelity of neural representations is reflected in the ability to remember specific details of encoded events. Furthermore, the fidelity of representations can be investigated in terms of their distinctiveness from other representations (e.g., Kuhl et al., 2012) and their stability over time (e.g., Xue et al., 2010) (see Figure 1).

The neural correlates of successful memory encoding have mostly been studied in young adults and include the interplay of activity in neocortical regions that process incoming information and hippocampal activity binding different features into coherent memory representations (Eichenbaum, 2017; Griffiths, Parish, et al., 2019; Hanslmayr et al., 2016; Moscovitch et al., 2016; Parish et al., 2018; Simons & Spiers, 2003). The compromise between accurately representing and remembering specific details while allowing for enough overlap to represent regularities in order to adapt future behavior is a fundamental challenge of the memory system (Keresztes et al., 2018; Xu & Südhof, 2013). As the ability to retrieve specific details of past experiences differs across the lifespan (Brainerd et al., 2008; Fandakova et al., 2018; Koutstaal & Schacter, 1997; Ngo et al., 2018; Ofen & Shing, 2013; Sloutsky & Fisher, 2004), it is reasonable to assume that these differences are based on the ability to form high-fidelity neural representations (cf. Bowman et al., 2019; Fandakova et al., 2019). Yet, the neural mechanisms underlying the formation of highly specific memories, especially with regard to the potential differences during maturation and aging, are not fully established.

Regarding the neural representational properties underlying episodic memory encoding, there is evidence for both high similarity and high distinctiveness of neural representations benefiting memory performance (e.g., Davis, Xue, et al., 2014; Koen et al., 2019; Kuhl et al., 2012; LaRocque et al., 2013; Y. Lu et al., 2015). In line with cognitive models (e.g., Clark & Gronlund, 1996; Gillund & Shiffrin, 1984), high similarity of activation patterns may give rise to a sense of familiarity and thus recognition (Davis, Xue, et al., 2014). However, highly similar representations may also result in incorrect memory (Ye et al., 2016), for example, if the hippocampus fails to separate the respective cortical inputs (LaRocque et al., 2013; Schlichting et al., 2015; Stark, Kirwan, & Stark, 2019; Wing et al., 2020; Yassa & Stark, 2011). Furthermore, in addition to absolute similarity as such, it may be particularly the specificity of information representation that is critical for memory performance, namely the specifcity of category (Koen et al., 2019; Kuhl et al., 2012) and item (Hasinski & Sederberg, 2016; Zheng et al., 2018) information represented in the neural patterns. Thus, it is indicated that the formation of similar yet distinctive neural representations is crucial for cognition, however, the "right balance" remains an open question, and may be particularly dependent on the specific memory requirements. Moreover, there may be fine-grained temporal variations in the relation of representational similarity and memory performance while information is encoded, which may be identified by focusing more strongly on the temporal and oscillatory nature of neural information representation. Forming high-fidelity item-specific neural representations furthermore entails that the representations are stable over time, indicated by accurate reactivation of the underlying neural activity patterns when information is re-encountered or remembered (e.g, Kuhl & Chun, 2014; Y. Lu et al., 2015; Michelmann et al., 2018; Xue et al., 2010). However, how the stability of neural representations relate to their distinctiveness from other representations, especially with regard to specificity at different representational levels, requires more extensive investigation.

In line with the memory-benefiting characteristics of representational distinctiveness and stability, aging-related cognitive deficits may be caused by impaired neuromodulation that results in less stable and less distinct neural representations (S.-C. Li et al., 2000, 2001; S.-C. Li & Sikström, 2002). Supporting evidence comes from neuroimaging studies showing age-related reduced category-selective processing in functionally specialized VVC regions (e.g., Koen et al., 2019; D. C. Park et al., 2004) and less category-specific neural activation patterns (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010), which was partly related to cognitive performance (e.g., Koen et al., 2019; J. Park et al., 2010; for reviews, see Koen & Rugg, 2019; Koen et al., 2020). Some evidence furthermore points towards age differences in item-level representational specificity and stability (cf. St-Laurent et al., 2014; Zheng et al., 2018). However, these different representational levels and properties have mostly been studied separately, and also the discrepancy with the findings from general memory research – showing that high similarity between neural representations profits memory – has not been specifically addressed.

Whereas the contribution of the degradation of neural representational properties to cognitive performance in old age has gained considerable attention, how the development of neural representations during childhood relates to advancing cognition in children has only barely been studied. Many cognitive abilities including episodic memory performance improve across childhood (Ngo et al., 2018; Ofen et al., 2007; W. Schneider, 2014), which is linked to the maturation of relevant brain structures and functions (Keresztes et al., 2017; Ofen, 2012; Tang et al., 2018) and is likely related to improved representational fidelity. However, little is known about the specific properties of neural representations shaping memory in children (cf. M. A. Cohen et al., 2019; Fandakova et al., 2019). Crucially, full lifespan comparisons on memory development are sparse (but see Fandakova, Shing, & Lindenberger, 2013a; Friedman, de Chastelaine, Nessler, & Malcolm, 2010; Shing, Werkle-Bergner, Li, & Lindenberger, 2008) and particularly with respect to memory specificity and the underlying neural representations. Such lifespan studies would provide a better understanding of the neural underpinnings of episodic memory in general as well as its ontogenetic development.

The following chapters comprise three empirical studies that examined age-related differences in the formation of memory representations, using a combination of neuroimaging techniques and memory performance assessments. Study I investigated the encoding mechanisms that facilitate the formation of memory representations with varying specificity. Studies II and III directly assessed the neural representational properties underlying memory formation with a focus on distinctiveness and stability.

Specifically, I hypothesized that children, young adults, and older adults differ in the specificity of their memories and the underlying neural correlates. To this end, I tested whether EEG repetition effects (Grill-Spector et al., 2006; Penney et al., 2001; Stefanics et al., 2018) are related to inter-individual and lifespan age differences in item recognition and lure discrimination (Keresztes et al., 2017; Stark & Stark, 2017), indicating potential differences in representational fidelity across the lifespan (Study I; Nordt et al., 2016; Ofen & Shing, 2013; Turk-Browne et al., 2006). Furthermore, I expected adult age differences in the distinctiveness of neural representations which predict the subsequent memory fate of the respective material. I therefore examined within-subject differences in the global (dis)similarity of EEG frequency patterns (Kerrén et al., 2018; Michelmann et al., 2016; Zhang et al., 2015) in relation to memory performance in a cued recall task in young and older adults (Study II; S.-C. Li et al., 2000; Y. Lu et al., 2015; D. C. Park et al., 2004). Finally, I investigated how age differences at different representational levels and in different brain regions are associated with inter- and intra-individual differences in memory success. For this, I assessed category-level and item-level specificity and stability (Carp, Park, Polk, & Park, 2011; D. C. Park et al., 2004; St-Laurent et al., 2014; Xue et al., 2010; Zheng et al., 2018) in fMRI-based neural representations in relation to recognition memory performance in young and older adults (Study III; S.-C. Li et al., 2000; Koen et al., 2020; Xue, 2018). Overall, the goals of these studies were to identify the neural factors supporting episodic memory across the lifespan, specifically concerning the neural representational properties during memory encoding.

4 Study I: Memory Specificity Is Linked to Repetition Effects in Event-Related Potentials Across the Lifespan

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Contents

Abstract

Our memories depend on our brain's ability to form internal representations of relevant aspects of the world that can later be retrieved. The specificity with which past experiences can be remembered may be reflected in the fidelity of the underlying neural representations. This memory specificity varies across the lifespan, possibly due to differences in how precisely information is encoded. Memory formation can be investigated through repetition effects, the common finding that neural activity is altered (suppressed or enhanced) when stimuli are repeated. However, the association between this indirect measure of memory and actual performance across lifespan development, especially regarding memory specificity, has not yet been established. In the present study, we examined repetition effects in event-related potentials and their relation to recognition specificity across the lifespan. During incidental encoding, children (aged 7–9 years), young adults (18–30 years), and older adults (65–76 years) viewed repeated object images from different categories. During subsequent recognition, old, similar, and new objects were presented, allowing for a differentiation of memory for the specific item versus the general category. We identified neural repetition suppression in all age groups and repetition enhancement for adults. Furthermore, individual item recognition performance comprising lure discrimination was positively associated with the magnitude of the neural repetition effects. These brain–behavior associations did not differ between age groups, indicating common neural mechanisms of memory formation. In sum, our findings demonstrate that neural repetition effects reflect encoding mechanisms that facilitate the formation of highly specific memory representations and highlight their significance as a neural indicator of individual differences in episodic memory encoding across the lifespan.

Introduction

Memories of past events vary in their degree of specificity from very unique and detailed to more general and gist-like. Most likely, the variability in memory specificity partly reflects how precisely incoming information has been encoded (McClelland & Rumelhart, 1985; Robin & Moscovitch, 2017). Forming precise memory representations is critical in many situations as it enables remembering concrete details and avoiding confusion with similar information. This ability changes across lifespan development (cf. Ofen & Shing, 2013). Understanding how memory representations are formed is therefore crucial in the study of memory, particularly with regard to differences in memory competences across the lifespan.

One way to study the formation of neural representations is to examine brain activity in response to repeated stimulus input (Barron, Garvert, & Behrens, 2016; Grill-Spector et al., 2006). If the neural response differs between first and repeated encounters, this indicates that an internal representation of the repeated stimulus has been formed (Rugg & Doyle, 1994). Indeed, such repetition effects are widely observed: Repetition suppression describes the finding that neural activity evoked by a repeated stimulus is reduced (Barron, Garvert, & Behrens, 2016; Grill-Spector et al., 2006). In addition to a reduction of activity in response to repeated stimuli, increased activity (repetition enhancement) has also been reported, especially in the ERP literature (Desimone, 1996; Doniger et al., 2001; M. E. Nagy & Rugg, 1989; Rugg, Soardi, & Doyle, 1995), but also in fMRI (for a review, see Segaert et al., 2013).

The neural mechanisms underlying these repetition effects are still debated (e.g., Gotts et al., 2012; Grill-Spector et al., 2006; Henson & Rugg, 2003; Krekelberg et al., 2006; Larsson et al., 2016). Several theories have been proposed including a neural sharpening model that entails narrowed tuning curves of neurons and thus a sparsening of neural representations (Desimone, 1996; Wiggs & Martin, 1998) based on further inhibition of weakly activated neurons (Grill-Spector et al., 2006; Norman & O'Reilly, 2003). Accordingly, the neural basis of the occurrence of suppression versus enhancement effects is still under discussion (Henson & Rugg, 2003; Segaert et al., 2013) but may reflect an involvement of different processes at repeated encoding (Henson & Rugg, 2003; Henson et al., 2000; see Discussion). Although the underlying neural mechanisms are not yet fully explained, the observation of an altered neural response to repeated input implies that the first encounter must have left some neural trace that is re-accessed upon repetition (Koen et al., 2020; Rugg & Doyle, 1994), which provides a useful tool to investigate the nature of neural representations (Grill-Spector et al., 2006). Differences in the formation of neural representations, reflected in repetition effects, may be associated with differences in memory performance across the lifespan.

Repetition effects can be leveraged to investigate particular properties of neural memory representations, for example, their specificity and overlap (cf. Barron, Vogels, et al., 2016; Schacter et al., 2004). Jiang et al. (2006) modulated the similarity of face images by morphing and showed that moderately similar faces elicited smaller fMRI repetition suppression effects than identical faces but larger effects than clearly distinct faces did. This association between face similarity and the level of repetition suppression was furthermore linked to participants' face discrimination performance (Gilaie-Dotan & Malach, 2007; Jiang et al., 2006). These findings suggest that repetition effects can track the specificity of neural representations that is directly related to behavior (see also Grill-Spector et al., 2006; Lueschow, Miller, & Desimone, 1994). Furthermore, suppression effects for different but previously associated stimuli allow investigation of the overlap between memory representations and they proved to be related to associative memory performance (Barron, Vogels, et al., 2016) and the ability to differentiate similar memories (Koolschijn et al., 2019). In summary, these results demonstrate the potential of neural repetition effects in elucidating neural representational properties during encoding and how they are related to memory components such as memory specificity.

Although the repetition effect (primarily suppression) has been mainly implicated as the neural correlate of implicit memory, namely repetition priming (Doniger et al., 2001; Gotts et al., 2012; Henson & Rugg, 2003; Wiggs & Martin, 1998), it has also been associated with explicit memory. M. E. Nagy and Rugg (1989) suggested that the ERP repetition effect may be related to consciously recognizing the repeated stimulus. To date, however, this relationship has not been established fully. For example, Rugg (1990) did not identify an association between the size of the ERP repetition effect and the probability that the respective stimulus (word) would subsequently be recalled. In contrast, Turk-Browne et al. (2006) showed that subsequently remembered scenes elicited greater fMRI repetition suppression and behavioral priming than scenes that were not remembered, thus linking repetition effects to both explicit and implicit memory. The authors suggested that both memory systems may be influenced by the quality of the neural representations during encoding as was reflected in the representations' sensitivity to repetitions. However, other fMRI studies found no relation (Ward et al., 2013) or even a negative relation (A. D. Wagner et al., 2000; Xue et al., 2011) between repetition suppression and subsequent explicit memory. On the between-person level, individual differences in fMRI repetition suppression were shown to be related to individual differences in memory performance and thus linked to memory deficits in autism spectrum conditions (Ewbank et al., 2017) as well as mild cognitive impairments and Alzheimer's disease (Pihlajamäki et al., 2011). All in all, although previous findings are mixed, there is accumulating evidence that the magnitude of repetition effects may be a useful indicator for successful episodic memory.

Memory abilities vary across the lifespan, especially the ability to remember specific details versus the general gist of an episode (Graf & Ohta, 2002; Hultsch, Hertzog, Dixon, & Small, 1998). Compared with adults, children's memories have been shown to rely more on perceptual properties than on abstract/semantic knowledge that is still developing (Ofen & Shing, 2013; Sloutsky & Fisher, 2004). Thus, children have proved to be less likely than young adults to falsely recognize items that were conceptually similar to ones previously encountered (Brainerd et al., 2002, 2008; but see Keresztes et al., 2018; Ngo et al., 2018). The opposite is observed at the other end of the lifespan: Older adults rely more on general concepts and similarities, leading to more false memories (Fandakova et al., 2018; Koutstaal & Schacter, 1997; Schacter et al., 1997). The developmental differences in memory abilities are accompanied by age-dependent changes in the underlying brain structures and functions during maturation and senescence (S.-C. Li et al., 2004; Ofen & Shing, 2013; Sander et al., 2020; Shing et al., 2010; Van Petten, 2004). Specifically, differences in the neural encoding of memory representations may determine the specificity of mnemonic contents and may thus account for performance differences across the lifespan (Bowman et al., 2019; Fandakova et al., 2019; Morcom, 2015; H. Park, Kennedy, Rodrigue, Hebrank, & Park, 2013).

Adaptive memory systems need to balance the affordance of representing information with high specificity, while allowing for sufficient overlap to detect regularities (McClelland & Rumelhart, 1985; Wiltgen & Silva, 2007; Xu & Südhof, 2013), for example, when forming categories (Ashby & Maddox, 2005). With regard to age differences in memory performance, it has been suggested that neural representations become less specific in old age, which may be linked to aging-related cognitive decline (Carp, Park, Polk, & Park, 2011; S.-C. Li & Sikström, 2002; S.-C. Li et al., 2001; D. C. Park et al., 2004; J. Park et al., 2010). Indeed, a positive relation between the specificity of the neural activity patterns during encoding (of different categories) and memory performance could be demonstrated for young and older adults (Koen et al., 2019). In children (aged 7–12 years), higher neural specificity of scene representations was associated with better memory performance, too (Fandakova et al., 2019). In addition to measuring neural specificity as the discriminability of neural activation patterns according to stimulus content (Fandakova et al., 2019; Koen et al., 2019), the stimulus-specificity of neural repetition effects can indicate how precisely information is represented (see above; Jiang et al., 2006) and how these representations may vary across the lifespan (cf. Nordt et al., 2016). With this approach it has been shown that the specificity with which faces of modified similarity were represented in face-selective brain regions was lower in children (5–12 years) than young adults (Natu et al., 2016), and lower in older adults (61–72 years) than in young adults (Goh et al., 2010). Furthermore, both studies showed that the neural specificity reflected in fMRI repetition suppression was associated with face discrimination performance (Goh et al., 2010; Natu et al., 2016), suggesting a behaviorally relevant improvement of how precisely information is encoded from childhood to adulthood followed by a decline during aging. All in all, crucial aspects of neurocognitive lifespan development including representational specificity have been linked to repetition-related changes in neural activity, however, age-comparative studies directly testing the association between repetition effects and memory abilities, particularly memory specificity, are lacking.

In summary, differences in the neural response to repeated input are suggested to reflect the formation of memory representations indicating successful encoding such that the respective information can be remembered in the future. However, the association between repetition effects and individual explicit memory performance has not yet been fully established. Furthermore, the question arises whether repetition effects reflect rather general memory formation, indicated by remembering the gist or broader concept of past experiences and encountered stimuli, or whether it reflects encoding of specific details allowing very similar information, for example, stimuli from the same category, to be discriminated. Finally, differences in the neural trace formation may underlie differences in memory specificity across the lifespan.

In the current EEG study, we aimed to investigate how memory formation is affected by stimulus repetition and whether neural repetition effects are directly associated to the specificity of later recognition. Furthermore, we asked whether potential age differences in the formation of memory representations manifest in age-differential relations of repetition effects and memory performance. Specifically, we studied ERP repetition effects in response to object images that were either repeated twice or four times in children (7–9 years), young adults (18–30 years), and older adults (65–76 years). We investigated whether repetition effects differed across the lifespan with respect to their magnitude and their behavioral significance by examining how individual differences in repetition effects were related to differences in subsequent recognition performance of the presented objects. During recognition, exact repetitions from encoding (old targets), new exemplars from old object categories (similar lures), as well as items from novel categories (new foils) were presented (cf. Stark et al., 2019). The three respective response options “old,” “similar,” and “new” enabled us to dissociate mere category memory from precise exemplar memory and thus to investigate whether repetition effects reflected general concept or detailed item-specific encoding.

Materials and methods

Participants

A total of 19 healthy children, 41 healthy young adults, and 61 healthy older adults participated in the EEG study. We excluded one child and three older adults due to low performance in the vigilance task during encoding (see Experimental design and Behavioral performance) and two young adults and two older adults due to missing or noisy EEG data. One additional older adult was excluded based on low performance in the dementia screening (see below). The remaining 18 children (age: $M(SD) = 8.44(0.70)$, 7–9 years, 13 female, 5 male), 39 young adults (age: $M(SD) = 24.77(3.30)$, 18–30 years, 23 female, 16 male), and 55 older adults (age: $M(SD) = 70.15(3.39)$, 65–76 years, 27 female, 28 male) are included in the analyses presented here.

Children and adults were recruited at different sites. The children were recruited from a database of children who had previously participated in studies at the Developmental Neuropsychology Lab at the Ruhr-Universität Bochum (RUB), Germany. Adults were recruited from a participant database at the Max Planck Institute for Human Development in Berlin, Germany, as well as via flyers, circular emails, and internet advertisements. Due to technical issues with the EEG system at RUB and relocation of the laboratory, testing of children had to be aborted before the targeted number of 31 subjects could participate.

All participants were native German speakers, reported normal or corrected-to-normal vision, no history of psychiatric or neurological disease, and no use of psychiatric medication. In addition to participants' subjective report, their visual acuity was tested with the Landolt-C Freiburg Vision Test (Bach, 1996; decimal acuity: children: $M(SD) = 1.65(0.87)$; young adults: $M(SD) = 1.67(0.74)$; older adults: $M(SD) = 1.18(0.75)$; higher values indicate better visual acuity). We screened older adults with the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). One had a score below the threshold of 24 points (namely 21) and was excluded (see above). The remaining older adults reached a mean score of 28.95 ($SD = 1.21$, 25–30 points).

To control for the different task versions (see below), behavioral performance of 23 additional young adults on the shorter children's task was assessed at RUB.

All experiments were approved by the respective local ethics committee. All adult participants and the children's parents gave written informed consent to taking part in the experiment and all participants or their parents could abort the study at any time without giving reasons.

Experimental design

Data for this study were collected at two different sites. Children were tested at the Developmental Neuropsychology Lab at the Ruhr-Universität Bochum, Germany, and adults were tested at the Center for Lifespan Psychology at the Max Planck Institute for Human Development in Berlin, Germany. The experimental procedures, such as collected covariates, also differed for children and adults (see Supplemental material). However, the same visual object encoding and recognition tasks were at the core of the study (see Figure 2A), the only difference being that children performed a shorter version of the tasks, namely only the first half. Other than that, the selection and order of stimuli in both tasks were identical for all participants. During encoding and recognition, participants viewed color photographs of objects from different categories (e.g., hats, trees, guitars). The pictures were partly selected from a published stimulus set (”Massive Memory” Object Categories; https://konklab.fas.harvard.edu; Konkle, Brady, Alvarez, & Oliva, 2010) and partly obtained from internet searches. The stimuli were scaled to 500 × 500 pixels and all text, such as brand names, were removed using Adobe Photoshop CC 2017. Stimuli were presented using Psychtoolbox (Psychophysics Toolbox, RRID: SCR_002881) for MATLAB (The MathWorks Inc., Natick, MA, USA; RRID: SCR_001622). During the tasks, EEG was acquired for all participants, and – for the adult samples only – also electrocardiography (ECG), electrooculography (EOG), and eye-tracking. In the following, we describe the task paradigm for the adults, followed by the specific differences for the children’s sample.

Encoding task

During the encoding task (see Figure 2), adult participants viewed objects from 80 different categories. Participants were not instructed to memorize the stimuli and they did not know that their memory would be tested. Stimuli were presented successively on a white background on the center of the screen. A central fixation cross was superimposed on the objects and remained on the screen throughout the task. Stimulus duration was 1500 ms with an inter-stimulus-interval (ISI) jittered between 1500 and 2000 ms, during which only the fixation cross was presented on a white screen. Subjects were instructed to attend to the objects but to fixate on the cross in order to minimize eye movements. To ensure that participants attended to each trial, they performed a target detection task in which they were asked to press a button whenever the fixation cross changed its color from black to magenta. In all other trials, no response was required in order to minimize the impact of response-related components to the ERPs elicited by the items of experimental interest. The target trials appeared in approximately 7% of all trials, that is 54 times in total, with 1–25 (on average 14.7) trials between two target trials. The color change occurred

100–500 ms after onset of the stimulus. The target trials showed objects from additional categories and were excluded from further analyses.

After the first half of the trials, adult participants could take a voluntary break. The two halves of the encoding task were independent of each other in that categories from the first half were not part of the second half. To motivate participants for the second half, they received visual feedback on how many color changes they had successfully detected so far. They could continue with the task by button press.

The 80 object categories were equally divided into four conditions that differed with respect to (a) the number of different presented exemplars from one category (either two or four), and (b) the number of exemplar repetitions (either two or four times). This resulted in four encoding conditions: (1) Baseline (BL) condition with two exemplars per category that were each presented twice, (2) High-Repetition (HR) condition with two exemplars per category that were each presented four times, (3) High-Exemplar (HE) condition with four exemplars per category that were each presented twice, (4) High-Repetition-and-Exemplar (HRE) condition with four exemplars per category that were each presented four times (see Figure 2B).

Twenty categories were randomly selected for each condition. For those conditions with two exemplars per category (BL and HR), two of the four available exemplars were randomly selected for presentation. The stimulus order was pseudorandomized with the restriction that 3–10 stimuli (from other categories) appeared between repetitions of the same item, with the same mean distance for all conditions. Furthermore, at least five other items were presented after the last repetition of a category exemplar before the next exemplar of that category was shown. In this way, exemplars from the same category were not presented interleaved.

Since the number of exemplars and repetitions differed between conditions, the number of trials in each condition varied accordingly: 80 in the BL condition, 160 in the HR condition, 160 in the HE condition, and 320 trials in the HRE condition. This adds up to a total of 720 experimental trials. In addition to these experimental trials, 54 target trials (see above) and 6 filler trials were presented. Filler trials were needed when the distance restrictions of the pseudorandomization could not be met otherwise. Like target trials, filler trials showed objects from additional categories and they were excluded from further EEG analyses. Altogether, the encoding task consisted of 780 trials and lasted 42 minutes plus the self-paced break, which lasted approximately 2 minutes on average. After the last trial, subjects again received feedback on their performance.

A shorter version of the task was used for the children. They performed only the first half of the adult task, comprising 40 distinct object categories, i.e., 10 in each encoding condition, which results in 360 experimental trials (40 BL, 80 HR, 80 HE, 160 HRE), plus 27 target trials, and 3 filler trials. In contrast to the adults, children had more breaks, namely every 85 trials (approximately every 4 minutes). The breaks were voluntary and self-paced and could be ended in agreement with the child via button press by the experimenter. In total, the encoding task for children lasted 25 minutes on average – depending on the lengths of their breaks.

Recognition task

After a 15-minute break, a surprise recognition task followed (see Figure 2A). Again, object images were presented successively on a white screen and with a black fixation cross on top. The presented objects were either "old," i.e., identical to an item of the encoding task (targets), "similar," i.e., of a category that was already presented in the encoding task but a different exemplar (lures), or "new," i.e., of a novel category (foils). Stimulus duration was again 1500 ms. After each stimulus presentation, participants were asked to indicate whether the object was "old," "similar," or "new" by pressing one of three buttons on a button box. The response was self-paced but limited to 2000 ms. The three response options remained on the screen until a response was made. Thereupon, the fixation cross was shown for 1500–2000 ms before the next stimulus item appeared.

For adults, the task consisted of 160 targets ("old"), 160 lures ("similar"), and 160 foils ("new"), resulting in a total of 480 trials and a chance level of 33%. The targets contained the same 80 object categories that were presented in the encoding task, but for each category, only two exemplars were presented in the recognition task (see Figure 2C). For those categories that belonged to an encoding condition with four exemplars (HE and HRE), two of these were randomly selected to be tested in the recognition task. Two more novel exemplars from the same categories were presented as similar lures. The foils consisted of two exemplars from each of the 80 novel object categories.

The stimuli were pseudorandomized with the restriction that there were at least three trials between items from the same object category, and maximally four stimuli with the same correct response ("old," "similar," "new") were presented in a row. Targets that were presented in the first/second half of the encoding task were also tested in the first/second half of the recognition task, respectively.

The children only performed the first half of the recognition task, i.e., the first 240 trials, containing 80 targets, 80 lures, and 80 foils. Two exemplars of the same 40 object categories from the encoding were tested as targets, two new exemplars from the same 40 categories were used as similar lures, and two exemplars from 40 novel categories were used as foils. In contrast to the adults who had no breaks in the recognition task, the children could again take a self-paced break every 85 trials.

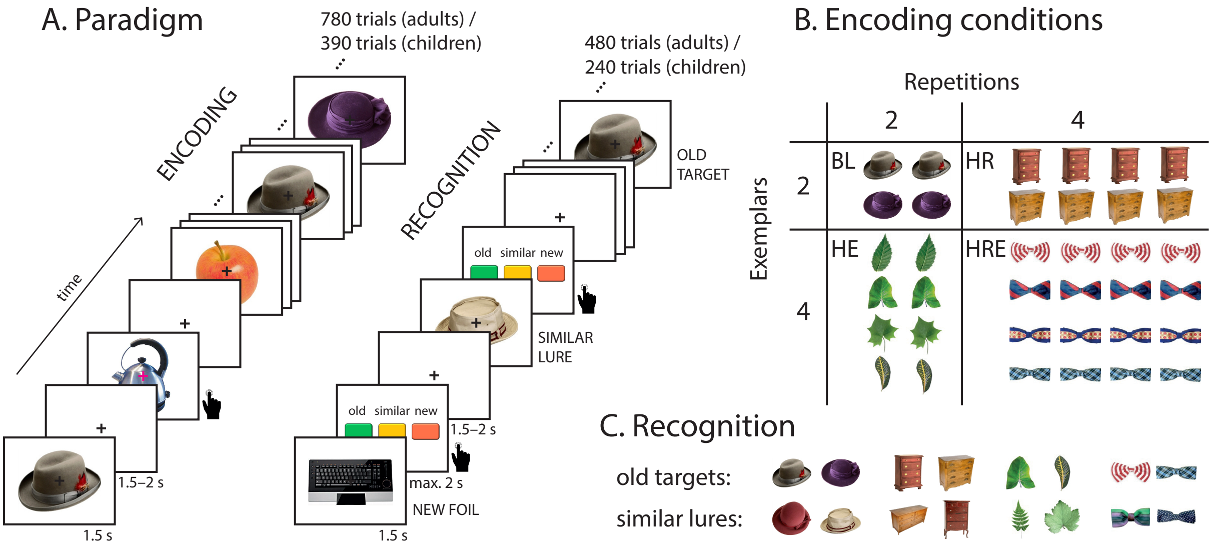

Figure 2: A. Overview of the experimental paradigm. In the encoding task, objects were sequentially presented, and subjects were asked to press a button whenever the fixation cross changed its color. Stimulus presentation lasted 1.5 s and ISIs were jittered between 1.5 s and 2 s. Items were repeated either 2 or 4 times (see B), with 3 to 10 items from other categories shown between repetitions. Either 2 or 4 exemplars from each object category were presented (see B), with at least 5 trials in-between. The task consisted of 780 trials for adults and only the first 390 trials for children. During recognition, objects were sequentially presented, and subjects were asked to decide for each object whether it was old, similar, or new. Stimulus presentation lasted 1.5 s, response time was self-paced but limited to 2 s, and ISIs were jittered between 1.5 s and 2 s. Objects were either already shown during encoding (old targets), or from categories that were shown during encoding but new exemplars (similar lures), or from novel categories (new foils). Each item was shown only once. The recognition task consisted of 480 trials for adults and only the first 240 trials for children. **B.** Encoding conditions. The number of item repetitions (2 or 4) and category exemplars (2 or 4) were manipulated during encoding, resulting in 4 encoding conditions: Baseline (BL) with 2 repetitions of 2 exemplars, High-Repetition (HR) with 4 repetitions of 2 exemplars, High-Exemplar (HE) with 2 repetitions of 4 exemplars, and High-Repetition-and-Exemplar (HRE) with 4 repetitions of 4 exemplars. Each condition comprised 20 object categories for adults, and 10 object categories for children. One sample category per condition is shown for illustration. **C.** Recognition. From each category presented during encoding, 2 exemplars were presented as old target items plus 2 new exemplars as similar lures. Not depicted: 2 exemplars from novel categories were presented as new items.

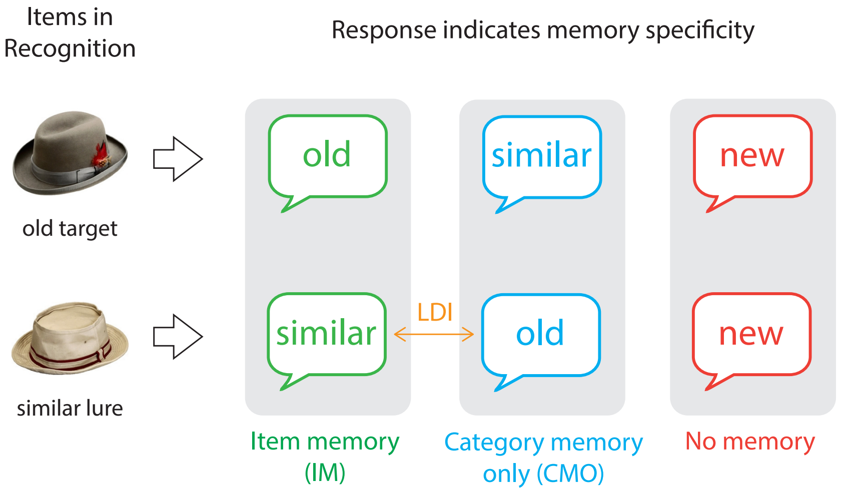

Figure 3: Illustration of memory specificity measures. Correctly identifying targets as old and lures as similar reflects specific item memory (IM; green), incorrectly identifying targets as similar and lures as old reflects mere category memory (CMO; blue), and incorrectly identifying targets and lures as new reflects no memory (red). The difference between identifying lures as similar and mistaking them as old is the lure discrimination index (LDI; yellow). The measures of IM and CMO are furthermore corrected for the tendency to respond "old" or "similar" (not depicted).

Analysis of behavioral data

Encoding task

Performance in the encoding task was measured as the proportion of correctly detected color changes of the fixation cross (see Table 1).

Recognition task

In the recognition task, participants were asked to indicate for each presented object whether it was old (target), similar (lure), or new (foil) (see Experimental design). The same number of targets, lures, and foils were presented, resulting in a 33% chance level of giving the correct response. To quantify performance, one can regard the given responses (old, similar, new) separately for each item class (target, lure, foil) and as a function of the encoding condition, i.e., the number of item repetitions and number of exemplars of the same object category (see Encoding task). One way of quantifying memory performance, independent of conditions, is to calculate the proportion of correct answers: $\Pr(\text{“}old\text{”} \mid target) + \Pr(\text{“}similar\text{”} \mid lure) + \Pr(\text{“}new\text{”} \mid foil)$. However, the two respective incorrect responses for each item class can be evaluated as not equally incorrect but as reflecting the level of memory specificity. For example, incorrectly responding "similar" to a target is less precise than responding "old," but it shows that the general category has been correctly identified as known, whereas a “new” response would reflect no memory for either the item or category.

On this basis, we computed performance measures that focus on different levels of specificity, namely on precise item memory and more general category memory (see Figure 3). These measures are equivalent to the classic performance measure *d’* in old/new recognition tasks that assess correctly recognized old items (hits) corrected for falsely recognized new items or the tendency to respond “old” (false alarms). The current recognition task comprised three response options with graded precision. Thus, different levels of memory specificity can be measured by scoring different responses as correct versus incorrect.

Item memory (IM): Only if specific details of the objects were encoded, were participants able to distinguish previously presented targets from similar lures and vice versa. In this measure, only responses of correct target memory and lure detection were scored as accurate, corrected for both unspecific category memory (see below) as well as the general tendency to respond “old” or “similar.”

$$\begin{aligned} IM = {} & \Pr(\text{“}old\text{”} \mid target) + \Pr(\text{“}similar\text{”} \mid lure) \\ & - \Pr(\text{“}old\text{”} \mid lure) - \Pr(\text{“}similar\text{”} \mid target) - \Pr(\text{“}old\text{”} \mid foil) - \Pr(\text{“}similar\text{”} \mid foil) \end{aligned} \tag{1}$$

Category memory only (CMO): This performance measure captures the ability to successfully remember the general category of presented objects but a failure to distinguish individual exemplars, corrected for the general response bias.

$$\begin{aligned} CMO = {} & \Pr(\text{“}old\text{”} \mid lure) + \Pr(\text{“}similar\text{”} \mid target) \\ & - \Pr(\text{“}old\text{”} \mid foil) - \Pr(\text{“}similar\text{”} \mid foil) \end{aligned} \tag{2}$$

These performance measures emphasize different degrees of memory specificity. Combining IM and CMO provides a measure for general category memory that aggregates all responses in which the category was correctly recognized, independent of specific items (see Supplemental material). Whereas for general category memory a sense of familiarity of the object categories is sufficient, high IM performance requires remembering specific object details in order to recognize the exact exemplar and to reject a similar lure.

In terms of probability, since IM is corrected for four incorrect response combinations while only two combinations are counted as correct, it is more likely to give an incorrect than a correct response. Because of this imbalance of correct and incorrect response probabilities, the chance level of IM is below 0, namely –0.22 (as opposed to, for example, *d’* or CMO, which include the same probability of correct and incorrect responses and therefore have a chance level of 0). To have all measures on the same scale, we adjusted IM such that it denotes the deviation from its chance level (see Figure 4).

Lure discrimination index (LDI): One part of IM (see above) is lure discrimination. The ability to discriminate lures has been assessed separately in a number of studies and associated with hippocampal pattern separation and age differences therein (e.g., Keresztes et al., 2017; Morcom, 2015; Ngo et al., 2018; Stark, Yassa, Lacy, & Stark, 2013; Toner et al., 2009; Yassa, Mattfeld, Stark, & Stark, 2011). The measure reported here computes the difference between correct lure detection and the susceptibility to mistake lures as old[6] (cf. Ngo et al., 2018; Toner et al., 2009).

$$LDI = \Pr(\text{“}similar\text{”} \mid lure) - \Pr(\text{“}old\text{”} \mid lure) \tag{3}$$

EEG recording and preprocessing

EEG was recorded during the object encoding and recognition tasks. In adults, EEG was recorded continuously with BrainVision amplifiers (BrainVision Products GmbH, Gilching, Germany) from 61 Ag/AgCl electrodes embedded in an elastic cap (EASYCAP GmbH, Herrsching, Germany). Two additional electrodes were placed at the outer canthi and one below the left eye to monitor eye movements (horizontal and vertical EOG). During recording, all electrodes were referenced to the right mastoid electrode, and the left mastoid electrode was recorded as an additional channel. Electrode AFz served as ground. The EEG was recorded with a pass-band of 0.1 to 250 Hz and digitized with a sampling rate of 1000 Hz. During preparation, electrode impedances were kept below 5 kΩ.

In children, EEG was recorded continuously with BrainVision amplifiers (BrainVision Products GmbH, Gilching, Germany) from 64 active Ag/AgCl electrodes in an ActiCAP cap (EASYCAP GmbH, Herrsching, Germany). Electrode FCz served as reference and AFz as ground. The sampling rate was 1000 Hz and electrode impedances were kept below 5 kΩ.

For all age groups, the same EEG data preprocessing pipeline was used, except that adults' EEG and eye-tracking data were first integrated using the Eye-EEG toolbox (Dimigen, Sommer, Hohlfeld, Jacobs, & Kliegl, 2011; RRID: SCR_012903). EEG preprocessing was performed with the EEGLab (Delorme & Makeig, 2004; RRID: SCR_007292) and Fieldtrip (Oostenveld, Fries, Maris, & Schoffelen, 2011; RRID: SCR_004849) toolboxes as well as custom MATLAB code (The MathWorks Inc., Natick, MA, USA; RRID: SCR_001622). For analyses, EEG data were de-meaned, re-referenced to an average reference,

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[6] Note that a slightly different score, namely subtracting "similar" responses to foils instead, i.e., correcting for the tendency to respond "similar," has also been used in previous work (e.g., Keresztes et al., 2017; Morcom, 2015; see also Stark et al., 2019), but is not reported here (the age group pattern was similar for both scores).

downsampled to 250 Hz, and band-pass filtered (0.2–125 Hz; fourth order Butterworth). Data were visually screened for excessive muscle artifacts, followed by an independent component analysis (ICA) to identify components related to eye, muscle, and cardiac artifacts (Jung et al., 2000). Microsaccadic artifacts were detected by using an algorithm for the correction of saccade-related transient spike potentials (COSTRAP; Hassler, Trujillo Barreto, & Gruber, 2011). Artifact components were automatically detected, visually checked, and removed from the data. Following the FASTER procedure (Nolan, Whelan, & Reilly, 2010), automatic artifact correction was then performed for any residual artifacts. Channels excluded prior to ICA were interpolated after artifact correction with spherical splines (Perrin, Pernier, Bertrand, & Echallier, 1989). Finally, 10% of the remaining trials were again visually screened to determine successful cleansing. For further analysis, data epochs of 5.5 s were extracted from –2 s to 3.5 s with respect to the onset of the object presentation.

EEG analysis

The current paper only covers analysis of the EEG recorded during encoding. We computed the ERPs by averaging the time-locked EEG data over the respective trials, separately for each electrode. For the ERP group comparison, we applied an absolute pre-stimulus baseline correction (200 ms before onset). To examine repetition effects, we calculated the ERPs separately for the first and second presentation of the object items. For plotting only, data were low-pass filtered at 30 Hz (fourth order Butterworth).

Statistical analysis

Memory performance

For each age group, we tested whether participants performed better than chance in the recognition task by contrasting the proportion of correct responses to chance level (0.33) (one-sample t-tests). We tested for age differences in all reported behavioral measures by conducting one-way ANOVAs contrasting children, young adults, and older adults, followed by post-hoc t-tests. For item memory, we investigated the effects and possible interactions of age and the number of item repetitions and category exemplars during encoding using three-way mixed effects ANOVAs with age group (children, young adults, older adults) as the between-subjects factor, number of repetitions (two or four) and number of exemplars (two or four) as within-subjects factors, and item memory performance as the dependent variable. The influence of item repetitions independent of exemplar manipulations was further investigated using paired sample t-tests contrasting memory for objects from the HR condition and the BL condition.

Event-related potentials

On the first (within-subject) level, we compared the ERPs of every encoding trial in which an object item was presented for the first time with the ERPs of the respective second presentation using two-sided paired sample *t*-tests.

On the second (between-subject) level, the individual *t*-maps of the first-level analysis were contrasted against zero using two-sided independent samples *t*-tests. We controlled for multiple comparison by conducting non-parametric, cluster-based, random permutation tests (Fieldtrip toolbox; Maris & Oostenveld, 2007; Oostenveld et al., 2011; see also Fields & Kuperberg, 2019). All scalp electrodes (60 for adults, 64 for children) and the trial time points from –0.1 to 1.6 s relative to stimulus onset were included in the analysis. Clusters were formed by grouping neighboring channel × time samples with a *p*-value below 0.05 (spatially and temporally). The respective test statistic was then determined as the sum of all *t*-values within a cluster. The Monte Carlo method was used to compute the reference distribution for the summed cluster-level *t*-values. Samples were repeatedly (10,000 times) assigned into two classes and the differences between these random classes were contrasted with the differences between the actual two conditions (e.g., first and second presentation). For every permutation the *t*-statistic was computed, and the *t*-values summed for each cluster. This was done separately for each age group to reveal the group-specific repetition effects.

On the third (between-group) level, we tested whether the identified effects differed between age groups. For this, we extracted and averaged the individual *t*-values from the first-level analysis within the time–electrode clusters identified in the second-level analysis. For all group comparisons, *t*-values were transformed to *z*-values. For each repetition effect, these values were entered into a one-way ANOVA contrasting children, young adults, and older adults, or underwent a two-sample *t*-test if only two groups were compared. We tested whether the identified clusters may be different reflections of the same repetition suppression/enhancement effect by correlating the extracted mean *t*-values (see above) across subjects (Pearson correlation). If clusters correlated highly ($r > 0.7$), we pooled them together as one composite effect by averaging across the individual mean *t*-values.

Brain–behavior relationship

We tested for a relationship between ERP repetition effects (first versus second presentation) and memory performance by modeling their correlations using maximum likelihood estimations (in Ωnyx 1.0-1010; von Oertzen, Brandmaier, & Tsang, 2015). Specifically, the correlations of the individual mean *t*-to-*z*-transformed *t*-values extracted from the identified time–electrode clusters (see above) and the individual measures of memory performance were modeled (a) separately for each age group, and (b) across all age groups. Since we observed overall age differences in both effect sizes and memory performance, we standardized both measures within groups in order to test for the brain–behavior association independent of overall age differences. We tested whether the models (a and b) showed significantly different model fits using likelihood-ratio (Chi-squared) tests. Significant differences between the model fits (H1) would show that the model allowing for group-specific correlations (a) explains the data better, indicating that the correlations differed between groups, which would then require follow-up analyses of the pairwise differences. In turn, if the model fits did not differ significantly (H0), this would indicate that the brain–behavior relationship was not different between groups.

Results

Behavioral performance

Encoding task

During encoding, the participants' task was to detect when the fixation cross changed its color, which occurred in about 7% of the trials. The task mainly served to keep the participants vigilant and make sure they attended to the stimuli. We expected close-to-ceiling performance when participants attended to the stimuli and therefore excluded everyone who detected less than 80% of the respective trials (i.e., fewer than 43 out of 54 for adults, and fewer than 21 out of 27 for children). One child (66.7% hit rate) and two older adults (72.2% and 50% hit rate, respectively) were excluded based on this criterion. A cut-off based on false alarms was not used as they barely happened. The encoding performance results of the remaining participants are shown in Table 1.

Table 1: Mean (± *SD*) target detection performance of all age groups, excluding participants with a hit rate below 80%. Absolute numbers of trials and percentages (%) for hits (responses to targets) and correct rejections (no responses to non-targets). The task comprised 780 trials including 54 targets and 726 non-targets for the adults, and 390 trials including 27 targets and 363 non-targets for the children.

Group	Hits (targets)		Correct rejections (non-targets)	
	absolute *M* (*SD*)	% *M* (*SD*)	absolute *M* (*SD*)	% *M* (*SD*)
Children	26.5 (1.0)	98.1 (3.6)	362.5 (1.2)	99.9 (0.3)
Young adults	53.4 (1.1)	98.8 (2.1)	724.4 (1.1)	99.8 (0.2)
Older adults	52.1 (1.9)	96.4 (3.5)	722.4 (4.2)	99.5 (0.6)

M = mean, SD = standard deviation

Recognition task

In the recognition task, participants were asked to decide for each presented object whether it was old (target), similar (lure), or new (foil). One way to measure performance is to calculate the proportion of correct and incorrect responses. The mean (±*SD*) proportion of correct responses was 0.63 (0.14) for children, 0.57 (0.15) for young adults, and 0.56 (0.15) for older adults (chance level: 0.33). On average, subjects of all age groups gave more correct than incorrect responses, and they performed better than chance (children: $t(17) = 15.38$, $p < 0.001$; young adults: $t(38) = 18.09$, $p < 0.001$; older adults: $t(54) = 19.13$, $p < 0.001$; one-sample *t*-tests of proportion correct responses against chance level).

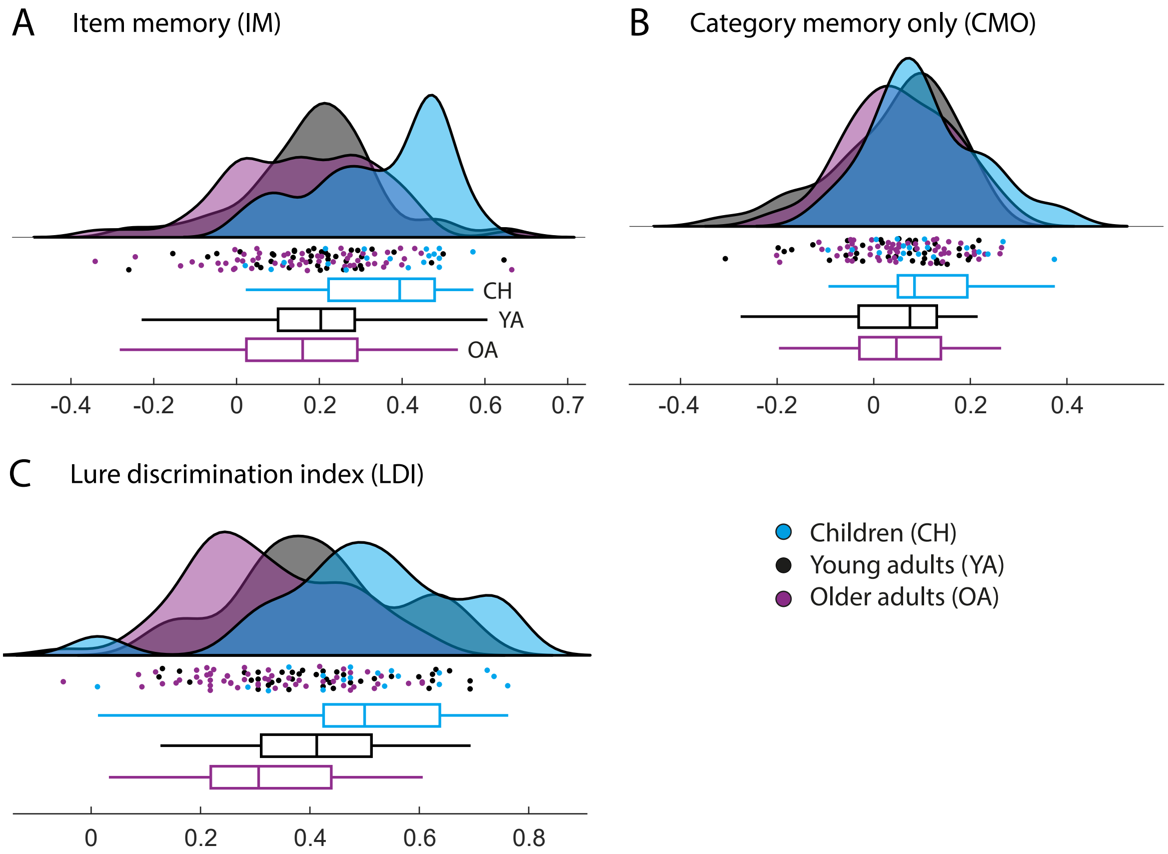

Figure 4: Behavioral performance of the children (CH; blue), young adults (YA; black), and older adults (OA; purple). **A.** Correct item memory (IM). **B.** Category memory only (CMO). **C.** Lure discrimination index (LDI) indicating bias towards pattern separation (positive) or completion (negative). Group distributions as un-mirrored violin plots (probability density functions), boxplots with 1st, 2nd (median), and 3rd quartiles, whiskers with 2nd and 98th percentiles, and individual (vertically jittered) data points (Allen et al., 2019). Zero denotes the chance level of the respective measure; above-chance performance (larger proportion of correct responses than incorrect responses in the respective measure) is indicated by positive values and below-chance performance by negative values.

Age differences in memory specificity. We distinguished different degrees of memory specificity by computing memory measures that differentiate trials in which the specific exemplar could be correctly identified as old or similar versus trials in which targets were confused as lures and vice versa. Considering only correct item-specific responses to targets and lures, corrected for all incorrect "old" and "similar" responses (IM; Eq. (1); Figure 4A), showed significant age differences ($F(2,109) = 7.48$, $p < 0.001$; one-way ANOVA). Post-hoc t-tests revealed higher performance of children compared with young adults ($t(55) = 3.27$, $p = 0.002$) as well as older adults ($t(71) = 3.75$, $p < 0.001$) but no differences between the adult groups ($t(92) = 0.78$, $p = 0.435$). In contrast, the measure of correct category memory but incorrect item memory, corrected for the tendency to respond "old" or "similar" (CMO; Eq. (2); Figure 4B), showed no age differences ($F(2,109) = 1.90$, $p = 0.155$). That is, the age groups differed in their specific exemplar memory but not mere concept memory.

Descriptively, the lure discrimination index (LDI; e.g., Ngo et al., 2018; Toner et al., 2009; Eq. (3); Figure 4C) showed a clear lifespan trajectory in that, on average, children exhibited the highest scores, older adults the lowest scores, and young adults fell in-between. A high score is achieved by a large proportion of trials in which lures could be identified as similar and a low proportion of trials in which lures were mistaken as old, indicating pattern separation. A lower score, in contrast, indicates greater generalization or a bias towards pattern completion (cf. Keresztes et al., 2017). A one-way ANOVA contrasting all groups revealed significant age differences ($F(2,109) = 10.65, p < 0.001$). Post-hoc t-tests showed no significant differences between children and young adults ($t(55) = 1.73, p = 0.089$) whereas both children ($t(71) = 4.26, p < 0.001$) and young adults ($t(92) = 3.15, p = 0.002$) showed a higher LDI than older adults did. Thus, whereas all groups generally exhibited a bias towards pattern separation (i.e., positive values), older adults were driven more towards pattern completion than children and young adults.

To control for the different task versions (see Experimental design), 23 additional young adults performed the shorter children's task. In the shorter task, children and young adults did not differ in either IM ($t(39) = –0.95, p = 0.348$), CMO ($t(39) = –0.748, p = 0.459$), or LDI ($t(39) = –1.66, p = 0.105$), whereas young adults with the shorter task performed better than young adults with the longer task (IM: $t(60) = 3.94, p < 0.001$; CMO: $t(60) = 2.96, p = 0.004$; LDI: $t(60) = 3.14, p = 0.003$), indicating that children's high performance was largely due to lower task difficulty.

The effect of repetitions on item memory. In the following, we asked whether item and category repetitions might affect memory performance differentially in children, young adults, and older adults. We initially expected better item-specific memory performance when items were repeated more often and worse performance when more exemplars were presented during encoding. This was based on the hypothesis that more repetitions would provide more opportunity to encode item-specific details leading to both better target recognition as well as rejection of similar lures (Benjamin, 2001; but see Reagh & Yassa, 2014), whereas more exemplars would create stronger interference, making it harder to distinguish between similar items (M. C. Anderson, 2015). The latter is supported by previous findings showing that increasing the number of exemplars from the same object category, reduced participants' ability to discriminate between lures and targets from that category (Gallo, 2004; Konkle et al., 2010; Koutstaal & Schacter, 1997; Omohundro, 1981; Poch, Prieto, Hinojosa, & Campo, 2019). Alternatively, interference from similar memories can also trigger a repulsion of memory representations, suggested by the findings of less overlapping activation patterns in the hippocampus (pattern separation), which was associated with less memory interference, that is, better performance (Chanales et al., 2017, 2020; Favila et al., 2016). That is, both scenarios – better or worse item memory when more exemplars were presented – are conceivable.

To examine these predictions, we conducted a three-way mixed ANOVA with age group as the between-subjects factor, number of repetitions and number of exemplars as within-subjects factors, and item memory performance as the dependent variable. The results revealed a main effect of age ($F(2,109) = 7.48$, $p < 0.001$) with the same pattern of age differences as reported above, and a main effect of the number of exemplars ($F(1,109) = 8.53$, $p = 0.004$). Post-hoc t-tests demonstrated better item memory when four rather than two exemplars were presented ($t(111) = 3.58$, $p < 0.001$), revealing a beneficial effect of a higher number of category exemplars. This is in line with the repulsion prediction (see above), whereas the number of repetitions did not influence item memory ($F(1,109) = 0.99$, $p = 0.321$). To better disentangle the effect of repetitions and exemplars for item-specific memory, we further examined the potential effect of repetitions by directly contrasting memory performance for items from the HR and BL condition, i.e., independently of the exemplar manipulation. Across age groups, this revealed better IM for the HR condition ($t(111) = 2.72$, $p = 0.008$; paired-sample t-test).

Since there were no interactions between age and item manipulations, we largely disregard the encoding conditions and do not separate the trials accordingly in the following analyses.

Lifespan differences in ERPs

The ERPs of children, young adults, and older adults at selected representative electrode sites are shown in Figure 5. Children exhibited overall higher amplitudes than adults, which is consistent with previous findings in the literature (Coch, Skendzel, & Neville, 2005; Dustman & Beck, 1969; Mueller, Brehmer, von Oertzen, Li, & Lindenberger, 2008). This could, for example, be due to differences in skull thickness (Frodl et al., 2001), but in the current study it may also be a result of the different EEG systems and laboratories used to test the children and adults.

Repetition effects in ERPs

Using paired sample t-tests (first level) and non-parametric cluster-based permutation analysis (second level), we derived group-specific time–electrode clusters that indicated the trial time points and electrodes in which first and second object presentations showed reliable differences. We considered clusters whose test statistic exceeded the 97.5th percentile for its respective reference distribution as showing reliable repetition effects.

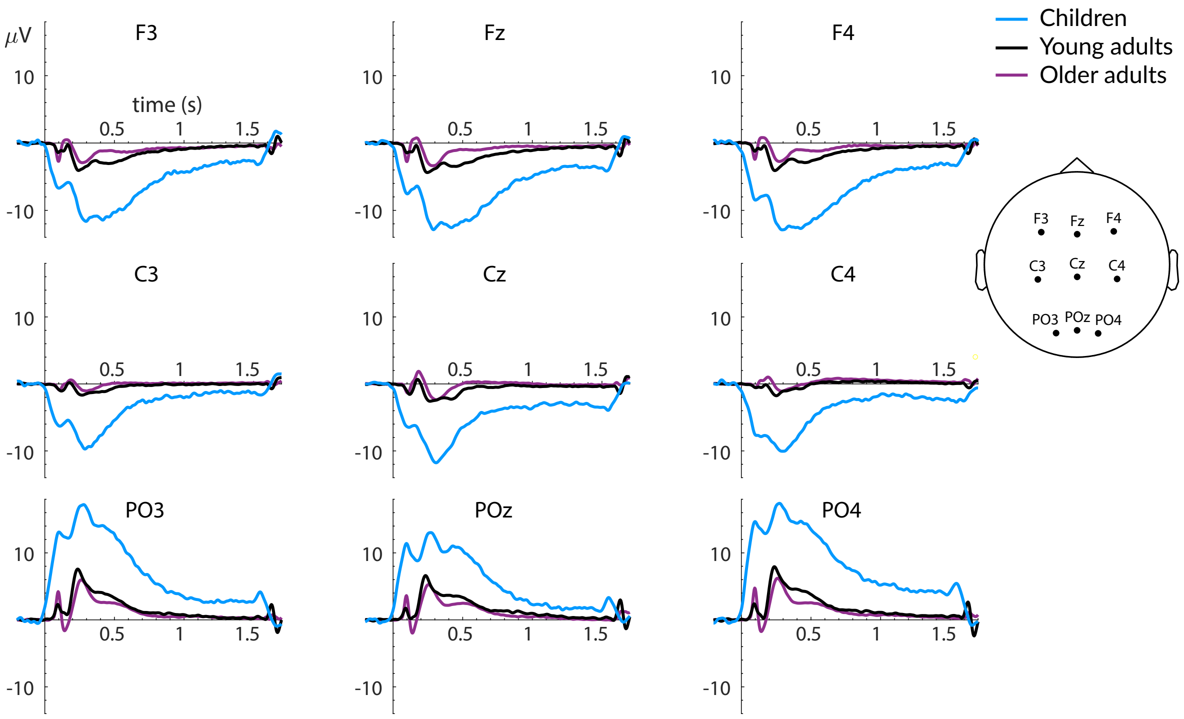

Figure 5: Event-related potentials (ERPs) at selected electrode sites, averaged over all trials in which an object was shown for the first time, for all children (blue), young adults (black), and older adults (purple). The x-axis shows trial time (s) with stimulus onset at 0 (origin) and offset at 1.5 s, the y-axis shows amplitude (μV) with negative values plotted downwards. Data were baseline-corrected with an absolute pre-stimulus baseline of 200 ms.

With this procedure, we identified two clusters in children, three in younger adults, and four in older adults (all clusters $p \leq 0.002$) with broadly overlapping topography and latency (see Figure 6 for details). For all age groups, there was a cluster over posterior electrodes showing lower positive amplitudes for the second versus first stimulus presentation (i.e., repetition suppression; RS1; Figure 6A). This cluster appeared earliest in children (372–852 ms after stimulus onset), slightly later and with shorter duration in young adults (492–840 ms), and latest and with the shortest duration in older adults (568–884 ms). Within similar time windows another repetition suppression cluster (RS2) was identified at frontal and central electrodes which showed reduced negativity for repeated stimuli (Figure 6B). This cluster appeared earliest in young adults (224–756 ms), followed by children (304–864 ms), and latest, as well as with much shorter duration in older adults (676–848 ms). For all age groups, both of these suppression effects occurred mainly while the ERP deflections peaked off back to baseline, starting right at or after the peak in children and starting only shortly before returning to baseline in older adults. As the effects appeared at similar times but at different locations, and with opposite polarity, they could be two reflections of the same repetition suppression effect (perhaps resulting from the two sides of the dipole).

To test this, we assessed whether the magnitudes of the effects correlated across subjects (see below).

Furthermore, we identified a repetition enhancement effect (RE1) for both young and older adults that showed stronger (more negative) activity for the second than for the first object presentations over mainly frontal and temporal electrode sites (young adults: 244–368 ms; older adults: 308–548 ms; Figure 6C). An opposite enhancement effect (RE2) was only identified for older adults over centro-parietal regions at 308–640 ms after stimulus onset (Figure 6D). According to our definition of suppression/enhancement, the latter effect in older adults actually started as a suppression effect since negativity was reduced for the ERPs of the second presentations. As the polarity of the ERPs change from negative to positive, the difference between first and second presentations becomes an enhancement effect, where the ERPs of the second presentations show a steeper rise and end in a higher peak compared with the first presentations. Since most of the effect occurred during the positive part, we classified it as an enhancement effect. In analogy to the two suppression effects, the opposite enhancement clusters identified in older adults could be two reflections of the same effect, which would be indicated by a high correlation between the effect sizes.

To test for correlations between the repetition effects, we extracted the individual *t*-values (first-level analysis) from the identified time–electrode clusters (second-level analysis) and averaged them across the respective time points and channels for each subject. These *t*-values were then correlated across subjects. High correlations would indicate that participants who showed large effect sizes in, for example, RS1 also showed a large RS2 effect, indicating that they are not two independent effects potentially serving different functions. Indeed, for all age groups as well as across groups, the magnitudes of the RS1 and RS2 effects correlated strongly (children: $r = 0.92$, $p < 0.001$; young adults: $r = 0.72$, $p < 0.001$; older adults: $r = 0.81$, $p < 0.001$; across groups: $r = 0.82$, $p < 0.001$; Pearson correlation). Likewise, the two enhancement effects of the older adults were highly correlated ($r = 0.72$, $p < 0.001$). Hence, we pooled the two suppression effects for each group and the two enhancement effects for older adults into composite RS and RE effects by averaging the respective effect sizes for each subject. RS and RE effects did not correlate, potentially indicating two functionally different effects.

Age differences in ERP repetition effects

Repetition effects were identified for all age groups (see Figure 6). In the next step, we examined whether the size of the effects differed between age groups (see Figure 7 left). Because of overall age differences in EEG amplitudes (see Figure 5), rather than computing and comparing the raw amplitude difference between the ERPs to first and second presentations, it is more appropriate to compare the effect sizes,

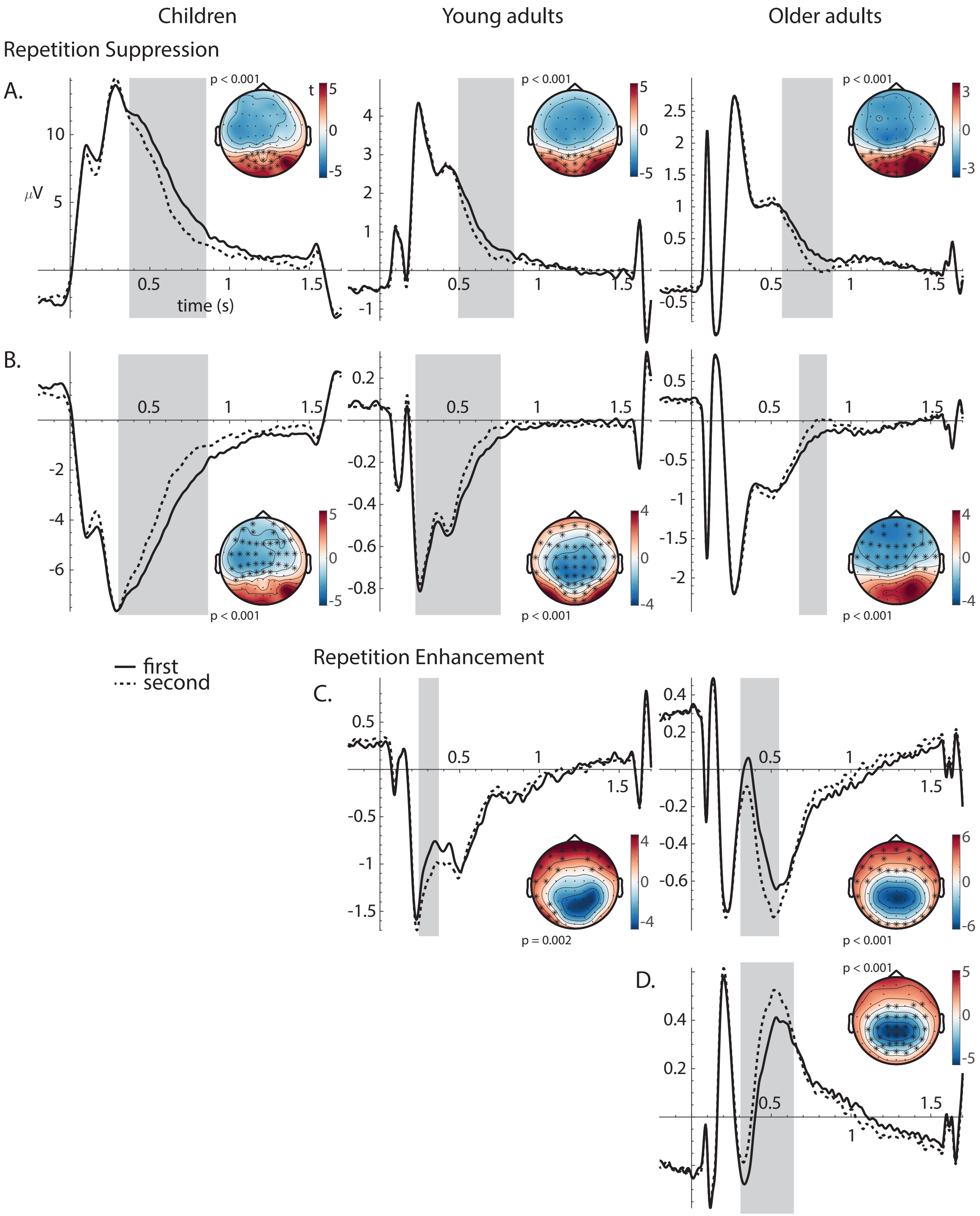

Figure 6: Group-specific repetition suppression (A, B) and repetition enhancement (C, D) effects. **A.** Positive posterior suppression effect (RS1). **B.** Negative fronto-central suppression effect (RS2). **C.** Negative frontal enhancement effect (RE1). **D.** Positive centro-parietal enhancement effect (RE2). ERPs are averaged over all trials in which objects were shown for the first time (solid line) or for the second time (dashed line) for children (left), young adults (middle), and older adults (right). The *x*-axis shows trial time (s) with stimulus onset at 0 (origin) and offset at 1.5 s, the *y*-axis shows amplitude (μV) with negative values plotted downwards. The time windows in which reliable differences between first and second presentation were identified (cluster-based permutation analysis) are shaded in gray. All ERPs are averaged over the respective electrodes in which the effects were identified, highlighted by asterisks in the respective topographical distributions plotted next to the ERPs. Topographies show the resulting *t*-values from contrasting ERPs of first and second presentations, averaged over the respective significant time windows. The *p*-values from the cluster-based permutation analysis are provided for each time–electrode cluster.

i.e., the respective *t*-values of the contrast, which are independent of the overall amplitude. For group comparisons, *t*-values were transformed into *z*-values.

The composite RS effect sizes (*z*-values) differed between the age groups ($F(2,109) = 4.88, p = 0.009$; one-way ANOVA) with children showing larger effects than adults (children vs. young adults: $t(55) = 2.10$, $p = 0.040$; children vs. older adults: $t(71) = 2.83, p = 0.006$; post-hoc *t*-tests) and no differences between young and older adults ($t(92) = 1.46, p = 0.150$) (see Figure 7A left). The enhancement effects identified for young adults (RE1) and older adults (composite of RE1 and RE2) did not differ in their effect sizes ($t(92) = –0.13, p = 0.896$) (see Figure 7B left).

Repetition effects are positively linked to memory performance

We examined the relationship between the individual mean effect sizes of the composite repetition effects (see above) and the individual performance measures (see Behavioral analysis) by modeling their correlations using maximum likelihood estimates, (a) separately for each age group, and (b) across all groups. Because there were overall age differences in both ERP effects and memory performance (see above), we standardized both measures within groups to test for the brain–behavior association independent of age differences. The resulting estimated correlation coefficients are presented in Table 2.

Across groups, the composite RS effect correlated significantly with IM (see Figure 7A right) in the direction that larger RS were associated with better memory performance. The RE effect that only occurred in adults also showed a positive association to IM across young and older adults (Figure 7B right). In contrast, CMO and LDI did not show significant brain–behavior correlations across groups (see Table 2).

We tested whether the models (a and b) differed in their model fits using likelihood ratio (LR) tests. For all repetition effects (RS, RE) and performance measures (IM, CMO, LDI), the model fits were not significantly different from each other (see Table 2). That is, the model that allowed age group-specific brain–behavior relations did not explain the data significantly better than the model with fixed correlations across groups. This indicates that the brain–behavior associations did not differ across the age groups. Therefore, in the following we do not interpret the group-specific but only the cross-group brain–behavior correlations.

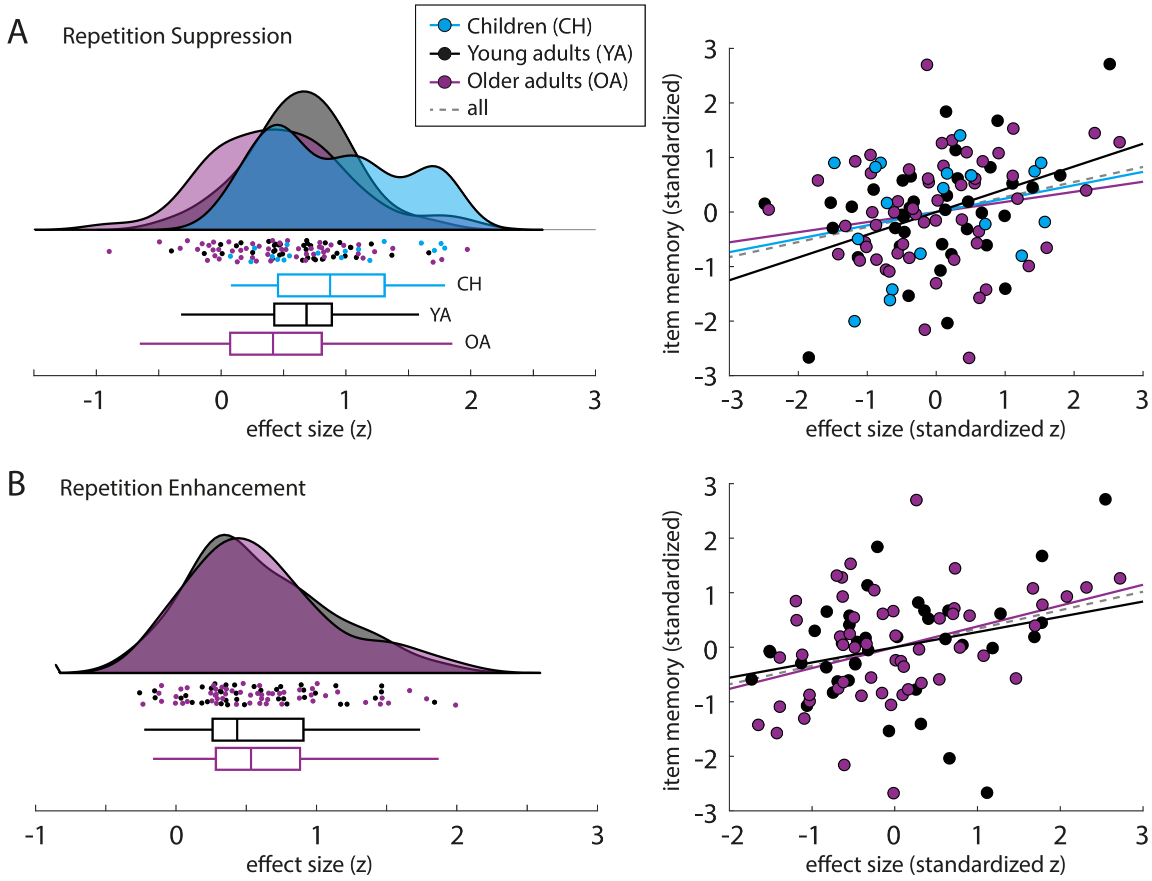

Figure 7: Repetition suppression (A) and enhancement (B) effect sizes for each group (left) and correlations between effect sizes and item memory performance (right). Left: Group distributions as un-mirrored violin plots (probability density functions), boxplots with 1st, 2nd (median), and 3rd quartiles, whiskers with 2nd and 98th percentiles, and individual (vertically jittered) data points (Allen et al., 2019) of the mean effect sizes (z-transformed t-values within the respective clusters) in the children (blue), young adults (black), and older adults (purple). Right: Association (Pearson correlation) between individual standardized effect sizes (z-transformed t-values; x-axis) and standardized item memory performance (IM; y-axis) indicated by least-squares lines, separately for each group (colors as above) and across groups (gray dashed line). For statistics and correlations with other performance measures, see Table 2.

Table 2: Estimated correlation coefficients (*r*) for modeled correlations of individual ERP effect sizes (standardized *z*-transformed *t*-values) of the composite repetition suppression (RS) and repetition enhancement (RE) effects with memory performance measures (IM, CMO, LDI; standardized) for all age groups separately as well as across groups (All). Correlations for item memory (IM) are also plotted in Figure 7. Likelihood ratio (LR) tests were used to compare the models of group-specific versus group-independent brain–behavior correlations. Significant LR would indicate that correlations differed between age groups.

Memory	Effect	Children	Young adults	Older adults	All	Model comparison		
		r	*r*	*r*	*r*	*LR*	*df*	*p*
IM	RS	0.26	0.43	0.19	0.28	1.66	2	0.436
	RE		0.29	0.39	0.35	0.33	1	0.568
CMO	RS	–0.22	0.10	–0.06	–0.03	1.23	2	0.540
	RE		–0.07	0.17	0.07	1.28	1	0.258
LDI	RS	0.03	0.35	–0.07	0.10	4.26	2	0.119
	RE		0.33	–0.02	0.12	2.85	1	0.091

IM = item memory, CMO = category memory only, LDI = lure discrimination index,
RS = repetition suppression, RE = repetition enhancement,
LR = likelihood ratio, df = degrees of freedom

Discussion

The present study investigated whether processes of memory formation, as reflected in neural repetition effects, are associated with inter-individual and age differences in item and category memory. Specifically, we were interested in how far repetition-related neural mechanisms might “determine” the degree of memory specificity in a lifespan sample. For this, we compared repetition-related differences in ERPs during incidental object encoding in groups of 7–9-year-old children, 18–30-year-old young adults, and 65–76-year-old older adults in relation to their later recognition performance. We distinguished memory for specific items and for the general stimulus category. We identified reliable ERP repetition suppression effects for all age groups and repetition enhancement among young and older adults. Across groups, item-specific memory performance was positively associated with the magnitude of repetition suppression and enhancement. In sum, we demonstrate common neural mechanisms of memory encoding across the lifespan.

Memory performance partially differed between age groups. Children showed better item-specific memory compared with adults who performed a longer task. However, there were no performance differences between children and control young adults who also performed the children’s task version. This is in accordance with previous findings showing worse memory for faces and houses in children compared with adolescents and young adults, but not for objects (Golarai et al., 2007). The specific item memory depended on a high hit rate for old and similar items as well as a low false alarm rate for similar and new items, which includes high lure discrimination (LDI) performance. Whereas some previous work suggested that pre-school children tend to have fewer false memories than adults (Brainerd et al., 2002, 2008), other studies showed higher false alarm rates for foils and, in particular, similar lures (Ngo et al., 2018). Especially children below the age of 6 years were shown to be biased towards pattern completion (negative LDI), whereas older children already revealed a bias toward pattern separation responses (positive LDI) (Ngo et al., 2018; Rollins & Cloude, 2018), which is in line with the current results. Despite a general trend towards improved lure discrimination across childhood and adolescence (Keresztes et al., 2017; Rollins & Cloude, 2018), there are considerable inter-individual differences in memory specificity among children, which may be linked to uneven maturation of regions within the hippocampus (Keresztes et al., 2017, 2018).

At the other end of the lifespan, young and older adults did not differ with respect to recognition memory, which is in accordance with previous work showing much less pronounced or no age differences for item compared to associative memory, especially under incidental encoding conditions (Old &

Naveh-Benjamin, 2008). However, one might have expected that older adults would tend to generalize more and thus show worse item-specific memory than young adults, perhaps accompanied by greater reliance on category memory (Koutstaal & Schacter, 1997; Tun, Wingfield, Rosen, & Blanchard, 1998). Although this was not the case in these aggregated performance assessments, evidence in this direction is nevertheless provided by age-related differences in lure discrimination and false alarms. The ability to recognize lures as "similar" and not "old" is only achievable if the original targets have been encoded with high specificity. Here, young adults outperformed the older adults, which corroborates previous findings (Schacter et al., 1997; Stark & Stark, 2017; Stark et al., 2013; Stark, Stevenson, Wu, Rutledge, & Stark, 2015) and has been shown to be related to age-associated disruptions of the intra-hippocampal circuitry (Shing et al., 2011; Wilson, Gallagher, Eichenbaum, & Tanila, 2006; Yassa et al., 2011). This was related to generally higher false alarm rates in older adults, which is also in agreement with previous studies (e.g., Fandakova et al., 2018).

All in all, the age pattern shows that 7–9-year-old children already have adult-like item-specific memory and lure discrimination abilities. Further, aggregated performance measures did not show differences between young and older adults while individual elements of the measures (e.g., lure detection) did, indicating aging-related behavioral disparity in specific memory aspects.

With regard to our ERP results, we showed that all age groups exhibited repetition-related changes in the neural responses during encoding, suggesting common neural mechanisms of memory formation overall. We identified repetition suppression (for all age groups) and repetition enhancement (only for adults) with overlapping topographies and time windows across age groups but age-related differences with regard to the magnitudes of the effects. Taken together, these observed repetition effects are in line with the effects described in the ERP literature (on adults). Whereas many early ERP experiments only found repetition enhancement effects, usually with repeated words (for a review, see Rugg & Doyle, 1994), similar suppression effects have also been reported, usually with repeated images (Penney et al., 2001; Rugg et al., 1995; Van Petten & Senkfor, 1996). However, suppression and enhancement can also co-occur (e.g., Henson, Rylands, Ross, Vuilleumeir, & Rugg, 2004; Lawson, Guo, & Jiang, 2007; Stefanics et al., 2018). Our effects are in line with, for example, Lawson et al. (2007) who also reported an earlier enhancement effect and a later suppression effect for both young and older adults.

The repetition suppression effects may be linked to modulations in the P600 ERP component, which is sensitive to word frequency and familiarity (Rugg & Doyle, 1994; Rugg, 1990), and in FN400, which is also associated with familiarity (Curran, 2004; Friedman & Johnson, 2000; Mecklinger, 2000). Thus, modulations in these components may suggest differences in stimulus familiarity that are certainly to be expected when items are repeated. The repetition enhancement effect that we observed only for adults partially resembles the original ERP repetition effect described in early studies (Rugg & Doyle, 1994). It has been argued that this reflects modulations in several ERP components, mainly a decrease in N400, which is related to priming and contextual integration, and an increase in P300, which is related to working memory and stimulus categorization (Friedman, 2000; Lawson et al., 2007; Rugg & Doyle, 1994; Van Petten & Senkfor, 1996). The observation that the ERPs of repeated stimuli show changes in these components may indicate successful integration of the items into internal object representations. However, this contrasts with the suggestion by Henson et al. (2000) that repetition enhancement may reflect the formation of new representations of previously unfamiliar stimuli, whereas suppression may reflect the strengthening of already existing representations. According to this interpretation, children may have had less experience with the presented objects (cf. Brod, Werkle-Bergner, & Shing, 2013) and therefore show more enhancement than adults, who presumably had previously well-established representations of all the objects. As the effects described by Henson et al. (2000) were found in fMRI, the suggested functional distinction between enhancement and suppression may be specific to the fusiform cortex in which they were identified, and represent generally different effects than those found in the current study. The absence of repetition enhancement in children may also be due to deficient statistical power as the children's group was smaller and they had fewer trials than the adult groups. Since other studies on repetition effects in children of this age are lacking, we can only speculate on whether children may indeed exhibit no enhancement. If this is the case, it may indicate that the underlying neural mechanisms related to context integration and working memory, for example (see above), are not yet fully developed. This would be largely consistent with previous studies showing developmental differences in context integration and binding in general (Káldy & Kovács, 2003; Raj & Bell, 2010), and also in relation to working memory (Fandakova, Sander, Werkle-Bergner, & Shing, 2014) in the course of childhood.

While similar patterns of suppression effects occurred in all three age groups, we observed differences in the magnitudes of the effects between groups. Comparing the composite suppression effect between age groups yielded the largest effect sizes for the children's group. Young and older adults differed in neither the magnitudes of suppression nor enhancement, which is generally in line with previous studies (e.g., Hamberger and Friedman (1992), but see Friedman, Hamberger, and Ritter (1993), who showed stronger repetition effects in older than in young adults). However, these studies may not be entirely comparable as they contrasted raw amplitudes rather than standardized effect sizes. On this between-group level, the co-occurrence of children's strong memory performance and larger repetition effects while the adult groups differed in neither, may suggest that memory success is associated to strong repetition suppression, in line with the hypothesis that repetition effects reflect successful memory formation. To expand on this proposition, especially with regard to the degree of memory specificity, we further examined the relation of individual differences in repetition effects and memory on the item- and category-level both within and across age groups.

The central finding of the present study is the observed positive relationship of the extent to which neural activity is altered in response to repeated input and individual explicit memory performance. In line with the hypothesis that these repetition-related activation differences reflect the formation of memory representations, across groups, individuals exhibiting larger repetition effects during encoding showed better item recognition memory than individuals with smaller repetition effects did. Importantly, this was not due to overall age group differences, such as children showing both larger effects and better performance (see above), but the association remained when overall age differences were eliminated by standardizing the measures within groups. Although not all age groups separately showed significant correlations between individual memory performance and the repetition effects, the estimated brain–behavior associations did not significantly differ between the groups, suggesting largely common neural correlates of successful memory encoding across the lifespan. The finding that the repetition effects were linked to specific item memory and not to mere category memory furthermore suggests that repetition-sensitive neural responses reflect highly detailed memory encoding. Moreover, repetition effects were not related to mere lure discrimination but specific item memory, including correct target recognition, lure detection, and foil rejection, indicating that the LDI alone may provide an incomplete picture with regard to the abilities reflecting highly specific memory representations. All in all, we show that ERP repetition effects provide an age-independent indicator of individual differences in successful encoding of item-specific details.

To conclude, we found that memory formation processes that manifest in repetition-sensitive ERP components are related to individual differences in item recognition performance across the lifespan. The effects did not differ between age groups, indicating age-independent reflections of memory encoding that have not been shown before. These novel findings highlight the significance of encoding mechanisms that facilitate the formation of high-quality memory representations and enable highly specific recognition and item distinction.

Supplemental material

Supplemental experimental methods

Other tasks and measurements

In addition to the main tasks, participants completed several further paper-and-pencil and computer-based tests and questionnaires that varied between age groups. Adults' blood pressure was assessed once at the beginning and end of the testing session. While their EEG was prepared, the adult participants filled out a paper questionnaire concerning demographic information about their gender, age, education, occupation, physical activities, handedness, drug use (caffeine, tobacco, alcohol, medicines), and a questionnaire on their sleep quality (Pittsburgh Sleep Quality Index; PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Before and after the encoding task, resting-state EEG and ECG were assessed. Between the encoding and recognition tasks, we took photos of the participants to record the position of the EEG cap and electrodes. After the recognition task, the adult participants' vision acuity was tested with the Landolt-C Freiburg Vision Test (Bach, 1996) and they performed an additional memory task on the computer in which they were asked to associate photographs of faces with spoken names (Keresztes et al., 2017). Furthermore, they completed the Digit-Symbol Substitution Task measuring processing speed (DSST; Wechsler, 1981) and a test of verbal knowledge (Lehrl, 1977) on paper. Only older adults additionally took the Mini-Mental State Examination (MMSE; Folstein et al., 1975) for dementia screening.

In the children's sample, both the child and their parent filled out a questionnaire before the experiment started. The parents' questionnaire contained items concerning the child's gender, age, handedness, and the previously screened inclusion criteria of normal or corrected-to-normal vision and psychiatric and neurological health. The children's questionnaire comprised six questions regarding tiredness, motivation, focus, and hours spent looking at a mobile phone or computer screen on that day. Then, working memory was assessed by a verbal digit span task (Petermann & Petermann, 2011) and they completed the same DSST as the adults (Wechsler, 1981). After EEG preparation during which the children could play games on a tablet, resting-state EEG was measured, followed by the object encoding task. In the break between encoding and recognition, children's vision acuity was tested with the same Freiburg Vision Test (Bach, 1996).

All eligible adult participants were invited for a second session several months afterwards in order to record structural magnetic resonance images (MRI) including T1, T2, and high-resolution hippocampus scans. These data are not part of the current analysis.

Supplemental Results

The basis of age differences in memory performances

We separately contrasted the individual response components from the assessed memory performance measures between groups to identify the basis of the age differences. First, children, younger adults, and older adults did not differ in the proportions of false responses to foils (novel categories), which can be seen as an indicator of their general tendencies to give "old" or "similar" responses ($\mathrm{Pr}(\text{“}old\text{”} \mid foil)$: $F(2,109) = 2.05$, $p = 0.133$; $\mathrm{Pr}(\text{“}similar\text{”} \mid foil)$: $F(2,109) = 1.87$, $p = 0.159$). This shows that age differences in our aggregated performance measures were not due to age differences in general response biases.

Second, the performance differences between children and young adults could mainly be explained by children's better target detection performance, i.e., their higher proportion of correct "old" responses ($\mathrm{Pr}(\text{“}old\text{”} \mid target)$: $t(55) = 2.80$, $p = 0.007$), which was the only response component in which children and young adults differed significantly. In contrast, the differences between children and older adults were due to children's higher lure detection rate ($\mathrm{Pr}(\text{“}similar\text{”} \mid lure)$: $t(71) = 3.14$, $p = 0.003$) and lower susceptibility to lures ($\mathrm{Pr}(\text{“}old\text{”} \mid lure)$: $t(71) = –4.17$, $p < 0.001$).

Third, young and older adults differed in all performance components related to targets and lures: Older adults were better at correctly recognizing targets ($\mathrm{Pr}(\text{“}old\text{”} \mid target)$: $t(92) = –2.55$, $p = 0.013$), but they were also more susceptible to lures ($\mathrm{Pr}(\text{“}old\text{”} \mid lure)$: $t(92) = –5.12$, $p < 0.001$). Young adults, in turn, were better at correctly detecting similar lures ($\mathrm{Pr}(\text{“}similar\text{”} \mid lure)$: $t(92) = 3.55$, $p = 0.001$), but they more often confused targets as being lures ($\mathrm{Pr}(\text{“}similar\text{”} \mid target)$: $t(92) = 2.65$, $p = 0.009$). This may suggest that when young adults were uncertain, they tended to respond "similar" whereas older adults tended to respond "old". Thus, when aggregating these measures either as general category memory or specific item memory, young and older adults' strengths and weaknesses in the respective components canceled each other out, resulting in no overall performance differences. For the LDI, in contrast, only lure detection mattered, resulting in young adults outperforming the older adults.

Age differences in general category memory

We calculated an additional measure of general category memory that included all trials in which the object category was remembered, that is, combining item memory (IM) and category memory only (CMO).

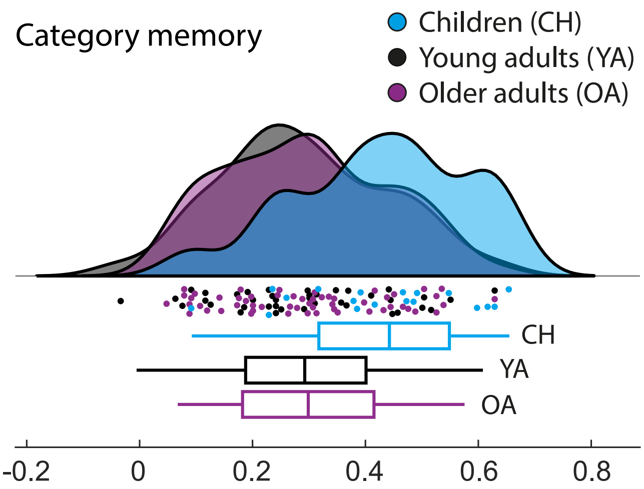

Figure 8: Category memory (CM) performance of children (CH; blue), young adults (YA; black), and older adults (OA; purple). Group distributions as un-mirrored violin plots (probability density functions), boxplots with first, second (median), and third quartiles, whiskers with second and 98th percentiles, and individual (vertically jittered) data points (Allen et al., 2019). Zero denotes chance level.

Category memory (CM): This measure aggregates all responses in which the category was correctly recognized, independent of specific item memory, and corrected for false responses to foils, i.e., the general tendency to respond "old" or "similar."

$$\begin{aligned} CM &= \Pr(\text{"}old\text{"} \mid target) + \Pr(\text{"}similar\text{"} \mid target) + \Pr(\text{"}old\text{"} \mid lure) + \Pr(\text{"}similar\text{"} \mid lure) \\ &\quad - \Pr(\text{"}old\text{"} \mid foil) - \Pr(\text{"}similar\text{"} \mid foil) \end{aligned} \tag{4}$$

For the same reasons as presented for IM in the main text, the chance level of this measure is above 0, namely 0.22.

A one-way ANOVA contrasting children, young adults, and older adults indicated significant age differences ($F(2,109) = 5.99$, $p = 0.003$) in CM (see Figure 8). Post-hoc t-tests showed that children, who had a shorter task version, performed better than both young adults ($t(55) = 3.13$, $p = 0.003$; two-sample t-tests) and older adults ($t(71) = 3.24$, $p = 0.002$). There were no differences between young and older adults ($t(92) = -0.16$, $p = 0.872$).

Age differences in separate (not composite) repetition effects

In addition to pooling together the repetition suppression and enhancement effects, respectively, we also analyzed the separate repetition effects. In analogy to the main analyses, we extracted the individual

z-transformed t-values (first level analysis) from the identified time–electrode clusters (second level analysis) and averaged them across the respective time points and channels for each subject. For both the positive posterior, and the negative fronto-central repetition suppression findings, effect sizes differed between age groups (positive posterior: $F(2,109) = 4.15$; $p = 0.018$; negative fronto-central: $F(2,109) = 3.94$; $p = 0.022$; one-way ANOVAs). For the posterior cluster, the suppression effect was significantly larger in children than in young and older adults (children vs. young adults: $t(55) = 2.03$, $p = 0.047$; children vs. older adults: $t(71) = 2.72$, $p = 0.008$; young adults vs. older adults: $t(92) = 1.18$, $p = 0.243$; post-hoc t-tests). For the frontal cluster, the suppression effect was significantly larger for children compared with older adults (children vs. young adults: $t(55) = –1.65$, $p = 0.104$; children vs. older adults: $t(71) = –2.40$, $p = 0.019$; young adults vs. older adults: $t(92) = 1.62$, $p = 0.109$). The repetition enhancement effect that only occurred in young and older adults did not differ between the groups ($t(92) = 0.03$, $p = 0.978$). These results are not significantly different than the main results, justifying the merging of highly correlating effects.

5 Study II: Neural Pattern Similarity Differentially Relates to Memory Performance in Younger and Older Adults

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This study is published in *The Journal of Neuroscience*, October 9, 2019, 39(41):8089–8099.

Contents

Abstract

Age-related memory decline is associated with changes in neural functioning but little is known about how aging affects the quality of information representation in the brain. Whereas a long-standing hypothesis of the aging literature links cognitive impairments to less distinct neural representations in old age ('neural dedifferentiation'), memory studies have shown that overlapping neural representations of different studied items are beneficial for memory performance. In an electroencephalography (EEG) study, we addressed the question whether distinctiveness or similarity between patterns of neural activity supports memory differentially in younger and older adults. We analyzed between-item neural pattern similarity in 50 younger (19–27 years old) and 63 older (63–75 years old) male and female human adults who repeatedly studied and recalled scene–word associations using a mnemonic imagery strategy. We compared the similarity of spatiotemporal EEG frequency patterns during initial encoding in relation to subsequent recall performance. The within-person association between memory success and pattern similarity differed between age groups: For older adults, better memory performance was linked to higher similarity early in the encoding trials, whereas young adults benefited from lower similarity between earlier and later periods during encoding, which might reflect their better success in forming unique memorable mental images of the joint picture–word pairs. Our results advance the understanding of the representational properties that give rise to subsequent memory as well as how these properties may change in the course of aging.

Significance statement

Declining memory abilities are one of the most evident limitations for humans when growing older. Despite recent advances of our understanding of how the brain represents and stores information in distributed activation patterns, little is known about how the quality of information representation changes during aging and thus affects memory performance. We investigated how the similarity between neural representations relates to subsequent memory in younger and older adults. We present novel evidence that the interaction of pattern similarity and memory performance differs between age groups: Older adults benefited from higher similarity during early encoding whereas young adults benefited from lower similarity between early and later encoding. These results provide insights into the nature of memory and age-related memory deficits.

Introduction

A long-standing hypothesis in the cognitive neuroscience of aging holds that neural representations become less specific with advancing age, with detrimental effects on cognitive performance (S.-C. Li et al., 2001). Previous neuroimaging studies have shown reduced neural distinctiveness between different stimulus items or categories in older compared to younger adults (Carp, Park, Polk, & Park, 2011; Goh et al., 2010; Koen et al., 2019; D. C. Park et al., 2004; J. Park et al., 2010, 2012; Payer et al., 2006; St-Laurent et al., 2014), whereby different definitions and measures of distinctiveness impede comparability between studies (see also Multivariate EEG analysis and Discussion). More importantly, most of these studies did not provide evidence for the direct link between reduced neural distinctiveness and behavior, either by not assessing performance or by assessing it separately. An exception is a recent functional magnetic resonance imaging (fMRI) study by Koen et al. (2019) that showed an age-invariant association between individual neural category selectivity during encoding (measured as differences between preferred and non-preferred stimuli) and recognition performance (see also Abdulrahman et al., 2017, for a link between task context reinstatement and performance). However, memory-related differences in distinctiveness on the item-level were not investigated. Such a subsequent memory approach was taken by Zheng et al. (2018) who showed stronger item-specific representations (defined as higher similarity of fMRI patterns across item repetitions than between different items) for later remembered compared to not remembered items which explained age-related memory performance differences.

Surprisingly, the hypothesis of the cognitive aging literature suggesting that reduced neural specificity underlies cognitive decline is in stark contrast to the prevalent evidence in general memory research that increased neural similarity is actually advantageous for performance: In young adult samples, various studies have shown that the representational similarity between different items is positively related to memory for these items (Davis, Xue, et al., 2014; LaRocque et al., 2013; Y. Lu et al., 2015; I. C. Wagner et al., 2016), which is in line with cognitive and computational models (Clark & Gronlund, 1996; Gillund & Shiffrin, 1984). Global similarity may support memory by capturing regularities (LaRocque et al., 2013) and creating familiarity (Davis, Xue, et al., 2014).

To date, most studies have used fMRI to assess neural representations, prioritizing the spatial distribution of representational patterns over their temporal dynamics. In contrast, time-sensitive magneto-/electroencephalography (M/EEG) measurements are able to identify the temporal distribution and oscillatory dynamics in which information is encoded in neural patterns as well as the processing stages at which representational similarity supports performance. For example, Y. Lu et al. (2015) showed that at approximately 420–580 ms after stimulus onset, global spatiotemporal EEG pattern similarity was higher for later remembered than for not remembered symbols. In addition, concurrent power increases and decreases in different frequency bands have consistently been related to memory performance (Hanslmayr & Staudigl, 2014). Beyond the relevance of power in single frequency bands, recent scalp (Kerrén et al., 2018; Michelmann et al., 2016, 2018) and intracranial EEG studies (Staresina et al., 2016; Zhang et al., 2015) have demonstrated the importance of considering the rich information profile carried by a wide range of frequencies for item-specific neural signatures. However, there are no previous reports on the relation of the similarity between these dynamic time–frequency patterns to later memory success for the studied items, neither in young nor in older adults.

To our knowledge, the apparent conflict between the observed beneficial effect of global similarity in memory studies with young adults, and the potentially detrimental effect of decreasing distinctiveness in the aging literature has not been explicitly addressed. Here, we aimed to resolve the question whether distinctiveness or similarity (which we define as each other's inverse) between patterns of neural activity is beneficial for memory performance by systematically investigating the relation between representational similarity and memory performance in young and older adults. For this, we examined the similarity of EEG frequency patterns elicited when encoding scene–word pairs in relation to age and subsequent recall performance.

Materials and Methods

Experimental design

The research presented here comprises data from two associated studies that investigated age-related differences in associative memory encoding, consolidation, and retrieval (Fandakova et al., 2018; Muehlroth et al., 2019; Sander et al., 2020). Despite subsequent procedural differences, an identical picture–word association task paradigm during which EEG was recorded was at the core of both studies (see Figure 9). In this task, participants were asked to memorize scene–word pairs by applying a previously trained mnemonic imagery strategy. Specifically, they were instructed to imagine the scene and word content together in a unique and memorable mental image. Stimuli consisted of color photographs of indoor and outdoor scenes randomly paired with concrete German nouns (4–8 letters). During the initial study phase, scenes and words were presented next to each other on a black background for 4 s. After studying a pair, participants indicated on a four-point scale how well they were able to integrate the presented scene and word. Young and older adults studied 440 and 280 pairs, respectively. During the subsequent cued recall phase, scenes served as cues for participants to verbally recall the associated word. Recall time was not constrained. After each trial, the correct scene–word pair was presented again for 3 s and subjects were instructed to restudy the pair, independent of previous retrieval success. This recall and restudy phase was repeated one more time for the older adults (similarly to Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Duverne, Habibi, & Rugg, 2008; J. Li, Morcom, & Rugg, 2004; Morcom, Li, & Rugg, 2007). Finally, both young and older participants underwent a final cued recall round in which no feedback was presented.

After each phase, we asked participants to indicate on a four-point scale how often they used the instructed imagery strategy or other specific memory strategies to memorize a pair. For a detailed description of the study design and stimulus selection, see Fandakova et al. (2018).

Since older adults often remember less and need more repetitions to learn the same information as young adults (e.g., J. Li et al., 2004), the numbers of to-be-studied pairs as well as recall repetitions were adjusted between age groups in order to achieve comparable recall success of about half of the studied items. It can be assumed that an equivalent relative amount of information remembered by both groups indicates that the task was similarly difficult for them. These kinds of age-adapted procedures help to identify memory-relevant age differences in brain activity without the influence of confounding variables that correlate with age (Rugg & Morcom, 2005), and thus unconfound task and age difference. Here, extensive pilot experiments showed that the reported numbers of pairs for young and older adults

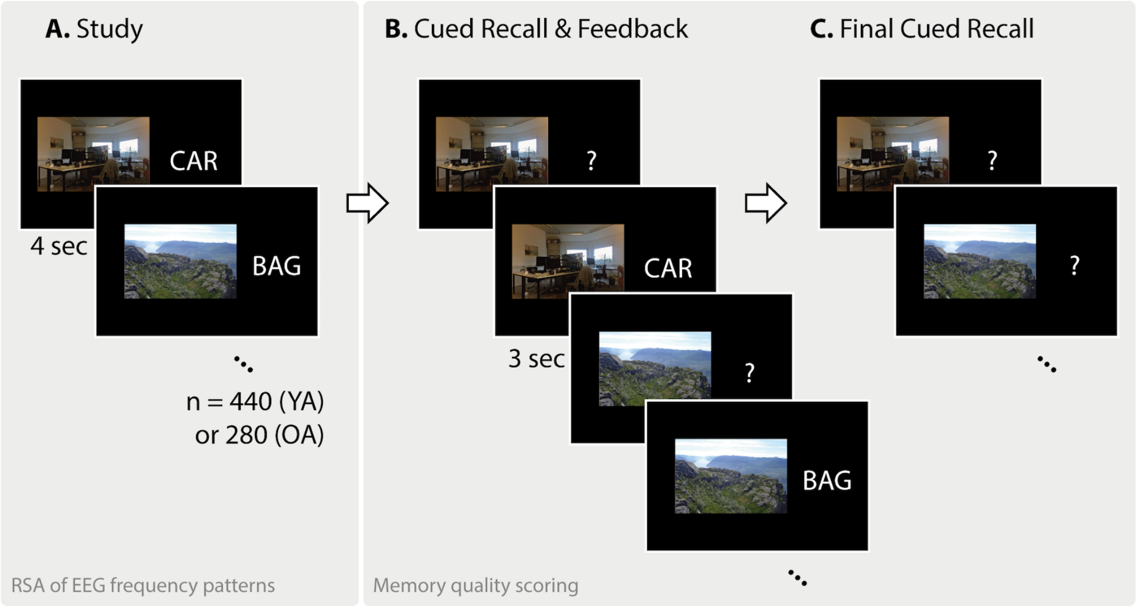

Figure 9: Memory task paradigm (cf. Fandakova et al., 2018). **A**. In the study phase, participants were asked to associate 440 (young adults; YA) or 280 (older adults; OA) scene–word pairs using an imagery strategy. RSA was conducted on EEG data during this phase. **B**. During the cued recall and feedback phase, the scene was presented as a cue to verbally recall the associated word. Subsequently, the original pair was presented again for restudy. The cued recall and feedback phase was performed once for younger and twice for older adults. **C**. During final recall, no feedback was provided. Scene–word pairs were sorted into three memory quality categories based on recall performance in phases B and C (see Figure 10).

as well as one additional recall and feedback phase for older adults produced the desired results. The adequacy of the chosen number of pairs and repetitions for producing the desired performance levels was recently confirmed by a replication in an independent (third) sample of younger and older adults (Fandakova et al., 2020).

Subjects

The original sample of study 1 (Fandakova et al., 2018) consisted of 30 healthy young adults and 44 healthy older adults. Due to technical failures, one young adult and three older adults did not complete the study. Study 2 (Muehlroth et al., 2019) involved 34 healthy young adults and 41 healthy older adults, with 4 younger and 4 older participants not completing the experiment for technical reasons. Due to missing or noisy EEG data, we additionally excluded 9 younger and 15 older adults, resulting in a total of 50 younger adults and 63 older adults across both studies, who are included in the analyses presented here (young adults: M(SD)age = 24.3(2.5) years, 19–27 years, 27 female, 23 male; old adults: M(SD)age = 70.4(2.6) years, 63–75 years, 33 female, 30 male).

All participants were right-handed native German speakers, reported normal or corrected-to-normal vision, no history of psychiatric or neurological disease, and no use of psychiatric medication. We screened older adults with the Mini-Mental State Examination (MMSE; Folstein et al., 1975) and none had a score below the threshold of 26 points. Both studies were approved by the ethics committee of the Deutsche Gesellschaft für Psychologie and took place at the Max Planck Institute for Human Development in Berlin, Germany. All participants gave written consent to take part in the experiment.

Behavioral analysis

During the cued recall phases, participants had to verbally recall the word associated with the presented image. We report the proportion of correctly recalled words. False responses occurred rarely and were treated as no responses. Following the rationale of a subsequent memory analysis (Paller & Wagner, 2002) we sorted all trials according to whether the associated word was successfully recalled during the experiment or not. Items that were not remembered after repeated encoding were assumed to have only created a weak memory trace, that was not sufficient for successful recall (although maybe strong enough for successful recognition, see Fandakova et al., 2018). Importantly, given the repeated recall phases, we were able to further differentiate successfully recalled items, distinguishing those that were immediately learned from those that were only acquired later in the experiment. We refer to those items as high memory quality and medium memory quality items, respectively (see Figure 10). Because the pattern similarity between items of a given memory quality was computed (see Multivariate EEG analysis), a certain number of trials in that quality category was required. Due to close-to-floor performance of older adults in their initial recall phase (16 older adults recalled only one or no item), we only started scoring older adults' performance in the second recall phase. To keep the scoring of stimulus pairs as evincing high, medium, or low memory quality comparable across age groups, items that were recalled successfully in the final recall cycle were divided into those that were also already recalled in the previous cycle (high quality) and those that were only remembered in the last recall (medium quality) in contrast to never-recalled items (low quality). In other words, memory performance in older adults' very first recall phase was omitted for memory quality scoring. For both age groups, the few items that were remembered in an earlier but not later recall (i.e., forgotten), were excluded from further EEG analyses (see Results and Figure 12). All EEG analyses were conducted on the activity patterns elicited during the first learning phase such that all pairs were novel to the participants and no retrieval-related processes could influence the evoked activity patterns.

The fact that the current study design did not allow us to include older adults' first recall attempt because performance was too low is a limitation as we cannot completely rule out the possibility that the

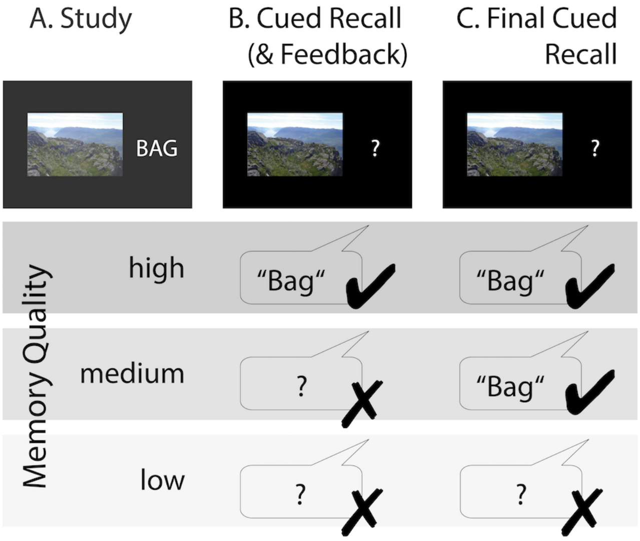

Figure 10: Scoring of stimulus pairs into high, medium, or low memory quality categories based on learning history. For both younger and older adults, items that were correctly recalled in the last recall cycle (**C**) as well as the previous one (**B**) were scored as high memory quality items. Pairs that were solely recalled in the final recall were scored as medium memory quality items, and items that were never correctly recalled were scored as low memory quality items. Not depicted: Items that were recalled in the earlier but not later recall were excluded. Older adults performed one more cued recall and restudy cycle (between **A** and **B**) that was not included in item scoring due to close-to-floor performance. Note that wrong and missing responses were treated equally.

obtained age effects arise from the different memory quality scoring for young and older adults. However, subjecting both age groups to identical procedures in the current study (for example, by also omitting young adults' first recall) eliminates the strength of our approach, which is the ability to differentiate more fine-grained differences in the memory fate of the stimulus material, which are already observable in the EEG patterns during first encounter. This is the great advantage of our study design in comparison to the usual contrast of subsequently remembered and not remembered items (see also Discussion).

EEG recording and preprocessing

EEG was recorded continuously with BrainVision amplifiers (BrainVision Products GmbH, Gilching, Germany) from 61 Ag/AgCl electrodes embedded in an elastic cap. Three additional electrodes were placed at the outer canthi (horizontal electrooculography (EOG)) and below the left eye (vertical EOG) to monitor eye movements. During recording, all electrodes were referenced to the right mastoid electrode, and the left mastoid electrode was recorded as an additional channel. The EEG was recorded with a pass-band of 0.1 to 250 Hz and digitized with a sampling rate of 1000 Hz. During preparation, electrode impedances were kept below 5 kΩ.

EEG data preprocessing was performed with the Fieldtrip software package (developed at the F. C.

Donders Centre for Cognitive Neuroimaging, Nijmegen, The Netherlands; http://fieldtrip.fcdonders.nl; RRID: SCR_004849) and custom MATLAB code (The MathWorks Inc., Natick, MA, USA; RRID: SCR_001622). Data were downsampled to 250 Hz and an independent component analysis was used to correct for eye blink, (eye) movement, and heartbeat artifacts (Jung et al., 2000). Artifact components were automatically detected, visually checked, and removed from the data. For analyses, the EEG was demeaned, re-referenced to the mathematically linked mastoids, and band-pass filtered (0.2–100 Hz; fourth order Butterworth). Following the FASTER procedure (Nolan et al., 2010), automatic artifact correction was performed for the remaining artifacts. Excluded channels were interpolated with spherical splines (Perrin et al., 1989). Finally, data epochs of 4 seconds were extracted from -1 s to 3 s with respect to the onset of the scene–word presentation during the study phase (Figure 9A).

EEG analysis

Time–frequency representations (TFRs) of the data were derived using a multitaper approach. For the low frequencies (2–20 Hz), we used Hanning tapers with a fixed width of 500 ms, resulting in frequency steps of 2 Hz. For higher frequencies (25–100 Hz), we used DPSS (discrete prolate spheroidal sequences) tapers with a width of 400 ms in steps of 5 Hz with seven Slepian tapers resulting in ±10 Hz smoothing. In this way, we obtained a TFR for each trial and electrode. Trial lengths were reduced to –0.752 s to 3 s relative to stimulus onset.

To counter the effect of intrinsically high correlations between frequency patterns due to the 1/frequency power spectrum (Schönauer et al., 2017), we removed the mean background noise spectrum from the log-transformed TFRs following previously established procedures (i.e., as suggested by the “Better oscillation detection” (BOSC) method; Caplan, Madsen, Raghavachari, & Kahana, 2001; Kosciessa et al., 2020; Whitten, Hughes, Dickson, & Caplan, 2011). Because of structured noise, correlations between different activity patterns are usually very high and almost never at or below zero, meaning that the true null-distribution is higher than zero. For detailed discussions of these issues (in fMRI), see Allefeld, Görgen, and Haynes (2016); Cai et al. (2016).

Multivariate EEG analysis

In the aging literature, different measures of neural distinctiveness (also called specificity, selectivity, differentiation, fidelity) have been used, for instance, the differences in univariate activation levels to preferred and non-preferred stimuli (e.g., D. C. Park et al., 2004), increased similarity (e.g., St-Laurent et al., 2014) or reduced discriminability (e.g., J. Park et al., 2010) between multivariate neural activity patterns, or the difference between within-category and between-category representational similarity (e.g., Carp, Park, Polk, & Park, 2011). Reduced neural distinctiveness in older compared to younger adults has been observed in encoding and retrieval phases between different memory tasks (Carp et al., 2010; St-Laurent et al., 2011), in the reinstatement of encoding task context during retrieval (Abdulrahman et al., 2017; but compare T. H. Wang et al., 2016), between different stimulus categories (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; D. C. Park et al., 2004; J. Park et al., 2010, 2012; Payer et al., 2006), and between different individual stimuli (Goh et al., 2010; St-Laurent et al., 2014). In turn, neural similarity in the general memory literature has been quantified by distance measures based on correlations (e.g., Davis, Xue, et al., 2014) or directly as (usually Pearson) correlation (e.g., LaRocque et al., 2013; Y. Lu et al., 2015; I. C. Wagner et al., 2016) between activation patterns. In the current paper, EEG data were analyzed using representational similarity analysis (RSA; Kriegeskorte et al., 2008). RSA assesses the resemblance of patterns of neural activity, with similar patterns assumed to represent mutual information and/or processes. Similarity was measured as Pearson correlation, which is insensitive to absolute power and variance of the time–frequency representations. Similarity and distinctiveness were defined as inverses of each other.

Although the pattern of neural activity elicited by a stimulus is commonly defined as the neural representation of that stimulus (Carp, Park, Polk, & Park, 2011; S.-C. Li & Sikström, 2002), the measured activity pattern does not only contain information of that stimulus but also about the context, the current task etc. Furthermore, activity patterns cannot keep apart the content of a memory (the memory representation in the original sense; e.g., Tulving & Bower, 1974) and the underlying processes of, for example, encoding it (if these are distinct entities). However, the term “neural/memory representations” usually denotes the respective activation patterns, and the two terms are therefore used synonymously in this paper.

In the current study, we investigated frequency-transformed EEG activity patterns (see EEG analysis). In addition to their spatial and temporal domains, the (often) strong oscillatory nature of electrochemical brain signals allows information to be encoded in their frequency, power, and phase dimensions, which are largely independent of each other (M. X. Cohen, 2011). Oscillations reflect rhythmic and synchronous fluctuations in the excitability of neural populations that have been shown to be functionally relevant for cognition (Buzsáki & Draguhn, 2004; X.-J. Wang, 2010). Our decision to examine EEG frequency patterns is largely based on findings of recent studies that have demonstrated the importance of the rich information profile carried by a wide range of frequencies for item-specific neural signatures (Kerrén et al., 2018; Michelmann et al., 2016; Staresina et al., 2016; Zhang et al., 2015).

We analyzed between-item representational similarity during the first encoding phase in relation to memory quality. “Item” or “stimulus” always refers to a scene–word pair. Figure 11 illustrates the procedure for analyzing the similarity between stimulus-specific spatiotemporal frequency representations. RSA was conducted for each participant and EEG channel independently. Stimuli were grouped according to high, medium, and low memory quality (see Figure 10). In order to examine whether between-item representational similarities differed as a function of memory quality, we correlated the noise-corrected and log-transformed frequency patterns of every item with the frequency patterns of all other items of the same memory quality. That is, for each participant we ran three similarity analyses, namely for high, medium, and low memory quality items. In order to use the same number of items for each RSA of a given participant, we reduced them to the number of items available in the condition with the least items. For example, if there were 50 items with high, 180 items with medium, and 210 items with low memory quality for a given participant, the number of items used in the RSAs of medium and low quality items, respectively, was reduced to 50 as well. Note that the category containing the fewest items was in most cases the group of high memory quality items (except for 6 younger and 6 older participants). We randomly sampled the respective number of items from all available trials of the respective memory quality. As the actual measure of similarity, we employed pairwise Pearson correlations between the corresponding frequency patterns. In each of these correlations, every pair of frequency vectors (with 26 frequency bins) of all time points from the two respective trials were correlated with each other (470 time points, from 752 ms before stimulus onset to 3000 ms after stimulus onset). The resulting time–time similarity matrices were Fisher z-transformed. In order to prevent bias towards the randomly picked items, the item sampling was repeated 20 times. Finally, the matrices were averaged to obtain one between-item similarity matrix for each scene–word pair, which indicates the similarity of this pair to all other pairs of the same memory quality. The similarity matrices of all items within one memory quality were then again averaged to obtain the mean similarity matrices between all high, medium, and low memory quality items, respectively. This procedure was performed separately for each of the 60 scalp electrodes.

The resulting similarity matrices contain the time dimension on both the x- and the y-axis, revealing the frequency pattern similarity not only at identical within-trial time points (diagonal) but also between all combinations of time points (in analogy to the temporal generalization method; Cichy et al., 2014; King & Dehaene, 2014). This enables us to determine whether certain parts of the memory representations were similar to each other at different times during encoding of the respective scene–word pairs.

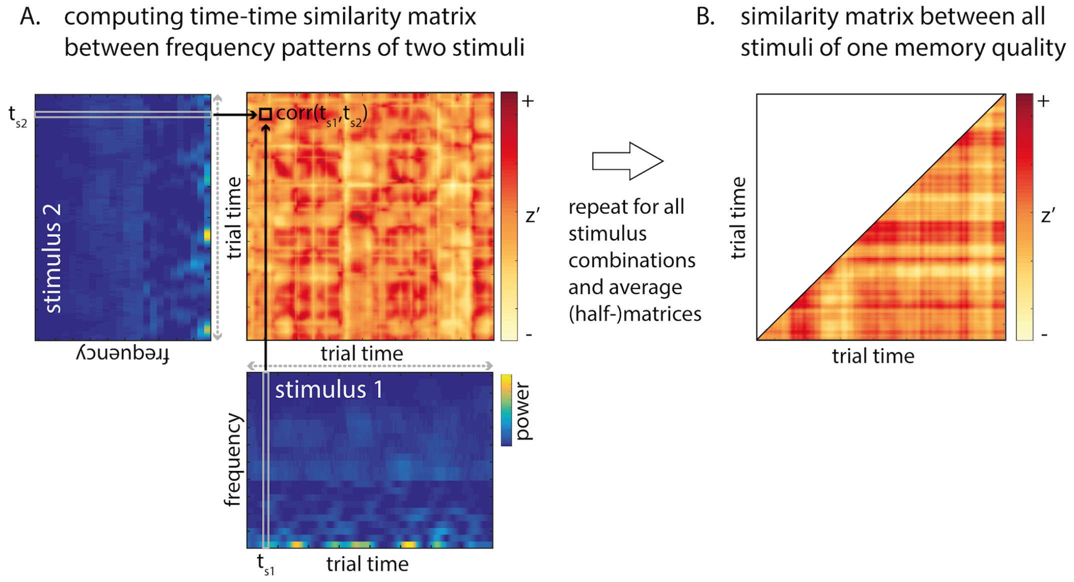

Figure 11: Spectral RSA methodology. **A**. Frequency vector from every time point (i.e., column) of the noise-corrected and log-transformed time–frequency pattern (from one electrode) corresponding to stimulus 1 (bottom) is Pearson-correlated with the vectors from every time point of stimulus 2 (left; rotated by 90°). For illustration, sample vectors of stimulus 1 (t_{s1}) and stimulus 2 (t_{s2}) are highlighted. Correlating these two vectors gives one correlation coefficient, i.e., one coordinate (indicated by black box) on a matrix with time on both axes. Computing all pairwise time vector correlations results in a time–time similarity matrix representing the similarity of those two frequency patterns at all time point combinations. This procedure is repeated for all items of a certain memory quality (i.e., similarity of stimulus 1 with all others, stimulus 2 with all others, etc.). **B**. Averaging across all similarity matrices yields the mean similarity matrix showing the pattern similarity among all items of the same memory quality. Only one triangle and the diagonal of the matrix are relevant because the similarity of every frequency pattern pair is computed twice, resulting in an identical correlation coefficient on both sides of the diagonal. Similarity is quantified as the Fisher's z-transformed Pearson correlation coefficient (z'). Not depicted: This procedure was repeated for all 60 electrodes, the three memory quality categories, and all subjects.

Because the similarity of any two items is computed twice and thus the identical correlation coefficients appear twice, namely on both sides of the diagonal, the similarity matrix was reduced to only one of the triangles plus the diagonal.

Representational similarity analyses were computed parallelized on a high-performance computing cluster. All computations and statistics were conducted with Matlab (The MathWorks, Inc., RRID: SCR_001622) versions R2014b or R2016b. The Matlab-based Fieldtrip Toolbox (Maris & Oostenveld, 2007; Oostenveld et al., 2011; RRID: SCR_004849) was used to perform time–frequency transformations and cluster-based permutation analyses.

Statistical analysis

Memory performance, imagery ratings, and strategy use

We analyzed the relationship between age group and the number of items in the three memory quality categories (high, medium, low) by conducting a Chi-Squared test. For post-hoc analyses, we computed two-sided independent samples t-tests in order to test for age differences in the proportion of items within each memory quality category (high, medium, low, as well as forgotten/excluded) and the proportion of items remembered in the final recall task. The imagery ratings after each trial were analyzed by computing frequencies of how often which ratings were given for items of each memory quality. The strength of the relationship between imagery rating and memory quality on the group and within-person level was tested by conducting non-parametric Goodman and Kruskal's Gamma correlations for ordinally scaled data. The association between these individual Gamma correlations and the individual effect of pattern similarity and memory quality (regression coefficients; see Age and memory quality effects in the identified clusters) was further analyzed using Pearson correlations. To compare younger and older adults' overall strategy use in the first encoding phase (post-encoding strategy questionnaire), we used the Wilcoxon rank sum test to examine differences in their median responses of how often they used the imagery strategy.

Differences in representational similarity

Within both groups, we tested for differences in the representational similarity matrices between different memory quality categories (i.e., low $<$ medium $<$ high) by conducting non-parametric, cluster-based, random permutation tests (Fieldtrip Toolbox; Maris & Oostenveld, 2007). Univariate two-sided, dependent samples regression coefficient t-statistics were calculated for the time–time similarity matrices at all channels. Clusters were formed by grouping neighboring channel × time × time samples with a p-value below 0.05 (spatially and temporally). The respective test statistic was then determined as the sum of all t-values within a cluster. The Monte Carlo method was used to compute the reference distribution for the summed cluster-level t-values. Samples were repeatedly (1000 ×) assigned into three groups and the differences between these random groups were contrasted to the differences between the three actual conditions (high, medium, and low memory quality). The t-statistic was computed for every repetition and the t-values summed for each cluster. The t-values were z-transformed for further analysis.

In addition to the linear regression of all three memory qualities mentioned above, we also compared each pair of memory quality categories using a two-sided, dependent samples t-test in the permutation analysis (1000 permutations).

We examined overall age differences in the level of between-item pattern similarity independently of memory success by conducting independent samples *t*-statistics within a cluster-based permutation analysis. For simplicity, similarity matrices were averaged across one time dimension (y).

We regarded clusters whose test statistic exceeded the 97.5th percentile for its respective reference probability distribution as significant. If such clusters were obtained, we furthermore assessed the time–time intervals and the topographic distributions of the channels showing when and where, respectively, the differences were reliable. The clusters that were identified for each age group were further examined for age and memory quality effects (see below). In addition, we tested for main age group differences in a separate permutation analysis using independent samples *t*-tests.

In order to demonstrate that the effects obtained for the young adult group and the older adult group appeared at different times during stimulus encoding, we formally contrasted the times at which the clusters showed significant differences. For this, we extracted the most extreme *z*-value (*z*-transformed regression coefficients) within the respective cluster from each subject and compared their coordinates in time–time space. We fitted two models to test whether it was more likely that the time points come from an identical multivariate normal distribution (single model) or from two distinct distributions (two-group model). We then compared the two models using a Chi-Squared test for model comparison with the null hypothesis that both models fit equally well.

Age and memory quality effects in the identified clusters

To explore potential age differences more closely, we further investigated the relationship between pattern similarity and memory quality by conducting independent samples regression coefficient *t*-statistics for each participant. We extracted and averaged the individual *z*-transformed regression coefficients within the time–time–electrode clusters that were identified in younger and older adults (see above). For both clusters and age groups we performed one-sample *t*-tests to test whether the correlation coefficients come from a distribution with a mean different from zero. Furthermore, we tested for differences between the age groups in both clusters using independent samples *t*-tests.

Code Accessibility

Custom MATLAB code of the main analyses as well as control analyses are available on https://osf.io/p7v3s/.

Results

Memory performance and strategy use

During the cued recall phases, participants had to respond verbally with the word they had previously learned to associate with the presented image. We sorted the trials according to whether recall was successful, and when, into high, medium, and low memory quality items (see Methods). A Chi-Squared test revealed a significant association between memory quality and age ($\chi^2(2) = 19.71$, $p < 0.001$). Post-hoc *t*-tests furthermore showed that the proportion of high memory quality items did not differ between younger adults and older adults ($M_{\text{(young adults)}} = 0.17$, $SD_{\text{(young adults)}} = 0.11$, $M_{\text{(older adults)}} = 0.18$, $SD_{\text{(older adults)}} = 0.15$; $t(111) = –0.40$, $p = 0.690$, two-sample *t*-test; see Figure 12). In contrast, the proportion of items with medium memory quality was significantly larger for younger than older participants ($M_{\text{(young adults)}} = 0.39$, $SD_{\text{(young adults)}} = 0.11$, $M_{\text{(older adults)}} = 0.23$, $SD_{\text{(older adults)}} = 0.09$; $t(111) = 8.48$, $p < 0.001$), while older adults had a significantly higher proportion of low memory items ($M_{\text{(young adults)}} = 0.43$, $SD_{\text{(young adults)}} = 0.19$, $M_{\text{(older adults)}} = 0.56$, $SD_{\text{(older adults)}} = 0.23$; $t(111) = –3.31$, $p = 0.001$). Note that in older adults we observed a higher proportion of items that were remembered in an early but not later recall phase, i.e., that were forgotten in the course of the experiment ($M_{\text{(young adults)}} = 0.007$, $SD_{\text{(young adults)}} = 0.005$, $M_{\text{(older adults)}} = 0.025$, $SD_{\text{(older adults)}} = 0.02$; $t(111) = –7.04$, $\text{p} < 0.001$). Those item pairs were excluded from further analyses.

Our experimental procedure was successful in inducing variability in memory performance such that both groups could remember approximately half of the studied items: Young adults successfully recalled on average 56.64% (*SD* = 10.70) and older adults successfully recalled on average 41.60% (*SD* = 12.06) of the items (440 and 280, respectively). However, our procedure did not completely eliminate age differences since young adults still performed significantly better than older participants in the final recall task ($t(111) = 3.82$, $p < 0.001$, two-sample *t*-test).

Due to the different number of items that younger and older adults studied in the course of the experiment and the fact that the number of items included in the RSA was reduced based on the smallest memory quality category (usually high quality), the number of items that were compared to each other in the RSA also differed between groups: The median number of items included in the RSA was 48 (range 10 to 101) for younger adults and 32 (range 5 to 79) for older adults. The groups differed significantly in their respective item numbers ($z = 3.76$, $p < 0.001$; Wilkoxon rank sum test) which, however, did not affect group differences in pattern similarity (control analysis code are available on https://osf.io/p7v3s/).

After the first study phase was completed, we asked participants to indicate on a four-point scale

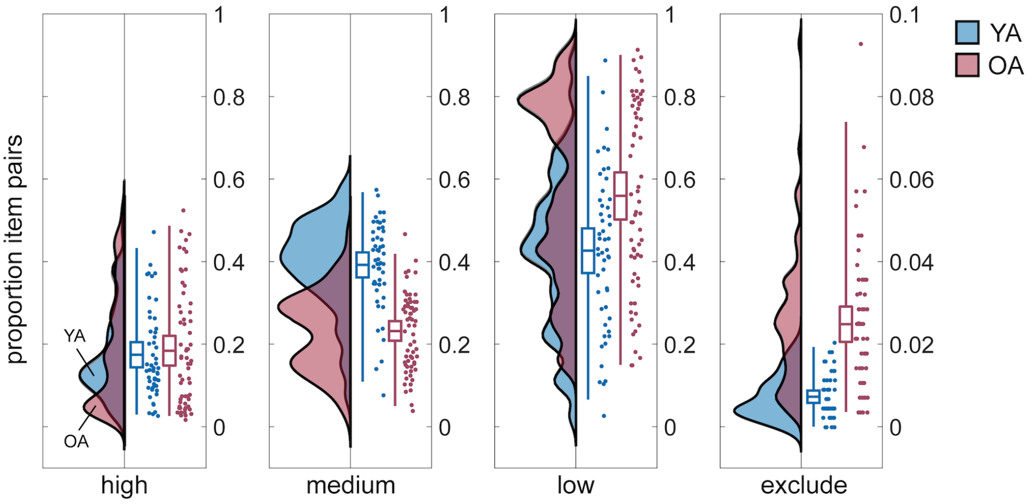

Figure 12: Proportion of item pairs with high, medium, and low memory quality as well as proportion of excluded items for 50 young adults (YA; blue) and 63 older adults (OA; red). Group distributions as unmirrored violin plots (probability density functions), boxplots with means and 95% confidence intervals, whiskers with second and 98th percentiles, and individual data points (horizontally jittered) (modified from Allen et al., 2019). Note that the *y*-axis for excluded items differs from that of the other categories. YA studied 440 pairs and OA studied 280 pairs.

how often they had used specific memory strategies for the task (1: almost always, 4: almost never). With regard to the imagery strategy, young adults indicated that they had used it significantly more often than older adults did (younger adults: median = 1.5, min = 1, max = 3; older adults: median = 2, min = 1, max = 4; $z = -5.09$, $p < 0.001$, Wilcoxon rank sum test). We further analyzed the relationship between memory quality, imagery rating, and representational similarity (see below).

Representational similarity

Calculation of between-item representational similarity was based on the initial encoding phase (Figure 9A). To identify whether high pattern similarity or high pattern distinctiveness during learning was beneficial for later memory success, we sorted all items according to subsequent memory performance and correlated the evoked spatiotemporal frequency pattern of each item with every other item in the same memory quality category. The resulting mean similarity matrices over all channels and scene–word pairs are shown in Figure 13A. These matrices display the similarity of the frequency representations at all possible within-trial time point combinations (0.752 s to 3 s relative to stimulus onset at 0). In contrast, the diagonals of the similarity matrices (also plotted separately in Figure 13B) only show the similarity between items at identical time points and facilitate a visual comparison of the time courses of representational similarities for the different memory quality categories and age groups. Although this omits much of the similarity information, elevated similarities do occur largely along the diagonal. Note that the diagonals are only plotted for illustration purposes and all statistical tests were performed on the complete matrices as presented in Figure 13A.

Older adults generally exhibit higher representational similarity than young adults

Just before stimulus onset, similarity increased in both age groups and reached a peak around the time of onset (cf. Figure 13A and B). Elevated similarity occurred mainly between identical trial time points (diagonal) with slightly more persistent activity (elevated off-diagonal similarity) in older adults compared to young adults. Irrespective of later memory success, between-item pattern similarity was generally higher in older adults than in young adults (cf. Figure 13A and B; averaged across the whole time–time matrix and all 60 channels: $M_{(\text{young adults})} = 0.21$, $SD_{(\text{young adults})} = 0.06$, $M_{(\text{older adults})} = 0.25$, $SD_{(\text{older adults})} = 0.06$; 5000 cluster permutations, $p = 0.001$). Furthermore, the level of pattern similarity and final memory performance were negatively correlated across age groups ($r = -0.22$, $p = 0.020$; Pearson correlation). This is in line with previous “dedifferentiation” findings and suggests that also on the within-person level better remembered items should be less similar to each other. However, an across-group correlation may completely differ from a within-group or even within-person correlation (Simpson’s Paradox; Kievit, Frankenhuis, Waldorp, & Borsboom, 2013). Therefore, we further investigated the association of pattern similarity and memory quality on the within-group and individual level.

Representational similarity differentially relates to memory performance in younger and older adults

Within both age groups, we tested for differences in the levels of representational similarity between scene–word pairs of different memory quality by conducting linear regressions (low < medium < high). We controlled for multiple comparisons by using non-parametric cluster-based permutation tests. In both age groups we identified a cluster with a Monte Carlo p-value below 0.025, which indicates a reliable linear relationship between representational similarity and memory quality (young adults: $p = 0.020$; older adults: $p = 0.003$; see Figure 13C). Importantly, the direction of this relationship differed between groups: while the relation between similarity and memory quality was positive in older adults (low < medium < high), it was negative in young adults (low > medium > high) (Figure 13E).

The cluster obtained in older adults included most of the diagonal from 50 ms to 830 ms after stimulus onset and extended off-diagonally to 470 ms before and 1240 ms after stimulus onset (Figure 13C). Elevated similarity along the diagonal indicates similarity between neural representational patterns at identical trial time points, whereas off-diagonal time windows suggest similar activation patterns at different trial time points. The larger the distance of a coordinate from the diagonal, the more distant are the compared time points in the respective frequency patterns. Differences between memory quality categories were reliable in most (49 out of 60) occipital, parietal, temporal, and central electrodes in older adults (Figure 13D).

In contrast to the cluster found in older adults, an off-diagonal cluster was identified for young adults, in which low memory quality items displayed significantly more similarity than medium and high memory quality items (Figure 13C). Compared to older adults, where differences between memory qualities were found to be most pronounced between early and neighboring trial time points, i.e., close to the diagonal, the off-diagonal cluster identified in young adults indicated that differences occurred at later and more distant trial time points. Specifically, differences were found between earlier (450 ms to 1400 ms after stimulus onset) and later time points (2640 ms to 2800 ms after onset) and at 34 mainly parietal-occipital and central electrodes (Figure 13D). Despite the relatively poor spatial resolution in EEG, the large electrode clusters in both young and older adults indicate that the encoding-related patterns of neural activity that proved to be indicative of subsequent memory were broadly distributed across the brain rather than specific to a particular region.

Additional analyses of pairwise comparison of the three memory quality categories instead of linear regression resulted in a significant cluster that extended over similar time–time intervals and electrodes only for high versus medium memory quality items in younger adults (high vs medium: $p = 0.008$; high vs low: $p = 0.030$; medium vs low: $p = 0.600$; 1000 cluster permutations), and high versus medium as well as high versus low quality in older adults (high vs medium: $p = 0.004$; high vs low: $p = 0.006$; medium vs low: $p = 0.300$; 1000 cluster permutations).

In order to demonstrate that the effects obtained for the young adult group and the older adult group appeared at different times during stimulus encoding, we extracted the most extreme z-value (z-transformed regression coefficients) within the respective cluster from each subject and compared their coordinates in time–time space. We fitted two models to test whether it was more likely that the time points come from an identical multivariate normal distribution (single model) or from two distinct distributions (two-group model). We then compared the two models using a Chi-Squared test for model comparison with the null hypothesis that both models fit equally well. The two models differed in model fit ($p < 0.001$), and the two-group model showed significantly better fit. This demonstrates that the effects obtained for young and older adults appeared at different times during stimulus encoding.

Age and memory quality effects in the identified clusters

The cluster-based analyses reported above suggested differential memory-related representational similarity in younger and older adults. To explore potential age differences in more depth, we additionally tested for a linear relationship between representational similarity and memory quality in each participant by conducting individual linear regressions. We then extracted and averaged the individual z-transformed regression coefficients within each time–time–electrode cluster (see Figure 13E). In the young-adult cluster only the mean regression coefficients of the young adults differed from zero (young adults: $t(49) = –3.42$, $p = 0.001$; older adults: $t(62) = 1.79$, $p = 0.078$; one-sample t-tests) and vice versa in the older-adult cluster (young adults: $t(49) = 0.75$, $p = 0.457$; older adults: $t(62) = 5.27$, $p < 0.001$). In both clusters the regression coefficients differed significantly between younger and older adults (young-adult cluster: $M_{\text{(young adults)}} = –0.27$, $SD_{\text{(young adults)}} = 0.57$, $M_{\text{(older adults)}} = 0.086$, $SD_{\text{(older adults)}} = 0.38$, $t(111) = –4.03$, $p < 0.001$; older-adults cluster: $M_{\text{(young adults)}} = 0.058$, $SD_{\text{(young adults)}} = 0.55$, $M_{\text{(older adults)}} = 0.29$, $SD_{\text{(older adults)}} = 0.43$, $t(111) = –2.50$, $p = 0.014$; independent samples t-tests) implying that age differences do exist in the relation between representational similarity and memory quality in these clusters.

Stronger links among pattern similarity, memory quality, and imagery ratings in young adults

After each study trial, participants indicated on a four-point scale how well they were able to integrate the presented scene and word (1: not well, 4: very well). We calculated the frequencies of how often each rating was given by each participant. To test the strength of the relationship between participants' imagery ratings and memory quality (see Memory performance and strategy use) on the group and within-person level, we conducted non-parametric Goodman and Kruskal's Gamma correlations for ordinally scaled data. For both groups, we obtained significant positive relationships showing that higher imagery ratings were given to items of higher memory quality (young adults: $\gamma = 0.28$, $z = 32.04$, $p < 0.001$; older adults: $\gamma = 0.13$, $z = 11.04$, $p < 0.001$). The individual z-values from the within-person correlations of young and older adults differed significantly ($t = 7.08$, $p < 0.001$; two sample t-test) indicating a stronger link between imagery ratings and memory success in young adults.

We further analyzed the association between these individual gamma correlations and the individual regression coefficients from the representational similarity analyses (see Age and memory quality effects in the identified clusters). Across both groups (but not within either group), individual z-values from the gamma correlations and the individual regression coefficients (Figure 13E) showed a negative association ($r = –0.27$, $p = 0.005$, Pearson correlation). This means that the lower (more negative) the individual regression coefficient (lower similarity in higher memory quality; i.e., the effect seen in young adults),

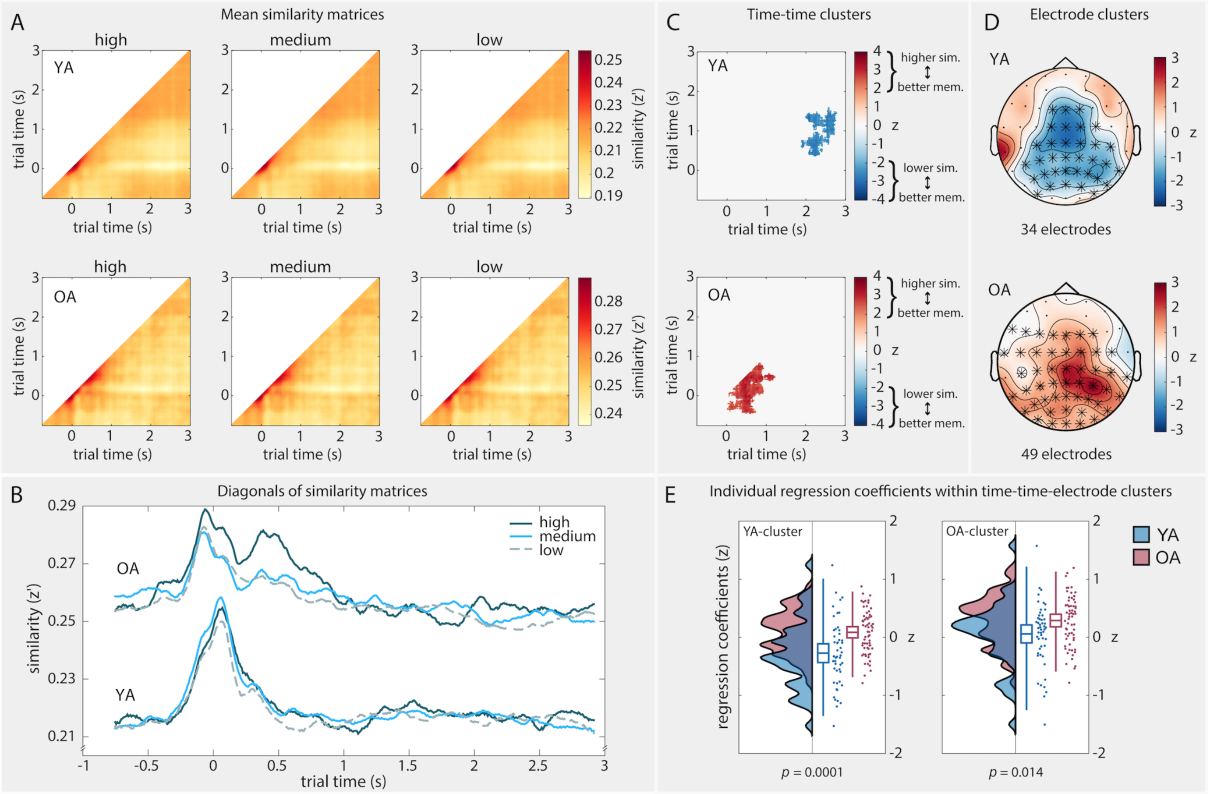

Figure 13: Between-item pattern similarities and statistics. Similarity is quantified as Fisher's z-transformed Pearson correlation coefficient (z'). On time axes, zero denotes stimulus onset. C and D show results from cluster-based permutation analyses for each age group, E shows results from individual regression analyses (see Materials and Methods). **A**. Mean time–time similarity matrices across all 60 channels and items within each memory quality category (high, medium, low) for all 50 young adults (YA; top) and 63 older adults (OA; bottom). Note that the scales differ between age groups. **B**. Diagonals from the time–time similarity matrices (see A). **C**. Time–time clusters (masked z-scores) in which the three memory quality categories differ significantly within each age group (averaged across reliable electrodes, see D). Positive z-values (red) reveal a positive relationship between pattern similarity and memory quality (higher similarity is associated with higher memory quality), negative z-values (blue) reveal a negative relationship (lower similarity is associated with higher memory quality). **D**. Topographic representations of the electrode clusters that revealed reliable differences between memory quality categories within each age group (averaged across reliable time windows, see C). **E**. z-transformed regression coefficients extracted from time–time–electrode clusters identified in YA (left) and OA(right) (see C and D). Group distributions (probability density functions), boxplots with means and 95% confidence intervals, whiskers with second and 98th percentiles, and individual data points (horizontally jittered) for YA (blue) and OA (red) (modified from Allen et al., 2019). p-values are given for group differences within each cluster (independent-samples t-tests). Note the difference between z' (Fisher's z-transformed correlation coefficients) and z (z-transformed regression coefficients).

the stronger was the link between imagery rating and memory quality. Equivalently, the higher (more positive) the individual regression coefficient (higher similarity in higher memory quality; i.e., the effect seen in older adults), the weaker was the link between imagery rating and memory quality.

These post-hoc analyses underline our interpretation of the main results showing an age-dependent effect of between-item representational similarity and memory. We suggest that older adults' benefit from more similar activation patterns may reflect their reliance on gist extraction whereas young adults' benefit from distinct patterns reflects the encoding of more specific details (see Discussion). It seems likely that implementing the imagery strategy allowed the younger participants to create novel, salient mental images from the rather common and similar stimuli, as reflected in more distinct memory representations (McDaniel & Einstein, 1986).

Discussion

The present study aimed to reconcile an evident tension between theories relating neural pattern similarity and memory in the fields of cognitive neuroscience and cognitive aging research. We addressed the central question whether high pattern similarity or high pattern distinctiveness benefits memory performance. To this end, we computed the similarity between the EEG frequency patterns elicited during encoding of different scene–word pairs at each electrode and related this measure of between-pair similarity to the subsequent recall performance of younger and older adults.

For older adults, between-item representational similarity was generally higher compared to young adults, supporting the "dedifferentiation" hypothesis of declining neural distinctiveness with age (Baltes & Lindenberger, 1997; Carp, Park, Polk, & Park, 2011; S.-C. Li et al., 2004; D. C. Park et al., 2004; J. Park et al., 2012; Payer et al., 2006; St-Laurent et al., 2014). Previous studies suggested that the loss of neural specificity in old age may underlie age-related cognitive impairments. This was, for example, supported by the finding that neural distinctiveness and fluid intelligence were correlated (J. Park et al., 2010). However, most previous studies were not able to link neural item specificity directly with participants' performance since memory for the items themselves was not assessed. By measuring between-item representational similarity during the encoding phase of an associative memory task and sorting the trials according to subsequent memory performance, we were able to relate measures of neural distinctiveness during encoding directly to later recall success. Notably, results obtained from multivariate analyses like those carried out here mostly reflect within-subject variability rather than differences between individuals (Davis, LaRocque, et al., 2014). We found that although older adults remembered significantly fewer items and revealed overall higher between-item pattern similarity than younger adults, on the within-subject level, items represented with high similarity to other items were actually those that older adults remembered best.

Specifically, based on their learning history, we sorted the studied pairs into high, medium, and low memory quality items and, on the within-subject level, measured the linear relationship between the level of representational similarity and memory quality. Importantly, the direction of this relationship and the time window in which representational similarity mattered for subsequent memory performance, differed between younger and older participants: For older adults, high similarity early during encoding supported memory performance. For young adults, low similarity between earlier and later time points benefited memory performance.

Beneficial effects of representational similarity for memory have been reported before (Davis, Xue, et al., 2014; LaRocque et al., 2013; Y. Lu et al., 2015; Visser et al., 2013; I. C. Wagner et al., 2016; Ye et al., 2016) and have been located to medial temporal lobe regions, whereas pattern distinctiveness supported memory in the hippocampus (LaRocque et al., 2013). These pattern separation computations were shown to be impaired for older adults (Shing et al., 2011; Wilson et al., 2006; Yassa et al., 2011). While high distinctiveness may be beneficial for memory performance to prevent false memories, high similarity may support mnemonic decisions by capturing regularities across experiences (LaRocque et al., 2013) and by giving rise to a feeling of familiarity (Davis, Xue, et al., 2014). Higher pattern similarity may also reflect more consistent processing that facilitates associative memory formation (I. C. Wagner et al., 2016).

Because neural activity patterns contain information on both content and processes (cf. Multivariate EEG analysis), the age differences reported here could reflect differences in the similarity of memory representations, processes, or both. The observed benefit of early high pattern similarity in older adults may indeed reflect similarities in processing, e.g., increased attention to the stimuli and/or gist extraction. Trials in which similar, memory-beneficial processes occur would be associated with higher between-item pattern similarity and they would have a higher recall probability. However, our findings may also refer to age differences on the representational level: A tendency toward more generalized memories (Koutstaal & Schacter, 1997; Koutstaal, Schacter, & Brenner, 2001; Tun et al., 1998) is often reported for older adults and may also be associated with increased neural similarity. In our study, age differences in the subjective judgements of imagery strategy use during encoding suggest that older adults did indeed rely more on encoding the general gist of scene–word pairs while young adults more often used the imagery strategy to create and encode unique details (cf. Hertzog, Price, & Dunlosky, 2012). Moreover, imagery and memory success were more strongly associated in young compared to older adults, and more strongly linked to the association of pattern similarity and memory quality. Older adults' benefit from successful early gist extraction may thus be reflected in increased early similarity, whereas young adults' formation of mental images with distinct details may be reflected in increased later dissimilarity.

The negative relationship between pattern similarity and memory performance in younger adults that we report in the current study contrasts with other memory studies that showed a positive relation, namely for recognition memory (LaRocque et al., 2013; Y. Lu et al., 2015; Ye et al., 2016), memory confidence and categorization (Davis, Xue, et al., 2014), fear memory (Visser et al., 2013), and associative memory (I. C. Wagner et al., 2016). This could be due to the fact that most previous studies showed a beneficial effect of neural similarity for performance in recognition tasks (but compare I. C. Wagner et al., 2016), in which a sense of familiarity due to high pattern similarity (Davis, Xue, et al., 2014; Gillund & Shiffrin,

1984) can be sufficient. In contrast to that, recall tasks as adopted in the current study typically require retrieval of specific details of the studied items (Craik & Tulving, 1975). Therefore, the observed benefit of distinct neural activation patterns for young adults' performance here may be due to the deployed intentional learning task in which participants were explicitly instructed to form very distinct mental images of the corresponding scene–word pairs. Furthermore, similarity of event-related potentials such as that observed by Y. Lu et al. (2015) may result in different effects than in the time–frequency domain.

The current study used an age-adapted procedure with adjusted numbers of items and repetitions to identify memory-relevant age differences in neural patterns. Although procedural differences may have contributed to the observed age differences in pattern similarities, we argue that avoiding differences in task difficulty, a typical confound in age-comparative studies (Rugg & Morcom, 2005) which have shown to be reflected in differences in brain activity (e.g., Nagel et al., 2009) outweigh this concern. In fact, minimizing this confound enables us to conclude that the identified differences between groups are indeed related to age. Nevertheless, it is a limitation that we cannot completely rule out the possibility that the different effects identified in the two groups arise from the different memory quality scoring procedures that were necessary in order to appropriately handle the age-related performance differences. It is possible that both effects may play an important role for memory encoding in the two age groups but the early similarity seems to be more critical for older adults whereas the later dissimilarity may be more critical for young adults. Alternatively, it is possible that the differences in memory from first to second recall arise from unmeasured differentiation during the second encoding phase.

So far, the prevailing evidence on the relationship between representational similarity and memory has been based on fMRI studies and therefore lacks insights into the temporal dynamics of pattern similarity during the formation of memory representations. Here, we demonstrate the advantage of dissociating different parts within the trial time course that reveal distinctions in the way representational similarity relates to memory performance of younger and older adults. Furthermore, the present study provides further evidence for the high relevance of the rich neural signatures offered by a wide range of frequencies and across multiple topographical sites for memory encoding and extends previous research with similar approaches (cf. Kerrén et al., 2018; Michelmann et al., 2016; Staresina et al., 2016; Zhang et al., 2015).

The question remains how between-item similarity links to within-item similarity, i.e. item-specific representational stability (across item repetitions) and reinstatement (between encoding and retrieval). Recent research suggests that within-item similarity benefits memory performance (Y. Lu et al., 2015; Xue, 2018; Xue et al., 2010) and declines during aging (St-Laurent et al., 2014; Zheng et al., 2018).

Understanding the mutual influences of between-item similarity, pattern stability, and pattern reinstatement may be crucial to complete our comprehension of how memories are represented and processed in the brain across the lifespan.

In summary, we provide critical new evidence countering the assumption that a decrease in neural distinctiveness underlies age differences in memory. Although older adults showed generally higher between-item representational similarity and performed worse on the memory task, they actually best remembered the items with the highest peak in pattern similarity early during encoding. Moreover, we show that young adults benefited from eliciting distinct memory representations later during the encoding trial, which presumably reflects the implementation of the imagery strategy for scene–word binding. The work presented here extends our knowledge about between-item pattern similarity as a memory-relevant representational property. In particular it shows how its relation to cognitive performance may change in the course of aging.

6 Study III: From Age Differences in Category Distinctiveness to Item Level Specificity and Stability: Bridging Representational Levels

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Contents

Abstract

The distinctiveness of neural information representation is crucial for successful memory performance but suggested to decline with advancing age. Age-related neural dedifferentiation regarding category information is apparent, but whether age differences exist at the level of item representations is an ongoing debate based on limited evidence. In this age-comparative fMRI study, we combined ROI-based univariate analysis and whole-brain searchlight pattern similarity analysis to elucidate age differences in neural specificity both at the category and item level, and their relation to memory performance. Young and older adults incidentally encoded images of repeated faces and houses and were subsequently tested in an old/new recognition memory task. We showed that age differences in neural distinctiveness during encoding coexisted at various levels and took the form of reduced category-selective processing in the VVC and less item-specific activation patterns in occipital regions. A multivariate distinctiveness score revealed the joint contribution of both categorical distinctiveness and item specificity to memory performance and age group differences, with item specificity being the strongest contributor to the latent distinctiveness score. Age differences in occipital item specificity were driven by higher item representation stability across repetitions in young compared to older adults, which was related to successful subsequent memory performance. Thus, we demonstrated that differences in the fidelity of neural representations during encoding accounted for age, inter-individual, and intra-individual differences in recognition performance. We discuss the potential implications of these results in light of the neural dedifferentiation hypothesis.

Introduction

Aging is associated with declining memory functions (Fandakova et al., 2020; Naveh-Benjamin & Ohta, 2012; Shing et al., 2010). Recently, the question of whether a phenomenon called “neural dedifferentiation” is underlying this reduction in memory performance has obtained much interest (cf. Koen & Rugg, 2019; Koen et al., 2019, 2020; Srokova et al., 2020; St-Laurent et al., 2014; Zheng et al., 2018). Neural dedifferentiation describes the finding that neural information representation is less distinctive in older compared to young adults (e.g., Carp, Park, Polk, & Park, 2011; Koen & Rugg, 2019; D. C. Park et al., 2004; J. Park et al., 2010). Since neural representations link brain activity to the contents of the mind and thus form the basis of cognition (cf. Dudai et al., 2007; Kriegeskorte & Diedrichsen, 2019; Tulving, 2007), neural dedifferentiation may indeed compromise cognition in old age (Koen & Rugg, 2019; Koen et al., 2020; S.-C. Li et al., 2001).

However, while general evidence for neural dedifferentiation is accumulating (for reviews, see Koen & Rugg, 2019; Koen et al., 2020), the extent of the representational change with age and its role in cognitive decline may still be underestimated, since most age-comparative studies have so far focused on age-related differences in the representation of broader categories such as faces, houses, or objects within the ventral temporal cortex, but have largely neglected item-specific representations (Koen et al., 2019; D. C. Park et al., 2004; J. Park et al., 2012; Payer et al., 2006; Srokova et al., 2020; Voss et al., 2008). Given the widespread structural (Raz et al., 2005; Shing et al., 2011), functional (Cappell, Gmeindl, & Reuter-Lorenz, 2010; Reuter-Lorenz & Park, 2010; Sander et al., 2020), and neurochemical (Bäckman et al., 2010) changes across the lifespan and the key role of neural representations on both item and category level for episodic memory (Hasinski & Sederberg, 2016; Kuhl et al., 2011; Y. Lu et al., 2015; Xue, 2018), it seems plausible that representational differences on a multitude of different informational levels coexist. In particular, we argue that age differences at the item level may be an essential but yet underappreciated aspect of neural dedifferentiation. Furthermore, if age differences coexist at various representational levels, their joint contribution to age-related memory decline remains to be determined.

Our reasoning is based on a prominent model of cognitive aging proposed by Li and colleagues (S.-C. Li & Sikström, 2002; S.-C. Li et al., 2000, 2001) that has inspired the investigation of neural dedifferentiation from the beginning (cf. D. C. Park et al., 2004). This model suggests that deficient neuromodulation in the aging brain can be conceived as a flattening of the activation function leading to reduced neural responsivity. Importantly, reduced neural responsivity accumulates in increased neural noise, that is, haphazard activation to identical informational input leading to lower fidelity of representations at the item level. Furthermore, increasing random activation variability within the network leads to a decrease in the distinctiveness of the network's representations. Thus, the model suggests that a common factor, namely deficient neuromodulation, causes a cascade of both proximal and distal changes at different representational levels, ranging from a loss of fidelity of neural information representation at the item level to reduced distinctiveness of larger network units that represent information at a higher (category) level. We here argue that most age-comparative studies so far have focused on the distal effects and have neglected proximal effects that may underlie representational change in old age.

The model by Li and colleagues emphasizes that an age-related increase in processing variability and differences in early information processing manifest as age differences in item-level representations. However, most fMRI studies investigating neural dedifferentiation focused on broader concept representations, namely by assessing univariate category-selective processing (e.g., D. C. Park et al., 2004) and/or multivariate category-specific representations (e.g., Carp, Park, Polk, & Park, 2011). These studies made use of the observation that regions in the ventral visual cortex (VVC) respond maximally to specific visual stimulus categories and less to others. For instance, the fusiform face area (FFA) maximally responds to face images, while the strongest responses in the parahippocampal place area (PPA) are typically reported for scene or house images (Epstein & Kanwisher, 1998; Grill-Spector & Malach, 2004; Kanwisher et al., 1997). Using conventional univariate analysis, D. C. Park et al. (2004) demonstrated that, compared to young adults, older adults exhibited less category-selective blood oxygen level dependent (BOLD) responses to stimuli of faces, houses, chairs, and pseudowords, providing the first evidence for age-related neural dedifferentiation in the VVC (see also J. Park et al., 2012; Payer et al., 2006, and, accounting for trial-wise BOLD variability: Koen et al., 2019; Voss et al., 2008). In addition to the comparison of (univariate) activation differences between brain regions in response to stimuli of different categories, multivariate activation patterns have been used to characterize the representational content in a region (e.g., Davis & Poldrack, 2013; Mur et al., 2009; Xue, 2018), for example, with multivariate analysis approaches such as representational similarity analysis (Kriegeskorte et al., 2008) and decoding (Haynes & Rees, 2006; Mitchell et al., 2004; Rissman et al., 2010). Investigating the similarity or distinctiveness of distributed, multivariate activation patterns, later studies revealed that different stimulus categories were represented less distinctively in category-selective areas in the VVC and other regions in older compared with younger adults (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010; Trelle et al., 2019). Thus, the available evidence is generally in line with the notion of age-related neural dedifferentiation of category information.

While multivariate analyses complement the picture obtained by univariate analyses, most age-comparative multivariate studies still focused on distinctiveness defined as categorical differences (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010; Srokova et al., 2020) and did not address the question of how precise and specific older adults' neural patterns are at the item level, over and above their specificity with regard to category information. Until now, only few age-comparative studies have aimed to investigate neural distinctiveness at the within-category or even item level, mostly focusing on predefined category-specific regions (e.g., Goh et al., 2010; Trelle et al., 2019). However, it is highly likely that item-specific representations are also supported by other brain regions than those showing category selectivity (see e.g., Kriegeskorte, Formisano, Sorger, & Goebel, 2007). Thus, age differences in item specificity may have easily gone unnoticed in age-comparative studies with region-of-interest approaches that focus on category-specific brain regions such as the FFA and PPA. Indeed, evidence from two studies without such a focus point into the direction of age differences in item specificity. First, a study by St-Laurent et al. (2014) showed that BOLD patterns elicited by different video clips were more similar to each other in older adults than in young adults, supporting the notion of neural dedifferentiation on the item level. Similarly, Sommer et al. (2019) found that electroencephalographic (EEG) frequency patterns of unique image–word pairs were generally more similar in older adults than young adults. Nevertheless, in both studies, the studied items were not divided into broader categories, therefore not allowing for a comprehensive account of both item-level specificity and category-level distinctiveness. In addition, in these two studies, the relation of between-item similarity to memory performance was not reported (St-Laurent et al., 2014) or only observed on the within-person level (Sommer et al., 2019), leaving open the question of how age differences in item specificity contribute to age-related memory decline.

Nevertheless, findings of these studies provide the first evidence that in addition to the primarily observed age differences in categorical representations, also item-specific representations are altered in old age. Importantly, assuming that an altered signal-to-noise ratio in neural information processing leads to more variable neural responses in old age (S.-C. Li et al., 2001), item-level specificity in older adults may depend critically on the consistency with which individual items are represented across several instances of encoding, so-called item stability. However, while several studies using young adults samples have already revealed the importance of item stability (inside and outside of category-selective areas including, for instance, the occipital cortex) for memory performance (Ward et al., 2013; Xue et al., 2010), so far only one study by Zheng et al. (2018) compared item stability across repeated encodings between young and older adults. They found that, independent of their distinctiveness from other representations, item stability in the visual cortex was reduced in older adults and was associated with lower memory performance compared with young adults. Moreover, item stability was an important contributor to memory performance as indicated by subsequent memory effects. However, age differences were less clear regarding item specificity, that is, when item stability was corrected for similarity of items from the same category, which provoked criticism regarding the validity of the results (see Koen & Rugg, 2019).

All in all, while previous studies generally supported the notion of an age-related degradation of neural representations, most provided evidence for differences in the distinctiveness of categorical information representation. Few studies have investigated item-level specificity over and above categorical information representation, and only one of these has provided evidence for age differences in item stability with unclear consequences for item-level specificity. Thus, whether age differences exist at the level of item representations is an ongoing debate in the field based on highly limited evidence (see, e.g., Koen & Rugg, 2019). Furthermore, a comprehensive account simultaneously regarding age differences at various representational levels is needed to unravel the joint contribution to age-related memory decline.

In the current age-comparative fMRI study, we combined conventional ROI-based univariate analysis and whole-brain searchlight pattern similarity analysis to elucidate age-related differences in neural specificity both at the level of categorical information as well as at the level of the individual item, and their relation to memory performance. Young and older adults incidentally encoded repeated images of faces and houses and were subsequently tested in an old/new recognition memory task. We found age differences in neural distinctiveness during encoding at multiple representational levels, specifically in the form of reduced category-selective neural processing in the VVC and less item-specific activation patterns in occipital regions. Category-selective processing and item representation specificity could account for how well the respective information was later remembered in both young and older adults. Importantly, age differences in occipital item specificity were driven by higher item stability in young adults than older adults, with higher item stability also being related to successful subsequent memory performance on the within-person level. We discuss the potential implications of these results in light of the neural dedifferentiation hypothesis.

Materials and methods

Participants

The face–house task described in the current report was embedded in a larger study with an overall sample consisting of 47 young and 49 older healthy adults who participated in several structural MRI scans and behavioral tasks inside and outside the MRI scanner on two study days. Thirty-nine young and 37 older adults completed the face–house task. We excluded 3 participants (2 young adults and 1 older adult) due to memory performance below chance level and 6 participants (2 young adults and 4 older adults) due to a failure to detect category-selective clusters (see below). Therefore, final analyses were based on a sample of 35 young (age: M = 22.11, SD = 2.70, 18–27 years) and 32 older adults (age: M = 70.72, SD = 2.26, 67–75 years) with normal or corrected-to-normal vision and no history of neurological or psychiatric diseases. No participant was taking any medications known to affect brain functions. Furthermore, we screened all older adults with the Mini-Mental State Examination (Folstein et al., 1975) and none scored below the threshold of 26 points. All participants gave written informed consent to take part in the experiment. All procedures were approved by the ethics committee of the German Society for Psychological Research (DGPs).

Stimuli and procedure

Stimulus material. Overall, the stimulus set comprised 300 grey-scale pictures from three different categories: 120 neutral faces (adapted from the FACES database; Ebner, Riediger, & Lindenberger, 2010), 120 houses (in part adapted from D. C. Park et al., 2004 and in part obtained through web search) and 60 phase-scrambled images (30 faces and 30 houses, constructed from randomly chosen pictures of the face/house sets) as control stimuli. Face stimuli furthermore consisted of four subcategories, split by age group (i.e., young and older adults) and gender (i.e., female and male). Similarly, house stimuli comprised four subcategories, namely apartment buildings, family houses, sheds, and warehouses. In addition, three target stimuli were used for the encoding task, comprising a specific face image, a specific house image, and a phase-scrambled image with a white square in the center, that participants were familiarized with before the task. All 240 non-target face and house stimuli were split into two sets of 120 items (60 faces and 60 houses comprising 15 stimuli of each subcategory) to present one set during encoding and recognition (old items) and the other set only during recognition (new items). The same item sets were used as old or new items across subjects.

Procedure. Here, we focused on the face–house task consisting of an incidental encoding phase and a surprise recognition test, both conducted inside the MRI scanner (see Figure 14A). After verbal and written instructions, giving consent, and performing several behavioral tasks including a short training of the encoding task, participants were positioned into the scanner. Here, they again practiced the task for a few trials. The encoding phase consisted of two identical runs including nine stimulus blocks each (see Figure 14B). Stimuli were presented using Psychtoolbox (Psychophysics Toolbox) for MATLAB (The MathWorks Inc., Natick, MA, USA). During each block, one target (for which participants had to respond) and 20 non-target images of the same category (i.e., faces, houses, or phase-scrambled controls) were presented for 1200 ms with a fixation cross shown between trials (jittered; ranging from 500 ms to 8000 ms). While face or house blocks included five images from each of the four subcategories, phase-scrambled blocks comprised ten scrambled-face images and ten scrambled-house images. Stimuli were randomly distributed into the blocks. Stimulus order was pseudo-randomized with the restriction that no subcategory appeared twice in a row and the target image was presented neither in the first four nor last four trials of a block. The order of the blocks was alternating and counterbalanced across participants, either starting with a face or house block. Due to a technical failure, the identical stimulus order was used for all participants starting with a face block and in 36 participants starting with a house block. To ensure attention to all stimuli during encoding, subjects were instructed to engage in a vigilance task asking them to press a button with their right index finger whenever one of the three target images was presented. Such target trials were excluded from further analyses. In the second run, blocks and trials were repeated exactly as in the first run, i.e., each image was presented twice during encoding. In total, the encoding task lasted 22 minutes.

After encoding, several structural scans were conducted (see below). Then, subjects had a break outside the scanner in which the surprise recognition test was explained to them. The recognition test consisted of two runs, each including three face and three house blocks presented in alternated and counterbalanced order. Each block contained 20 previously seen and 20 new images. Subjects were instructed to indicate whether a presented image was old or new via button press during stimulus presentation (1200 ms) or the following grey screen (3000 ms). The order of the trials was pseudo-randomized with the restriction that images from the same subcategory or four old or new images did not appear successively. Furthermore, trials were separated by a jittered fixation cross (500–8000 ms). Again, due to a technical issue an identical stimulus order was used for 13 participants starting with a face block and for 14 participants starting with a house block. The recognition task lasted about 26 minutes.

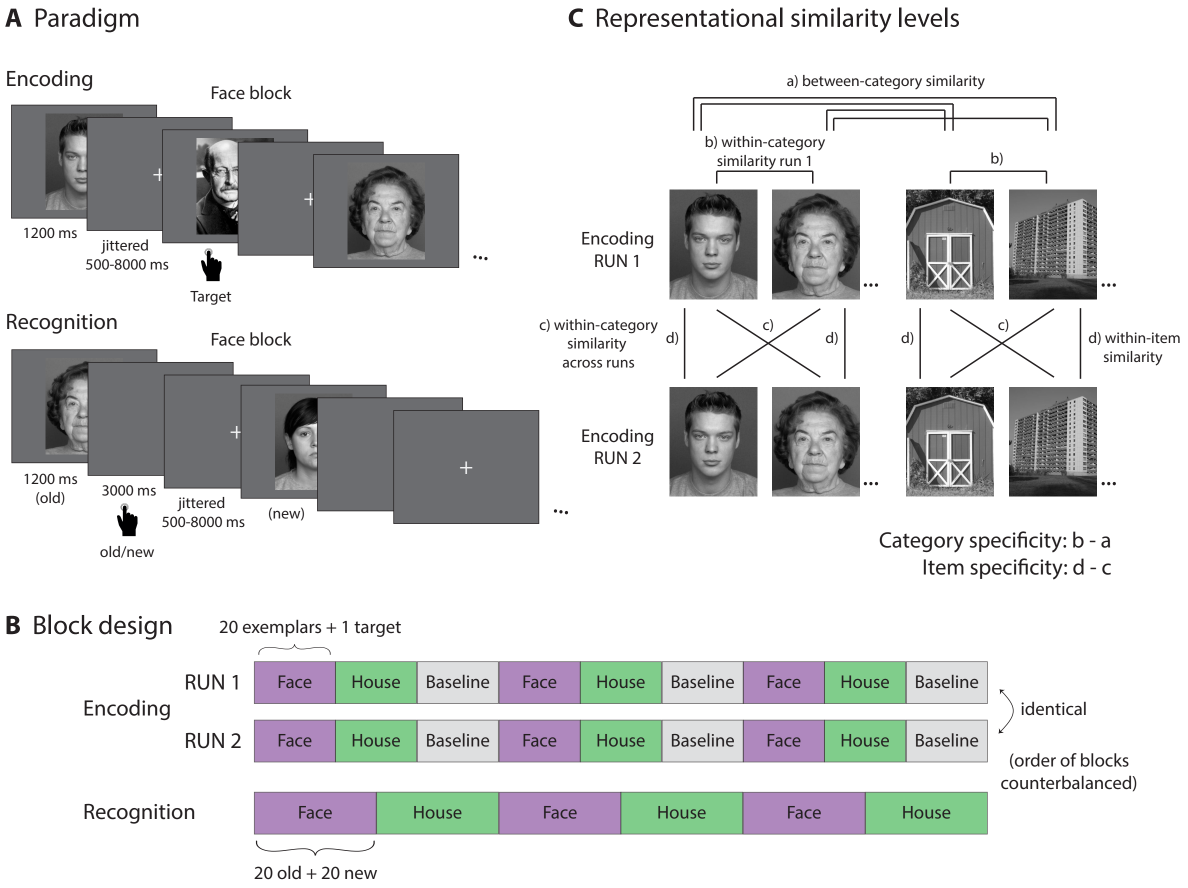


Figure 14: Task design and representational similarity levels. **A.** The paradigm comprised an encoding (top) and recognition (bottom) task. During encoding, participants were asked to press a button whenever a previously trained target image appeared. During recognition, participants responded via button press whether each presented image was old or new. Here, only sample stimuli from a face block are shown for illustration but also houses and baseline control stimuli were presented. **B.** Illustration of the block design of encoding and recognition tasks. The encoding task consisted of two identical runs, each of which comprised 3 face, 3 house, and 3 baseline (phase-scrambled faces and houses) blocks in alternating and counterbalanced order (either starting with a face or house block). In each block, 20 exemplars of the respective category (face, house, baseline) were presented plus one target stimulus. The recognition task consisted of 3 face and 3 house blocks in alternating and counterbalanced order. In each block, 20 old and 20 new faces/houses were presented. **C.** Simplified illustration of the computed representational similarity levels. For each item presented in encoding run 1, neural pattern similarity was computed as the Pearson correlation of the BOLD pattern elicited by that item and the BOLD pattern(s) elicited by (a) all items of the respective other category in run 1 (between-category similarity), (b) all other items of the same category in run 1 (within-category similarity in run 1), (c) all other items of the same category in run 2 (within-category similarity across runs), (d) the same item in run 2 (within-item similarity; stability). For each subject, the respective similarity measure was averaged across items, resulting in one similarity value for each representational level. Category representation specificity was calculated as the difference of between-category and within-category similarity (within–between category similarity; b–a). Item representation specificity was calculated as the difference of within-category (across runs) and within-item similarity (between–within item similarity; d–c). These similarities were assessed based on regions of interest as well as a searchlight approach, see main text.

Behavioral data analysis

Behavioral data were analyzed using custom-written MATLAB scripts. Performance in the target detection task during encoding was measured as percentage of correct responses to targets. Memory performance in the recognition task was assessed by calculating the discrimination index *Pr* (Snodgrass & Corwin, 1988), which is an unbiased parameter for recognition performance. The parameter *Pr* was calculated by the difference between the hit-rate (proportion of old responses to old images) and the false-alarm-rate (proportion of old responses to new images). We used *t*-tests to test whether recognition performance was different from chance level, and whether memory performance differed for face and house images. We tested for age differences in memory performance by computing an independent samples *t*-test. For effect sizes, we report Cohen's *d*.

FMRI data collection and preprocessing

All MR images were acquired with a 3T Siemens Magnetom Tim Trio scanner. MRI data acquisition included a T1-weighted structural image (MP-RAGE sequence: TR = 2.5 ms, TE = 4.77, flip angle = 7°, TI = 1.1 ms , voxel size = $1\times1\times1$ mm^3) and T2*-weighted echo planar images (EPIs; TR = 2 s, TE = 30 ms, pixel size = 3×3 mm^2) sensitive to blood oxygenation level-dependent (BOLD) contrast. EPIs were acquired in two separated encoding and retrieval sessions, each of which comprised 270 volumes with 36 axial slices of 3 mm thickness, separated by 3.3 mm. As part of the larger study context, we additionally acquired turbo spin-echo proton density images (PD), diffusion tensor images (DTI), and fluid attenuation inversion recovery (FLAIR).

MRI data were first organized according to "Brain Imaging Data Structure" specifications (BIDS; Gorgolewski et al., 2016). Data processing was performed using the fMRIPrep toolbox (1.4.0) (Esteban et al., 2019) with the default processing steps incorporating the software packages: FSL, FreeSurfer, ANTs and AFNI. First, each T1-weighted volume was corrected for intensity non-uniformity and skull-stripped to reconstruct brain surfaces. Brain-extracted T1-weighted images were spatially normalized to the ICBM 152 Nonlinear Asymmetrical template version 2009c through nonlinear registration. Brain tissue segmentation of cerebrospinal fluid, white-matter and grey-matter was performed on the brain-extracted T1-weighted image. Functional data were slice time corrected, motion corrected and co-registered to the normalized T1-weighted template. For further details including software packages for each preprocessing step in FMRIPrep, please refer to https://fmriprep.readthedocs.io/en/stable (online documentation).

For univariate brain imaging analyses, functional images were resampled to 4 mm isotropic voxels by performing spatial smoothing with a kernel of 4 mm full width half maximum. We computed a voxel-wise general linear model (GLM) including the first and second encoding run using SPM12. BOLD signal changes were modeled using separate regressors for face, house, and phase-scrambled control image blocks and 6 nuisance motion regressors, which were all convolved with a canonical hemodynamic response function (HRF).

Pattern similarity analyses were conducted on functional images resampled to 2 mm isotropic voxels to enhance signal-to-noise ratio (Dimsdale-Zucker, Ritchey, Ekstrom, Yonelinas, & Ranganath, 2018) and were based on single trial beta weights including one trial-specific regressor, one regressor for all other trials, six motion regressors and one run-specific mean (Mumford, Turner, Ashby, & Poldrack, 2012). Trial-specific regressors were modeled as a 1.2 second duration delta function convolved with a canonical HRF.

FMRI data analysis

Defining regions of interest

We used a cluster-based approach to define individual functional ROIs most strongly involved in processing faces or houses during both encoding runs. To restrict our analyses to category-selective processing areas, we defined an anatomical mask of the VVC using the automated anatomical labeling atlas (AAL) including the bilateral fusiform gyrus, parahippocampal gyrus, and the inferior temporal gyrus (D. C. Park et al., 2004). Within this mask, we then contrasted BOLD responses to face vs. phase-scrambled control image blocks and BOLD responses to house vs. phase-scrambled control image blocks for each subject. All adjacent voxels exceeding the uncorrected threshold of $p < 0.005$ were defined as one cluster. As mentioned above, 2 young and 4 older participants were excluded because clusters included less than 10 voxels. The face-selective ROI was defined as the cluster with the highest averaged t-value for faces compared to phase-scrambled images and the house-selective ROI as the cluster with the highest averaged t-value for houses compared to phase-scrambled images leading to the formation of two individual functional ROIs. Within participants, on average only 4.15% (fusiform gyrus: 4.74%; parahippocampal gyrus: 1.64%; inferior temporal gyrus: 2.40%) of all voxels of the face- and house-selective ROIs overlapped, indicating separated category-selective clusters in the VVC.

ROI analysis of category-selective processing

To estimate the neural response magnitude evoked by face and house images within each individual ROI, we first contrasted the BOLD signal elicited by face and house image blocks against the BOLD signal of phase-scrambled control image blocks within the same encoding run. Then, we averaged all *t*-values within each ROI to obtain a standardized neural response value to faces or houses, respectively. Selectivity scores were computed by contrasting standardized neural responses to the preferred vs. non-preferred image category within each individual ROI, e.g., neural response to faces vs. neural response to houses in the face-selective ROI. To analyze selectivity scores at the group level, we used a 2 (Age Group) × 2 (ROI) mixed factorial ANOVA.

We only used the selectivity score within the first encoding run to estimate category-selective processing. It is suggested that repeated stimulus presentation is accompanied by decreased BOLD responses in neural populations especially in high-level visual brain areas, which is called repetition suppression (Barron, Garvert, & Behrens, 2016; Grill-Spector et al., 2006). According to previous work (Goh et al., 2010), young adults show repetition suppression in face selective areas to repeated identical faces only, whereas older adults also showed reduced BOLD responses to similar faces indicating age-related neural dedifferentiation. Indeed, we found that in young adults, repetition suppression for preferred categories was higher than for non-preferred categories (e.g., higher repetition suppression for faces than houses in face-selective regions), while there was no difference in repetition suppression between preferred and non-preferred categories in older adults (see supplements for details). Therefore, selective repetition suppression effects reduced selectivity scores in young adults but not in older adults during the second encoding run. Thus, selectivity scores during the second encoding run are confounded by repetition suppression effects and therefore may not be a suitable parameter to test age-related differences in category-selective processing.

Selectivity scores of the first encoding run were collapsed across ROIs to calculate mean selectivity scores within each participant. This selectivity score index was correlated with *Pr* across all participants using Pearson correlation. Furthermore, we conducted partial correlations between selectivity scores and *Pr* with age group as a control variable to test whether this relationship was independent of age.

ROI analysis of category representation specificity

To estimate the specificity of neural category representations within category-selective clusters, we compared the within-category similarity to the between-category similarity using pattern similarity analysis (Kriegeskorte et al., 2008) (see Figure 14C). In line with category-selective processing analyses, we calculated within- and between-category similarity only for trials from the first encoding run to eliminate potential confounds due to repetition suppression effects (see supplements). Within- and between-category similarities were calculated separately in both ROIs. Within-category similarity was only calculated for items from the preferred category of the selected area (Koen et al., 2019) and was only computed for items from different blocks to control for potential confounds due to time-dependent correlations in hemodynamic responses (Dimsdale-Zucker et al., 2018). The within-category similarity was computed as the averaged across-voxel Pearson correlation of the neural activity pattern of each item to all other items from the same preferred category in a category-selective area (e.g., similarity of a face trial to all other face trials in the face area). For each subject, we averaged within-category similarity across items resulting in one within-category similarity value for each region of interest. The between-category similarity of each item was calculated as the across-voxel Pearson correlation of the neural activity pattern of the item to the neural activity pattern of all items from the other category (e.g., similarity of a face trial to all house trials in the face area). We again averaged between-category similarity across items to estimate one between-category similarity value for each region of interest. To test for differences in pattern similarity values, we used a 2 (Age Group) $\times$ 2 (within-/between-category similarity) $\times$ 2 (ROI) mixed factorial ANOVA.

Searchlight analyses of category representation specificity

We conducted separate searchlight analyses for faces and houses. For each voxel in the brain, we measured the difference of within-category and between-category similarity, that is, within-minus-between (within–between) category similarity, in an 8 mm-radius sphere centered on that voxel (Nili et al., 2014). Within- and between-category similarity was calculated as described in the previous section. Thus, we derived a whole-brain map for each subject where each value indicated the within–between category similarity of the according sphere.

We used non-parametric, cluster-based, random permutation statistics adapted from the Fieldtrip toolbox (Oostenveld et al., 2011) to test for age differences in within–between category similarity across the brain. First, independent *t*-tests were conducted comparing within–between category similarity of young and older adults for each voxel. Adjacent voxels exceeding the defined threshold of $p < 0.005$ were grouped into clusters. The sum of all *t*-values of these empirical clusters was determined as the respective test statistic. We used the Monte Carlo method to compute a reference distribution for the summed cluster *t*-values. Within–between category similarity of both age groups was randomly assigned (1,000 permutations) into two new within–between category similarity sets. In every permutation an independent *t*-test was conducted between the new generated sets to reveal random clusters. The highest sum of *t*-values during each permutation was included in the estimation of the reference distribution.

To correlate category representation specificity and memory performance across participants, we averaged the within–between category similarity of each participant across face and house selective areas. The resulting category specificity score was correlated with *Pr* across participants using Pearson correlations. To control for age, we also calculated partial correlations of the category specificity score and *Pr* with age group as control variable.

Searchlight analysis of item representation specificity

To investigate the specificity of item representations, we compared within-item similarity to between-item similarity (within–between item similarity) using pattern similarity searchlight analysis (see Figure 14C). Matching the category specificity searchlight analysis, we compiled the within–between item similarity for each voxel within an 8 mm-radius sphere. For each item, within-item similarity was calculated as the across-voxel Pearson correlation of the neural activity pattern of a given item from the first encoding run to the neural activity pattern of the same item from the second encoding run in each sphere. Between-item similarity was computed as the correlation of the neural activity pattern of an item of the first encoding run to the neural activity pattern of all other items from the same category of the second encoding run. For each participant, we then averaged within- and between-item similarity across items. We used the resulting within- and between-item similarity brain maps of each participant to calculate one within–between item similarity brain map for each subject. To test for age differences in within–between item similarity across the brain, we used non-parametric, cluster-based, random permutation statistics (see above). First-level statistics compared within–between item similarity of young and older adults for each voxel. Second-level statistics compared the summed t-value of the empirical clusters to a reference distribution computed using the Monte Carlo procedure.

Furthermore, we averaged within–between item similarity for faces and houses for each participant to estimate one item specificity score per participant. Respective item specificity scores were correlated with *Pr* across participants using Pearson correlations and partial correlations to control for age group differences.

Analyzing the multivariate relationship between dedifferentiation at multiple representational levels and age using partial least squares correlation (PLSC)

We performed PLSC which allows to investigate the joint impact of the multiple distinctiveness levels on age/memory relations (Keresztes et al., 2017; Krishnan, Williams, McIntosh, & Abdi, 2011; A. McIntosh, Bookstein, Haxby, & Grady, 1996). To compile PLSC, we first calculated a between-subject correlation matrix between an $n \times 2$-matrix containing age (in years) and memory performance (*Pr*) and an $n \times 3$-

matrix of distinctiveness levels. *Pr* was inverted to create consistent directionality between variables of interest. Thus, increasing age was positively related to Pr indicating worse memory performance. The correlation matrix was decomposed using singular value decomposition (SVD) resulting in two latent variables consisting of a diagonal matrix of the correlation strength (i.e., a singular value) and one vector representing the neural distinctiveness profile best describing the brain-age/behavior relationship in our data (distinctiveness weights). We tested the significance of the detected latent variables (LVs) using 10,000 permutation tests of the singular value corresponding to the LV, which revealed one significant LV ($P < 0.001$). For the significant LV, we tested the robustness of the within-LV distinctiveness weights using a bootstrapping procedure (10,000 resamples). These distinctiveness weights were divided by their bootstrapped standard errors to calculate bootstrap ratios (BSRs) as normalized estimates of robustness. Comparable to z-values, BSRs below or above ± 1.96 are considered as reliably robust. By calculating the dot product of the model-based distinctiveness weights and each subject's empirical distinctiveness scores, we compiled an individual LV profile for each participant – the dedifferentiation-aging/memory score. This single value indicates the degree of a subject's distinctiveness profile which characterizes aging and memory decline.

Disentangling the relations of age, memory performance, and item similarity

We aimed to disentangle whether lower item representation specificity in older adults occurred due to lower item stability or higher between-item similarity in older adults compared to young adults and which of these two factors was related to memory performance. Therefore, we averaged within- and between-item similarity for later remembered and forgotten items separately in the significant face and house clusters of the conducted searchlight analyses. To test for differences in item similarity, we conducted a 2 (Age Group) × 2 (within-item/between-item similarity) × 2 (Memory: remembered/forgotten) × 2 (ROI) mixed factorial ANOVA.

Results

Behavioral results

Healthy young adults (n = 35, age: M = 22.11, SD = 2.70, 18–27 years) and older adults (n = 32, age: M = 70.72, SD = 2.26, 67–75 years) incidentally encoded images of faces and houses, followed by a surprise recognition test (see Figure 14). During encoding, all images were presented twice in two subsequent runs. To ensure adequate processing of the presented face and house images, participants performed a low-level vigilance task during encoding (i.e., pressing a button whenever an interspersed predefined target image appeared). Both young and older participants performed near ceiling in the vigilance task (percentage of correct answers: M_{young} = 98.95%, SD_{young} = 4.69% M_{old} = 98.77%, SD_{old} = 3.54%), reflecting high engagement in encoding the presented images. Memory performance in the recognition task was assessed by the discrimination index Pr ranging from –1 to 1 with 0 representing chance level. In both age groups, the mean memory performance exceeded chance level (Pr_{young} = 0.24, $t_{\text{young}}(34)$ = 12.18, $p_{\text{young}} < 0.001$, d_{young} = 2.06, Pr_{old} = 0.19, $t_{\text{old}}(31)$ = 9.16, $p_{\text{old}} < 0.001$, d_{old} = 1.62) and did not differ between face and house images ($t_{\text{young}}(35)$ = 0.93, p_{young} = 0.358, $t_{\text{old}}(31)$ = 1.67, p_{old} = 0.105). Compared to young adults, older adults gave more “old” responses for both previously learned images (hit-rate$_{\text{young}}$ = 0.50, hit-rate$_{\text{old}}$ = 0.61, $t(65)$ = –3.08, p = 0.003, d = 0.75) and new images (false-alarm-rate$_{\text{young}}$= 0.26, false-alarm-rate$_{\text{old}}$= 0.41, $t(65)$ = –4.92, $p < 0.001$, d = 1.34). An independent samples t-test revealed no significant difference in memory performance (Pr) between age groups ($t(65)$ = 1.62, p = 0.110, d = 0.40).

Category-selective processing in the VVC differs between age groups and is related to memory performance

Age-related neural dedifferentiation has previously been shown as less distinct recruitment of category-selective areas located in the ventral visual cortex (VVC; D. C. Park et al., 2004). Using a cluster-based approach, we defined two regions of interest (ROIs; see Figure 15) in the bilateral VVC showing the highest BOLD response to images of faces compared to phase-scrambled control images (face-selective ROI) and to houses compared to control images (house-selective ROI). Within these category-selective functional ROIs, we calculated a selectivity score as the difference in BOLD responses to images of the preferred and non-preferred category (e.g., the difference in BOLD responses to images of faces versus houses in the face-selective ROI). During the first encoding run, a 2 (Age Group) × 2 (ROI) mixed factorial analysis of variance revealed that older adults showed reduced category-selective processing

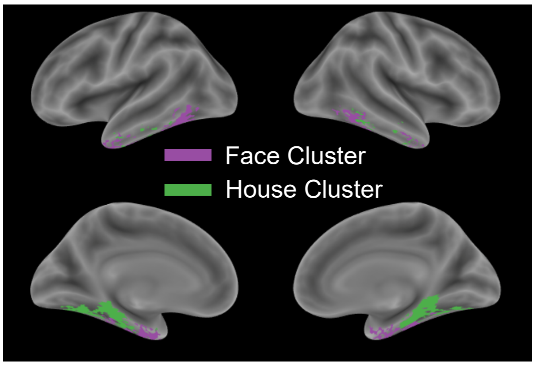


Figure 15: Category-selective clusters. Surface rendered illustration of non-overlapping category-selective ROIs. Purple color indicates face-selective ROI. Green color depicts house-selective ROI. Notably, the face-selective ROI is predominantly located in the lateral VVC and house-selective ROI in the medial VVC. This closely resembles the category-selective areas observed by J. Park et al. (2012).

compared to young adults (F(1,65)= 12.59, $p < 0.001$; see Figure 16A). Furthermore, the magnitude of the selectivity score did not differ between ROIs (F(1,65) = 0.22, p = 0.643) and there was no interaction between ROI and age (F(1,65)= 0.06, p = 0.813). Thus, replicating previous observations (Koen et al., 2019; D. C. Park et al., 2004), our findings emphasize that older adults engaged category-selective areas in the VVC less distinctively compared to young adults when encoding visual information.

We only used the selectivity score within the first encoding run to estimate category-selective processing because category-selective repetition suppression effects diminished the age differences in category selectivity during the second run with repeated images (see supplements; cf. Barron, Garvert, & Behrens, 2016; Goh et al., 2010; Grill-Spector et al., 2006).

If neural dedifferentiation occurred due to age-related increases of haphazard neural activation as suggested by Li and colleagues (S.-C. Li et al., 2001), lower category selectivity should result from increased neural noise reflected in increased responses to images of the non-preferred category in older adults (neural broadening). However, current evidence is mixed as there are studies supporting neural broadening and studies showing the opposite effect – reduced neural responses to images of the preferred category (neural attenuation; for review see Koen & Rugg, 2019). To unravel whether age-related reductions in category-selective processing occurred due to a) neural broadening, b) neural attenuation, or c) a mixture of both processes (see J. Park et al., 2012), we conducted post hoc t-tests and used Bonferroni correction to control for multiple comparisons (see Figure 16B). Across ROIs, older adults showed increased BOLD responses to images of the non-preferred category compared to young adults (t(65) = 2.38, p = 0.040), while BOLD responses to preferred images did not differ between age groups (t(65) = –1.13, p = 0.526). Hence, the observed age-related neural dedifferentiation in category pro-

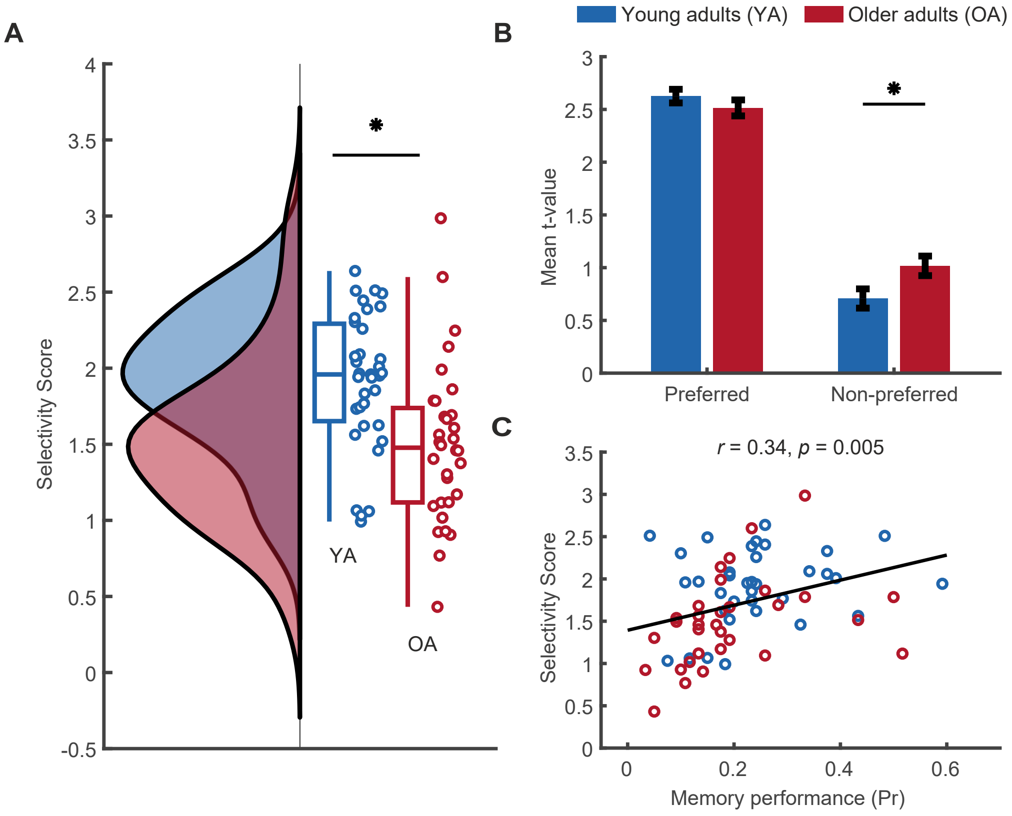


Figure 16: Category-selective processing during encoding. **A.** Selectivity score for young adults (YA; blue) and older adults (OA; red). Group distributions as unmirrored violin plots and boxplots with medians and 95% confidence interval and whiskers with 98th percentiles (Allen et al., 2019). **B.** Neural response to preferred and non-preferred categories within functionally defined VVC ROIs. The neural response is expressed as the averaged t-values for preferred/non-preferred categories against phase-scrambled images within the respective ROIs. Errorbars indicate standard error of the mean. **C.** Scatterplot illustrating the association between selectivity scores and corrected recognition (Pr) over all participants independent of age. Each circle represents an individual young or older adult. For illustrative purposes, the best fitting least-squares line is plotted. Significant group differences ($p < 0.05$) indicated by asterisk.

cessing most likely results from an increased engagement of category-specific regions by non-preferred stimuli in line with the theoretical assumption that broadening effects of the neural tuning curve underlie the loss of neural distinctiveness in older adults (S.-C. Li et al., 2001).

To test whether inter-individual variability in category-selective processing is related to memory performance in the recognition task, zero-order and partial correlations were computed across participants using Pearson's *r*. Selectivity scores were averaged across face- and house-selective ROIs in the VVC. Across participants, selectivity scores were related to memory performance ($r = 0.34$, $p = 0.005$; see Figure 16C). Importantly, this correlation remained significant when controlling for age group using partial correlations ($r = 0.29$, $p = 0.019$). Thus, dedifferentiated visual processing in category-selective areas, as primarily observed in older adults, was related to poorer memory performance independent of age.

Age differences in category representation specificity are restricted to the VVC

Since category selectivity as assessed with univariate methods relies on averaged BOLD signal changes and does not allow for quantifying the distinctiveness of specific item representations, we next used pattern similarity analysis (Kriegeskorte et al., 2008) to investigate the categorical specificity of item representations. These analyses still focus on differences at the categorical level, but use item-level information instead of averaged activation changes. Thus, we defined the specificity of neural category representations as the difference of within-category similarity and between-category similarity (within–between category similarity; cf. Carp, Park, Polk, & Park, 2011). Similarity indices were based on single-trial beta weights and calculated as across-voxel Fisher *z*-transformed Pearson correlations (Koen et al., 2019).

First, we focused on the previously-defined category-selective ROIs following an approach widely used in previous studies (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; Trelle et al., 2019). Within those areas, the within-category similarity was computed as the mean similarity between neural patterns evoked by different images of the same preferred category, whereas between-category similarity was defined as the mean similarity of neural activity patterns of images from the preferred to the non-preferred category (see Figure 14C). For example, for the face area, within-category similarity for each participant was calculated as the mean correlation between all face trials, whereas between-category similarity was defined as the mean correlation of all face trials to all house trials. Therefore, higher within–between category similarity reflects more distinct neural category representations for the preferred category within each ROI.

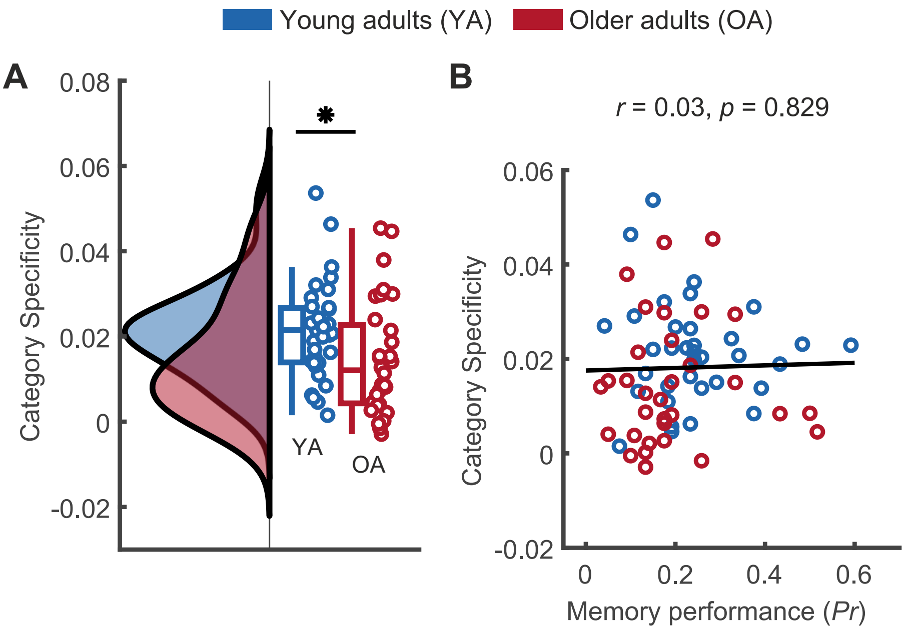


Figure 17: Category representation specificity in the VVC. **A.** Within–between category similarity in both age groups. Group distributions as unmirrored violin plots and boxplots with medians, 95% confidence intervals, and whiskers marking 98th percentiles. **B.** Pearson correlation of within–between category similarity and corrected recognition (*Pr*) across subjects including best fitting least-squares line. Significant group differences ($p < 0.05$) indicated by asterisk.

We used a 2 (Age Group) × 2 (within-/between-category similarity) × 2 (ROI) mixed factorial ANOVA to investigate age differences in category representation specificity. Across age groups, within-category similarity was higher than between-category similarity ($F(1,65) = 146.70, p < 0.001$). Moreover, the difference of within- and between-category similarity depended on age ($F(1,65) = 4.85$, $p = 0.031$) indicating lower specificity of neural category representations in older than in young adults (see Figure 17A). Neither the main effects of age ($F(1,65) = 2.07$, $p = 0.155$) nor ROI ($F(1,65) = 0.05$, $p = 0.820$) nor any further interaction reached significance (*p*s > 0.268).

Next, we used a whole-brain searchlight approach (Nili et al., 2014) to test for age differences in category representation specificity (cf. Carp, Park, Polk, & Park, 2011). For each voxel in the brain, we calculated the specificity of neural category representations as the difference of within-category similarity and between-category similarity (within–between category similarity) for faces and houses within an 8 mm-radius-sphere centered on that voxel. To control for multiple comparisons, we used cluster-based permutation statistics to compare within–between category similarity between age groups. In contrast to the ROI analysis, whole-brain analyses revealed no group differences in within–between category similarity for houses ($p > 0.336$) and furthermore indicated that older adults showed higher within–between category similarity for faces in the superior temporal gyrus (p = 0.006). Thus, while the ROI-based multivariate approach provided evidence for an age-related decline in category specificity as reported by several previous studies (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010), the whole-brain approach did not. This result indicates that an age-related decline regarding item-level differences for category information may be restricted to category-specific brain regions and less pronounced than thought, such that it does not survive exploratory whole-brain analyses.

We also tested whether specificity of neural category representations in category-specific brain regions was related to memory performance across subjects (see Figure 17B). Specificity of neural category representations was calculated as the within–between category similarity averaged over face and house selective areas. Neural category representation specificity was not related to memory performance using zero-order (r = 0.03, p = 0.829) or partial Pearson correlations (r = –0.03, p = 0.829). Thus, we found no evidence that the specificity of neural category representations was related to memory performance.

Item representation specificity in the occipital cortex differs between age groups and is related to memory performance

In contrast to previous studies (Carp, Park, Polk, & Park, 2011; Koen et al., 2019) our results only partially support lower *category* representation specificity in older adults (namely, when restricting the analyses to category-specific ROIs). However, theoretical accounts based on computational models emphasize that age-related dedifferentiation is particularly reflected in reduced specificity of neural representations of *individual items* (S.-C. Li et al., 2001) which are not restricted to category-selective areas but are found in large-scale neural networks (Xue, 2018). Therefore, we applied pattern similarity analyses across the whole brain to investigate age-related differences in neural item representation specificity.

Similar to the previously described searchlight analysis at the category level, we defined an 8 mm-radius sphere around each voxel. Within each sphere, within-item similarity was calculated as the similarity of neural activity patterns across the two repetitions of a given face or house item. We compared such item similarity to the respective within-category similarity (within–between item similarity) to capture the specificity of neural item representations. To control for potential confounds due to item repetition, we also calculated within-category similarity as the similarity between different images of the same category across runs. Cluster-based permutation statistics were used to compare within–between item similarity between age groups for face and house images separately. For faces, older adults showed smaller within–between item similarity compared to young adults in occipital regions ($p < 0.001$) including bilateral intracalcarine cortex, lateral occipital cortex, and occipital fusiform cortex (see Figure 18A). For houses,

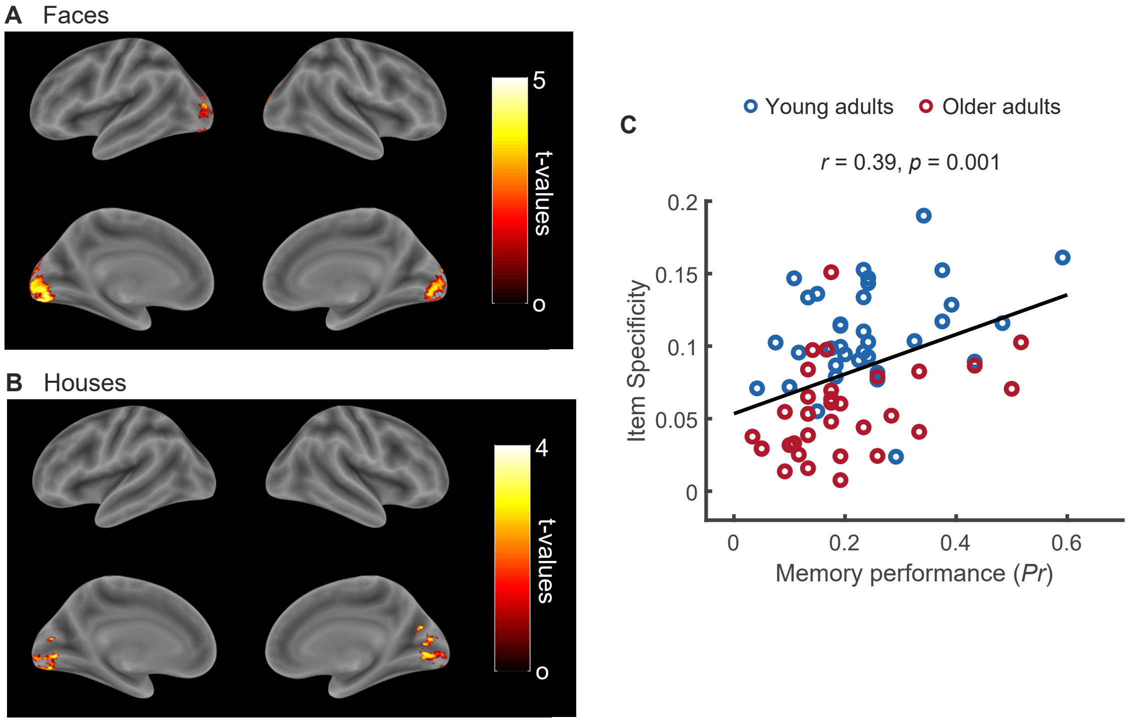


Figure 18: Item representation specificity in the whole brain. **A.** Significant age differences in within–between item similarity for faces indicated by *t*-values. Young adults showed higher within–between item similarity in occipital areas compared to older adults as depicted by the presented cluster. **B.** Significant age differences in within–between item similarity for houses. Again, young adults showed higher within–between item similarity in occipital areas than older adults. **C.** Pearson correlation of within–between item similarity and corrected recognition (*Pr*) over all subjects including best fitting least-squares line.

older adults also showed smaller within–between item similarity than young adults in occipital areas ($p = 0.006$) comprising bilateral lingual gyrus, intracalcarine cortex, and left occipital fusiform cortex (see Figure 18B). Thus, our findings underline that older adults form less specific item representations in occipital areas than young adults.

We also tested whether inter-individual differences in item representation specificity were related to overall memory performance (see Figure 18C). We calculated item representation specificity as the within–between item similarity averaged over both categories in their respective occipital clusters. Neural item representation specificity was related to memory performance using zero-order ($r = 0.39$, $p = 0.001$) and partial Pearson correlations ($r = 0.35$, $p = 0.004$). Thus, high item representation specificity account for inter-individual differences in memory performance of young and older adults.

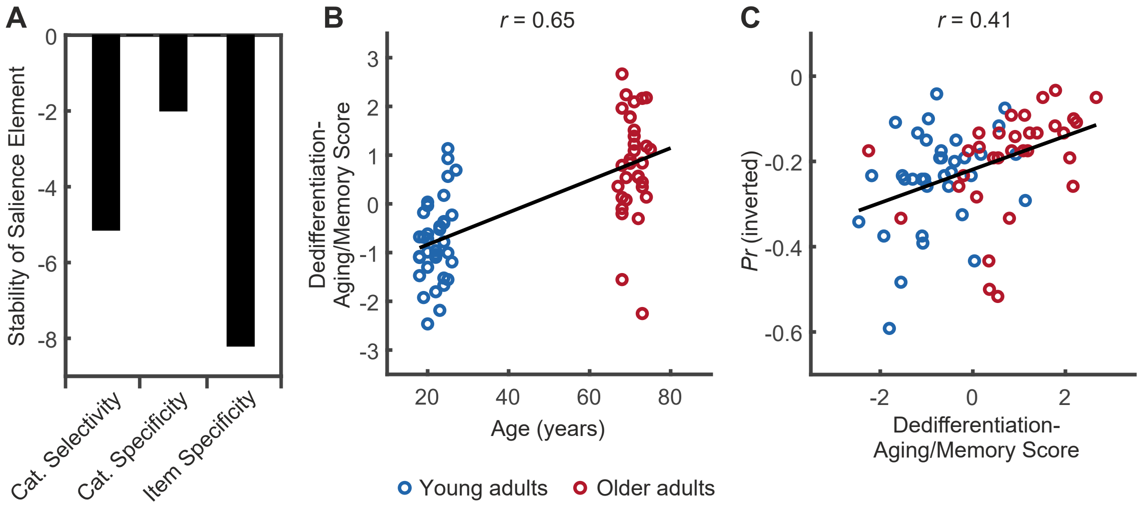


Figure 19: Specific dedifferentiation profile associated with age and memory performance. **A.** Latent variable weights (brain saliences) for each distinctiveness level used to transform individual empirical distinctiveness scores into one latent variable expressing the largest amount of information common to the multivariate pattern of distinctiveness levels and age/memory. *Z*-score-like values of stability suggest a negative relationship between distinctiveness levels and age/memory mostly pronounced in occipital item specificity. **B.** The resulting dedifferentiation-aging/memory score is positively related to age and **C** inverted memory performance (*Pr*) meaning that higher expression of the dedifferentiation profile is related to worse memory performance.

Evidence for the joint contribution of neural distinctiveness at different representational levels to age group and inter-individual differences in memory performance

To take into account the coexistence of age differences in category selectivity, category specificity, and item specificity, and delineate their joint contribution for memory performance, we used PLSC analysis to extract a single composite score of neural dedifferentiation – the dedifferentiation-aging/memory score. Our PLSC analysis identified a single reliable latent variable (LV; $P < 0.001$; see Figure 19A) that optimally represents the association between participants' age/memory performance and neural dedifferentiation ($r = 0.65$; see Figure 19B) as well as between participants' memory performance and neural dedifferentiation ($r = 0.41$; see Figure 19C). Bootstrap ratios (BSRs) indicated lower category selectivity (BSR = –5.13) and lower item specificity (BSR = –8.03) as the two stable components of the LV with category specificity only contributing marginally reliable information (BSR = –1.98). Importantly, in line with our proposal that item-level specificity is an important factor for age and performance differences, item specificity expressed by far the largest amount of information common to age group, performance, and the multivariate neural distinctiveness.

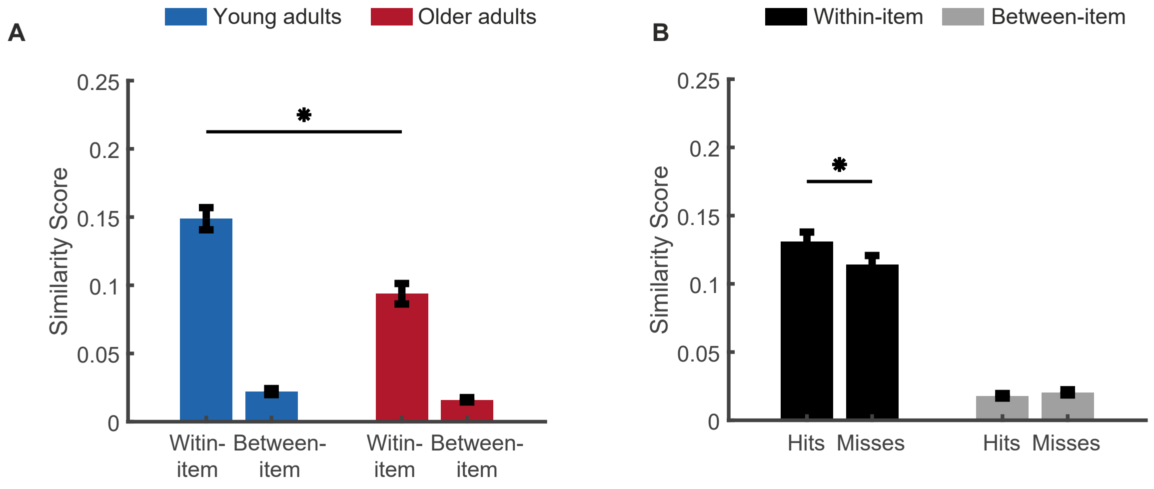


Figure 20: Item representation specificity and memory performance. **A.** Within (WI) and between-item similarity (BI) in both age groups indicates that lower item specificity in older adults is mostly driven by lower item stability. **B.** Comparing within- and between-item similarity for subsequently remembered and not-remembered items across age groups shows that item stability is higher for later remembered than not-remembered items independent of age.

Age and performance differences in occipital item specificity are driven by item stability

Our PLSC analysis revealed that in particular differences in item specificity account for age group differences as well as inter-individual differences in memory performance. Importantly, if, as assumed by Li and colleagues, more variable neural responses are at the core of age-related reductions in neural specificity (S.-C. Li et al., 2001), item-level specificity in older adults depends critically on the consistency with which individual items are represented across several instances of encoding, that is, item stability. To test whether lower item specificity in older adults was indeed due to lower item stability (within-item similarity) or higher between-item (within-category) similarity compared to young adults and whether differences in these similarities were related to a higher probability of successful memory retrieval, we compared similarity indices in the observed occipital clusters with a 2 (Age Group) $\times$ 2 (within-/between-item similarity) $\times$ 2 (Memory: remembered/forgotten) $\times$ 2 (ROI) mixed factorial ANOVA.

In line with the searchlight analysis, young adults showed higher similarity scores compared to older adults ($F(1,65) = 22.25$; $p < 0.001$) and within-item similarity was higher than between-item similarity ($F(1,65) = 435.87$; $p < 0.001$). Crucially, age interacted with within-/between-item similarity ($F(1,65) = 25.05$; $p < 0.001$; see Figure 20A). Furthermore, within- and between-item similarity differences were not affected by ROIs ($F(1,65) = 3.53$; $p = 0.064$). Specifically, post hoc tests revealed that within-item similarity was lower in older adults compared to young adults ($t(65) = 4.94$, $p < 0.001$), while between-item similarity did not differ between age groups after multiple error correction ($t(65) = 2.16$, $p = 0.069$).

Furthermore, subsequently remembered items showed higher similarity scores compared to subsequently forgotten items ($F(1,65) = 7.85$, $p = 0.007$) which interacted with within-/between-item similarity ($F(1,65) = 17.51$; $p < 0.001$; see Figure 20B). We found no interaction between memory and age group ($F(1,65) = 3.90$; $p = 0.052$) or other significant effects (ps < 0.316). Post hoc t-tests revealed that within-item similarity was higher for subsequently remembered than forgotten items ($t(66) = 3.90$, $p < 0.001$), while there was no difference in between-item similarity ($t(66) = -1.17$, $p = 0.248$). Thus, item representation stability was lower in older than young adults and supported subsequent recognition performance, emphasizing the role of neural dedifferentiation at the item level for age-related memory decline.

Discussion

A prominent theory of cognitive aging assumes that neural representations become less distinctive in old age and that this so-called neural dedifferentiation underlies age-related cognitive impairments (e.g., Koen & Rugg, 2019; S.-C. Li et al., 2001; J. Park et al., 2010). Age differences have been ascribed to deficient neuromodulation that causes a chain of consequences, namely a) increased neural noise, i.e., haphazard activation to identical informational input leading to lower fidelity of representations at the item level as well as b) increased random activation variability within the network leading to a decrease in the distinctiveness of the network's representations (S.-C. Li & Sikström, 2002; S.-C. Li et al., 2000, 2001). Importantly, such a common cause results in age differences in neural information representation that coexist at various levels (i.e., at the level of item representation and the level of category representation) and jointly affect memory performance. However, previous age-comparative studies have mostly focused on age-related dedifferentiation in categorical representation, neglecting age differences at the level of item representations. We therefore set out to investigate age differences at different representational levels ranging from category-selectivity to item-level specificity and stability and delineate their contribution to memory performance in young and older adults.

Age-related neural dedifferentiation coexists at different representational levels

We found evidence for age-related neural dedifferentiation in terms of reduced univariate category-selective neural processing in older compared with young adults within category-specific regions of interests in the VVC. This finding replicates previous studies that have used such a conventional analytical approach (Koen et al., 2019; D. C. Park et al., 2004). As predicted by the computational model by Li and colleagues, age differences in neural differentiation resulted from a broadening of the neural tuning curve, that is, increased activation to non-preferred stimuli in the older adults, with no age differences in activation differences for preferred stimuli. This prediction was previously supported by findings in single neurons (Leventhal et al., 2003; Schmolesky et al., 2000) and in fMRI, namely in the FFA (J. Park et al., 2012). However, the alternative prediction, that is, decreased responses to preferred stimuli (neural attenuation), has also received supporting evidence, namely in the extended face network (J. Park et al., 2012) and PPA (Koen et al., 2019). These results suggest that different processes may contribute to neural dedifferentiation depending on the level of observation and brain region.

Since category selectivity as assessed with univariate methods relies on averaged BOLD signal changes and does not allow for quantifying the distinctiveness of specific item representations, we next used pattern similarity analysis (Kriegeskorte et al., 2008) to investigate the categorical specificity of item representations. This analysis still focuses on differences at the categorical level, but uses item-level information instead of averaged signal change across items. When we restricted our analysis to category-specific regions in the VVC, we observed reliable age differences in category specificity, with older adults showing lower levels of categorical specificity than young adults. Again, this observation confirmed results from previous studies (Carp, Park, Polk, & Park, 2011; Koen et al., 2019; J. Park et al., 2010). However, when we used a whole-brain searchlight procedure and directly searched for age differences in category specificity, we did not observe age-related neural dedifferentation, but instead identified one region with higher categorical specificity in the older than in the younger adults. This result challenges the relevance of prior findings that used predefined regions of interest within the VVC, often based on univariate analysis, and suggest that age differences in categorical specificity may be more locally restricted (i.e., to category-specific regions in the VVC) and less pronounced than previously thought. One possible explanation is that the engagement of category-specific brain regions is more relevant for the representation of abstract category information, and contains little information about specific items.

In order to target specificity of neural representations on the item level (i.e., item specificity), we compared activation patterns across stimulus repetitions in relation to their similarity to different stimuli of the same category (cf. Hasinski & Sederberg, 2016; Koen & Rugg, 2019). Thus, this analysis focuses on age differences in the stability of item representations while correcting for possible age differences in between-item similarity. (Note that between-category distinctiveness does not contribute to this analysis.) We found clear evidence for age group differences in item-specific neural activation patterns in occipital regions, suggesting that older adults' neural representation of item-specific information over and beyond categorical differences is indeed reduced compared to young adults. In sum, our results suggest that age differences in neural information representation coexist at various levels, i.e., at the level of item representation and the level of category representation. In particular, whether neural dedifferentiation occurs at the item level is an ongoing debate. Previous studies with young adult samples demonstrated that item specificity was positively related to subsequent memory (Hasinski & Sederberg, 2016; Xue et al., 2010), suggesting that reduced item specificity may result in poorer memory performance. We argue that a predefined focus on category-specific regions in the VVC prevented previous studies to reveal age differences in item-level specificity. Instead, the current study suggests that age differences in item specificity are most prominent in occipital regions (faces: bilateral intracalcarine cortex, lateral occipital cortex, and occipital fusiform cortex; houses: bilateral lingual gyrus, intracalcarine cortex, and left occipital fusiform cortex; see Figure 18), and probably reflect differences in early processing of the incoming information which has in turn detrimental consequences for downstream processing. Occipital regions are involved in visual processing, for example, together with the fusiform gyrus, the lateral occipital cortex has shown to be critical for visual object (including face) perception (Grill-Spector & Malach, 2004; Grill-Spector et al., 1999; K. Nagy, Greenlee, & Kovács, 2012). Furthermore, the occipital face area, which is connected to the FFA and lateral occipital cortex, constitutes the lowest level in the face perception network and is suggested to represent and integrate facial components (Kadosh, Walsh, & Kadosh, 2011; K. Nagy et al., 2012; Pitcher, Walsh, Yovel, & Duchaine, 2007; Pitcher, Walsh, & Duchaine, 2011). Thus, precise item-specific activation patterns in these regions are likely to be related to the ability to subsequently recognize the items based on specific perceptual features. Furthermore, sensory and cognitive functions have been shown to be increasingly linked to each other in the course of aging, which further reinforces the close connection of age-related deficits in perceptual processing and declining cognitive abilities (Baltes & Lindenberger, 1997; K. Z. H. Li & Lindenberger, 2002; Lindenberger & Baltes, 1994; B. A. Schneider & Pichora-Fuller, 2000). The current study substantiates this association by identifying reduced representational specificity coexisting at different representational levels but most prominently in early visual regions, which was furthermore linked to inter- and intra-individual differences in memory performance.

Inter- and intra-individual differences in neural distinctiveness are related to memory performance

Our results suggest that neural dedifferentiation coexists at both the level of category information as well as item information. However, the mere observation of age differences does not necessarily imply an important role for cognition. A few recent studies have explicitly addressed the relation between representational distinctiveness and memory performance. Most of these asked whether between-person differences in neural distinctiveness (ranging from categorical selectivity to item specificity) account for inter-individual differences in memory performance and whether this relation is age-invariant or differs by age group. For example, Koen et al. (2019) reported that neural distinctiveness in the PPA (measured as univariate activation differences and multivariate pattern similarities) was linked to memory performance across participants, but this relationship was not moderated by age. They argue that age-invariant associations might challenge (Koen et al., 2019) but do not preclude (Koen & Rugg, 2019) the notion that neural dedifferentiation is a determinant of cognitive aging. In any case, the findings highlight the importance of accurate category-level representations for memory success. Of course, a related yet different question is whether within-person variation, that is, item-level differences in distinctiveness, also relates to memory performance in terms of subsequent memory effects, and whether this relation differs by age group. Evidence for an age-differential relation between the similarity of neural representations and subsequent memory performance was recently provided by Sommer et al. (2019). Using pattern similarity analysis on EEG time–frequency representations, the study showed that higher similarity between neural patterns during scene–word pair encoding was related to subsequent memory (cued recall) performance in older adults, whereas lower similarity was related to subsequent memory in young adults. This finding provides evidence that young and older adults differed in the neural representational properties that benefited their memory encoding and thus led to successful retrieval. However, a comprehensive account how age differences at different representational levels jointly contribute to differences in memory performance has not yet been provided.

Our results show that neural distinctiveness at various representational levels is positively related to memory performance. We found that high-performing young and older adults showed highly category-selective neural processing in the VVC, that is, larger BOLD amplitudes for preferred than for non-preferred stimuli compared with lower performing participants (see also Koen et al., 2019). We did not observe such a relationship when using multivariate analysis focusing on differences between stimuli belonging to different categories, suggesting that categorical distinctiveness of specific items may be less relevant for recognition performance (in contrast to Koen et al., 2019). However, we found a clear relationship between item-specific neural activation patterns in occipital regions and memory performance, again independent of age group, supporting our argument that item-level representational specificity is an important determinant of memory performance.

To delineate the joint contribution of category selectivity, category specificity, and item specificity for memory performance, we used a PLS analysis with memory performance and age group as dependent variables. This analysis revealed a reliable latent distinctiveness score that compromised the three representational levels. The latent distinctiveness score showed high correlations with age group ($r = 0.65$) and with memory performance ($r = 0.41$), indicating that lower neural distinctiveness is more common in older adults and low performing individuals. Importantly, item specificity was the strongest contributor to the latent distinctiveness score. Thus, while our results nicely illustrate the coexistence of age differences at different representational levels, they clearly identify item specificity in early visual areas as the driving force for inter-individual differences in memory performance and age differences. Since the recognition memory task used in the current study required participants to distinguish between highly similar face and house exemplars, rather than simply discriminating faces from houses, high item specificity was required to perform well. Category selectivity instead may rather be a general indicator of representational quality and a potential downstream effect of item-specific perceptual representations.

Our results further revealed the importance of item specificity for memory both for performance differences between persons as well as for the mnemonic fate of single items, that is, subsequent memory effects at the within-person level. In line with others we defined item specificity as the comparison of activation patterns across stimulus repetitions in relation to their similarity to different stimuli of the same category (cf. Hasinski & Sederberg, 2016; Zheng et al., 2018; Xue et al., 2010). In that way, item specificity is a joint effect of representational stability and representational distinctiveness. Thus, theoretically, reduced item specificity in old age may be due to decreased item stability (Zheng et al., 2018), increased within-category similarity (Goh et al., 2010), or both (cf. Koen & Rugg, 2019). However, the computational model by Li and colleagues suggests that item-level specificity in older adults is reduced due to increased variability, thus reduced item stability. In line with this proposal, we observed that age differences in item specificity were due to a reduction in item stability in the older age group, whereas no age differences were observed for between-item (within-category) similarity. Furthermore, higher item stability was related to a higher probability of later recognition, thus, displayed an age-independent relation to memory. Higher item stability in young than in older adults in visual regions has been related to subsequent memory effects as reported by one previous age-comparative study (Zheng et al., 2018), however, the validity of that finding has been doubted by others (Koen & Rugg, 2019) since age differences in item specificity were not reliable. Our results clearly align with these prior results and speak to the necessity of acknowledging the important contributions of item specificity and item stability to age differences in memory performance.

Neural dedifferentiation as a consequence of age-related neurotransmitter changes

In the current study, we proposed that age differences at various representational levels coexist based on a computational model (S.-C. Li & Sikström, 2002; S.-C. Li et al., 2000, 2001) that proposes deficient neuromodulation as the causal mechanism for reduced neural information processing fidelity with ensuing consequences for representational distinctiveness and age-related cognitive deficits. Of course, in the current study the causal mechanism underlying the observed representational differences at the various levels remains speculative. Nevertheless, evidence from other studies support the proposal of age differences in neuromodulation as a driving factor for neural dedifferentiation. While the original proposal emphasized age-related changes in dopamine (cf. Abdulrahman et al., 2017; Bäckman, Nyberg, Lindenberger, Li, & Farde, 2006; Bäckman et al., 2010; S.-C. Li et al., 2001; Rieckmann, Johnson, Sperling, Buckner, & Hedden, 2018; Wong et al., 1984), more recently, several studies have revealed the contribution of age-related declines in gamma-aminobutyric acid (GABA) to cognition and neural information representation (cf. Leventhal et al., 2003). For example, using MR spectroscopy to quantify GABA concentrations in occipital voxels, Simmonite et al. (2019) found that lower occipital GABA levels in older adults were associated with declines in fluid processing abilities. Furthermore, Chamberlain et al. (2019) reported that individual differences in the category specificity of face versus house representations were linked to individual differences in VVC GABA concentrations in older adults, indicating a contribution of GABA in age-related neural dedifferentiation (see also Cassady et al., 2019; Gagnon et al., 2019; Lalwani et al., 2019). These findings substantiate the key role of proficient (particularly GABAergic) neuromodulation for high-fidelity neural representation and cognitive performance, with age-related deficits in neurotransmission being related to neural dedifferentiation across representational levels and cognitive decline.

Conclusion

The present fMRI study investigated age differences in the neural information representations supporting episodic memory performance. We provided a comprehensive account of age differences at different representational levels ranging from category selectivity to item-level specificity and stability and delineate their contribution to memory performance in young and older adults. Combining conventional ROI-based univariate analysis and whole-brain multivariate pattern similarity analysis we showed that age differences in representational distinctiveness coexist at various levels, and take the form of reduced category-selective neural processing in VVC regions, and reduced specificity of distributed item-specific activation patterns in occipital areas. A multivariate distinctiveness score revealed the joint contribution of both categorical distinctiveness and item specificity to memory performance and age group differences, with item specificity being the strongest contributor to the latent distinctiveness score. The particularly important functional role of item specificity for memory performance was further supported by subsequent memory effects with later remembered items showing higher item specificity than not remembered ones. Age differences in occipital item specificity were largely due to reduced representational stability across repetitions in older adults. We argue that our results are in line with the assumptions of computational models, namely that increased neural variability manifests as degraded item representations in early visual areas and reduced category selectivity during aging. Longitudinal studies are needed to elucidate to what extent the different levels depend on or precede each other, and whether a general mechanism (e.g., changes in neuromodulation) accounts for changes in representational properties.

Supplemental material

Less selective repetition suppression in older adults diminishes selectivity scores during second encoding

Reduced BOLD responses in a neural population after repeated stimulus presentation are suggested to indicate the formation of an internal representation (Koen & Rugg, 2019; Rugg & Doyle, 1994). If repetition suppression therefore predominantly occurs for the preferred image category in category-selective neural areas, this would underline neural differentiation. To investigate age-related differences in repetition suppression, we calculated the difference between BOLD responses from the first to the second encoding run for faces and houses. Crucially, a 2 (Age Group) × 2 (ROI) × 2 (Image Preferredness) mixed factorial ANOVA with repetition suppression as the dependent variable revealed a significant main effect for image preferredness ($F(1,65) = 8.48$, $p = 0.006$) and a two-way interaction between image preferredness and age group ($F(1,65) = 6.25$, $p = 0.015$). Since we found no other significant effects (ps < 0.190) including all main and interaction effects of selected ROIs, repetition-related activity changes were averaged across ROIs to conduct further post hoc t-tests. Contrasting averaged repetition suppression over all participants showed that repeated encoding resulted in larger repetition suppression for images from preferred compared to non-preferred categories ($t(66) = 2.91$, $p = 0.005$). Testing both groups separately showed that this selective repetition suppression for preferred images was evident in young adults ($t(34) = 4.83$; $\mathrm{p} < 0.001$), but not in older adults ($t(31) = 0.24$, $p = 0.810$).

We assumed that the observed age differences in selective repetition suppression confounded the analysis of category selectivity in the second encoding run. Higher selective repetition suppression reduces the difference between the magnitude of neural responses to preferred and non-preferred image categories. As young adults showed higher selective repetition suppression than older adults, this may indicate that age differences in selectivity scores are reduced in the second encoding run. To unravel age differences in selectivity scores after repeated encoding, we calculated a 2 (Age Group) × 2 (ROI) mixed factorial ANOVA on selectivity scores during second encoding as the dependent measure. In contrast to initial encoding, selectivity scores did not differ between young and older adults during second encoding ($F(1,65) = 3.71$, $p = 0.058$). Furthermore, there was no difference between ROIs ($F(1,65) = 3.17$, $p = 0.080$) and no interaction between age group and ROI ($F(1,65) = 0.55$, $p = 0.459$). Taken together, our findings underline that selective repetition suppression is reduced in older adults emphasizing age-related neural dedifferentiation. However, selective repetition suppression may confound other measures. Therefore, category-selective processing and category representation specificity was calculated on the initial encoding run only.

7 Discussion

This dissertation addresses the neural factors that support successful episodic memory encoding across the lifespan. Based on the hypothesis that the quality of the neural representations during memory formation crucially influences later retrieval success, the studies in the preceding chapters asked the following questions:

1. How are the neural representations during encoding, particularly their distinctiveness and stability, related to memory performance?
2. How do the neural indicators of successful episodic memory formation differ across the lifespan and potentially explain performance differences between age groups?

In my dissertation, I aimed to answer these questions using different neural and behavioral measures. In Study I, I investigated the neural correlates of memory formation using ERP repetition effects in relation to item-specific versus general concept memory in children, young adults, and older adults. In Study II, I linked the global similarity of time-resolved neural representations (EEG time–frequency patterns) to subsequent memory in a cued associative recall task for young and older adults. In Study III, I examined the specificity and stability of spatial neural representations (fMRI BOLD patterns) at the item and category level in association with old/new recognition performance in young and older adults. Through these means, I studied how the neural representations during encoding explained inter-individual (Studies I and III) and intra-individual (Studies II and III) differences in memory success in children, young adults, and older adults.

In this discussion, I will summarize my findings and integrate them into the current state of scientific knowledge. First, my focus will be on the general question of how neural representational properties support episodic memory (that is, across age groups or in young adults, as will be denoted). Second, I will discuss age differences in the relationship of neural representations and memory performance between children, young adults, and older adults. Third, I will acknowledge and comment on the methodological challenges and limitations of age-comparative cognitive neuroscience in general and of the current studies in particular. Finally, I will provide general conclusions and directions for future research.

7.1 How neural representations shape memory

The way information is encoded into neural representations and the properties of these representations influence whether and how well information will be remembered in the future (cf. Rissman & Wagner, 2012; Tulving, 2007; Xue, 2018). The three studies in this dissertation carefully delineate the relation between brain activity during memory encoding and later retrieval performance. Specifically, they revealed neural indicators of why an individual can remember some information better than other information (Studies II and III) as well as why some individuals have overall better memory capabilities than others (Studies I and III). Study I showed that the neural sensitivity to stimulus repetitions reflects memory specificity, the degree to which subjects were able to distinguish highly similar contents, thereby indicating the fidelity of the underlying memory representations. Studies II and III directly examined the properties of the neural representations during memory acquisition and found that their distinctiveness from other representations (Studies II and III) as well as their stability over time (Study III) were positively associated with memory, namely with cued recall (Study II) and recognition (Study III) performance. Adding to this, Study III furthermore investigated representations at different specificity levels, revealing that especially the amount of represented item information, rather than general concept information, relates to how well items will be remembered.

The current findings indicate that the fidelity in which sensory input is represented may determine how well details about it will be retrievable in the future (see also Rissman & Wagner, 2012; Watanabe et al., 2011; Xue et al., 2010; Xue, 2018; Zheng et al., 2018). The memory system has to balance the level of memory specificity and generalization, that is, the ability to recollect specific aspects of past events which enables the differentiation of highly similar memories versus the abstraction from event-specific details to a more general level that can be applied to future events, both of which are important abilities that enable survival (Keresztes et al., 2018; McClelland & Rumelhart, 1985; Norman & O'Reilly, 2003; Xu & Südhof, 2013; Yassa & Stark, 2011). Failing to remember specific details may result in interference from similar events and false memories (e.g., Favila et al., 2016; Koutstaal & Schacter, 1997). Thus, studies that use very similar stimuli that need to be differentiated by the participants are able to measure the specificity of acquired memories. Studies I–III employed in part highly similar stimuli (object exemplars in Study I, scenes asssociated with words in Study II, face and house exemplars in Study III) and in all tasks, participants benefited from encoding specific details rather than the general gist, especially in the mnemonic similarity task used in Study I (Stark et al., 2013, 2019). Versions of the mnemonic similarity task have been used to measure the behavioral bias toward pattern separation and completion

(Keresztes et al., 2017; Kirwan & Stark, 2007; Stark et al., 2019). Study I showed that participants across age groups (school children, young adults, older adults) were more often able to discriminate previously seen items from similar lure items than not (cf. Keresztes et al., 2017; Ngo et al., 2018; Rollins & Cloude, 2018, in contrast to younger children: Rollins & Cloude, 2018). That is, compliant with the task instructions, they showed an overall bias toward pattern separation, which was, however, significantly reduced in older adults (cf. Stark & Stark, 2017; see next section for details concerning age differences). Furthermore, we found that highly specific item memory, which includes lure discrimination, was related to the magnitude of neural repetition suppression and enhancement, two effects that have previously been linked to implicit memory (Doniger et al., 2001; Gotts et al., 2012; Henson et al., 2000; Henson & Rugg, 2003; Wiggs & Martin, 1998) but so far only inconsistently to explicit memory (e.g., Rugg, 1990; Turk-Browne et al., 2006; A. D. Wagner et al., 2000; Ward et al., 2013). Thus, we showed that the repetition sensitivity of neural activity is an indicator of representational fidelity that accounts for inter-individual differences in memory specificity. Furthermore, this brain–behavior relationship showed to be consistent across the lifespan. The reasons why this study was able to identify an association between repetition effects and explicit memory while others were not may include the large heterogeneity of the lifespan sample and, more importantly, the particular focus on very specific memory formation (versus, for example, simple old/new recognition memory, cf. Ward et al., 2013). In support of this, there was no relation between ERP repetition effects and mere category memory in Study I, as well as between fMRI repetition effects and old/new recognition in Study III (supplemental analyses; see below). Hence, repetition-related differences in neural activation may not reflect explicit memory formation in general (therefore the mixed evidence) but particularly the formation of highly specific memories that relies on the precise encoding of perceptual details. These findings extend our knowledge on the significance of encoding mechanisms that facilitate the formation of high-fidelity memory representations and thus enable highly specific recognition and item distinction across the lifespan.

To further scrutinize what makes a neural activation pattern a high-fidelity representation, Studies II and III directly examined the neural representational properties supporting successful memory formation. In line with the literature, the neural representation of a stimulus was defined as the pattern of neural activity it elicited during encoding (e.g., Carp, Park, Polk, & Park, 2011). High fidelity entails that different information elicits distinct neural representations (representational distinctiveness), whereas identical information is represented by stable, similar neural patterns (representational stability), which are the two main representational properties addressed in this dissertation.

Regarding representational distinctiveness, Study II showed that young adults' memory performance benefited from forming distinct (dissimilar) neural representations during encoding. Specifically, the neural representations while studying scene–word pairs that showed the highest dissimilarity between earlier and later trial time points were those that were best remembered by young adults. This positive effect of distinctiveness for young adults in Study II may have been especially pronounced in the given task in which participants were instructed to memorize the presented scene–word pairs by using a mnemonic imagery strategy, that is, by creating unique mental images of the studied material. Successfully doing so, as was the case for young adults, formed more distinctive memory representations, diverging from one another during the time of encoding, for those items that were subsequently remembered than those that were not remembered. This is in line with the predictions and findings that cognitive performance profits from neural distinctiveness (e.g., Koen et al., 2019; Kuhl et al., 2012; S.-C. Li et al., 2000; S.-C. Li & Lindenberger, 2006). However, the opposite relationship could have also been expected on the basis of cognitive models suggesting that memory strength arises from the *similarity* between memory representations (Clark & Gronlund, 1996; Hintzman, 1984; Humphreys, Bain, & Pike, 1989). Based on the understanding of memory as a network of nodes that are connected by the features they share (Arbib, 2002; Raaijmakers & Shiffrin, 1992), representations that are closer to each other in this memory space, that is, more similar, should be associated with better memory than representations farther apart. Accordingly, previous studies showed that high global representational similarity between neural patterns was positively related to memory performance (e.g., Davis, Xue, et al., 2014), which was only observed for the older adults group in Study II (see below). However, at the same time there may be a drawback of similarity, such as stronger interference between memories (M. C. Anderson, 2015; Chanales et al., 2017; Favila et al., 2016; Postman & Underwood, 1973), which may explain why older adults, although they benefited from similar representations, remembered significantly fewer pairs than young adults who relied on representational distinctiveness. Taken together, it may not be the absolute (dis)similarity between neural representations that shapes memory but the right balance of being similar yet distinctive, which may also depend on the goals and strategies during learning. These findings enhance our understanding of the relationship of neural representations to each other as a representational property that influences the memory fate of the respective contents.

In addition to (absolute) similarity or dissimilarity as such, another aspect of representational fidelity is the specificity of neural representations, which was investigated in Study III. Representational specificity, as defined in Study III, means that related information is represented more similarly than less related information. Accordingly, neural patterns contain category-specific information if they are more similar to each other in response to items from the same category as opposed to items from different categories (cf. Kuhl et al., 2012). Furthermore, neural representations are item-specific if their stability over repetitions is higher than their similarity to representations of other, similar items (cf. Hasinski & Sederberg, 2016). In Study III, young and older adults indeed showed category-specific as well as item-specific representations of faces and houses, while especially item specificity was associated with memory and reduced in older adults (see below; cf. Zheng et al., 2018). In particular, item specificity in occipital regions was linked to later recognition, demonstrating that accurate representation of item-specific details already during early visual processing "determined" the further quality of the memory representations. Thus, differences in item specificity of the neural representations during encoding could explain differences in memory outcomes within and between participants across the adult lifespan. By focusing on brain regions that show category-selective processing, earlier studies may have underestimated the significance of item specificity in lower visual areas for memory (cf. Koen et al., 2019; J. Park et al., 2010). All in all, the findings of Study III improve our comprehension of the coexistance of information representation at different specificity levels and their joint contribution to memory performance in young and older adults. Together, Studies I–III indicate that in order to make highly specific memory judgments, high-fidelity memory representations need to be acquired that not only contain general but profound item-specific information.

One essential part of forming high-fidelity item-specific neural representations is that the representations are stable over time, indicated by accurate reactivation of the underlying neural activity patterns when information is re-encountered or remembered (e.g., Kuhl & Chun, 2014; Michelmann et al., 2018; Xue, 2018). This was reflected in a positive relationship between the item stability of neural representations and memory performance in Study III (see also Y. Lu et al., 2015; Ward et al., 2013; Xue et al., 2010). Specifically, both young and older adults' recognition performance profited from high representational stability, measured as within-item pattern similarity across repeated encoding. First, highly stable neural patterns may generally indicate high-fidelity representation, reflecting that the information has been encoded in a precise and reproducible manner, which is beneficial for memory. Second, the precise reactivation during repeated exposure itself may strengthen and further stabilize the underlying memory representation allowing for successful later retrieval (Sievers et al., 2019; Xue et al., 2010; Xue, 2018). Furthermore, it can be speculated that neural representations that show high stability across repeated encoding are likely to also show stable reactivation during retrieval, which would further explain why they were more likely to be associated with correct recognition (cf. Kuhl et al., 2011; Michelmann et al., 2016; Ritchey et al., 2013; Staresina et al., 2012).

Representational item specificity involves both of the two representational properties discussed in this dissertation, namely the distinctiveness and stability of neural activation patterns, and how they relate to and differ from each other. In particular, according to the way item specificity was measured in Study III and other studies (e.g., Hasinski & Sederberg, 2016; Zheng et al., 2018), if a representation is item-specific, this means that its stability over time is higher than its similarity to other representations (cf. Poh & Chee, 2017; Xue et al., 2010; Zheng et al., 2018). Moreover, the higher the item specificity of a given representation, the larger the difference between its stability and its similarity to other representations. That is, theoretically, some representations may be item-specific – and thus associated with successful memory – because they are very stable and some because they are very distinct. Furthermore, lacking stability may be compensated through high distinctiveness, and vice versa. However, considering also the finding that high similarity between neural representations is actually beneficial for memory, too (see above; Clark & Gronlund, 1996; Davis, Xue, et al., 2014), item specificity may be mainly depending on high representational stability, rather than high distinctiveness. In line with this, Study III showed that the benefit of item specificity was primarily due to highly stable representations. Similar results have demonstrated that stability accounted for subsequent memory more than the global similarity of different representations (Ward et al., 2013), and that stability and global similarity had independent effects on subsequent memory (Davis, Xue, et al., 2014; Y. Lu et al., 2015). To sum up, both stability and distinctiveness independently of one another as well as their relationship, for example, their difference (i.e., item specificity), are representational properties that influence successful memory encoding and thus profit performance (see Figure 21).

The neural repetition effects observed in Study I and representational stability, measured as neural pattern similarity across repetitions, identified in Study III both revealed the importance of high-fidelity neural representations during memory formation. However, on the methodological level, repetition effects and representational stability rely on seemingly contradictory assumptions and it is an unsolved question of how they may relate to each other (e.g., Ward et al., 2013). Whereas repetition effects mark differences in neural activity upon repeated presentations, representational stability is characterized by high similarity in neural activity between repetitions, both of which are associated with positive effects for memory. However, repetition effects describe an overall increase or decrease in the averaged univariate magnitude of the neural response (e.g., measured as ERP in Study I or BOLD activity in the supplements of Study III). In contrast, representational stability takes into account the whole multivariate pattern of neural activation (e.g., distributed BOLD patterns in Study III) which is independent of overall magnitudes. That is, in principle, although the overall activation magnitude changes from first to repeated stimulation, the similarity (e.g., correlation) between the distributed neural representations can still be high if the pattern of (relatively) high and low activation remains. However, it has also been suggested that it may be particularly the most selective neural units that show reducd activation by repeated input (Barron, Garvert, & Behrens, 2016; Grill-Spector et al., 2006; L. Li, Miller, & Desimone, 1993), resulting in a smaller or no magnitude difference between higher and lower activated units. Alternatively, it has been suggested that the lower activated neural units are the ones that are suppressed, leading to even less engagement during repetitions and thus a sparsening of the underlying neural representation (Grill-Spector et al., 2006; Norman & O'Reilly, 2003). Both of these possible mechanisms would change the overall pattern of activity and would result in relatively low pattern stability. Given that Studies I and III assessed repetition effects and representational stability in very different modalities, it is hard to speculate what their exact relationship is. However, in supplemental analyses of Study III, we also looked at repetition effects in the BOLD responses in category-selective VVC regions. Here, the effect of repetition suppression was found to be category-selective in young adults, that is, more pronounced for the preferred stimulus category than for the non-preferred category, which resulted in overall less category-selective responses for the repeated stimulus blocks (repetition effects were measured on the level of repeated stimulus presentation blocks and not the level of individual items). Despite these selective suppression effects in the *VVC*, representational stability in *occipital* areas was high, suggesting that repetition effects and pattern stability may coexist in disparate brain regions involved during encoding. So far, to my knowledge only one study (Ward et al., 2013) directly compared repetition effects and representational stability. In contrast to our results, they found that suppression effects and pattern stability co-occurred in overlapping occipitotemporal regions. Interestingly, whereas repetition suppression predicted implicit memory performance, pattern stability predicted explicit memory performance (within-person). Thus, their results suggest that these effects track different aspects of neural representations during encoding. As opposed to this, the observations of Studies I and III and other studies suggest that both repetition effects (e.g., Turk-Browne et al., 2006) and stability (e.g., Xue et al., 2010) can be positively related to (explicit) memory . More studies are needed to solve this conundrum and explicitly address the association of repetition effects and representational stability in relation to memory performance. The results so far may suggest that both phenomena can co-occur, whereby the stability of neural representations is a reliable neural indicator of memory performance – supported by Study III and other work (e.g., Y. Lu et al., 2015; Xue et al., 2010) – and neural repetition effects capture representational qualities more indirectly and thus show a less consistent association to behavior.

Mnemonic representations as examined in the presented studies were based on different, complementary aspects of the neural code in which information is written and retained in neural activity. In the (mainly) temporal code of EEG amplitude changes over trial time assessed in Study I, small-scale differences in the timing and magnitude of responses were detectable, which was therefore well suited for investigating the formation of memory representations indicated by neural repetition effects. In that way, alterations at specific and well-established ERP components could be identified, namely those associated with, for example, stimulus categorization, familiarity, and contextual integration (Curran, 2004; Friedman, 2000; Friedman & Johnson, 2000; Lawson et al., 2007; Mecklinger, 2000; Rugg & Doyle, 1994; Van Petten & Senkfor, 1996). These specific neurocognitive mechanisms may be critical for integrating information into a coherent representation, and thus enabling detailed memory encoding. Furthermore, oscillatory neural activity has been shown to be critical for high-fidelity content representation (e.g., Griffiths, Mayhew, et al., 2019; Zhang et al., 2015) and memory formation (e.g., Düzel et al., 2010; Fell & Axmacher, 2011; Hanslmayr & Staudigl, 2014; Sander et al., 2020). In Study II, we investigated the similarity of EEG time–frequency patterns, taking into account the highly dynamic nature of neural activity by including power at a broad range of frequencies across trial time and electrodes. Comparing these patterns allowed a fine-grained examination of the similarity between neural representations, also between different time points during the encoding of a stimulus (i.e., within-trial; cf. King & Dehaene, 2014). As such, we were able to observe that young adults' memory performance profited from pattern dissimilarity between earlier and later time points, indicating a differentiation of memory representations in the course of successful memorizing, a finding that would not have been detectable without the applied time–time similarity analyses. In contrast, the vast majority of previous studies primarily focused on spatial activation patterns when investigating the nature and quality of neural information representation, neglecting the temporal dynamics of neural coding, a gap in the literature that our study helps to close. However, the high temporal resolution of EEG comes at the price of poorer spatial resolution, allowing only a broad differentiation of regions across the cortex in Studies I and II. In comparison, the fMRI BOLD signal assessed in Study III could localize neural activity at precise, also subcortical, areas which enabled the study of neural representations as spatially distributed activation patterns at various regions throughout the brain. Thus, we could identify that it was the item specificity of neural representations in occipital cortex that was related to later memory success, indicating the significance of accurate information representation during early visual processing for the quality of downstream higher-order representation and possibly later consolidation mechanisms. To sum up, making use of different brain recording and analysis techniques allowed us to study neural representations from different perspectives, focusing rather on temporal, spectral, and/or spatial aspects of neural representational properties and how they may influence memory encoding. Albeit approaching the neural representations underlying episodic memory from largely different angles, our findings reveal a consistent picture. Studies I–III jointly demonstrate the importance of accurate and specific neural representations for memory performance.

Altogether, we show that neural activity during memory acquisition reflects and potentially determines whether memory representations are formed in such a manner that the respective contents can be remembered in the future (cf. Brewer et al., 1998; Rissman & Wagner, 2012; Xue, 2018). Specifically, we identified (1) repetition sensitivity as a (age-independent) neural indicator of inter-individual differences in the successful encoding of item-specific details. Furthermore, we showed that (2) the relation of different neural representations to each other, in terms of their absolute similarity as well as their specificity, and (3) their stability over time are important neural properties that are related to memory success. In particular, the right balance between similarity and distinctiveness of neural representations benefits subsequent memory performance, which may be inclined towards representational distinctiveness in situations in which focusing on unique details is required (at least for young adults; see next section). Moreover, the accurate neural representation of item-specific details, which entails larger representational stability than similarity to other representations, accounts for memory differences within and between individuals. All in all, our results emphasize the importance of the fidelity of neural representations for episodic memory performance.

7.2 Age group differences in neural representations and their contribution to memory performance

Differences in episodic memory performance across the lifespan are associated with age differences in brain structure, function, and neurochemistry (Bäckman et al., 2010; Cabeza et al., 2017; Casey et al., 2000; Fjell & Walhovd, 2010; Grady, 2012; Keresztes et al., 2017; Ofen et al., 2007; Ofen & Shing, 2013; Sander et al., 2020). It is plausible to assume that such widespread changes cause age differences in the way information is neurally represented. Here, I discuss to what extent performance differences between age groups may be explained by differences in the neural representational properties indicating successful memory formation as elaborated above. In the discussed studies, we mainly compared samples of young (18–30 years old) and older (63–76 years old) adults (Studies I–III) as well as a group of children (7–9 years old; Study I).

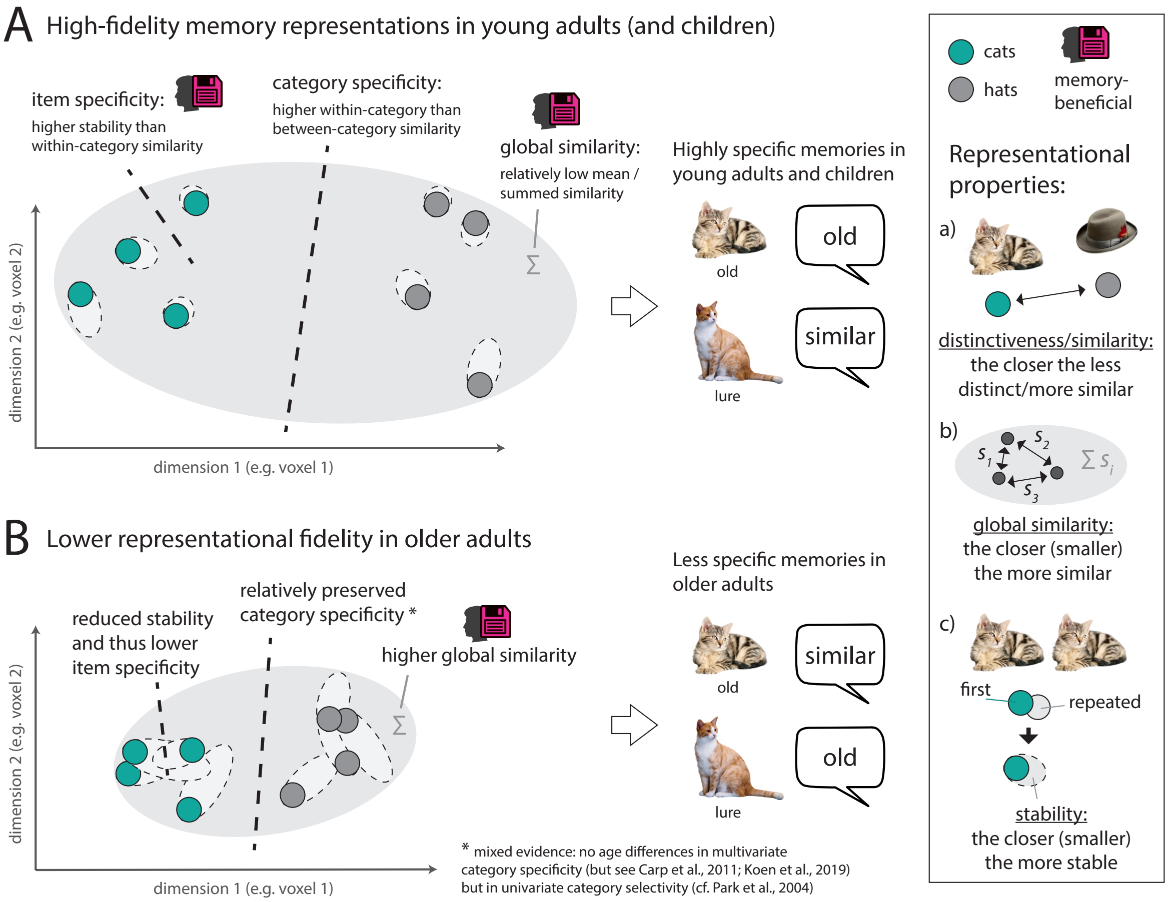
In line with the neural dedifferentiation hypothesis of cognitive aging (Carp, Park, Polk, & Park, 2011; Koen & Rugg, 2019; Koen et al., 2020; J. Park et al., 2012), we found less distinctive neural representations in older adults compared with young adults across different brain recording and analysis approaches as well as representational levels. In Study II, we measured the global similarity between the neural time–frequency patterns elicited by different items during memory encoding. The general age group comparison, independent of memory, revealed that neural patterns were less distinct, that is, more similar to one another, in older compared with young adults. In Study III, age-related dedifferentiation was identified as reduced univariate category selectivity in the VVC (cf. D. C. Park et al., 2004) and less item-specific distributed neural patterns in occipital areas during encoding (cf. Zheng et al., 2018), while evidence for less category-specific multivariate spatial patterns in the VVC was less clear (cf. Koen et al., 2019). These results corroborate the literature (for a review, see Koen & Rugg, 2019) and suggest that declining fidelity of neural representations, in the form of lower distinctiveness, is a common pattern in old age that occurs in several brain regions in both temporal and spatial representations (S.-C. Li et al., 2001; S.-C. Li & Sikström, 2002).

Besides a general loss of representational distinctiveness in old age, the notion of age-related neural dedifferentiation assumes that this reduced distinctiveness is detrimental for cognitive performance (Koen & Rugg, 2019; Koen et al., 2020; D. C. Park et al., 2004), which in turn would mean that high distinctiveness benefits performance. Studies I–III show indeed that the fidelity of neural representations, which includes their distinctiveness, is critical for memory performance. However, regarding distinctiveness in the sense of dissimilarity between neural representations, the relationship to memory performance is more complex because also high similarity between neural patterns can be beneficial for memory (e.g., Davis, Xue, et al., 2014). Accordingly, our findings regarding the contribution of age-related neural dedifferentiation to memory performance need a more fine-grained elaboration. Although in Study II older adults showed more similar neural representations than young adults, their memory actually profited from forming these similar neural representations during learning. This finding may seem to oppose the assumptions of neural dedifferentiation, however, they show a within-subject association between distinctiveness and memory, whereas neural dedifferentiation is mainly assumed to explain differences between individuals, especially between young and older adults. The positive relation of similarity and memory is in turn in line with cognitive models of memory (Clark & Gronlund, 1996; Gillund & Shiffrin, 1984) that are supported by neural evidence (Davis, Xue, et al., 2014; LaRocque et al., 2013; Y. Lu et al., 2015; I. C. Wagner et al., 2016; Ye et al., 2016). This contrasted with the findings for young adults whose performance profited from distinct representations (see above). Besides the opposite directions, also the timing of the effects differed between young and older adults: In contrast to young adults' distinctiveness effect between earlier and later time points during encoding trials, older adults' similarity effect occurred during very early encoding time points. These results for older adults may indicate that they relied more on successful early gist extraction and more generalized memories overall (cf. Koutstaal & Schacter, 1997; Koutstaal et al., 2001; Tun et al., 1998), which is also supported by the finding that they used the instructed imagery technique less successfully than young adults (cf. Hertzog et al., 2012). Hence, the study may suggest that older adults' difficulty in memorizing the material by forming unique mental images was related to the formation of less distinct neural representations, which required them to rely on other strategies that are supported by more similar neural activity (cf. Gillund & Shiffrin, 1984; Hertzog et al., 2012), resulting in opposite relationships between performance and neural similarity in young and older adults.

In Study III, age differences coexisted at different representational levels, but memory performance of both young and older adults was mainly linked to the amount of item information represented by the neural activation patterns in occipital regions (see above). Although, in contrast to Study II, young and older adults in Study III did not show overall memory performance differences, the combination of higher age and poorer performance was associated with less item specificity. This finding provides evidence for age-related neural dedifferentiation as a factor contributing to performance decline. The observation that it is particularly item specificity that links to memory performance indicates that not only the relation of different representations changes during aging but also their stability. Indeed, Study III demonstrated that reduced item specificity was due to less stable neural representations across encoding repetitions for older adults. This finding underscores the significant role of altered neural stability for age-related cognitive deficits, which may promote differences in neural distinctiveness, such as the often observed reduced category specificity (e.g., Carp, Park, Polk, & Park, 2011; Koen et al., 2019). This pattern was also predicted in the computational model by Li and colleagues proposing that deficient neuromodulation made neural responses more variable, that is, less stable, and thus less distinct (S.-C. Li et al., 2000, 2001; S.-C. Li & Sikström, 2002). Accordingly, in Study III young and older adults' recognition memory benefited from high item specificity due to high representational stability (as opposed to high distinctiveness).

Together, Studies I–III provide evidence that the fidelity of neural representations decreases in old age, which manifests in generally less distinctive and less stable activation patterns during encoding (Studies II and III) as well as poorer lure discrimination performance (Study I) (see Figure 21). In Study III, the age-related neural differences occurred at both the level of specific items and more general category representations, but especially the former was able to explain inter- and intra-individual differences in memory performance (see 7.1; cf. Zheng et al., 2018). As highlighted previously, the significance of accurate representation of item-specific details may be especially pronounced in the studies discussed here as they required differentiation of highly similar stimuli, perhaps more than in other studies. Therefore, accurate representation of more general information may not have been sufficient to perform well in the present studies. The diminished representational fidelity in old age is assumed to underlie older adults' impaired ability to remember specific details, indicated by a stronger reliance on general concepts and similarities which leads to more false memories (Fandakova et al., 2018; Koutstaal & Schacter, 1997; Schacter et al., 1997). This was also observed in Study I where older adults more often confused similar lure items as known, which suggest a stronger tendency towards pattern completion (cf. Stark et al., 2013; Keresztes et al., 2017). All in all, we show diminishing representational quality during aging which is associated to memory performance.

With regard to the development of episodic memory during childhood and the maturation of the underlying brain structures and functions (cf. Casey et al., 2000; Keresztes et al., 2018; Ofen et al., 2007; Ofen, 2012; Tang et al., 2018), so far there has been much less focus on the quality of neural information representation compared to the literature on senescent development across adulthood. First evidence indicated that 5–7-year-old children already show adult-like representational similarity patterns (M. A. Cohen et al., 2019), and that 7–12-year-olds show similar distinctiveness of individual scene representations than young adults, which was positively related to memory performance (Fandakova et al., 2019). Adding to this, Study I suggests that children at age 7–9 are already able to form high-fidelity



* mixed evidence: no age differences in multivariate category specificity (but see Carp et al., 2011; Koen et al., 2019) but in univariate category selectivity (cf. Park et al., 2004)

Figure 21: Simplified summary of age differences in the fidelity of neural representations in relation to memory performance in Studies I–III. Neural activity patterns that represent certain information (for example, different exemplars of cats and hats) are illustrated as coordinates in multidimensional space (green: cats, gray: hats). The distance between representations denotes their distinctiveness (a). Global similarity (b), that is, the mean or summed similarity of all activity patterns, is illustrated as a light gray area including all representations in the space. Representational stability (c) is illustrated as the area in which the neural activation patterns vary across time (repetitions). **A.** Young adults' neural representations are item-specific, indicated by higher pattern stability than pattern similarity to other representations of the same category, which is illustrated as a dashed line separating single item representations. This item specificity shows to be beneficial for memory performance (at the within- and between-person level; Study III). Young adults' neural representations are category-specific, indicated by higher similarity of representations from the same category than representations from different categories, which is illustrated as a dashed line separating cat and hat representations. Young adults' global similarity is lower than that of older adults (see B) and their memory benefits from such distinct representations (at the within-person level; Study II). Together, these representational properties indicate high-fidelity representations in young adults, which shape their memory performance, including their ability to form highly item-specific memories (Study I). Children (7–9 years old) also show high memory specificity, indicating that their representational fidelity may already be similar to that of young adults (Study I). **B.** Older adults' neural representations are less item-specific which is mainly due to reduced pattern stability. Older age and lower item specificity are associated with lower memory performance, reflecting neural dedifferentiation as a factor contributing to age-related memory decline (Study III). It is likely that reduced item stability also leads to reduced category specificity, but evidence for age differences in category specificity are less clear. Older adults show higher global similarity (again indicating neural dedifferentiation) but, at the within-person level, they actually benefit from highly similar neural representations (Study II). Together, these representational properties indicate reduced representational fidelity in older adults, which manifests as lower memory specificity (e.g., lure discrimination; Study I).

representations, indicated by their high item memory and lure discrimination performance. Children's memory abilities were as good as young adults' (in the same task version; see 7.3) which is partially in line with the literature (Golarai et al., 2007). Also on the neural level, performance for children and adults was related to similar neural encoding mechanisms reflected in repetition suppression, suggesting a common neural indicator of memory acquisition across the lifespan (see 7.1). In contrast, children did not show any repetition enhancement effects, that is, higher neural activity in response to repeated stimuli. In adults, previous work suggested that ERP enhancement effects may be associated with contextual integration, working memory, and stimulus categorization (Friedman, 2000; Lawson et al., 2007; Rugg & Doyle, 1994; Van Petten & Senkfor, 1996), abilities that may not be fully developed in children (Fandakova et al., 2014; Káldy & Kovács, 2003; Raj & Bell, 2010). However, if this was the case, this would not have diminished children's performance in the task. Furthermore, the absence of repetition enhancement in children may also be due to deficient statistical power as the child sample in Study I was considerably smaller and they had fewer trials than the adult samples. Remaining questions include when and how children's neural representations develop with respect to the specific representational properties discussed in this dissertation, namely neural distinctiveness and stability (see also 7.4). All in all, the results for children suggest that at the age of 7 to 9 forming high-fidelity neural representations is already relatively mature, but further studies on the specific representational properties are lacking.

Besides adding to the sparse research on how memory representations develop during childhood, Study I is one of the few studies investigating memory and its neural underpinnings across the lifespan, that is, in more than two stages of life at once (cf. Fandakova et al., 2014; Sander, Werkle-Bergner, & Lindenberger, 2011, 2012; Shing et al., 2008). While developmental research on the neural and cognitive changes during maturation and aging are largely separated (Craik & Bialystok, 2006), integrated accounts on lifespan differences and changes are needed for a comprehensive understanding of the interplay of brain and cognition during lifespan development as well as in general (cf. Baltes, Lindenberger, & Staudinger, 2007; Lindenberger, 2001; Ofen & Shing, 2013; Sander, Lindenberger, & Werkle-Bergner, 2012; Shing et al., 2010; Shing & Lindenberger, 2011; Werkle-Bergner et al., 2006). In particular, senescence is not the reverse of childhood development (Craik & Bialystok, 2006), and accordingly, it is likely that the changes in neural representational properties associated with age-related improving and declining memory abilities differ between children and older adults. We made a start by examining how neural activity links to memory specificity in children, young adults, and older adults, laying the ground for further research on the specific neural representational properties supporting episodic memory.

To sum up, the findings in this dissertation demonstrate that children, young adults, and older adults show overall similar memory encoding mechanisms that enable them to form highly specific memory representations (Study I), while the specific properties of the neural representations during encoding differ between young and older adults (Studies II and III) (see Figure 21). In particular, old age appears to be accompanied by differences in the distinctiveness and stability of the underlying neural patterns that shape memory performance. In addition to their absolute similarity to each other, older adults' neural activity patterns represent less content-specific information, both at the category and item level, the latter of which is due to decreased representational stability and associated with inter- and intra-individual differences in recognition performance (Study III). All in all, the results indicate that 7–9-year-olds' neural representations already exhibit young adult-like fidelity, which is linked to high memory specificity, whereas older adults' representational qualities show substantial impairments that are associated with their declining memory abilities.

7.3 Challenges and limitations of behavioral, electrophysiological, and neuroimaging comparisons between age groups

The studies in this dissertation identified neural representational properties supporting memory performance and how differences therein relate to memory differences across the lifespan. However, comparisons between age groups encounter considerable challenges with respect to their ability to infer age-related *changes*, and both concerning the cognition and brain part of the investigated relationships. Here, I will discuss these difficulties and limitations and how we approached them in the studies of my dissertation.

First, challenges exist on the age side of the “age–brain–cognition triangle” (Raz & Lindenberger, 2011). Specifically, cross-sectional age group comparisons do not allow inference about age-related changes (Hertzog & Nesselroade, 2003; S.-C. Li & Schmiedek, 2002; Lindenberger & Pötter, 1998; Lindenberger, von Oertzen, Ghisletta, & Hertzog, 2011; Raz & Lindenberger, 2011; Rönnlund, Nyberg, Bäckman, & Nilsson, 2005; Schaie, Labouvie, & Buech, 1973). The reasons for this include cohort differences and sampling biases that can result in age differences that are not due to longitudinal development (Hertzog & Nesselroade, 2003; Lindenberger et al., 2011; Schaie et al., 1973). Thus, since longitudinal studies are needed to make claims about actual lifespan changes in memory and the relation to representational properties, we need to be aware that the results of our cross-sectional studies only speak to age group differences, not age changes. However, such age group differences or commonalities can nevertheless yield essential insights into the neural principles enabling cognition across the lifespan.

Furthermore, memory performance differs between age groups (Naveh-Benjamin & Ohta, 2012; W. Schneider, 2014; Shing et al., 2010) which is one of the main research interests in the studies presented here, and at the same time poses a serious challenge for the study paradigms used to investigate these differences. If designing an age-comparative study, one faces the dilemma of either using the same task for all age groups and risking ceiling or floor effects for a group, or adapting the task to be age-fair but introducing differences, for example, in task lengths, between groups. The former may give an indication of the magnitude of performance differences, for example, the absolute number of items subjects of different ages are able to remember, which may seem like an objective measure that compares behavior in the same task. However, because of the performance differences, the tasks are actually *not* the same between age groups. If a young adult can successfully remember 70% of presented items and an older adult only 40%, the older adult performed a considerably more difficult task. Differences in difficulty and thus performance level often confound differences in neural activation level (e.g., Nagel et al., 2009) and, importantly, strategies may differ by perceived difficulty (cf. Huber, 1985; Oxford, Cho, Leung, & Kim, 2004). If instead, the tasks were age-adapted such that both young and old can remember about the same relative amount of items, the tasks can be seen as similarly difficult. Irrespective of equal overall difficulty, age groups may still differ in their motivation during study participation. Whereas for (young) adults it may be relatively easy to perform a monotonous task and minimize movements for a certain time, children need to be more engaged and often cannot sit or lay still for long uninterrupted periods. This argues for age-adapted study designs, but also poses the question what amount and kind of age adaption accomplishes the desired outcomes, which usually requires extensive piloting. Furthermore, age adaption introduces further variance, for instance, in study length and statistical power. Nevertheless, age-adapted procedures are often the sensible choice and necessary to identify memory-relevant age differences in brain activity without the influence of confounding variables that are correlated with age and thus help to unconfound task and age (Rugg & Morcom, 2005). This is especially the case in tasks in which age differences are often large, for example, in memory recall, whereas other task conditions may not need age adjustments (cf. Old & Naveh-Benjamin, 2008).

In Study I, we adjusted the number of objects presented during the tasks such that for the children sample only half of the objects were used as compared with the adults samples. This was based on the experience and evidence (Betts, Mckay, Maruff, & Anderson, 2006; McAvinue et al., 2012) that children may have limited ability to sustain attention for a task that was originally developed for adults and was thus not very engaging for 7–9-year-olds. Besides fewer items, children had the chance to take more breaks. Together, these measures were taken to keep children motivated and divide the total amount of time they were asked to focus and keep still. Although it was still challenging to keep the children motivated for the duration of the tasks, they performed very well, in both the target detection during encoding that was supposed to ensure attention to the stimuli as well as the recognition memory task such that they showed even better relative performance than young adults. An independent group of young adults additionally performed the short children's task to ensure that children's better performance was due to the shorter task version and not due to overall better memory performance, which was supported by the results. However, due to the smaller number of trials (and technical issues that stopped data collection) for the children sample, we cannot completely preclude that neural differences between children and adults may be the result of deficient statistical power. For older adults, task adjustment was not needed as previous studies have shown limited performance differences between young and older adults when memory was tested as recognition (Old & Naveh-Benjamin, 2008), which was confirmed in the piloting for Study I. For the same reason, we did not adapt the tasks for young and older adults in Study III. To sum up, it was necessary to adjust the task lengths for children, although their memory performance was in general already comparable to adults, whereas the task was designed such that both young and older adults could complete the identical version. In the future, more engaging tasks would be desirable such that children would be able to stay motivated for a longer time period and could potentially perform the same task as adults.

Study II comprised learning of associations between unrelated images and words, followed by a cued recall task in which only the images were presented and young and older adults were asked to retrieve the respective words. In such demanding tasks, older adults often learn more slowly (i.e., they need more repetitions to learn the same amount of information; e.g., Li et al., 2004) and they reach their limit of acquisition earlier than young adults do (i.e., they remember fewer items; e.g., Rugg and Morcom, 2005). Potential ceiling-level performance in the young or floor-level performance in the older adults would fairly constrain the analysis of subsequent memory effects. In order to have both age groups within the same range of performance, we therefore (a) provided the older adults with an additional learning occasion and (b) reduced the number of items for the older adults to learn. Both manipulations aimed to equate performance between the age groups. The choice of the number of repetitions as well as the number of presented items was based on extensive pilot testing. The behavioral learning pattern reported in Study II was also successfully replicated in an independent (third) sample (Fandakova et al., 2020), indicating that the specific choice of our parameters was robust across samples. The choice of one additional study round for older adults was furthermore based on previous studies that successfully used and/or evaluated this kind of age adaption (Daselaar et al., 2006; Duverne et al., 2008; Li et al., 2004; Morcom et al., 2007). Moreover, participants practiced an effective learning strategy before initial encoding. Previous studies have provided evidence that without instructions, young and older adults spontaneously adopt different encoding strategies. Importantly, while young adults are more likely to encode items elaboratively, older individuals are more likely to employ non-elaborative, rote-based strategies (Craik and Simon, 1980; see Rugg and Morcom, 2005, for this line of argument). Thus, age-related neural differences are often confounded with differences in strategies. The explicit strategy instruction in Study II was used to minimize this confound and gain control over study processing (although young and older adults still may have shown some differences in strategy use, see above). In Studies I and III the possible effect of diverging strategies was addressed by incidental encoding tasks, that is, participants did not know that their memory would be tested later on. Under such conditions, memory differences have shown to be less pronounced than under intentional learning instructions (Old & Naveh-Benjamin, 2008). All in all, the age-adapted procedures helped to unconfound task and age and to identify age-related differences in neural representational properties associated with memory, independent of confounding variables that, “by virtue of their correlation with age, might masquerade as differences inherent to the aging process” (Rugg & Morcom, 2005, p. 132).

On the neural level, similar reasoning applies. When observing performance differences between age groups, interpreting main effects of age on associated neural measures may become inconclusive as it is not apparent whether the neural differences are an effect of age or performance (Rugg & Morcom, 2005; Rugg, 2017). Furthermore, unspecific age differences may influence brain signal recordings without being directly related to performance. For example, age differences in eye and head movements might alter the quality of the recorded EEG (Studies I and II) and/or fMRI (Study III) signal. EEG, in particular, has also been shown to be influenced by inter-individual differences in brain and skull anatomy (Frodl et al., 2001; Leissner, Lindholm, & Petersén, 1970; Segalowitz & Davies, 2004; Werkle-Bergner, Shing, Müller, Li, & Lindenberger, 2009) that can be especially pronounced between different age groups. For example, differences in synaptic density, myelination, and skull thickness can influence ERP and oscillatory amplitudes, which often show to be different between groups (Beauchamp et al., 2011; Hämmerer, Li, Völkle, Müller, & Lindenberger, 2013; Knott, Hazony, Karafa, & Koltai, 2004; van Dinteren, Arns, Jongsma, & Kessels, 2014; Werkle-Bergner et al., 2009). Increased myelination from childhood to adulthood has also been shown to influence MRI contrasts (Natu et al., 2019). Furthermore, fMRI is based on an indirect effect of neural activity on cerebral blood flow and blood oxygenation (H. Lu & Liu, 2017) and thus influenced by the neurovascular system which is known to change across the lifespan, especially during aging (D’Esposito, Zarahn, Aguirre, & Rypma, 1999; Farkas & Luiten, 2001; Gazzaley & D’Esposito, 2005; H. Lu et al., 2011). These age effects can be reduced by carefully screening participants for comorbidities (and their medications) that are known to affect the BOLD signal, for instance, hypertension (Gazzaley & D’Esposito, 2005). Crucially, the influence of confounding factors in both age-comparative EEG and fMRI studies can be minimized by refraining from interpreting main effects of age (Rugg & Morcom, 2005), for example, regarding absolute differences in neural activation. Thus, in Study I, we did not interpret the overall age differences in ERP amplitudes or the absolute amplitude differences as repetition effects but the standardized effect sizes. Furthermore, the observed relationship of neural repetition effects and memory performance was not due to overall age group differences but remained even when age differences were eliminated by standardizing both measures within groups. In Study III, the mere observation that older adults showed less specific neural representations across representational levels could be potentially due to any unspecific age differences, but the interaction with memory performance indicated which of the neural differences may be actually behaviorally relevant.

In addition, in all three studies we avoided to exclusively rely on *a priori* selected regions of interests or time windows, as would be common practice in, for example, ERP studies in young adults (cf. Fields & Kuperberg, 2019). Pre-selecting specific electrodes or time windows based on established effects in young adults may miss effects in other age groups that might appear at different topographies and/or latencies. Therefore, non-parametric data-driven permutation-based statistical analyses (Maris & Oostenveld, 2007; Oostenveld et al., 2011) were used in Study I to identify the spatiotemporal clusters in which ERP repetition effects occurred (for arguments in favor of such approaches in general, see Fields & Kuperberg, 2019). Likewise, we identified the time–time–electrode clusters in which similarity of the neural patterns appeared to be critical for memory in Study II as well as the voxel clusters that showed significantly different neural specificity between age groups in Study III. These analysis procedures also account for differences between groups such as the number of included trials (for example, due to age-adapted task designs or differences in data quality). In a similar fashion, the searchlight analyses (Kriegeskorte et al., 2006; Nili et al., 2014) implemented in Study III allowed us to search for pattern information throughout the entire brain (in addition to ROI-based analyses). These methodological advances are still relatively scarcely used in age-comparative studies.

To conclude, age-comparative research faces various methodological challenges with regard to cross-sectional comparisons that do not necessarily reflect developmental lifespan changes, the paradigms used to measure cognition, and the non-invasive measures of neuronal activity that are influenced by many factors. At the same time, appropriate measures can be taken to address these challenges, such that age-comparative research has the potential to elucidate the fundamental mechanisms that enable cognition across the lifespan. In Studies I–III, we pursued to minimize such limitations by reducing the impacts of confounding factors and ensure age-fair comparisons.

7.4 Conclusions and future research directions

Conclusions

The aim of this dissertation was to identify the (potentially age-dependent) neural representational properties that support episodic memory across the lifespan, namely in children, young adults, and older adults. By utilizing various approaches to measure and analyze neural activity including temporal, spectral, and spatial aspects of neural representation (ERP, TFR, fMRI; univariate and multivariate) and memory performance (memory specificity, associative memory, recognition), as well as brain–behavior relationships on both the within- and between-person level, the three empirical studies in this dissertation substantiate the association between the fidelity of neural content representation at the time of encoding and the ability to remember such contents.

Deficient representational fidelity has been linked to aging-related cognitive deficits (e.g., Carp, Park, Polk, & Park, 2011; Koen et al., 2019; S.-C. Li et al., 2001; J. Park et al., 2010). Here, we further delineated the specific influences and interrelations of the similarity or distinctiveness between memory representations and their stability over time, in relation to memory performance. We bridged across representational measures and levels and their behavioral relevance and thus demonstrated that reduced neural specificity, particularly at the item level, is a crucial determinant of memory deficits in old age, adding to the previously scarce evidence (cf. Zheng et al., 2018). In contrast, the development of the quality of neural information representation in children is still largely uninvestigated, with the first evidence indicating that neural fidelity is already quite high during mid-childhood (M. A. Cohen et al., 2019; Fandakova et al., 2019), but the specific representational properties and their implications for memory performance are yet to be examined. Adding to our current knowledge of the maturation of relevant brain structures and functions in relation to age-related improvement in episodic memory (e.g, Keresztes et al., 2017; Ofen et al., 2007; Tang et al., 2018), we identified neural indicators of the formation of highly specific memories. We made the first foray into studying the underlying neural mechanisms of forming high-fidelity memory representations from childhood to old age, that can be the basis of the investigation and better understanding of the neural representations underlying episodic memory across the lifespan.

Identifying commonalities or differences between age groups, especially across full lifespan samples, does not only help our understanding of brain and memory development but also provides insights into general mechanisms and principles that ultimately increase our comprehension of how the brain encodes, maintains, and retrieves information.

Future research directions

Extending the presented work, there are multiple directions in which future studies can further elucidate the specific role of neural representational properties in supporting episodic memory across the lifespan. Here, I provide some of the, in my view, most critical further research questions and objectives, together with some concrete future plans with the data sets discussed in this dissertation.

So far, it is still largely unknown when and how children's neural representations develop with respect to the specific representational properties discussed in this dissertation. In particular, the relationship between different memory representations, both at the broad concept and specific item level, as well as representational stability over time, and the relation of distinctiveness and stability, have only scarcely been studied in children (cf. Fandakova et al., 2019). Examination of these representational properties, focusing both on spatial and temporal representations, and their relation to memory in children of different age groups and in comparison to young and older adults, would help our understanding of neurocognitive development in childhood, the specific differences occurring during maturation and senescence, and the neural representational principles underlying memory in general. Addressing some of these objectives, one of the remaining aims with the data from Study I is to examine how the distinctiveness and stability of neural representations, measured as representational similarity of the EEG time–frequency patterns during encoding, relate to subsequent memory. In addition to elucidating specific representational properties across the lifespan, this may also provide further insight into the relationship of neural repetition effects and representational stability.

This dissertation mainly covered the neural representations during encoding and how they are related to later memory success. Besides successful encoding, memory requires successful consolidation and retrieval of memory representations (e.g., Dudai et al., 2015; Frankland & Bontempi, 2005; Tulving & Thomson, 1973). Previous studies have shown that spontaneous reactivation of neural representations during wake and sleep periods as well as during retrieval are positively linked to memory performance (Deuker et al., 2013; Dimsdale-Zucker et al., 2018; Jonker et al., 2018; Kerrén et al., 2018; Rugg et al., 2008). Leveraging more on these findings and how they relate to representational distinctiveness and stability during encoding may help to further uncover the neural representational mechanisms supporting memory consolidation and retrieval. Furthermore, differences in the neural representational properties during successful retrieval may further explain age-related differences in memory performance across the lifespan (cf. Bauer, Pathman, Inman, Campanella, & Hamann, 2017; Shing et al., 2010; Trelle et al., 2019; T. H. Wang et al., 2016). Concretely, these questions will be addressed in the studies discussed in this dissertation, particularly Studies I and III, where neural activity has been recorded during the memory retrieval phases, allowing for testing of, for example, pattern reinstatement during recognition.

Another important direction of future research will be the investigation of the neural mechanisms causing the observed differences in neural representational quality in old age (and potentially childhood). The model by Li and colleagues proposed deficient neuromodulation, for instance, of the dopaminergic system, causing reduced neural distinctiveness in old age (e.g., S.-C. Li et al., 2001) which received its first supporting evidence from neuroimaging (e.g., Abdulrahman et al., 2017). Furthermore, recently GABAergic neurotransmission has received much attention in regard to its link to age-related neural dedifferentiation in rodent (e.g., Ding et al., 2017) and human studies (Cassady et al., 2019; Chamberlain et al., 2019; Gagnon et al., 2019; Lalwani et al., 2019). Further delineating the specific relationship of GABA concentrations, representational distinctiveness and stability, cognition, and age will largely contribute to a better mechanistic understanding of the neural basis of age-related cognitive decline. This may also offer a potential avenue for future investigation of neural representational properties during brain development where dopamine and GABA play critical roles (cf. Ben-Ari, Khalilov, Kahle, & Cherubini, 2012; Caballero & Tseng, 2016; Hoops & Flores, 2017; Larsen et al., 2020; Le Magueresse & Monyer, 2013; Yu, Wang, Fritschy, Witte, & Redecker, 2006).

Together, the proposed directions for future research promise a further refined understanding of the neural representational properties supporting episodic memory, how memory representations change across the lifespan, and how they contribute to the lifelong development of memory abilities.

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Glossary

The usage of terms to describe neural representational properties is highly inconsistent in the literature. Here I define the terms how they are mainly used throughout this dissertation, however, there may be inconsistencies across Studies I–III, especially in Study II which is already published.

Distinctiveness Superordinate term for the relation of different neural representations to each other, describing how dissimilar/distinguishable neural activation patterns are, e.g., measured as correlation distance or pattern classification (decoding) accuracy

Fidelity Precision, faithfulness with which information is represented in neural activation patterns, including their distinctiveness and stability

Global similarity Representational similarity between neural activation patterns elicited by all items, e.g., presented during encoding (also called global matching)

Neural dedifferentiation Aging-related reduction in representational distinctiveness

Selectivity Specialization of neurons or neural populations for certain stimulus types (e.g., categories), indicated by higher responsiveness to preferred than non-preferred stimuli (here, usually measured as univariate activity differences)

Similarity Overlap or resemblance of neural activation patterns elicited by the same content (within-item similarity) or different contents (between-item similarity), e.g., measured as correlation of multivariate patterns of neural activity

Specificity Precision with which category or item information is represented in neural activation patterns, e.g., measured as within-minus-between category similarity (category specificity) or within-minus-between item similarity (item specificity), or indirectly as memory specificity, i.e., how precisely information can be remembered

Stability Similarity of the neural activation patterns elicited by the same content (within-item similarity) across repeated encoding or between encoding and retrieval (also called reactivation or reinstatement)

List of Abbreviations

ANOVA analysis of variance

BL baseline

BOLD blood oxygen level dependent

BSR bootstrap ratio

CMO category memory only

ECG electrocardiography

EEG electroencephalography

EOG electrooculography

EPI echo planar image

ERP event-related potential

FFA fusiform face area

fMRI functional magnetic resonance imaging

GABA gamma-aminobutyric acid

HE high-exemplar

HR high-repetition

HRE high-repetition-and-exemplar

HRF hemodynamic response function

ICA independent component analysis

iEEG intracranial electroencephalography

IM item memory

ISI inter-stimulus-interval

IT inferotemporal

LDI lure discrimination index

LOC lateral occipital complex

LV latent variable

MEG magnetoencephalography

MRI magnetic resonance imaging

MRS magnetic resonance spectroscopy

MTL medial temporal lobe

MVPA multivariate pattern analysis

PET positron emission tomography

PLSC partial least squares correlation

PPA parahippocampal place area

RDM representational dissimilarity matrix

RE repetition enhancement

ROI region of interest

RS repetition suppression

RSA representational similarity analysis

tDCS transcranial direct current stimulation

TE echo time

TFR time–frequency representation

TI inversion time

TR repetition time

VVC ventral visual cortex

List of Figures

List of Tables

Appendix

Original publication of Study II

Sommer, V. R., Fandakova, Y., Grandy, T. H., Shing, Y. L., Werkle-Bergner, M., & Sander, M. C. (2019). Neural Pattern Similarity Differentially Relates to Memory Performance in Younger and Older Adults. *The Journal of Neuroscience*, 39(41), 8089–8099. doi: 10.1523/JNEUROSCI.0197-19.2019.

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