Aus der Klinik für Psychiatrie und Psychotherapie Campus Benjamin Franklin der medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

FMRI emotion research and its dependence on task specifics: comparing four standard paradigms

Die Abhängigkeit von fMRT-basierter Emotionsforschung von Aufgabenmerkmalen: Vergleich von vier Standardparadigmen

zur Erlangung des akademischen Grades

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I Abkürzungsverzeichnis

ACC	Anterior cingulate cortex
ALE	Activation likelihood estimation
AM	Amygdala
BAWL	Berlin Affective Word List
BOLD signal	blood-oxygen-level-dependent signal
dlPFC	Dorsolateral prefrontal cortex
dmPFC	Dorsomedial prefrontal cortex
dACC	Dorsal anterior cingulate cortex
fMRI	Functional magnetic resonance imaging
FWHM	full width at half maximum
IAPS	International Affective Picture System
ITI	Inter-trial-interval
MNI	Montreal Neurological Institute
OASIS	Open Affective Standardized Image Set
OFC	Orbitofrontal cortex
pgACC	Pregenual anterior cingulate cortex
ROI	Region of interest
SPM	Statistical parametric mapping
TE	Echo time
TR	Repetition time
l/r	Left/right

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IV Deutsche Zusammenfassung

Die affektiven Neurowissenschaften setzen zur Erforschung der neuronalen Grundlagen von Emotionsverarbeitung verschiedene fMRT-Aufgaben ein, bei denen den Versuchteil-nehmer:innen emotionale Stimuli gezeigt werden. Obwohl bereits bekannt ist, dass die spezifischen Eigenschaften von fMRT-Aufgaben einen substanziellen Effekt darauf haben können, welche Gehirnaktivierungen durch die Aufgabe ausgelöst werden, werden die Aufgaben gegenwärtig oft miteinander gleichgesetzt und direkte Vergleiche der Aufgaben sind selten. Das darin liegende Potential, Studiendesigns durch bewusste Auswahl der fMRT-Aufgabe zu optimieren, wird so meist vertan.

Diese Dissertation hat einen direkten Vergleich von vier häufig genutzten fMRT-Aufgaben zur Emotionsverarbeitung auf Grundlage der gleichen Analysepipeline durchgeführt, um zu untersuchen, welche Aufgabe am besten geeignet ist, um welche Gehirnregion zu untersuchen. Diese waren eine Arbeitsgedächtnisaufgabe mit emotionalen Wörtern (EMOBACK-Aufgabe), und drei Aufgaben mit impliziter Verarbeitung von entweder emotionalen Gesichtsausdrücken (FACES-Aufgabe) oder Fotos emotionalen Szenen (OASIS und IAPS-Aufgabe). Von drei Stichproben (je n=15) wurden blutsauerstoff-abhängige MRT-Daten gesammelt, während diese Aufgaben bearbeitet wurden. Verglichen wurden die Aktivierungen in vier *regions of interest,* die zentral für die Emotionsverarbeitung im Gehirn sind: in der Amygdala, der anterioren Insula, dem dorsolateralen präfrontalen Kortex (dlPFC) und dem pregenualen anterioren zingulären Kortex (pgACC). Für die FACES- und OASIS-Aufgaben, bei denen die Daten aus der gleichen Stichprobe stammten, wurden Korrelationsanalysen durchgeführt, um zu untersuchen, ob die Aktivierungen, die durch die beiden Aufgaben ausgelöst wurden, systematisch zusammenhängen.

Die EMOBACK-Aufgabe hat eine signifikante Deaktivierung im pgACC ausgelöst, sowie Aktivierungen im rechten dlPFC und in der bilateralen anterioren Insula. Im Gegensatz dazu hat die FACES-Aufgabe selektiv in der bilateralen Amygdala Aktivierungen ausgelöst. Die IAPS- und OASIS-Aufgabe haben beide zu Aktivierungen in der bilateralen anterioren Insula und Amygdala geführt. Obwohl die Aktivierungsmuster in diesen beiden Aufgaben ähnlich waren, gab es größere Varianz der Aktivierungen in der IAPS-Aufgabe. Die Amygdala-Aktivierungen, die durch die FACES- und OASIS-Aufgabe ausgelöst wurden, waren nicht signifikant korreliert.

Diese Dissertation schlussfolgert, dass die verschiedenen fMRT-Aufgaben nicht bedingungslos austauschbar sind. Stattdessen könnten sie in zukünftigen affektiven fMRT-Studien strategisch eingesetzt werden, abhängig davon auf welchen Gehirnregionen das konkrete Forschungsinteresse liegt.

V English Abstract

Affective neuroscience studies brain activity underlying emotion processing with the help of a variety of different fMRI paradigms that present subjects with emotionally valanced stimuli. It is known that the precise characteristics of fMRI tasks can have a substantial influence on the activation elicited by a paradigm, however, paradigms are currently used interchangeably and direct comparisons of tasks are scarce. This bears a potential for optimization in the planning of future studies that is not currently used.

This dissertation undertook a direct comparison of four common emotion processing tasks based on the same analysis pipeline to elucidate which tasks are best suited for the study of which brain regions. Studied here are a working memory task using emotional words (EMO-BACK task) and implicit processing tasks of emotional face stimuli (FACES task) and pictures of emotional scenes (OASIS and IAPS task). Blood oxygen level dependent (BOLD-) MRI data from these tasks were collected in three samples of healthy male adults (each n= 15). The tasks were compared regarding the activation they elicited in four regions of interest, that are central to emotion processing, namely the amygdala, anterior insula, dorsolateral prefrontal cortex (dlPFC) and pregenual anterior cingulate cortex (pgACC). For two tasks (FACES and OASIS) where data were available from the same sample correlation analyses were conducted to investigate whether activation between the tasks was systematically related.

In the EMOBACK task significant deactivation in the pgACC and significant activation in the right dlPFC and bilateral anterior insula was found, while the FACES task elicited activation selectively in the bilateral amygdala. The IAPS and OASIS task both recruited the bilateral anterior insula and amygdala. While the activation pattern of these two tasks was similar there was greater variability in activation in response to the IAPS task. The amygdala activation elicited by OASIS and FACES task was not significantly correlated.

This dissertation concludes that the different tasks should not be seen as interchangeable proxies for emotion processing but can rather be employed strategically in future affective neuroimaging studies depending on the parts of the emotion processing brain network, they are interested in.

VI Manteltext/Framework for the dissertation thesis[1]

[1]The following parts of the framework are adapted with permission from my previously published article, in which I am the sole first author Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525.:

1.1 Study rationale 1.4 Choice of regions of interest, 2. Methods, 3.1 ROI analyses: mean activations by tasks, 3.2 Direct comparisons between tasks, 4.1 Summary, 4.2 Comparison with the literature, 4.4 Limitations

1. Introduction

1.1 Study rationale[2]

A variety of fMRI paradigms have been used to probe emotion processing to study its neural underpinnings in healthy subjects (García-García et al., 2016) and how it evolves over the lifespan (Wu et al., 2016), and is affected by psychopathology (McTeague et al., 2020), or therapeutic interventions (Enneking et al., 2020; Outhred et al., 2014). These paradigms differ in the stimulus material that is used (e.g., printed words, pictures, or sounds), the task that is posed to participants (e.g., passive viewing, naming the depicted emotion, or working memory tasks involving the stimuli), and the cognitive effort that is needed to fulfill the task (e.g., the difficulty of working memory tasks). Previous research has shown that the specifics of the task and the stimuli used in emotional fMRI paradigms have a substantial impact on the neural activations found (Müller et al., 2018; Reisch et al., 2020; Sabatinelli et al., 2011). Furthermore, different tasks likely trigger different aspects of emotion processing (Riedel et al., 2018). Crucially, standard emotion processing paradigms for the study of target brain regions or aspects of emotion processing are yet to be established. This poses a challenge for planning new experiments as many different paradigms exist to choose from and the choice likely influences the brain activations found in the study. However, direct comparisons between tasks are scarce. And as fMRI studies often differ in their pre-processing routines and analysis software, activation differences between studies cannot safely be attributed solely to the task at use, which leaves a gap of knowledge about the specific neural activations to expect when using one of the different fMRI paradigms of emotion processing. The goal of this dissertation was to directly compare common emotion processing fMRI tasks based on the same analysis pipeline regarding the activation they elicit in core regions of emotion processing.

1.2 Paradigms used to study emotion processing

Paradigms used to study the processing of emotional information in the brain generally combine stimulus material of emotional valance with a task that participants are asked to do. Stimuli used can be of different modalities (e.g., sounds, words, pictures, scenes from movies), however, because of practicality and some evidence that they elicit brain activation most robustly (Costafreda et al., 2008; García-García et al., 2016) visual stimuli (i.e., photos or words) are the most common. Internal stimuli (emotional episodes from memory for example) have also been used in fMRI paradigms, however, they appear to be less effective in eliciting brain

[2] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission.

activation than external stimuli (Costafreda et al., 2008) and are relatively rare in use. Most commonly used are emotional faces, emotional scenes, and emotional words (García-García et al., 2016).

Paradigms employing facial stimuli usually use photos of actors showing different emotional expressions. Photos with neutral facial expression are often used as a control condition. This way, a subtractive contrast that compares the activation elicited by emotional and neutral expressions can be used to conclude about the neural response that is specific to the emotional content of the stimuli. Brain regions that have been shown to be activated by emotional faces are the amygdala, parahippocampal gyrus, fusiform gyrus, posterior cingulate cortex, dorsal anterior cingulate cortex (dACC), orbitofrontal cortex, visual cortices, and the cerebellum (Fusar-Poli et al., 2009; McDermott et al., 2018; Müller et al., 2018).

Paradigms that employ emotional scenes use pictures of pleasant or unpleasant emotional content of varying arousal. Aversive pictures can for example depict aggressions, wounded people or car accidents whereas pleasant pictures show animals or families. Emotionally neutral pictures of objects (e.g. pieces of furniture) or scrambled pictures matched for visual properties like brightness serve as control conditions. Databases such as the International Affective Picture System (IAPS; Lang et al., 1997) or the Open Affective Standardizes Image Set (OASIS; Kurdi et al., 2017) provide validated stimuli for which average ratings of arousal and valence from representative samples have been established. Brain regions that have been shown to be activated by emotional scenes are similar to those activated by emotional faces and include the amygdala, parahippocampal gyrus, posterior cingulate cortex, anterior insula, ventromedial prefrontal cortex, dACC, OFC, and visual cortices (McDermott et al., 2018; Phan et al., 2002)

Similarly, fMRI paradigms employing words usually recruit stimuli from different word lists with validated ratings of valence and arousal for the different languages, like for example the Berlin Affective Word List (BAWL; Võ et al., 2009) and the Affective Norms for English Words (ANEW; Bradley & Lang, 1999). These are usually single words (e.g., “corpse” for negative, “hall” for neutral and “kiss” for positive valence) matched for word type, length, frequency in the language and imaginiability. Emotional words have been shown to activate the amygdala, hippocampus, ventral or subgenual ACC, anterior insula, posterior cingulate cortex, dACC, middle temporal cortex, ventral striatum, and pallidum (Citron, 2012).

Stimuli are generally embedded in a task, which at the simplest can be passive viewing, i.e., participants being instructed to look at the stimuli that they are presented with. Other tasks aim at implicit processing of the emotion by instructing participants to process a non-emotional characterist of the stimulus (e.g., the gender of a presented face, the background colour of an object) or explicit processing of the emotion (e.g., naming the emotion). Participants can also be instructed to suppress or reduce their emotional reaction to the presented stimuli or to

reframe their thinking around them (cognitive reappraisal). These tasks, however go beyond the mere processing of emotion and are more apt to study the concept of emotion regulation (Costafreda et al., 2008; Kohn et al., 2014). Further more, emotional stimuli can be included in established cognitive tatsks (e.g., n-back, Stroop task) to target specific aspects (like attention capture or interference effects) of the multifaceted concept of emotion processing.

Generally, a common network of brain structures is thought to underlie emotion processing that is activated by emotionally valenced stimulation regardless of the precise induction context (Lindquist et al., 2012). Therefore, any of the described tasks could be used to activated and study this network of brain regions. However, the different stimulus types undeniably differ sensorically as well as in complexity, emotional intensity and ecological validity (e.g., single written words are rarely a source of emotion in human daily lives whereas emotional faces might be) (Grühn & Sharifian, 2021). These differences may plausibly influence neural processing routes and could e.g., lead to the predominant activation of some parts of the brain network concerned with emotion processing relative to others. Likewise, the instructions to the task (whether the emotional content needs to be memorized, categorzied, subjectively evaluated, etc.) has been shown to influence the precise pattern of activation elicited by emotional fMRI paradgims (García-García et al., 2016; Riedel et al., 2018).

Notably, for threat reactivity, a specific aspect of emotion processing, it appears that tasks intended to represent that same psychological function elicit different activation patterns. A study comparing several fMRI paradigms that had been used to study threat reactivity found that - against the authors' hypothesis - amygdala activation in the four studied tasks was not significantly correlated and the tasks were, hence, not interchangeable (Villalta-Gil et al., 2017). This finding highlights the importance of task characteristics and warns against rashly equating paradigms and psychological concepts such as, for example, threat reactivity. However, threat reactivity is a very specific aspect of the broader concept of emotion processing, and it is thus worth evaluating the evidence regarding differences between fMRI paradigms of emotion processing.

1.3 Comparative evidence on fMRI tasks for emotion processing

Direct comparisons between different fMRI paradigms probing emotion processing are relatively scarce. Recently, Reisch and colleagues (2020) compared the effects of a passive viewing task using three different types of emotional visual stimuli: printed words, photographs of emotional faces and photographs of emotional scenes. Apart from areas of visual processing and reading comprehension[3], they also found that reactivity to emotion differed between the stimulus types in a number of brain regions including the superior and inferior frontal gyrus, the amygdala and anterior insula. Across stimulus types, emotion effects converged in the left anterior insula. The authors conclude that the type of visual stimuli has a substantial impact on the resulting emotion effects, even after the basic visual perception effects are filtered out through subtractive contrasts. This underlines the importance of carefully choosing a task

[3] As the interest of this dissertation lies in the study of regions central to emotion processing, results about sensory brain areas lie beyond its scope and will not be discussed in detail.

when planning a study. However, while this study is very informative on different processing routes for the different stimuli categories, the paradigm used was created explicitly for this study and cannot speak with certainty to existing paradigms.

Beyond direct comparisons, information can also be gained via the meta-analytic approach. A meta-analytical comparison of 12 experiments each (matched for age and gender distribution) on negative images, negative faces and negative words found neural responses to faces and scenes to be more similar to each other than to activations elicited by words, with the activation maps showing no significant differences between faces and scenes and no significant overlap of either faces or scenes with emotional words. Amygdala activation was more reliably elicited by emotional scenes than by emotional words (García-García et al., 2016). A meta-analysis that solely focused on the neural response in the amygdala found a significantly higher probability of amygdala activation in response to faces and scenes than to emotional words (Costafreda et al., 2008). It has been argued however, that this is not a general effect of pictorial stimuli eliciting stronger neural responses than lexical stimuli but rather a function of stimulus complexity (Schlochtermeier et al., 2013).

Further direct comparisons exist between paradigms employing emotional faces and scenes. The first study to do that (Hariri et al., 2002) compared BOLD activations to emotional faces and picture stimuli. However, while the work is often cited and inspired the field, the results it reported are based on uncorrected statistics and can thus not grant definitive conclusions. In another direct comparison emotional scene stimuli elicited activation in largely similar regions as emotional face stimuli (amygdala, hippocampus, ventromedial pre-frontal cortex), however neural emotion effects were greater in response to faces than scenes bilaterally in the superior temporal gyrus and int the left anterior insula (Britton et al., 2006). A meta-analysis of 100 studies using paradigms based on face stimuli and 57 studies using emotional scenes also found extensive overlap in activations elicited by either, as well as, differences in extent and exact localization even after removing basic effects of stimulus perception by using subtractive contrasts (Sabatinelli et al., 2011). This reveals that despite extensive parallels specific emotion effects for picture and face stimuli exist, that should be considered when planning a study and that might strategically be used to an advantage. However, a meta-analysis combines activation maps from different paradigms that are similar in some regards (for example in employing face stimuli) but might differ in other aspects. Furthermore, studies likely differ in their analysis strategies. Both factors impede the use of meta-analytical results to predict the activations a specific fMRI paradigm will elicit. Hence, a direct comparison of activations elicited by fMRI paradigms probing emotion processing is warranted.

1.4 Choice of regions of interest[4]

Meta-analyses of fMRI research on emotion processing have robustly implicated several brain regions: Namely, the amygdala, anterior insula, pre- and subgenual anterior cingulate cortex (ACC) as well as dorsal ACC (dACC), dorsomedial prefrontal cortex (dmPFC), dorsolateral PFC (dlPFC), parahippocampus, orbitofrontal cortex, and visual and auditory cortices (García-García et al., 2016; Lindquist et al., 2012; Riedel et al., 2018). The constructionist approach (cf. Lindquist et al., 2012) assumes that emotion processing draws on more basic psychological operations and hence recruits the respective brain networks that underlie these operations. By this account, the brain regions activated in fMRI tasks of emotion can each be associated with a functional network that exerts a sub-process of emotion. The functional networks assumed to collaborate in emotion processing are the limbic network (realizing affective states within the body), salience network (detecting behaviorally relevant information), default-mode network (self-referential conceptualization of information), and the central executive network (evaluating or manipulating the incoming information; (Lindquist et al., 2012)).

A recent study on a databank of task-based fMRI studies of emotion processing clustered studies based on similar activation patterns elicited by the task in use, then performed meta-analyses for each of the cluster of studies. This approach dissociated five brain networks with convergent activations during different types of emotion processing tasks (Riedel et al., 2018). Apart from two networks in sensory cortices, these were largely overlapping with the salience, the default mode, and the limbic network. Subsequently, the meta-data of the experimental designs in each cluster were analyzed. Based on this the found networks were characterised as contributing to drawing attention to salient information, appraisal and prediction of emotional information, and induction of the emotional response, respectively. These results are in line with the constructionist notion (Lindquist et al., 2012) that emotion processing draws on psychological functions engendered by large-scale brain-networks.

Therefore, one hub of each of these networks was chosen for regions of interest for this dissertation: the bilateral amygdala, bilateral anterior insula, pregenual ACC (pgACC), and bilateral dlPFC. The amygdala is the region that is most robustly engaged in emotion processing (García-García et al., 2016; Müller et al., 2018; Sabatinelli et al., 2011) and shows the greatest functional connectivity with other regions involved in emotion processing (García-García et al., 2016). It is involved in signaling whether sensory information is motivationally salient (Whalen et al., 2009) guiding attention, perception and decision-making (Pessoa, 2010). It has also been thought of as realizing “core affect”, i.e., affective bodily sensations (Lindquist et al.,

[4] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission.

2012). In clinical neuroscience, altered amygdala function in emotion processing, specifically, hyperactivation to negative stimuli has been found in patients with depression, social anxiety, post-traumatic stress and borderline personality disorder (Gentili et al., 2016; McTeague et al., 2020; Stuhrmann et al., 2011).

The anterior insula is essential for the awareness of interoceptive information (Craig, 2002) as well as own affective experience (Zaki et al., 2012) and robustly activates during the perception of emotional stimuli (Duerden et al., 2013). It is part of the salience network (Seeley et al., 2007), where it proposedly integrates physiological information with emotional, cognitive, and motivational signals to detect salience of stimuli. Therefore, the activation of the anterior insula in emotion processing may be linked to the salience of emotional stimuli. The pregenual ACC is a part of the default mode network and typically deactivated in goal-directed tasks (Raichle, 2015), but activated during self-referential thought (Palomero-Gallagher et al., 2019), the assessment of internal emotional states (Vogt, 2014) as well as emotion perception (Phan et al., 2002). It has been suggested to serve the function of a hub that integrates emotion and cognition through its projections to several cortical regions (Tang et al., 2019), and its involvement in emotion processing may reflect cognitive appraisal of the emotional content of stimuli (Ochsner et al., 2012; Riedel et al., 2018). The pregenual ACC seems to play a crucial role in the cognitive regulation of emotions (Palomero-Gallagher et al., 2019). The dlPFC is a core region in the fronto-parietal control network, that supports executive attention, working memory, and complex problem-solving (Seeley et al., 2007). It has been found to activate in emotion processing tasks, especially when participants are asked to categorize or evaluate emotional information (Lindquist et al., 2012). DlPFC activity competes with amygdala activity in tasks that present an interference of emotional content and cognitive demand (Schweizer et al., 2019), such that cognitive load is negatively correlated with amygdala activation in presence of emotional stimuli (Van Dillen et al., 2009). Consistent with these findings, dlPFC activity has been associated with emotion regulation (Kohn et al., 2014).

1.5 Significance of the study

This dissertation aimed to establish a point of reference for activity patterns elicited by different emotional fMRI tasks in the four beforementioned regions of interest (amygdala, pgACC, anterior insula and, dlPFC). Knowing the location and intensity of activity elicited by emotional fMRI tasks should allow researchers to select an apt task when planning to study a specific region of the emotion processing network. By maximizing the effect sizes of elicited activations, this could reduce the sample size needed to detect a stable effect and thereby the cost of studies (Wall, 2018; Zuo et al., 2019). Currently, fMRI tasks in use for emotion research are mostly developed idiosyncratically by research groups and are often tailored for the specific investigation underway, not necessarily with re-use by other research groups (or potential

clinical application) in mind (McDermott et al., 2018). While this is at present common (and accepted) practice, it is suboptimal regarding transparency and efficiency. Furthermore, direct comparisons between fMRI paradigms are scarce. These are likely reasons why standard fMRI paradigms of emotion processing are yet to be established. This study's results might inform the design of future studies by providing information about the relative activation elicited by different fMRI paradigms probing emotion processing.

Ultimately, however ample the insights that the field of affective neuroscience has yielded about the neural processes underlying emotion processing, clinical applications are still lacking. The development of clinically useful fMRI biomarkers likely requires the establishment of psychometric properties and standardized norms for fMRI tasks (McDermott et al., 2018). This study considers itself part of this effort and might be a small step towards the clinical dissemination of affective neuroscience.

1.6 Research Question

The central question of this dissertation was what activations are elicited in the four chosen regions of interest central to emotion processing (amygdala, anterior insula, pgACC, and dlPFC) by four fMRI paradigms widely used in affective neuroscience. Out of the four paradigms, one was an emotional working memory task (EMOBACK; (Grimm et al., 2012)) and three were implicit emotion processing tasks. One of these used emotional face stimuli (FACES task) and the two others used pictures of emotional scenes, that were either positive and negative (IAPS task) or solely negative (OASIS task). All tasks used stimulus material from validated sets of pictures or words whose emotional valence has been established. I analyzed three datasets to investigate how the selected four core regions activate in response to the specific kind of emotional stimulation in each of the tasks.

2. Methods[5]

2.1 Population

This dissertation analyses data from 45 healthy males aged 18-58 belonging to three samples each consisting of 15 subjects. Mean age of the participants was 25.8 (±5.3) years for the sample from whom FACES and OASIS task were collected, 29.3 (±2.9) years for the EMOBACK task sample and 35.5 (±10.8) years for the IAPS task sample. Table 1 shows data on demographic variables and scanning sites. Exclusion criteria were standard MR exclusion

[5] This chapter is adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission

criteria, cardiovascular diseases, recent heart or head surgery, current pregnancy, history of psychiatric or neurological disorders and current use of any psychoactive medication. The study was conducted in accordance with the latest version of the Declaration of Helsinki. The full procedure and motivation were explained to each subject in detail as approved by the institutional review boards before they gave written informed consent to enter the study.

Table 1 Demographic variables and scanning site for the three samples.

	EMOBACK	FACES & OASIS*	IAPS
N	15	15	15
Gender	All male	All male	All male
Age (M±SD)	29.3 (±2.9)	25.8 (±5.3)	35.5 (±10.8)
Scanning site (n)	CCNB (15)	BCAN (15)	CCNB/UZH (5/10)

*FACES and OASIS task were assessed in the same sample; CCNB = Center for Cognitive Neuroscience Berlin, BCAN= Berlin Center for Advanced Neuroimaging; UZH = University of Zurich (Reprinted from Hartling et al., 2021 with permission).

2.2 Tasks

2.2.1 EMOBACK task

The EMOBACK task (Grimm et al., 2012) is a variant of the established n-back paradigm (Jaeggi et al., 2010), that is used to study working memory and executive function, in a “2-back” condition, meaning that subjects were required to monitor a series of words and to respond every time a word was presented that was the identical to the one presented 2 trials previously. The EMOBACK uses emotional word stimuli that were selected from the Berlin Affective Word List (BAWL; Võ et al., 2009). The stimuli were categorized as either positive, negative, or neutral and were matched with regard to length, imageability, emotional arousal and frequency of appearance. Stimuli were presented in 15 blocks, 5 each for the 3 valence categories (positive, negative, or neutral). Between the block a fixation cross appeared for 10–14 s. Each block contained 15 words presented for 500ms each. The interstimulus interval was 1500ms long. The task lasted for 12 minutes.

2.2.2 FACES task

In the faces task, participants were shown pictures from the Warsaw Set of Emotional Facial Expression Pictures (WSEFEP; Olszanowski et al., 2015). The block design task consisted of 12 blocks with 6 negative emotional faces displaying sadness, fear, and disgust (in randomized order) and 12 blocks with scrambled faces (control condition). In total, 72 negative

facial expressions of 24 actors (50% women) were presented for 3 seconds each. The inter-trial interval (ITI) was jittered between 10±1seconds. During the ITI, a white fixation cross on a black background was shown. To ensure their attention, participants were asked to indicate by button press whether the person was female for the portraits or for the scrambled faces whether the colored frame around the picture was blue (compared to green). The paradigm lasted 13 minutes.

2.2.3 IAPS task

The IAPS task consisted of 80 photographs (40 positive and 40 negative) from the International Affective Picture System (Lang et al., 1997) presented in a block-design. Five pictures were shown during a block of 20s duration. To ensure attention, after participants were presented a question after each block regarding the content of one of the five pictures for 8s (e.g., 'Was there a cat in the picture?'). After the rating, a fixation cross was shown for 20s to serve as a baseline condition. The fMRI-paradigm was composed of 16 blocks (8 positive and 8 negative) with an overall duration of 13 min.

2.2.4 OASIS task

The OASIS task is an implicit emotion processing task with attentional control. During the task, scenes from the OASIS picture set (Kurdi et al., 2017) with negative valence and high arousal rating were presented in a block-design. Scrambled pictures were used in a neutral control condition. There were 14 negative and 14 neutral blocks, each lasting 18 seconds. Within each block, three picture stimuli were presented consecutively for 6 seconds each, resulting in a set of 42 negative pictures and 42 scrambled pictures in total. The order of the blocks was semi-randomized. The inter-trial-interval was jittered within a range of 10±1 seconds to ensure reduced predictability of picture onset and optimized sampling of the blood-oxygen-level-dependent (BOLD) signal (Price et al., 1999). During the ITI, participants saw a fixation cross. To ensure their attention, participants were asked to indicate by button press whether there was a person present in the picture or for the scrambled pictures whether the bounding box was blue or green. The experiment lasted 15 minutes.

Supplementary Table 1 gives an overview of all task characteristics for the four tasks and Figure 1 shows example stimuli from each task. All tasks were presented via MRI compatible video goggles (VisuaStim digital, Resonance Technology, Inc., Los Angeles, CA, USA) using Presentation® (Neurobehavioral Systems, Inc., Albany, CA, USA). Participants responded by pushing a fiber-optic light sensitive key press. Participants completed a brief training session of the task they were to do inside the scanner outside in the laboratory before the scanning session started.

2.3 Data collection

Imaging was performed using 3T MR systems at three study sites (Berlin Center for Advanced Neuroimaging (BCAN), Center for Cognitive Neuroscience Berlin (CCNB) and University of Zurich (UZH). The exact scanner type and sequence parameters at each site can be found in Supplementary Table 2. For each sample, scanning consisted of functional imaging by an T2-weighted echo planar imaging sequence and one anatomical reference image using a 3-dimensional T1-weighted scan. The Faces and OASIS tasks were assessed in one session, following a 3D scan. For the two other tasks, subjects completed a 3D scan and one task-based functional scan (EMOBACK and IAPS, respectively). Imaging for all 4 tasks was collected in one run.

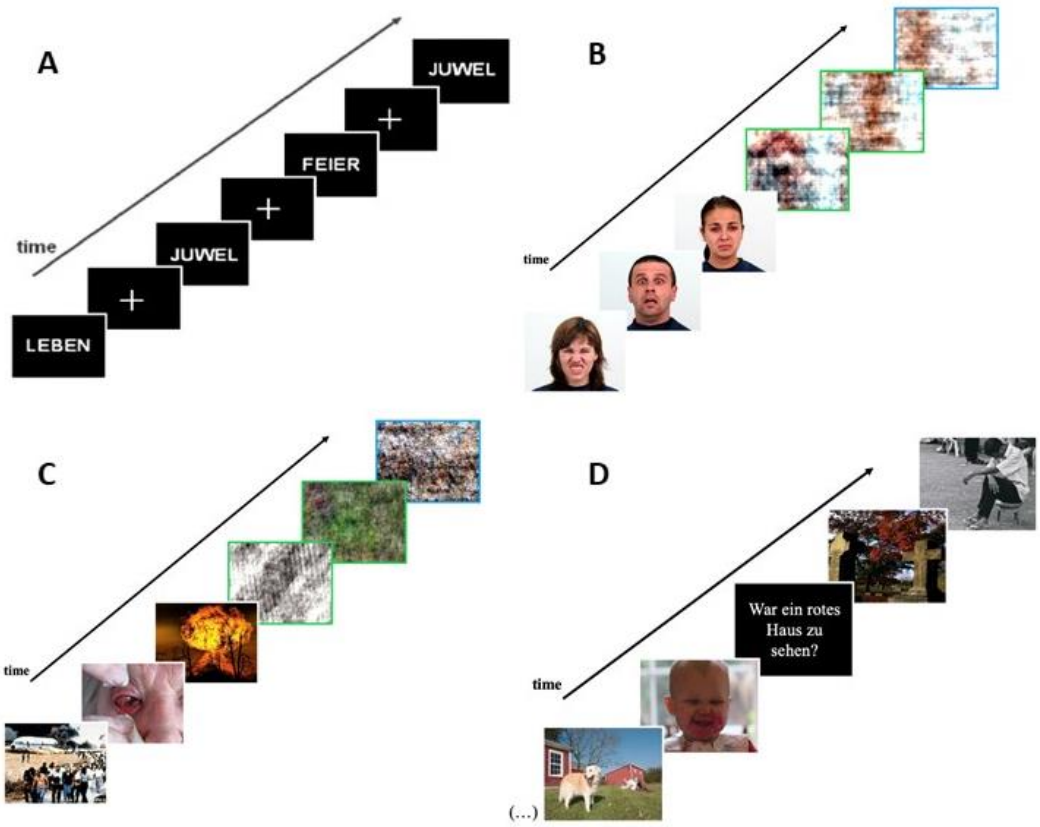


Figure 1 Example stimuli for A) EMOBACK B) FACES C) OASIS and D) IAPS task. (Reprinted from Hartling et al., 2021 with permission)

2.4 Data analysis

For behavioral data, accuracy was defined as accuracy= #correct responses/#trials for the FACES, OASIS and IAPS tasks and as accuracy = (#hits-#false alarms)/#targets in the EMOBACK task. A threshold of 80% accuracy for FACES, OASIS and IAPS tasks and 50% accuracy for EMOBACK task was defined for participants to be included in data analysis.

FMRI data were analyzed using MATLAB 2020a (The Mathworks Inc., Natick, MA, USA) and SPM12 revision 7771 (Statistical parametric mapping software, SPM; Wellcome Department of Imaging Neuroscience, London, UK; Penny et al., 2011; http://www.fil.ion.ucl.ac.uk). The first five volumes of each run were discarded to allow for T1 stabilization. The following pre-processing steps were realized: realignment according to the first volume for motion correction, normalization to the standard stereotactic space template from the Montreal Neurological Institute (MNI) and spatial smoothing using a 6 mm FWHM Gaussian kernel. The time series were high-pass filtered (filter width 128s) to eliminate low-frequency components and adjusted for systematic differences across trials. Data were checked for artifacts and a cut-off for motion parameters was set at 3mm or 3°; all volumes of all subjects passed this check. Statistical analysis on the subject level was performed by modeling the different conditions convolved with a hemodynamic response function as explanatory variables within the context of the general linear model on a voxel-by-voxel basis (Friston et al., 1999). Realignment parameters were included as additional regressors in the statistical model. A fixed-effect model was performed to create images of parameter estimates, which were then entered into a second-level random-effects analysis. For the fMRI data group analysis, the contrast images from the analysis of the individual participants were analyzed using one-sample t-tests.

For each subject, contrasts testing response to emotional stimuli relative to baseline or neutral stimuli were calculated. Specifically, for the four tasks, these were: 1. EMOBACK: emotional stimuli versus fixation condition (emotional > break); 2. OASIS: emotional stimuli versus control condition (emotional > scrambled) 3. IAPS: emotional stimuli versus fixation condition (emotional > break) 4. FACES: emotional stimuli versus control condition (emotional > scrambled).

Regions-of-interest (ROIs) were defined to examine emotion related brain activations. Specifically, the following ROIs previously linked to emotion processing (García-García et al., 2016; Lindquist et al., 2012) were selected (abbreviation and MNI coordinates in brackets): the bilateral dorsolateral prefrontal cortex (l/rdlPFC; ±40 36 32), the bilateral amygdala (l/rAM ±24 -2 -20), the bilateral anterior insula (l/rAI ±34 20 0) and the pregenual anterior cingulate cortex (pgACC; 0 42 2). Spherical ROI templates with a diameter of 10 mm were built with automated term-based meta-analyses on neurosynth.org or based on own previous studies (for pgACC; (Grimm et al., 2012)). All ROIs are illustrated in Figure 2. The mean parameter estimate of each ROI was extracted using the REX Toolbox (Duff et al., 2007; https://www.nitrc.org/projects/rex/). Significance tests for the ROI analyses were conducted with an α-level Bonferroni adjusted for the number of ROI of $p<.05/7=p<.0071$

Paired and independent sample t-tests were conducted to compare activation in the ROI between the tasks that have been collected in the same and different samples,

respectively. Further Pearson's correlation coefficients were calculated for amygdala activation in the tasks collected in the same sample (FACES and OASIS) to test whether individual differences in the level of amygdala activation were consistent across tasks. As exploratory analyses these are reported at an uncorrected α-level of p=.05.

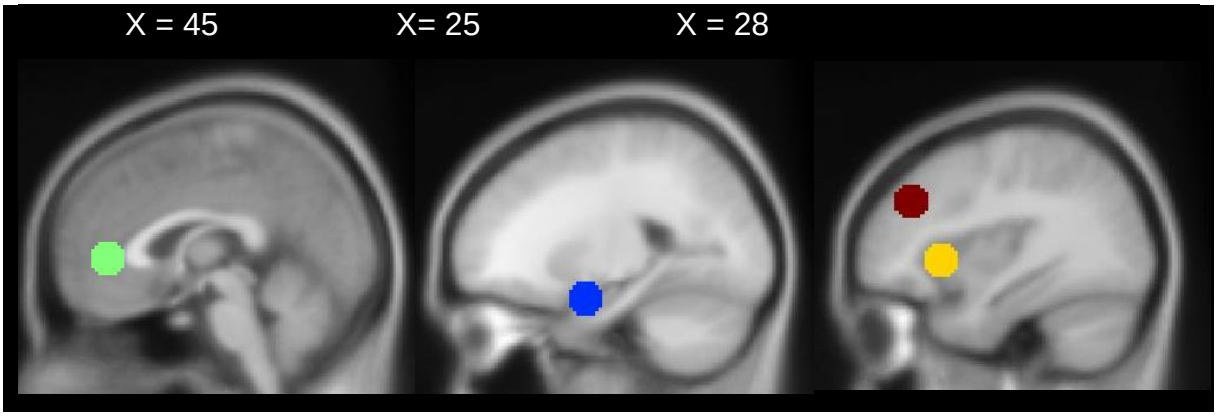


Figure 2 Region of interest (ROI) templates were spheres with 10mm diameter. Red = dorsolateral prefrontal cortex, yellow=anterior insula, green = pregenual anterior cingulate cortex, blue = amygdala. (Reprinted from Hartling et al. 2021 with permission)

3. Results

3.1 ROI analyses: mean activations by tasks[6]

Figure 3 shows an overview of the activations in the regions of interest for all 4 tasks. Activations in response to the emotional working memory condition compared to break in the EMOBACK task were found in bilateral anterior insula, right dorsolateral prefrontal cortex along with a significant decrease in activity in the pgACC (pgACC: mean β=-0.681 95% CI [-0.512, -0.849] t(14) = -8.666 p<.00001; lAI: mean β=1.004 95% CI [0.810,1.199] t(14) = 11.110 p<.00001; rAI mean β=0.910 95% CI [0.686,1.135] t(14) = 8.713 p<.00001; rdlPFC: mean β=1.310 95% CI [1.010,1.611] t(14) = 9.341 p<.00001;). There was also noticeable activation in the left dlPFC that was, however, not significant to a Bonferroni corrected alpha-level (ldlPFC: mean β=0.320 95% CI [0.046, 0.593] t(14) = 2.505 p = .0252).

The FACES task elicited significant activation in the bilateral amygdala (lAM: mean β=.469 95% CI=[.296,.644] t(14)=5.783 p=.00005; rAM: mean β =0.466 95% CI [0.278, 0.652] t(14) = 5.365 p = .00001).

The IAPS task elicited activation in the bilateral amygdala and bilateral anterior insula during presentation of emotional stimuli (activation in the left amygdala and bilateral anterior insula was not significant to an Bonferroni adjusted alpha-level of p=.007; rAM: mean β=0.898

[6] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission

95% CI [0.454,0.631] t(14) = 4.33 p = .0007; lAM: mean β = 0.646 95% CI [0.186,1.106] t(14) = 3.015 p = .009, lAI: mean β=0.404 95% CI = [0.026,0.781] t(14) = 2.295 p=.038 rAI: mean β=0.366 95% CI = [0.108,0.624] t(14) = 3.043 p = .009).

Activation elicited by emotional stimuli in the OASIS task was found in the bilateral amygdala as well as in the bilateral anterior Insula (Bonferroni-corrected significance not met for rAI; lAM: mean β=0.431 95% CI [.278,.584] t(14) = 6.063 p = .00003; rAM: mean β = 0.422 95% CI [0.245,0.601] t(14) = 5.103 p = .00016; lAI: mean β = 0.299 95% CI=[0.133,0.465] t(14) = 3.882 p = .002; rAI: mean β = 0.163 95% CI [.050,.276] t(14) = 3.091 p=.008).

3.2. Direct comparisons between tasks[7]

As data for the FACES and the OASIS task stem from the same subjects I further conducted exploratory paired t-tests to directly compare activation patterns between the two tasks. No significant difference arose except for the right anterior insula where activation in the OASIS task exceeded that in the FACES task (OASIS: M = 0.163±0.041 FACES: M =0.002± 0.027, Cohen's d = .633, p=.028). All results for paired t-tests between activations in the FACES and OASIS task can be found in Supplementary Table 4.

Further, I also conducted exploratory independent t-tests comparing activation elicited in each of the regions of interest between the tasks that were run in different samples. In the right dlPFC, the activation elicited by EMOBACK was found to be significantly stronger than that under any other task (EMOBACK: M= 1.310±.525 IAPS M=.245±.673 FACES: M=.094±.159 OASIS: M = .031±.270 Cohen's d >1.7 all p<.001 for all comparisons of EMOBACK with other tasks). In the left dlPFC the only significant difference that arose was between EMOBACK (M= .320±.477) and FACES task (M:.030±.162; Cohen's d=.982 p=.015).

In both the left and right amygdalae, the EMOBACK elicited significantly less activation than the other tasks (EMOBACK lAM: M=-.185±.255 rAM=-.210±.347 Cohen's d>1.4 p<.001 for all comparisons with other tasks), in the right amygdala the activation elicited by IAPS was also significantly stronger than that in the OASIS task. (IAPS: M=.898±.775 OASIS M=.422±.310 Cohen's d=.805 p=.042)

In the anterior insula the activation elicited by the EMOBACK was found to be significantly greater bilaterally than that by any other task (EMOBACK rAI: M=.910±.404 lAI: M=1.004±.350 Cohen's >1.1 p<.006 for all comparisons). For the right anterior insula, a significant difference was found also between the IAPS and the FACES task, (IAPS: M=.365±466

[7] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission

FACES: M= -.003±.158 Cohen's d=1.094 p=.007) with greater activation elicited by the IAPS task.

In the pgACC, no significant difference was found between the de-activations elicited by EMOBACK or IAPS task, however both differed significantly from the other two tasks, FACES and OASIS (EMOBACK M:-0.681±.294 IAPS: M=-0.331±.606 FACES: M= .033±.219 OASIS: M=.082±.301 Cohen's d>.75 p<.05 for all comparisons of EMOBACK or IAPS task with OASIS and FACES task).

3.3. Exploratory correlation analyses

I further explored whether activation in the amygdala, the only region significantly activated during both FACES and OASIS task, was correlated between the two tasks. The individual level of activation in the amygdala in one task was not significantly related to that in the other task, neither ipsi- nor contralaterally (all $r(13)<.15$, all $p>.05$; Supplementary Table 5 shows all correlation coefficients and Supplementary Figure 1 shows amygdala activation in one task plotted against that in the other task for left and right amygdala separately.

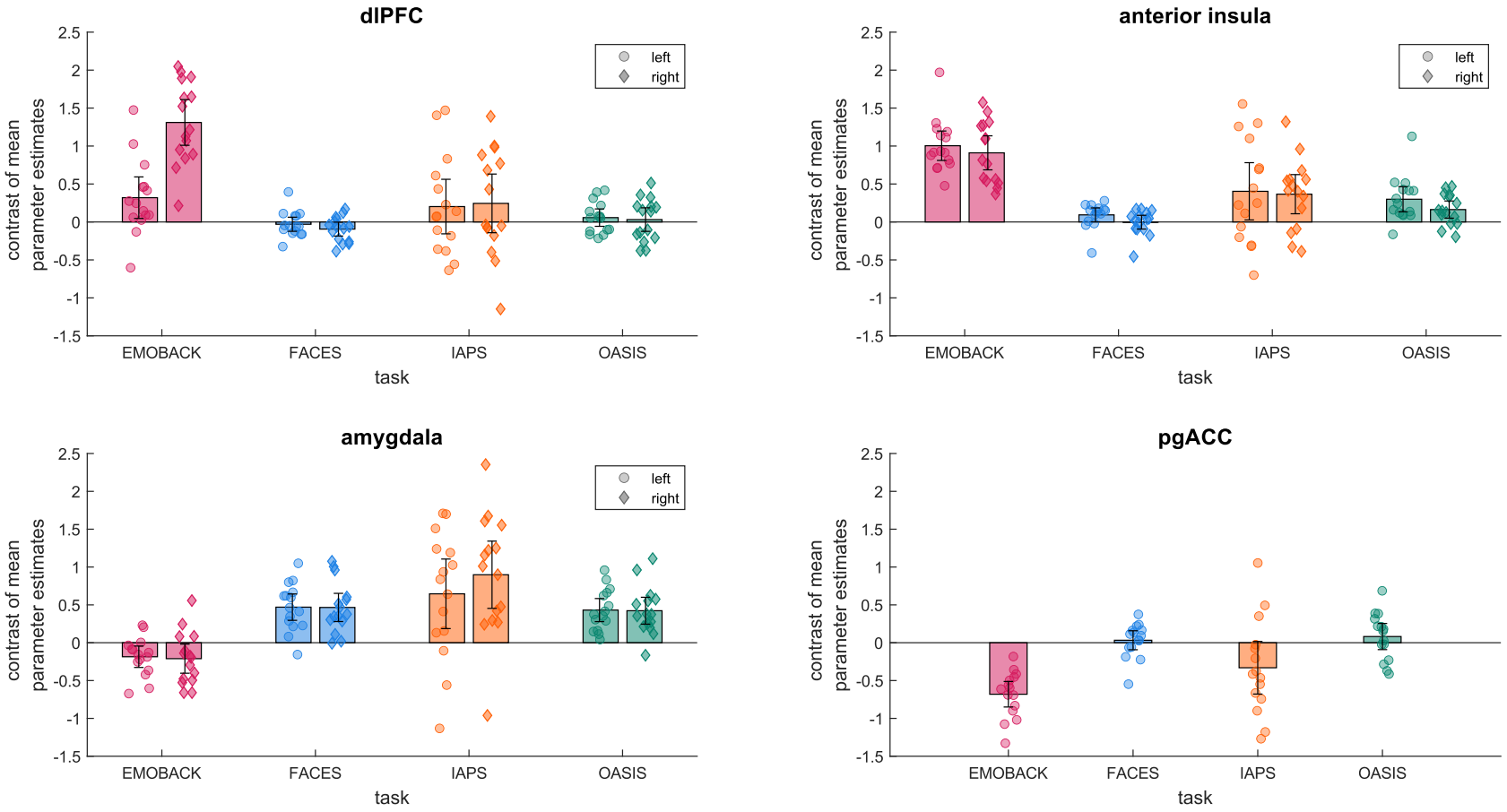


Figure 3 Contrasts of mean parameter estimates of neuronal activation in the prespecified regions of interest on the group (bars) and individual (dots) level. Error bars represent the 95% confidence interval. Colors represent the four tasks; pink: EMOBACK (Emotional > break), , blue: FACES (Negative > scrambled), orange: IAPS (Emotional > break), green: OASIS (Negative > scrambled). (Reprinted from Hartling et al., 2021 with permission)

4. Discussion

4.1 Summary[8]

This dissertation compared four fMRI paradigms that are often applied in the affective neurosciences regarding their potential of eliciting an activation in regions commonly associated with emotion processing. The results indicated that the different fMRI paradigms elicited different neural activation patterns. The EMOBACK task elicited activation in the right dlPFC and the bilateral anterior insula and deactivation in the pgACC (but no significant change in amygdala activation). The activation in the bilateral anterior insula in response to the EMOBACK was also significantly stronger than that of any other task recruiting the anterior insula. The FACES task induced activity selectively in the bilateral amygdala and the two tasks that used picture stimuli of emotionally valanced scenes, OASIS and IAPS, both induced activity in the bilateral amygdala and insula. While the activations in the right amygdala and anterior insula appeared stronger in the IAPS task, there was less variance in the OASIS task, which consisted solely of negative emotional scenes, resulting in more statistically significant activations. Activation in the amygdala, the region significantly activated in both the OASIS and FACES task, was not significantly correlated between the two tasks.

4.2 Comparison with the literature[9]

A meta-analysis of n-back tasks with neutral stimuli found activity in the bilateral middle frontal gyrus and left anterior insula (among other regions; Wang et al., 2019), pointing to the activation in the right anterior insula in the EMOBACK task being attributable to the emotional nature of the stimuli at use. The activation elicited by the emotional n-back task in this study is in line with previous research from our group that found activation in the bilateral dlPFC and anterior insula as well as deactivation in a region in the rostral anterior cingulate cortex (Grimm et al., 2012). While there was some activation in the left dlPFC, it was much less pronounced and not statistically significant. Previous studies have also reported predominant involvement of the right compared to the left dlPFC in coping with emotional distractors in working memory tasks (Erk et al., 2007; Van Dillen et al., 2009). The exploratory independent sample t-tests between the tasks revealed that the EMOBACK task elicited significantly greater right dlPFC and bilateral anterior insula activity than any other of the studied tasks. This finding is plausible given that the EMOBACK is the only task of those studied here that has a working memory

[8] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission.

[9] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission.

component on top of the emotional stimulation as well as the one with the shortest stimulus duration, likely requiring greater attention. No amygdala activation in response to the EMO-BACK task was found. This is in line with previous results showing high cognitive effort in emotion-cognition-interference tasks reducing amygdala activation in response to emotional stimuli (Erk et al., 2007) and the account that it is insular and not amydalar activation that mediates emotional capture of attention effects (Marxen et al., 2021). The EMOBACK also uses written words as stimuli, which have consistently been shown to be associated with a lower probability of amygdala activation compared to emotional pictures (Costafreda et al., 2008), possibly due to greater stimulus complexity of the latter (Schlochtermeier et al., 2013). The pregenual ACC is part of the default mode network, which is characterized by deactivation during goal-directed tasks but is activated in autobiographical and self-referential thought and social cognition (Raichle, 2015; Spreng, 2012). However, the pgACC is also implied in the cognitive regulation of affect (Palomero-Gallagher et al., 2019). The deactivation found here might thus represent an interaction of both reduced activity due to a cognitive process and involvement in the regulation of activity in emotion-reactive brain regions. A previous study from our group concordantly found the pgACC to deactivate less in an emotional compared to a neutral condition of the EMOBACK (Grimm et al., 2012).

The result regarding the FACES task eliciting amygdala activation distinctively is in line with meta-analytic findings on tasks using emotional faces (Müller et al., 2018; Sabatinelli et al., 2011), where several brain regions apart from the amygdala (e.g., fusiform gyrus) were significantly associated with viewing facial expressions of emotion, but none of the other ROIs studied here. Robust engagement of the bilateral amygdala has been found in response to facial stimuli regardless of valence (Müller et al., 2018). However, the amygdala is routinely implicated in orienting responses to behaviorally relevant stimuli, suggesting it is especially sensitive to the emotional content in facial expressions (Whalen et al., 2009).

The two tasks studied here that use pictures of naturalistic emotional scenes elicited activations in the anterior insula and amygdala. The tasks using naturalistic scene stimuli were found to elicit a wider set of neural activations than the FACES task, which is in line with a meta-analytic comparison of these two types of tasks (Sabatinelli et al., 2011). While this meta-analysis did not find an association of scenic emotional stimuli with activation in the anterior insula, a later meta-analysis did establish a robust association of anterior insula activation and emotional stimulation (Duerden et al., 2013). Although in direct comparison the IAPS task provoked a significantly greater activation in the right amygdala and right anterior insula, the OASIS task elicited more reliable (and significant) bilateral activation in both amygdala and anterior insula. This may be due to differences between the tasks: While the OASIS task shows only negative stimulus material to participants, the IAPS task uses both positive and negative scenes. The representation of positive and negative emotion in the brain seems to largely

overlap (Lindquist et al., 2016), however, there have been reports of negative emotions eliciting stronger activation in the amygdala (Wager et al., 2003) and the insula (Aldhafeeri et al., 2012) compared to positive emotions, which might explain the different activation patterns between the two tasks. It further seems plausible that showing aversive content exclusively, as in the OASIS task, might more likely induce a negative affective state as compared to alternating between pictures of positive and negative valence as in the IAPS task, hence triggering a more consistent neuronal response. As no ratings of subjective emotional experience were collected during the tasks, this remains speculative.

The results from the direct comparison of the FACES and the OASIS tasks is in line with another report of the right anterior insula being more strongly activated by emotional scene than by emotional face stimuli (Reisch et al., 2020). Both findings appear at odds with another study that compared passive viewing tasks of emotional facial expressions and scenes (Britton et al., 2006). In this study, the anterior insula activity was greater in response to emotional face stimuli compared to naturalistic scenes. The stimuli selection (a wider range of emotions including positive ones) and contrasts used (emotion – fixation), however, were different from the tasks studied here. It remains inconclusive, whether the activation profiles this dissertation report from the studied tasks generalize to similar paradigms or are rather specific to the exact task.

Correlation analyses revealed that individual amygdala activation in the FACES and OASIS tasks are not consistently related. This finding is in line with previous research that found that while group level activations were consistent across different threat probing tasks, individual amygdala activation in the different paradigms was not significantly correlated (Villalta-Gil et al., 2017). This indicates that individual brain activations in different emotional fMRI paradigms should not be regarded as interchangeable measures but should rather always be interpreted with regard to the specific features of the task. However, consistent group effects arising from unreliable individual activations in task-based fMRI have also been reported for intertemporal choice and reward processing tasks (Fröhner et al., 2019; Nielson et al., 2021). The phenomenon might hence also represent a challenge that is pervasive in task-based fMRI research. In the history of the field, fMRI measures were mostly designed to study within-subject group effects and hence optimized for robustness (Elliott et al., 2021). Robustness however does not guarantee good reliability of the measure, which is needed to study between-subject effects (Infantolino et al., 2018; Moriarity & Alloy, 2021) and determine correlations between different tasks.

4.3 Implications

The results of this study demonstrate that the different paradigms elicit different activation profiles and can be used to address different aspects of emotion processing. The pattern of

activation elicited by the EMOBACK task suggests that it is well suited for the study of emotion-cognition interactions in the anterior insula, pgACC, and (right) dlPFC, as might be of interest for example in the study of depression and its treatment (Korgaonkar et al., 2013; Phillips et al., 2015). Investigators primarily interested in amygdala activation and its potential change in response to interventions could deduct from this study's results to employ the FACES task, whereas the OASIS task showed robust activation in amygdala as well as in anterior insula, allowing for a broader study of brain regions involved in emotion processing. The results are less conclusive about recommendations concerning the IAPS task. It might have the greatest face validity to assess emotion processing among the tasks studied here as it presents naturalistic scenes of both positive and negative valence. However, in the present sample, there was substantial variability in the neural response during IAPS task performance and a statistically significant change in activation was found only in the right amygdala.

Currently, a vast variety of fMRI paradigms are in use for the study of emotion processing. This limits the comparability between studies and impedes concise meta-analyses (Riedel et al., 2018). Therefore, it can be difficult to extract from the literature which paradigm is best suited for a specific research question; especially, as it has become clear that analytic choices can considerably impact the results of fMRI studies (Botvinik-Nezer et al., 2020; Poldrack et al., 2017). To allow for a comparison between fMRI tasks, it is crucial that the data are studied using the same analysis pipeline, as was done here. The results from this dissertation showing activation elicited by different emotional fMRI paradigms in relevant pre-defined ROIs might thus provide guidance for planning studies on emotion processing. Being able to purposefully choose the fMRI task with the biggest effect sizes in a given study's target regions will increase the power of that said study, thereby reducing the risk of false positive findings. A well-powered study further requires fewer participants to produce stable effects, which can reduce its cost.

4.4 Directions for future research

The present dissertation is an effort toward improving fMRI research by systematically investigating activation patterns elicited by fMRI paradigms and thus enabling better informed and more strategical task employment. However, much further research is needed. The field of affective and clinical neuroscience would ultimately profit from standard task protocols specific to the study of certain brain regions or mental processes as this would grant optimized comparability of results and meta-analytic synthesis. The establishment of a centralized online repository for fMRI paradigms, where upon publication of the study researchers could upload the task material, is technically feasible and could support and accelerate the development of standardized paradigms (Wall, 2018).

Furthermore, recent studies have shown that the fMRI paradigms currently in use lack the reliability that would be needed for the use of fMRI as a biomarker in pathology and intervention research (Elliott et al., 2020; Fröhner et al., 2019; however, see also Chen, et al. 2021; Kragel

et al., 2020). Among the potential remedies that have been discussed is increasing the amount of individual data collected (i.e., longer scan time) (Chen et al., 2021; Gordon et al., 2017; Nee, 2019), which could be achieved by collecting several runs of the task in question. Another approach is increasing field strength. Good reliability for activations associated with emotional stimulation has been shown at 7T (Berboth et al., 2021; Geissberger et al., 2020). However, both these means are costly. In contrast, optimizing fMRI tasks for psychometric measures like reliability is relatively inexpensive and could maximize efficiency of fMRI research allowing researchers to collect smaller amounts of higher quality data instead of accruing high amounts of lesser quality data (McDermott et al., 2018; Moriarity & Alloy, 2021; Wall, 2018). Future research should strive to apply techniques from the field of psychometrics, such as item-response theory to the selection of stimuli to realize optimal psychometric properties for fMRI tasks (Wilson et al., 2021). Furthermore normative data on neural activation to fMRI paradigms should be collected from representative healthy and clinical populations as it would allow for the interpretation of individuals' neural responses to the tasks (McDermott et al., 2018).

4.5 Limitations[10]

The present dissertation has limitations that need to be considered when interpreting its results. Although the region of interest approach does increase power compared to whole-brain analyses, the size of the available samples was quite small, especially considering that the effects reported for emotion perception tasks are at best of moderate size (.5< Cohen's *d* <.8; (Poldrack et al., 2017)). The study thus had limited power to find 'true' effects and there is an increased likelihood of statistically significant results representing false positives. However, Bonferroni-correction was applied to account for multiple testing, limiting the risk of false positive results. Pre-registering the choice of ROIs would have been a way to further strengthen this dissertations results (Gentili et al., 2020) and while a clear rational for the choice is given, the lack of a time-stamped registration should be considered a limitation of this study. The data analyzed in this dissertation stem from different samples adding in-between subject variance and were collected on different MRI scanners (although with largely similar sequences). Therefore, systematic variability in the data stemming from the acquisition set-up (Jovicich et al., 2009) cannot be ruled out. Studies investigating multi-site-reliability of task-based fMRI found that a possible effect of site on the data is likely small (Forsyth et al., 2014; Gee et al., 2015). Nevertheless, it is a limitation of the present dissertation that acquisition site was not included in the statistical modelling of the data. The mean age of the samples studied differed notably, and although a recent meta-analysis (García-García et al., 2016) did not find an effect of age

[10] Adapted from Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain sciences*, *11*(5), 525. CC-BY 4.0. Adapted with permission.

on neural activations during emotion processing, such effects have been suggested (Cacioppo et al., 2011; MacCormack et al., 2020) and might have influenced the differences between activation patterns observed here. As all participants in this study were young to middle-aged, a possible impact of age differences on the data it is likely small. Lastly, the samples analyzed for this dissertation were confined to males, potentially limiting the generalizability of the results. There have been reports of gender differences in neural processes in emotion processing (e.g.,Wrase et al., 2003) and earlier meta-analyses found functional lateralization differences based on gender (Stevens & Hamann, 2012; Wager et al., 2003). However, their methodology has been contested (Bluhm, 2013), and the latest meta-analysis on emotion processing specifically (García-García et al., 2016) and neural activity in task-based fMRI research more generally did not find evidence for reliable gender differences (Eliot et al., 2021). However, a potential influence of selection bias on the results of this dissertation cannot be ruled out.

5. Conclusions

The present dissertation found that the four studied fMRI paradigms, that are frequently used to study emotion processing, elicit different neural activation patterns in core brain regions of emotion processing. These differences make the paradigms best suited for different research interest. Its results suggest that the FACES task can ideally be employed for the selective study of the amygdala, whereas the OASIS task evoked significant activations both in the left anterior insula and the amygdalae. The EMOBACK task elicited a deactivation of the pgACC and activation in the right dlPFC and bilateral anterior insula and is hence best suited for the study emotion-cognition interactions and the underlying interplay of brain regions from different networks. Amygdala activation in response to two of the tasks (FACES and OASIS) was not significantly correlated, warning of easily equating paradigms with each other. These results are valuable to inform the planning of future studies and the eventual development of functional MRI biomarkers.

6. References

Aldhafeeri, F. M., Mackenzie, I., Kay, T., Alghamdi, J., & Sluming, V. (2012). Regional brain responses to pleasant and unpleasant IAPS pictures: Different networks. *Neuroscience letters*, *512*, 94–98. https://doi.org/10.1016/j.neulet.2012.01.064

Berboth, S., Windischberger, C., Kohn, N., & Morawetz, C. (2021). Test-retest reliability of emotion regulation networks using fMRI at ultra-high magnetic field. *NeuroImage*, *232*, 117917. https://doi.org/10.1016/j.neuroimage.2021.117917

Bluhm, R. (2013). New research, old problems: Methodological and ethical issues in fMRI research examining sex/gender differences in emotion processing. *Neuroethics*, *6*, 319–330. https://doi.org/10.1007/s12152-011-9143-3

Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J. A., Adcock, R. A., Avesani, P., Baczkowski, B. M., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., Benoit, R. G., Berkers, R. M. W. J., Bhanji, J. P., Biswal, B. B., Bobadilla-Suarez, S., Bortolini, T., Bottenhorn, K. L., Bowring, A., Braem, S., Brooks, H. R., Brudner, E. G., Calderon, C. B., Camilleri, J. A., Castrellon, J. J., Cecchetti, L., Cieslik, E. C., Cole, Z. J., Collignon, O., Cox, R. W., Cunningham, W. A., Czoschke, S., Dadi, K., Davis, C. P., De Luca, A., Delgado, M. R., Demetriou, L., Dennison, J. B., Di, X., Dickie, E. W., Dobryakova, E., Donnat, C. L., Dukart, J., Duncan, N. W., Durnez, J., Eed, A., Eickhoff, S. B., Erhart, A., Fontanesi, L., Fricke, G. M., Fu, S., Galván, A., Gau, R., Genon, S., Glatard, T., Glerean, E., Goeman, J. J., Golowin, S. A. E., González-García, C., Gorgolewski, K. J., Grady, C. L., Green, M. A., Guassi Moreira, J. F., Guest, O., Hakimi, S., Hamilton, J. P., Hancock, R., Handjaras, G., Hawco, H. B. B., Herholz, C. P., Herman, G., Heunis, S., Hoffstaedter, F., Hogeveen, J., Holmes, S., Hu, C.-P., Huettel, S. A., Hughes, M. E., Iacovella, V., Iordan, A. D., Isager, P. M., Isik, A. I., Jahn, A., Johnson, M. R., Johnstone, T., Joseph, M. J. E., Juliano, A. C., Kable, J. W., Kassinopoulos, M., Koba, C., Kong, X.-Z., Koscik, T. R., Kucukboyaci, N. E., Kuhl, B. A., Kupek, S., Laird, A. R., Lamm, C., Langner, R., Lauharatanahirun, N., Lee, H., Lee, S., Leemans, A., Leo, A., Lesage, E., Li, F., Li, M. Y. C., Lim, P. C., Lintz, E. N., Liphardt, S. W., Losecaat Vermeer, A. B., Love, B. C., Mack, M. L., Malpica, N., Marins, T., Maumet, C., McDonald, K., McGuire, J. T., Melero, H., Méndez Leal, A. S., Meyer, B., Meyer, K. N., Mihai, G., Mitsis, G. D., Moll, J., Nielson, D. M., Nilsonne, G., Notter, M. P., Olivetti, E., Onicas, A. I., Papale, P., Patil, K. R., Peelle, J. E., Pérez, A., Pischedda, D., Poline, J.-B., Prystauka, Y., Ray, S., Reuter-Lorenz, P. A., Reynolds, R. C., Ricciardi, E., Rieck, J. R., Rodriguez-Thompson, A. M., Romyn, A., Salo, T., Samanez-Larkin, G. R., Sanz-Morales, E., Schlichting, M. L., Schultz, D. H., Shen, Q., Sheridan, M. A., Silvers, J. A., Skagerlund, K., Smith, A., Smith, D. V., Sokol-Hessner, P., Steinkamp, S. R., Tashjian, S. M., Thirion, B., Thorp, J. N., Tinghög, G., Tisdall, L., Tompson, S. H., Toro-Serey, C., Tresols, J. J. T., Tozzi, L., Truong, V., Turella, L., van 't Veer, A. E., Verguts, T., Vettel, J. M., Vijayarajah, S., Vo, K., Wall, M. B., Weeda, W. D., Weis, S., White, D. J., Wisniewski, D., Xifra-Porxas, A., Yearling, E. A., Yoon, S., Yuan, R., Yuen, K. S. L., Zhang, L., Zhang, X., Zosky, J. E., Nichols, T. E., Poldrack, R. A., & Schonberg, T. (2020). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, *582*, 84–88. https://doi.org/10.1038/s41586-020-2314-9

Bradley, M. M., & Lang, P. J. (1999). *Affective norms for English words (ANEW): Instruction manual and affective ratings*. Technical Report C-1, The Center for Research in Psychophysiology, University of Florida.

Britton, J. C., Taylor, S. F., Sudheimer, K. D., & Liberzon, I. (2006). Facial expressions and complex IAPS pictures: Common and differential networks. *Neuroimage*, *31*, 906–919. https://doi.org/10.1016/j.neuroimage.2005.12.050

Cacioppo, J. T., Berntson, G. G., Bechara, A., Tranel, D., & Hawkley, L. C. (2011). Could an aging brain contribute to subjective well-being? The value added by a social neuroscience perspective. In A. Todorov, S. Fiske & D. Prentice (Eds.), *Social neuroscience: Toward understanding the underpinnings of the social mind.* (pp. 249–262). Oxford: University Press. https://doi.org/10.1093/acprof:oso/9780195316872.003.0017

Chen, G., Pine, D. S., Brotman, M. A., Smith, A. R., Cox, R. W., & Haller, S. P. (2021). Beyond the intraclass correlation: A hierarchical modeling approach to test-retest assessment [Preprint]. *Neuroscience*. https://doi.org/10.1101/2021.01.04.425305

Chen, G., Pine, D. S., Brotman, M. A., Smith, A. R., Cox, R. W., Taylor, P. A., & Haller, S. P. (2021). Hyperbolic trade-off: The importance of balancing trial and subject sample sizes in neuroimaging. *BioRxiv*, 2021.07.15.452548. https://doi.org/10.1101/2021.07.15.452548

Citron, F. M. (2012). Neural correlates of written emotion word processing: A review of recent electrophysiological and hemodynamic neuroimaging studies. *Brain and language*, *122*, 211–226. https://doi.org/10.1016/j.bandl.2011.12.007

Costafreda, S. G., Brammer, M. J., David, A. S., & Fu, C. H. Y. (2008). Predictors of amygdala activation during the processing of emotional stimuli: A meta-analysis of 385 PET and fMRI studies. *Brain Research Reviews*, *58*, 57–70. https://doi.org/10.1016/j.brainresrev.2007.10.012

Craig, A. D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature reviews neuroscience*, *3*, 655–666. https://doi.org/10.1038/nrn894

Duerden, E. G., Arsalidou, M., Lee, M., & Taylor, M. J. (2013). Lateralization of affective processing in the insula. *NeuroImage*, *78*, 159–175. https://doi.org/10.1016/j.neuroimage.2013.04.014

Duff, E. P., Cunnington, R., & Egan, G. F. (2007). REX: Response Exploration for Neuroimaging Datasets. *Neuroinformatics*, *5*, 223–234. https://doi.org/10.1007/s12021-007-9001-y

Eliot, L., Ahmed, A., Khan, H., & Patel, J. (2021). Dump the “dimorphism”: Comprehensive synthesis of human brain studies reveals few male-female differences beyond size. *Neuroscience & Biobehavioral Reviews*, *125*, 667–697. https://doi.org/10.1016/j.neubiorev.2021.02.026

Elliott, M. L., Knodt, A. R., & Hariri, A. R. (2021). Striving toward translation: Strategies for reliable fMRI measurement. *Trends in Cognitive Sciences, 25*, 776-787. https://doi.org/10.1016/j.tics.2021.05.008

Elliott, M. L., Knodt, A. R., Ireland, D., Morris, M. L., Poulton, R., Ramrakha, S., Sison, M. L., Moffitt, T. E., Caspi, A., & Hariri, A. R. (2020). What is the test-retest reliability of common task-functional MRI measures? New empirical evidence and a meta-analysis. *Psychological Science*, *31*, 792–806. https://doi.org/10.1177/0956797620916786

Enneking, V., Dzvonyar, F., Dück, K., Dohm, K., Grotegerd, D., Förster, K., Meinert, S., Lemke, H., Klug, M., Waltemate, L., Goltermann, J., Hülsmann, C., Borgers, T., Böhnlein, J., Sindermann, L., Richter, M., Leehr, E. J., Repple, J., Opel, N., Baune, B. T., Dannlowski, U., & Redlich, R. (2020). Brain functional effects of electroconvulsive

therapy during emotional processing in major depressive disorder. *Brain Stimulation*, *13*, 1051–1058. https://doi.org/10.1016/j.brs.2020.03.018

Erk, S., Kleczar, A., & Walter, H. (2007). Valence-specific regulation effects in a working memory task with emotional context. *Neuroimage*, *37*, 623–632. https://doi.org/10.1016/j.neuroimage.2007.05.006

Esteban, O., Markiewicz, C. J., Blair, R. W., Moodie, C. A., Isik, A. I., Erramuzpe, A., Kent, J. D., Goncalves, M., DuPre, E., & Snyder, M. (2019). fMRIPrep: A robust preprocessing pipeline for functional MRI. *Nature methods*, *16*, 111–116. https://doi.org/10.1038/s41592-018-0235-4

Forsyth, J. K., McEwen, S. C., Gee, D. G., Bearden, C. E., Addington, J., Goodyear, B., Cadenhead, K. S., Mirzakhanian, H., Cornblatt, B. A., & Olvet, D. M. (2014). Reliability of functional magnetic resonance imaging activation during working memory in a multisite study: Analysis from the North American Prodrome Longitudinal Study. *Neuroimage*, *97*, 41–52. https://doi.org/10.1016/j.neuroimage.2014.04.027

Friston, K. J., Holmes, A. P., Price, C. J., Büchel, C., & Worsley, K. J. (1999). Multisubject fMRI Studies and Conjunction Analyses. *NeuroImage*, *10*, 385–396. https://doi.org/10.1006/nimg.1999.0484

Fröhner, J. H., Teckentrup, V., Smolka, M. N., & Kroemer, N. B. (2019). Addressing the reliability fallacy in fMRI: Similar group effects may arise from unreliable individual effects. *NeuroImage*, *195*, 174–189. https://doi.org/10.1016/j.neuroimage.2019.03.053

Fusar-Poli, P., Placentino, A., Carletti, F., Landi, P., Allen, P., Surguladze, S., Benedetti, F., Abbamonte, M., Gasparotti, R., & Barale, F. (2009). Functional atlas of emotional faces processing: A voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. *Journal of Psychiatry & Neuroscience, 34*, 418-432.

García-García, I., Kube, J., Gaebler, M., Horstmann, A., Villringer, A., & Neumann, J. (2016). Neural processing of negative emotional stimuli and the influence of age, sex and task-related characteristics. *Neuroscience and biobehavioral reviews*, *68*, 773–793. https://doi.org/10.1016/j.neubiorev.2016.04.020

Gee, D. G., McEwen, S. C., Forsyth, J. K., Haut, K. M., Bearden, C. E., Addington, J., Goodyear, B., Cadenhead, K. S., Mirzakhanian, H., Cornblatt, B. A., Olvet, D., Mathalon, D. H., McGlashan, T. H., Perkins, D. O., Belger, A., Seidman, L. J., Thermenos, H., Tsuang, M. T., Erp, T. G. M. van, Walker, E. F., Hamann, S., Woods, S. W., Constable , T., & Cannon, T. D. (2015). Reliability of an fMRI paradigm for emotional processing in a multisite longitudinal study. *Human Brain Mapping*, *36*, 2558–2579. https://doi.org/10.1002/hbm.22791

Geissberger, N., Tik, M., Sladky, R., Woletz, M., Schuler, A.-L., Willinger, D., & Windischberger, C. (2020). Reproducibility of amygdala activation in facial emotion processing at 7T. *NeuroImage*, *211*, 116585. https://doi.org/10.1016/j.neuroimage.2020.116585

Gentili, C., Cecchetti, L., Handjaras, G., Lettieri, G., & Cristea, I. A. (2020). The case for preregistering all region of interest (ROI) analyses in neuroimaging research. *European Journal of Neuroscience*, *53*, 357–361. https://doi.org/10.1111/ejn.14954

Gentili, C., Cristea, I. A., Angstadt, M., Klumpp, H., Tozzi, L., Phan, K. L., & Pietrini, P. (2016). Beyond emotions: A meta-analysis of neural response within face processing system in social anxiety. *Experimental Biology and Medicine*, *241*, 225–237. https://doi.org/10.1177/1535370215603514

Gordon, E. M., Laumann, T. O., Gilmore, A. W., Newbold, D. J., Greene, D. J., Berg, J. J., Ortega, M., Hoyt-Drazen, C., Gratton, C., Sun, H., Hampton, J. M., Coalson, R. S., Nguyen, A. L., McDermott, K. B., Shimony, J. S., Snyder, A. Z., Schlaggar, B. L.,

Petersen, S. E., Nelson, S. M., & Dosenbach, N. U. F. (2017). Precision Functional Mapping of Individual Human Brains. *Neuron*, *95*, 791-807.e7. https://doi.org/10.1016/j.neuron.2017.07.011

Grimm, S., Weigand, A., Kazzer, P., Jacobs, A. M., & Bajbouj, M. (2012). Neural mechanisms underlying the integration of emotion and working memory. *NeuroImage*, *61*, 1188–1194. https://doi.org/10.1016/j.neuroimage.2012.04.004

Grühn, D., & Sharifian, N. (2021). Chapter 9—Lists of emotional stimuli. In H. L. Meiselman (Ed.), *Emotion Measurement (Second Ed.)* (pp. 251–271). Woodhead Publishing. https://doi.org/10.1016/B978-0-12-821124-3.00009-0

Hariri, A. R., Tessitore, A., Mattay, V. S., Fera, F., & Weinberger, D. R. (2002). The amygdala response to emotional stimuli: A comparison of faces and scenes. *Neuroimage*, *17*, 317–323. https://doi.org/10.1006/nimg.2002.1179

Infantolino, Z. P., Luking, K. R., Sauder, C. L., Curtin, J. J., & Hajcak, G. (2018). Robust is not necessarily reliable: From within-subjects fMRI contrasts to between-subjects comparisons. *NeuroImage*, *173*, 146–152. https://doi.org/10.1016/j.neuroimage.2018.02.024

Jaeggi, S. M., Buschkuehl, M., Perrig, W. J., & Meier, B. (2010). The concurrent validity of the N-back task as a working memory measure. *Memory, 18*, 394–412. https://doi.org/10.1080/09658211003702171

Jovicich, J., Czanner, S., Han, X., Salat, D., van der Kouwe, A., Quinn, B., Pacheco, J., Albert, M., Killiany, R., Blacker, D., Maguire, P., Rosas, D., Makris, N., Gollub, R., Dale, A., Dickerson, B. C., & Fischl, B. (2009). MRI-derived measurements of human subcortical, ventricular and intracranial brain volumes: Reliability effects of scan sessions, acquisition sequences, data analyses, scanner upgrade, scanner vendors and field strengths. *Neuroimage*, *46*, 177–192. https://doi.org/10.1016/j.neuroimage.2009.02.010

Kohn, N., Eickhoff, S. B., Scheller, M., Laird, A. R., Fox, P. T., & Habel, U. (2014). Neural network of cognitive emotion regulation—An ALE meta-analysis and MACM analysis. *Neuroimage*, *87*, 345–355. https://doi.org/10.1016/j.neuroimage.2013.11.001

Korgaonkar, M. S., Grieve, S. M., Etkin, A., Koslow, S. H., & Williams, L. M. (2013). Using Standardized fMRI Protocols to Identify Patterns of Prefrontal Circuit Dysregulation that are Common and Specific to Cognitive and Emotional Tasks in Major Depressive Disorder: First Wave Results from the iSPOT-D Study. *Neuropsychopharmacol*, *38*, 863–871. https://doi.org/10.1038/npp.2012.252

Kragel, P. A., Han, X., Kraynak, T. E., Gianaros, P. J., & Wager, T. D. (2020). FMRI can be highly reliable, but it depends on what you measure [Preprint]. *PsyArXiv.* https://doi.org/10.31234/osf.io/9eaxk

Kurdi, B., Lozano, S., & Banaji, M. R. (2017). Introducing the Open Affective Standardized Image Set (OASIS). *Behavior Research Methods*, *49*, 457–470. https://doi.org/10.3758/s13428-016-0715-3

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International affective picture system (IAPS): Technical manual and affective ratings. *NIMH Center for the Study of Emotion and Attention*, *1*, 39–58.

Lindquist, K. A., Satpute, A. B., Wager, T. D., Weber, J., & Barrett, L. F. (2016). The Brain Basis of Positive and Negative Affect: Evidence from a Meta-Analysis of the Human Neuroimaging Literature. *Cerebral Cortex*, *26*, 1910–1922. https://doi.org/10.1093/cercor/bhv001

Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: A meta-analytic review. *Behav Brain Sci, 35*, 121–143. doi:10.1017/S0140525X11000446

MacCormack, J. K., Stein, A. G., Kang, J., Giovanello, K. S., Satpute, A. B., & Lindquist, K. A. (2020). Affect in the aging brain: A neuroimaging meta-analysis of older vs. younger adult affective experience and perception. *Affective Science*, *1*, 128–154. https://doi.org/10.1007/s42761-020-00016-8

Marxen, M., Jacob, M. J., Hellrung, L., Riedel, P., & Smolka, M. N. (2021). Questioning the role of amygdala and insula in an attentional capture by emotional stimuli task. *Human Brain Mapping*, *42*, 1257–1267. https://doi.org/10.1002/hbm.25290

McDermott, T. J., Kirlic, N., & Aupperle, R. L. (2018). Roadmap for optimizing the clinical utility of emotional stress paradigms in human neuroimaging research. *Neurobiology of stress*, *8*, 134–146. https://doi.org/10.1016/j.ynstr.2018.05.001

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., & Garrido, M. I. (2016). A rapid subcortical amygdala route for faces irrespective of spatial frequency and emotion. *BioRxiv*, 078097. https://doi.org/10.1101/078097

McTeague, L. M., Rosenberg, B., Lopez, J. M., Carreon, D., Huemer, J., Jiang, Y., Chick, C., Eickhoff, S., & Etkin, A. (2020). Identification of common neural circuit disruptions in emotional processing across psychiatric disorders. *The American Journal of Psychiatry*, *177*, 411–421. https://doi.org/10.1176/appi.ajp.2019.18111271

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., Vuilleumier, P., Gil-Nagel, A., & Strange, B. A. (2016). A fast pathway for fear in human amygdala. *Nature Neuroscience*, *19*, 1041–1049. https://doi.org/10.1038/nn.4324

Moriarity, D. P., & Alloy, L. B. (2021). Back to basics: The importance of measurement properties in biological psychiatry. *Neuroscience & Biobehavioral Reviews*, *123*, 72–82. https://doi.org/10.1016/j.neubiorev.2021.01.008

Müller, V. I., Höhner, Y., & Eickhoff, S. B. (2018). Influence of task instructions and stimuli on the neural network of face processing: An ALE meta-analysis. *Cortex*, *103*, 240–255. https://doi.org/10.1016/j.cortex.2018.03.011

Nee, D. E. (2019). FMRI replicability depends upon sufficient individual-level data. *Communications Biology*, *2*, 1–4. https://doi.org/10.1038/s42003-019-0378-6

Nielson, D. M., Keren, H., O'Callaghan, G., Jackson, S. M., Douka, I., Vidal-Ribas, P., Pornpattananangkul, N., Camp, C. C., Gorham, L. S., Wei, C., Kirwan, S., Zheng, C. Y., & Stringaris, A. (2021). Great expectations: A critical review of and suggestions for the study of reward processing as a cause and predictor of depression. *Biological Psychiatry*, *89*, 134–143. https://doi.org/10.1016/j.biopsych.2020.06.012

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: A synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*, *1251*, E1-24. doi:10.1111/j.1749-6632.2012.06751.x

Olszanowski, M., Pochwatko, G., Kuklinski, K., Scibor-Rylski, M., Lewinski, P., & Ohme, R. K. (2015). Warsaw set of emotional facial expression pictures: A validation study of facial display photographs. *Frontiers in psychology*, *5*, 1516. https://doi.org/10.3389/fpsyg.2014.01516

Outhred, T., Das, P., Felmingham, K., Bryant, R., Nathan, P., Malhi, G., & Kemp, A. (2014). Impact of acute administration of escitalopram on the processing of emotional and neutral images: A randomized crossover fMRI study of healthy women. *Journal of Psychiatry & Neuroscience: JPN*, *39*, 267–275. https://doi.org/10.1503/jpn.130118

Palomero-Gallagher, N., Hoffstaedter, F., Mohlberg, H., Eickhoff, S. B., Amunts, K., & Zilles, K. (2019). Human pregenual anterior cingulate cortex: Structural, functional, and connectional heterogeneity. *Cerebral Cortex*, *29*, 2552–2574. https://doi.org/10.1093/cercor/bhy124

Penny, W. D., Friston, K. J., Ashburner, J. T., Kiebel, S. J., & Nichols, T. E. (2011). *Statistical parametric mapping: The analysis of functional brain images*. Amsterdam: Elsevier.

Pessoa, L. (2010). Emotion and cognition and the amygdala: From "what is it?" to "what's to be done?". *Neuropsychologia*, *48*, 3416–3429. https://doi.org/10.1016/j.neuropsychologia.2010.06.038

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage*, *16*, 331–348. https://doi.org/10.1006/nimg.2002.1087

Phillips, M. L., Chase, H. W., Sheline, Y. I., Etkin, A., Almeida, J. R., Deckersbach, T., & Trivedi, M. H. (2015). Identifying predictors, moderators, and mediators of antidepressant response in major depressive disorder: Neuroimaging approaches. *American Journal of Psychiatry*, *172*, 124–138. https://doi.org/10.1176/appi.ajp.2014.14010076

Poldrack, R. A., Baker, C. I., Durnez, J., Gorgolewski, K. J., Matthews, P. M., Munafò, M. R., Nichols, T. E., Poline, J.-B., Vul, E., & Yarkoni, T. (2017). Scanning the horizon: Towards transparent and reproducible neuroimaging research. *Nature reviews neuroscience*, *18*, 115-126. https://doi.org/10.1038/nrn.2016.167

Price, C., Veltman, D., Ashburner, J., Josephs, O., & Friston, K. (1999). The critical relationship between the timing of stimulus presentation and data acquisition in blocked designs with fMRI. *Neuroimage*, *10*, 36–44. https://doi.org/10.1006/nimg.1999.0447

Raichle, M. E. (2015). The Brain's Default Mode Network. *Annual Review of Neuroscience*, *38*, 433–448. https://doi.org/10.1146/annurev-neuro-071013-014030

Reisch, L. M., Wegrzyn, M., Woermann, F. G., Bien, C. G., & Kissler, J. (2020). Negative content enhances stimulus-specific cerebral activity during free viewing of pictures, faces, and words. *Human Brain Mapping*, *41*, 4332–4354. https://doi.org/10.1002/hbm.25128

Riedel, M. C., Yanes, J. A., Ray, K. L., Eickhoff, S. B., Fox, P. T., Sutherland, M. T., & Laird, A. R. (2018). Dissociable meta-analytic brain networks contribute to coordinated emotional processing. *Human brain mapping*, *39*, 2514–2531. https://doi.org/10.1002/hbm.24018

Sabatinelli, D., Fortune, E. E., Li, Q., Siddiqui, A., Krafft, C., Oliver, W. T., Beck, S., & Jeffries, J. (2011). Emotional perception: Meta-analyses of face and natural scene processing. *Neuroimage*, *54*, 2524–2533. https://doi.org/10.1016/j.neuroimage.2010.10.011

Schlochtermeier, L. H., Kuchinke, L., Pehrs, C., Urton, K., Kappelhoff, H., & Jacobs, A. M. (2013). Emotional picture and word processing: An fMRI study on effects of stimulus complexity. *PLoS One*, *8*, e55619. https://doi.org/10.1371/journal.pone.0055619

Schweizer, S., Satpute, A. B., Atzil, S., Field, A. P., Hitchcock, C., Black, M., Barrett, L. F., & Dalgleish, T. (2019). The impact of affective information on working memory: A pair of meta-analytic reviews of behavioral and neuroimaging evidence. *Psychological Bulletin*, *145*, 566-609. http://dx.doi.org/10.1037/bul0000193

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience*, *27*, 2349–2356. https://doi.org/10.1523/JNEUROSCI.5587-06.2007

Spreng, R. N. (2012). The fallacy of a “task-negative” network. *Frontiers in Psychology*, *3*, 145. https://doi.org/10.3389/fpsyg.2012.00145

Stevens, J. S., & Hamann, S. (2012). Sex differences in brain activation to emotional stimuli: A meta-analysis of neuroimaging studies. *Neuropsychologia*, *50*, 1578–1593. https://doi.org/10.1016/j.neuropsychologia.2012.03.011

Stuhrmann, A., Suslow, T., & Dannlowski, U. (2011). Facial emotion processing in major depression: A systematic review of neuroimaging findings. *Biology of Mood & Anxiety Disorders*, *1*, 1–17. https://doi.org/10.1186/2045-5380-1-10

Tang, W., Jbabdi, S., Zhu, Z., Cottaar, M., Grisot, G., Lehman, J. F., Yendiki, A., & Haber, S. N. (2019). A connectional hub in the rostral anterior cingulate cortex links areas of emotion and cognitive control. *eLife*, *8*. https://doi.org/10.7554/eLife.43761

Van Dillen, L. F., Heslenfeld, D. J., & Koole, S. L. (2009). Tuning down the emotional brain: An fMRI study of the effects of cognitive load on the processing of affective images. *NeuroImage*, *45*, 1212–1219. https://doi.org/10.1016/j.neuroimage.2009.01.016

Villalta-Gil, V., Hinton, K. E., Landman, B. A., Yvernault, B. C., Perkins, S. F., Katsantonis, A. S., Sellani, C. L., Lahey, B. B., & Zald, D. H. (2017). Convergent individual differences in visual cortices, but not the amygdala across standard amygdalar fMRI probe tasks. *Neuroimage*, *146*, 312–319. https://doi.org/10.1016/j.neuroimage.2016.11.038

Võ, M. L., Conrad, M., Kuchinke, L., Urton, K., Hofmann, M. J., & Jacobs, A. M. (2009). The Berlin affective word list reloaded (BAWL-R). *Behavior research methods*, *41*, 534–538. https://doi.org/10.3758/BRM.41.2.534

Vogt, B. A. (2014). Submodalities of emotion in the context of cingulate subregions. *Cortex*, *59*, 197–202. ISSN 0010-9452

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: A meta-analysis of findings from neuroimaging. *Neuroimage*, *19*, 513–531. https://doi.org/10.1016/S1053-8119(03)00078-8

Wall, M. (2018). *Reliability starts with the experimental tools employed*. https://doi.org/10.31234/osf.io/upynr

Wang, H., He, W., Wu, J., Zhang, J., Jin, Z., & Li, L. (2019). A coordinate-based meta-analysis of the n-back working memory paradigm using activation likelihood estimation. *Brain and Cognition*, *132*, 1–12. https://doi.org/10.1016/j.bandc.2019.01.002

Whalen, P., Davis, F. C., Oler, J. A., Kim, H., Kim, M. J., & Neta, M. (2009). Human amygdala responses to facial expressions of emotion. In P. J. Whalen & E. A. Phelps (Eds.), *The human amygdala.* (pp. 265–288). The Guilford Press.

Wilson, K. A., Clark, D. A., & MacNamara, A. (2021). Using item response theory to select emotional pictures for psychophysiological experiments. *International Journal of Psychophysiology*, *162*, 166–179. https://doi.org/10.1016/j.ijpsycho.2021.02.003

Wrase, J., Klein, S., Gruesser, S. M., Hermann, D., Flor, H., Mann, K., Braus, D. F., & Heinz, A. (2003). Gender differences in the processing of standardized emotional visual stimuli in humans: A functional magnetic resonance imaging study. *Neuroscience Letters*, *348*, 41–45. https://doi.org/10.1016/S0304-3940(03)00565-2

Wu, M., Kujawa, A., Lu, L. H., Fitzgerald, D. A., Klumpp, H., Fitzgerald, K. D., Monk, C. S., & Phan, K. L. (2016). Age-related changes in amygdala-frontal connectivity during emotional face processing from childhood into young adulthood. *Human Brain Mapping*, *37*, 1684–1695. https://doi.org/10.1002/hbm.23129

Zaki, J., Davis, J. I., & Ochsner, K. N. (2012). Overlapping activity in anterior insula during interoception and emotional experience. *Neuroimage*, *62*, 493–499. https://doi.org/10.1016/j.neuroimage.2012.05.012

Zuo, X.-N., Xu, T., & Milham, M. P. (2019). Harnessing reliability for neuroscience research. *Nature human behaviour*, *3*, 768–771. https://doi.org/10.1038/s41562-019-0655-x

7. Appendix

Supplementary Table 1 Task characteristics of the four emotion tasks (Reprinted from Hartling et al., 2021 with permission)

	IAPS	EMOBACK	OASIS	Faces
Task design	block design	block design	block design	block design
Conditions	Positive/negative	Positive/negative/ neutral	negative/scrambled	negative/scrambled
Contrast of interest	Emotional - break	Emotional – break	Negative – scrambled	Negative – scrambled
Stimulus modality	Picture	Word	Picture	Picture
Stimuli database	IAPS	BAWL	OASIS	WSEFEP
Num. of conditions	2	3	2	2
Total num. of stimuli	80	225	84	144
Num. of blocks	16	15	28	24
Blocks per condition	8	5	14	12
Stimuli per block	5	15	3	6
Block duration	20s	21s	18s	18s
Stimuli per condition	40	75	42	72
Stimulus duration	4s	500ms	6s	3s
Inter-stimulus interval	none	1500ms	none	none
Break duration	20 s	10-14s	20-21s	20-21s
Attention check	Question for 8s after each block	n-back task	Indicate whether person is in the picture/ frame colour	Indicate gender/frame colour
break	fixation cross	fixation cross	fixation cross	fixation cross
Overall duration	13min	12min	15min	15min
Volumes collected	384	331	430	370

Supplementary Table 2 MRI sequence parameters at the different sites. (Reprinted from Hartling et al., 2021 with permission)

	BCAN	UZH	CCNB
Manufacturer, model name, field strength	Siemens MAGNETOM Prisma 3T	Philips Achieva TX 3T	Siemen MAGNETOM Tri-oTim 3T
Receiver coil	12-channel head coil	8-channel head coil	12-channel head coil
Functional imaging			
Imaging type	EPI	EPI	EPI
TE	30ms	35ms	30ms
TR	2000ms	2000ms	2000ms
Flip angle	80°	82°	70°
Number of slices placed along the anterior–posterior commissure plane	36	32	37
Slice thickness	3mm	4mm	3mm
FOV	192mm	220mm	192mm
Voxel size	3x3x3	2.75 x 2.75 x 4 mm	3x3x3mm
Parallel imaging method	GRAPPA	SENSE	GRAPPA
Slice order	Interleaved	Ascending	Interleaved
Fat suppression	Fat saturation	Fat saturation	Fat saturation
Anatomical imaging			
Imaging type	3D	3D	3D
TR/TE	3.03ms	4.6 ms	2.52ms
TR	2300ms	9.3ms	1900ms
Flip angle	9°	8°	9°
Number of slices	192	160	176
FOV	256x256mm	240x240mm	256x256mm
Voxel size	1x1x1mm	1x1x1mm	1x1x1mm

Supplementary Table 3 Region of interest analyses for the four tasks. Mean parameter estimates standard deviation, parameters for two-sided Student t-test (t, df, p) and confidence intervals. (Reprinted from Hartling et al., 2021 with permission)

A. EMOBACK

	leftAInsula	leftAM	leftDLPFC	pgACC	rightAInsula	rightAM	rightDLPFC
Mean β	1.48495	-0.24744	0.47400	-1.04277	1.32879	-0.28052	1.93647
SD	0.49629	0.50044	0.68464	0.55353	0.57498	0.55892	0.79502
t	11.58833	-1.91496	2,68142	-7,29613	8,95062	-1,94384	9,43357
df	14	14	14	14	14	14	14
p	0.00001	0.07616	0.01790	0.00001	0.00001	0.07229	0.00001
95% CI	[1.21012, 1.75979]	[-0.52458, 0.0297]	[0.09486, 0.85314]	[-1.3493, -0.73623]	[1.01038. 1.64720]	[-0.59004, 0.029]	[1.49620, 2.37674]

B. FACES

	leftAInsula	leftAM	leftDLPFC	pgACC	rightAInsula	rightAM	rightDLPFC
Mean β	0.09323	0.46985	-0.03039	0.03257	-0.00293	0.46597	-0.09403
SD	0.16553	0.31467	0.16785	0.22641	0.16341	0.33638	0.16507
t	2.18137	5.78297	-0.70129	0.55709	-0.06952	5.36501	-2.20631
df	14	14	14	14	14	14	14
p	0.04670	0.00005	0.49461	0.58627	0.94556	0.00010	0.04457
95% CI	[0.00156, 0.18490]	[0.29559, 0.64410]	[-0.12335, 0.06256]	[-0.09282, 0.15795]	[-0.09343, 0.08756]	[0.27969, 0.65225]	[-0.18544, -0.00262]

C. OASIS

	leftAInsula	leftAM	leftDLPFC	pgACC	rightAInsula	rightAM	rightDLPFC
Mean β	0.29931	0.43119	0.05705	0.08167	0.16307	0.42283	0.03093
SD	0.29854	0.27543	0.20688	0.31179	0.20431	0.32088	0.27998
t	3.88297	6.06322	1.06807	1.01444	3.09125	5.10350	0.42790
df	14	14	14	14	14	14	14
p	0.00166	0.00003	0.30356	0.32758	0.00797	0.00016	0.67523
95% CI	[0.13399, 0.46464]	[0.27866, 0.58372]	[-0.05752, 0.17162]	[-0.091, 0.25433]	[0.04993, 0.27622]	[0.24513, 0.60052]	[-0.12411, 0.18598]

D. IAPS

	leftAInsula	leftAM	leftDLPFC	pgACC	rightAInsula	rightAM	rightDLPFC
Mean β	0.40364	0.64603	0.20267	-0.33096	0.36585	0.89803	0.24453
SD	0.68117	0.82985	0.64881	0.62744	0.46560	0.80244	0.69763
t	2.29500	3.01507	1.20983	-2.04289	3.04322	4.33437	1.35752
df	14	14	14	14	14	14	14
p	0.03771	0.00927	0.24638	0.06036	0.00877	0.00069	0.19610
95% CI	[0.02642, 0.78086]	[0.18647, 1.10558]	[-0.15663, 0.56197]	[-0.67843, 0.01651]	[0.10801, 0.62369]	[0.45366, 1.34241]	[-0.14181, 0.63086]

Supplementary Table 4 Exploratory paired t-test (two-sided) parameters for mean parameter estimates in FACES and OASIS tasks collected in the same sample. (This table appears only this dissertation framework, its author holds the copyright. It has not previously been published.)

	leftAInsula	leftAM	leftDLPFC	pgACC	rightAInsula	rightAM	rightDLPFC
df	14	14	14	14	14	14	14
t	-1.944	.366	-1.195	- .480	-2.453	.383	-1.87
p	.072	.72	.252	.638	.028	.708	.082
Cohen’s d	.502	.095	.308	.124	.633	.099	.483

Supplementary Table 5 Exploratory independent sample t-test (two-sided) parameters for contrasts between mean parameter estimates for tasks collected in independent samples. (Reprinted from Hartling et al., 2021 with permission)

A. pgACC

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
T	-1.944	-7.286	-6.779	-2.111	-2.281
p	0.062	<.001	<.001	.044	.030
Cohen’s d	.734	2.753	2.562	.798	.862

B. right dlPFC

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	4.669	9.579	8.107	1.829	1.100
p	<.001	<.001	<.001	.078	.280
Cohen’s d	1.765	3.6216	3.064	.691	.41

C. left dlPFC

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	.556	2.598	1.898	.135	.828
p	.583	.015	.068	.188	.415
Cohen’s d	.210	.982	.718	.509	.313

D. right anterior insula

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	3.412	8.106	6.385	2.894	1.544
p	.002	<.001	<.001	.007	.134
Cohen’s d	1.292	3.064	2.413	1.094	.583

E. left anterior insula

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	3.037	9.111	5.933	1.715	.543
p	.005	<.001	<.001	.097	.591
Cohen’s d	1.148	3.443	2.243	.648	.205

F. right amygdala

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	-4.912	-5.424	-5.193	1.923	2.130
p	<.001	<.001	<.001	.065	.042
Cohen’s d	1.857	2.050	1.963	.727	.805

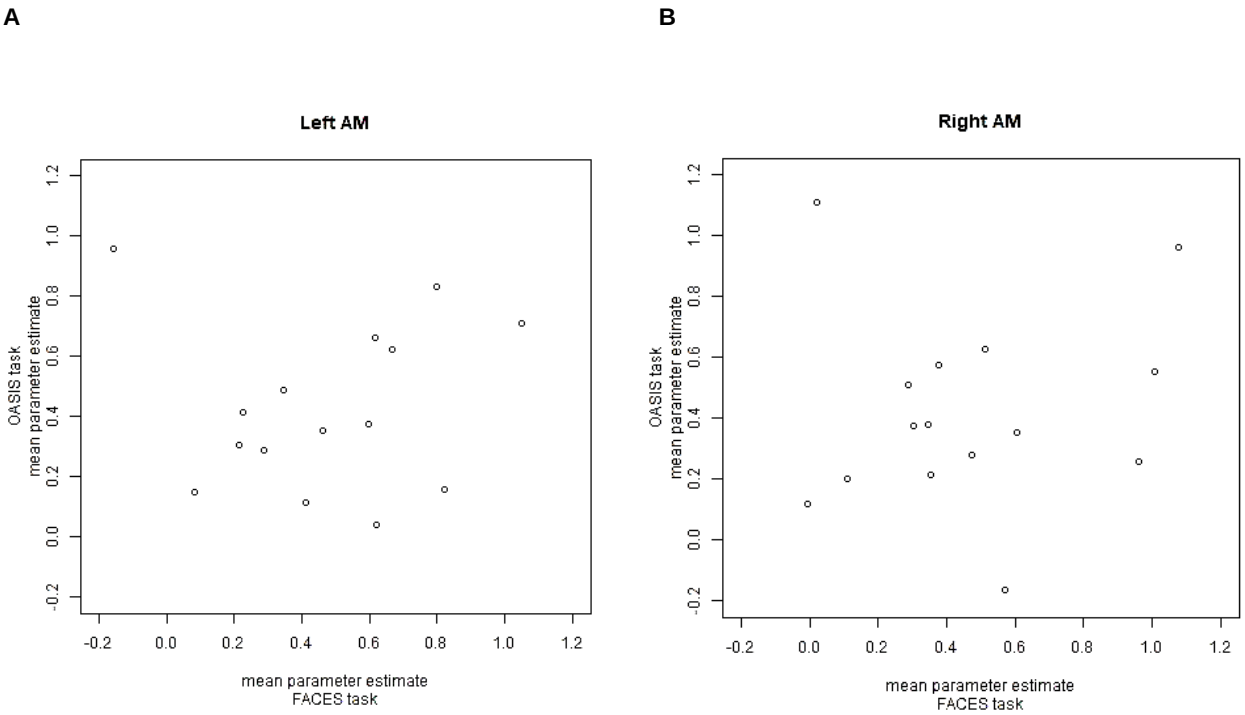
G. left amygdala

Contrast	EMOBACK / IAPS	EMOBACK / FACES	EMOBACK / OASIS	IAPS / FACES	IAPS / OASIS
df	28	28	28	28	28
t	-3.709	-6.264	-6.360	.769	.952
p	<.001	<.001	<.001	.448	.349
Cohen’s d	1.402	2.368	2.404	.291	.360

Supplementary Table 6 Correlation of mean parameter estimates of amygdala activation in FACES and OASIS task. This table only appears in this this dissertation framework, its author holds the copyright. It has not previously been published.

Variable	*M*	*SD*	1. leftAM FACES	2. rightAM FACES	3. leftAM OASIS
1. leftAM FACES	0.47	0.31			
2. rightAM FACES	0.47	0.34	.84** [.58, .95]		
3. leftAM OASIS	0.43	0.28	.05 [-.48, .55]	.10 [-.44, .58]	
4. rightAM OASIS	0.42	0.32	-.05 [-.55, .47]	.12 [-.42, .59]	.90** [.72, .97]

Note. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$.



Supplementary Figure 1 Scatterplots of mean parameter estimates of neural activation in FACES and OASIS tasks in A) left amygdala and B) right amygdala. (This figure appears only in this dissertation framework, its author holds the copyright. It has not previously been published).

VII Eidesstattliche Versicherung und Anteilserklärung

Eidesstattliche Versicherung

Ich, Corinna Hartling, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „FMRI emotion research and its dependence on task specifics: comparing four standard paradigms“ / „Die Abhängigkeit von fMRT-basierter Emotionsforschung von Aufgabenmerkmalen: Vergleich von vier Standardparadigmen“ selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.

_____ _____

Datum Unterschrift

Anteilserklärung an der erfolgten Publikation

Corinna Hartling ist alleinige Erstautorin der folgenden Publikation:

Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A. Weigand, A*. & Grimm, S.* (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain Sciences*, *11*(5), 525.

*These authors contributed equally

Der Beitrag im Einzelnen:

Die Fragestellung der vorliegenden Dissertation habe ich eigenständig unter Supervision von Prof. Dr. Simone Grimm und Dr. Anne Weigand entwickelt und habe nach umfassender Sichtung der Literatur die regions of interest (ROI) für die Studie selbst ausgewählt.

Für Teile der Daten, die in Berlin erhoben wurden, habe ich die Rekrutierung der Probanden übernommen und war für die Durchführung der MRT-Messungen als „Advanced User“ und die Anleitung von Praktikant:innen und Bachelorand:innen als „Basic User“ verantwortlich.

Weiterhin war ich für das Management der behavioralen und Bildgebungsdaten für diese Studie verantwortlich. Dazu habe ich zuvor an einer Schulung des Teams Forschungsdatenmanagement der FU Berlin teilgenommen, sowie an einem Workshop zu “Reproducible Neuroimaging” im Rahmen der Berlin Oxford Summer School on Open Research 2019, der spezifisch auf Standards für die Dokumentation und Sicherung von Bildgebungsdaten (Brain Imaging Data Structure, BIDS) einging.

Ich habe die behavioralen Daten mit MATLAB ausgewertet. Die MRT-Daten habe ich mit SPM12 vorverarbeitet und danach 1st und 2nd-Level-Analysen ebenfalls mit SPM12 durchgeführt. Die dazu verwendeten Skripte habe ich mit der Unterstützung von Dr. Corinna Pehrs selbst geschrieben. Für die dann folgenden *region of interest*(ROI)-Analysen habe ich ROI-Masken in Zusammenarbeit mit Dr. Matti Gärtner selbst mittels der SPM-toolbox Marsbar erstellt und die Analysen dann mit der REX-toolbox für SPM ausgewertet. Um die Validität der folgenden statistischen Auswertung mit R zu gewährleisten, habe ich eine statistische Beratung am Institut für Biometrie und klinische Epidemiologie der Charité wahrgenommen. Alle Grafiken und Tabellen in der Veröffentlichung, sowie Supplementary Figure 1, Supplementary Tables 4 und 6 die nur in dieser Dissertation erscheinen sind aus den oben genannten Analysen hervorgegangen und von mir selbst erstellt worden.

Mir oblag die kritische Interpretation der Ergebnisse im Kontext der Literatur und ich bin Verfasserin der Erstfassung des Manuskripts. Bei diesem Prozess bin ich durch engmaschiges Feedback von den beiden Letztautorinnen Dr. Anne Weigand und Prof. Dr. Simone Grimm unterstützt worden. Alle Ko-Autor:innen haben Stellung bezogen zur Erstfassung und alle Anmerkungen wurden von mir eingearbeitet. Ich habe die Korrespondenz im peer-review-Prozess mit dem Journal übernommen und das Manuskript gemäß der Reviewerkommentare überarbeitet.

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Unterschrift der Doktorandin

VIII Auszug aus der Journal Summary List[11]

[11] entnommen: https://intranet.charite.de/fileadmin/user_upload/microsites/sonstige/medbib/Impact_Faktoren_2019/ISI-WEB-Liste-Kategorie-Neurosciences.pdf

Journal Data Filtered By: **Selected JCR Year: 2019** Selected Editions: SCIE,SSCI Selected Categories: **"NEUROSCIENCES"** Selected Category Scheme: WoS **Gesamtanzahl: 271 Journale**

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	NATURE REVIEWS NEUROSCIENCE	42,809	33.654	0.055400
2	NATURE NEUROSCIENCE	62,933	20.071	0.144390
3	BEHAVIORAL AND BRAIN SCIENCES	9,395	17.333	0.008170
4	TRENDS IN COGNITIVE SCIENCES	27,705	15.218	0.036050
5	JOURNAL OF PINEAL RESEARCH	10,537	14.528	0.009430
6	NEURON	95,056	14.415	0.199640
7	ACTA NEUROPATHOLOGICA	21,908	14.251	0.040740
8	TRENDS IN NEUROSCIENCES	20,011	12.891	0.021220
9	Annual Review of Neuroscience	13,215	12.547	0.012740
10	MOLECULAR PSYCHIATRY	22,227	12.384	0.054730
11	Nature Human Behaviour	2,457	12.282	0.014190
12	BIOLOGICAL PSYCHIATRY	44,016	12.095	0.053910
13	BRAIN	53,282	11.337	0.067050
14	SLEEP MEDICINE REVIEWS	8,077	9.613	0.013000
15	Molecular Neurodegeneration	4,933	9.599	0.011840
16	PROGRESS IN NEUROBIOLOGY	12,791	9.371	0.011250
17	FRONTIERS IN NEUROENDOCRINOLOGY	4,491	9.059	0.007050
18	ANNALS OF NEUROLOGY	37,304	9.037	0.044120
19	NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS	28,873	8.330	0.051900
20	Neurology-Neuroimmunology & Neuroinflammation	2,232	7.724	0.008400
21	NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY	3,992	7.500	0.005960

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
22	Neurobiology of Stress	1,055	7.197	0.003840
23	NEUROPSYCHOPHARMACOLOGY	26,281	6.751	0.040680
24	npj Parkinsons Disease	662	6.750	0.002500
25	BRAIN BEHAVIOR AND IMMUNITY	16,285	6.633	0.028560
26	Brain Stimulation	6,537	6.565	0.015580
27	NEUROSCIENTIST	5,188	6.500	0.007220
28	Acta Neuropathologica Communications	4,070	6.270	0.014730
29	CURRENT OPINION IN NEUROBIOLOGY	14,959	6.267	0.028730
30	Alzheimers Research & Therapy	3,876	6.116	0.011650
31	Neurotherapeutics	4,998	6.035	0.009520
32	GLIA	14,220	5.984	0.017250
33	NEUROIMAGE	102,632	5.902	0.125360
34	Annual Review of Vision Science	601	5.897	0.003700
35	Molecular Autism	2,510	5.869	0.007450
36	Journal of Neuroinflammation	13,709	5.793	0.025870
37	Translational Stroke Research	2,274	5.780	0.004520
38	JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM	19,492	5.681	0.024230
39	JOURNAL OF NEUROSCIENCE	167,114	5.673	0.181170
40	BRAIN PATHOLOGY	5,308	5.568	0.007020
41	Translational Neurodegeneration	1,030	5.551	0.002790
42	NEURAL NETWORKS	14,065	5.535	0.018910
43	PAIN	37,753	5.483	0.035730

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
44	Multiple Sclerosis Journal	11,792	5.412	0.019460
45	BIPOLAR DISORDERS	4,838	5.410	0.006610
46	Dialogues in Clinical Neuroscience	3,842	5.397	0.005280
47	Biological Psychiatry-Cognitive Neuroscience and Neuroimaging	1,361	5.335	0.005880
48	NEUROBIOLOGY OF DISEASE	17,200	5.332	0.023770
49	Brain Connectivity	2,431	5.263	0.005180
50	Journal of Parkinsons Disease	2,244	5.178	0.005810
51	CEREBRAL CORTEX	30,815	5.043	0.056030
52	Developmental Cognitive Neuroscience	3,177	4.966	0.010180
53	CEPHALALGIA	11,053	4.868	0.011970
54	NEUROPSYCHOLOGY REVIEW	3,114	4.840	0.004050
55	SLEEP	22,296	4.805	0.024610
56	JOURNAL OF HEADACHE AND PAIN	3,898	4.797	0.007600
57	PSYCHONEUROENDOCRINOLOGY	19,287	4.732	0.027100
58	JOURNAL OF NEUROSCIENCE RESEARCH	13,098	4.699	0.010490
59	EXPERIMENTAL NEUROLOGY	20,154	4.691	0.020070
60	Molecular Brain	2,785	4.686	0.006510
61	Current Neuropharmacology	4,178	4.668	0.006280
62	JOURNAL OF PAIN	10,887	4.621	0.015040
63	JOURNAL OF PHYSIOLOGY-LONDON	50,045	4.547	0.037090
64	EUROPEAN JOURNAL OF NEUROLOGY	11,015	4.516	0.017330
65	MOLECULAR NEUROBIOLOGY	15,297	4.500	0.031350

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
66	ACS Chemical Neuroscience	6,881	4.486	0.015300
67	Fluids and Barriers of the CNS	1,331	4.470	0.002240
68	NEUROPHARMACOLOGY	21,682	4.431	0.033110
69	HUMAN BRAIN MAPPING	23,094	4.421	0.042760
70	JOURNAL OF PSYCHIATRY & NEUROSCIENCE	3,297	4.382	0.004290
71	Current Neurology and Neuroscience Reports	3,429	4.376	0.006810
72	Nature and Science of Sleep	728	4.375	0.001970
73	Frontiers in Aging Neuroscience	9,063	4.362	0.026120
74	PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY	11,179	4.361	0.013670
75	NEUROBIOLOGY OF AGING	23,002	4.347	0.032570
76	INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY	6,749	4.333	0.011150
77	Neuroscience Bulletin	2,338	4.326	0.004870
78	NEUROENDOCRINOLOGY	4,958	4.271	0.004820
79	CURRENT OPINION IN NEUROLOGY	5,437	4.207	0.008280
80	ASN Neuro	984	4.167	0.001580
81	Journal of Neural Engineering	7,240	4.141	0.011940
82	Journal of Neuroimmune Pharmacology	2,809	4.113	0.003520
83	CNS Neuroscience & Therapeutics	3,598	4.074	0.005870
84	JOURNAL OF NEUROCHEMISTRY	34,378	4.066	0.021840
85	Frontiers in Molecular Neuroscience	6,721	4.057	0.020190
86	NUTRITIONAL NEUROSCIENCE	2,110	4.028	0.002640
87	CORTEX	10,979	4.009	0.022870

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
88	Current Opinion in Behavioral Sciences	2,507	3.990	0.012580
89	Developmental Neurobiology	3,049	3.935	0.006120
90	Cognitive Neurodynamics	988	3.925	0.001690
91	Frontiers in Cellular Neuroscience	11,389	3.921	0.034000
92	JOURNAL OF ALZHEIMERS DISEASE	23,214	3.909	0.048080
93	NEUROCHEMISTRY INTERNATIONAL	8,928	3.881	0.008010
94	EUROPEAN NEUROPSYCHOPHARMACOLOGY	7,597	3.853	0.013120
95	JOURNAL OF NEUROTRAUMA	15,388	3.793	0.021530
96	Frontiers in Neuroscience	17,395	3.707	0.049650
97	HEARING RESEARCH	11,072	3.693	0.012480
98	PSYCHOPHYSIOLOGY	14,586	3.692	0.012670
99	Annals of Clinical and Translational Neurology	2,571	3.660	0.011170
100	JOURNAL OF SLEEP RESEARCH	5,945	3.623	0.007370
101	CELLULAR AND MOLECULAR NEUROBIOLOGY	4,732	3.606	0.006190
102	Social Cognitive and Affective Neuroscience	7,347	3.571	0.019570
103	eNeuro	3,237	3.544	0.015940
104	Journal of NeuroEngineering and Rehabilitation	5,164	3.519	0.008430
105	JOURNAL OF NEURAL TRANSMISSION	7,111	3.505	0.007930
106	EUROPEAN JOURNAL OF PAIN	7,579	3.492	0.009730
107	Journal of Neurodevelopmental Disorders	1,342	3.487	0.003300
108	HIPPOCAMPUS	8,587	3.404	0.010830
109	GENES BRAIN AND BEHAVIOR	3,639	3.397	0.005080

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
110	BRAIN RESEARCH BULLETIN	9,714	3.370	0.007920
111	REVIEWS IN THE NEUROSCIENCES	2,211	3.358	0.002840
112	PSYCHIATRY AND CLINICAL NEUROSCIENCES	3,696	3.351	0.004260
113	Brain Sciences	1,994	3.332	0.004980
114	NEUROINFORMATICS	1,457	3.300	0.003170
115	Brain Structure & Function	6,749	3.298	0.020660
116	Frontiers in Systems Neuroscience	4,943	3.293	0.012720
117	Frontiers in Neuroanatomy	3,672	3.292	0.011730
118	NEUROTOXICOLOGY AND TERATOLOGY	3,700	3.274	0.003460
119	CLINICAL NEUROPHYSIOLOGY	19,764	3.214	0.020260
120	MOLECULAR AND CELLULAR NEUROSCIENCE	6,348	3.182	0.005770
121	Neural Regeneration Research	4,834	3.171	0.009500
122	Frontiers in Neural Circuits	3,428	3.156	0.010970
123	PSYCHOPHARMACOLOGY	22,417	3.130	0.019820
124	CEREBELLUM	3,076	3.129	0.005430
125	JOURNAL OF NEUROIMMUNOLOGY	10,508	3.125	0.009210
126	JOURNAL OF PSYCHOPHARMACOLOGY	6,262	3.121	0.009340
127	EUROPEAN JOURNAL OF NEUROSCIENCE	24,806	3.115	0.018730
127	JOURNAL OF THE NEUROLOGICAL SCIENCES	18,170	3.115	0.022200
127	NEUROMUSCULAR DISORDERS	4,882	3.115	0.008260
130	JOURNAL OF COGNITIVE NEUROSCIENCE	16,520	3.105	0.015590
130	NEUROTOXICOLOGY	7,022	3.105	0.007110

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Article

Comparison of four fMRI paradigms probing emotion processing

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Abstract: Previous fMRI research applied a variety of tasks to examine brain activity underlying emotion processing. While task characteristics are known to have a substantial influence on the elicited activations, direct comparisons of tasks that could guide study planning are scarce. We aimed to provide a comparison of four common emotion processing tasks based on the same analysis pipeline to suggest tasks best suited for the study of certain target brain regions. We studied an n-back task using emotional words (EMOBACK) as well as passive viewing tasks of emotional faces (FACES) and emotional scenes (OASIS and IAPS). We compared the activation patterns elicited by these tasks in four regions of interest (amygdala, anterior insula, dorsolateral prefrontal cortex (dlPFC) and pregenual anterior cingulate cortex (pgACC)) in three samples of healthy adults (N=45). The EMOBACK task elicited activation in the right dlPFC, bilateral anterior insula and deactivation in pgACC, while the FACES task recruited the bilateral amygdala. IAPS and OASIS task showed similar activation patterns recruiting bilateral amygdala and anterior insula. We conclude that these tasks can be used to study different regions involved in emotion processing and that the information provided is valuable for future research and the development of fMRI biomarkers.

Keywords: fMRI paradigms; emotion processing; amygdala; anterior insula; pregenual ACC

1. Introduction

A variety of different fMRI paradigms have been used to probe emotion processing in order to understand its neural underpinnings in healthy subjects **[1]** and to study the effects that development**[2]**, psychopathology **[3]**, or therapeutic interventions **[4,5]** exert on it. Differences between these paradigms lie in the stimulus material used (e.g., printed words, pictures, melodies), the task posed to participants (e.g., passive viewing, matching, emotional Stroop or n-back), and the cognitive effort needed to fulfill the task (e.g., 0-back vs 2-back conditions, emotional judgements). Previous research has shown that the nature of the task and stimuli employed have a considerable impact on the effects **[6–8]** and that different tasks can trigger different aspects of emotion processing **[9]**. In some instances, even tasks intended

to represent the same concept appear to elicit different activation patterns: a study comparing amygdala activation in four different threat reactivity tasks found that amygdala activation did not correlate significantly across the tasks **[10]**. Importantly, standard emotion processing paradigms which aim to study certain target regions or aspects have not been established yet and direct comparisons between tasks are scarce. This can pose a challenge for planning new experiments. Furthermore, fMRI studies often differ in their pre-processing routines and analysis software, so that activation differences cannot safely be ascribed solely to the task at use. The goal of the present study was to compare common emotion processing fMRI tasks based on the same analysis pipeline regarding the activation they elicit in core regions of emotion processing.

Meta-analyses of fMRI research on emotion processing have robustly implicated several brain regions: Namely, the amygdala, anterior insula, pre- and subgenual anterior cingulate cortex (ACC) as well as dorsal ACC (dACC), dorsomedial prefrontal cortex (dmPFC), dorsolateral PFC (dlPFC), parahippocampus, orbitofrontal cortex, and visual and auditory cortices **[1,9,11]**. The constructionist approach (cf. **[11]**) assumes that emotion processing draws on more basic psychological operations and therefore recruits the respective brain networks underlying these operations. By this account, the brain regions activated in fMRI tasks of emotion can each be associated with a functional network that exerts a sub-process of emotion. The functional networks assumed to work together in emotion processing are the limbic network (realizing affective states in the body), salience network (detecting behaviorally relevant information), default-mode network (self-referential conceptualization of information), and the executive control network (evaluating or manipulating the incoming information; **[11]**).

A recent study on a databank of task-based fMRI studies of emotion processing clustered studies based on similar activation patterns elicited by the task in use, then performed meta-analyses for each of the cluster of studies. This approach dissociated five brain networks with convergent activations during different types of emotion processing tasks **[9]**. Apart from two networks in sensory cortices, these were largely overlapping with the salience, the default mode and the limbic network. Subsequently the metadata of the experimental designs in each cluster were analyzed. Based on this the found networks were characterized as contributing to drawing attention to salient information, appraisal and prediction of emotional information, and induction of the emotional response, respectively. These results are in line with the constructionist view **[11]** that emotion processing draws on psychological functions engendered by large-scale brain-networks.

Therefore, as regions of interest we chose one hub of each of these networks: the amygdalae, anterior insulae, pregenual ACC (pgACC), and bilateral dlPFC. The amygdala is the region that is most robustly engaged in emotion processing **[1,6,7]** and shows the greatest functional connectivity with other regions involved in emotion processing **[1]**. It is involved in signaling whether sensory information is motivationally salient **[12]** and has also been thought of as realizing "core affect", i.e., affective bodily sensations **[11]**. In clinical neuroscience, altered amygdala function in emotion processing, specifically, hyperactivation to negative stimuli has been found in patients with depression, social anxiety, post-traumatic stress and borderline personality disorder **[3,13,14]**.

The anterior insula is essential for the awareness of interoceptive information **[15]** as well as own affective experience **[16]** and robustly activates during the perception of emotional stimuli **[17]**. It is a core component of the salience network **[18]**, where it proposedly integrates physiological information with emotional, cognitive, and motivational signals to detect salience of stimuli. Therefore, the activation of the anterior insula in emotion processing may be linked to the salience of emotional stimuli. The pregenual ACC (pgACC) is a part of the default mode network and typically deactivated in goal-directed tasks **[19]**, but activated during self-referential thought **[20]**, the assessment of internal emotional states **[21]** as well as emotion perception **[22]**. It has been suggested to subserve a hub function integrating emotion and cognition through its projections to several cortical regions **[23]**, and its involvement in emotion processing may reflect cognitive appraisal of the emotional content of stimuli **[9,24]**. The pregenual ACC seems to play a crucial role in the cognitive regulation of emotions **[20]**. The dlPFC is a core

region in the fronto-parietal control network, that supports executive attention, working memory, and complex problem-solving **[18]**. It has been found to activate in emotion processing tasks, especially when participants are asked to categorize or evaluate emotional information **[11]**. DlPFC activity competes with amygdala activity in tasks that present an interference of emotional content and cognitive demand **[25]**, such that cognitive load is negatively correlated with amygdala activation in presence of emotional stimuli **[26]**. Consistent with these findings, dlPFC activity has been associated with emotion regulation **[27]**.

In this study we aimed to assess the different brain activation profiles elicited by four different tasks that have been widely used within the affective neurosciences. Thereby, we hope to inform the choice of experimental designs when aiming to examine specific parts of the emotion processing network. One task was an emotional working memory paradigm (EMOBACK; **[28]**) and three were passive emotion viewing tasks with attentional control. One of these used emotional face stimuli (FACES task) and the two others used pictures of emotional scenes, that were either positive and negative (IAPS) or solely negative (OASIS). All tasks used stimulus material from validated sets of pictures or words whose emotional valence has been established. We analyzed three datasets to investigate how the selected four core regions activate in response to the specific kind of emotional stimulation in each of the tasks.

2. Materials and Methods

2.1 Participants

This study analyses data from 45 healthy males aged 18-58 belonging to three samples each consisting of 15 subjects. Mean age of the participants was 25.8 (±5.3) years for the sample from whom FACES and OASIS task were collected, 29.3 (±2.9) years for the EMOBACK task sample and 35.5 (±10.8) years for the IAPS task sample. Supplementary Table 1 shows data on demographic variables and scanning sites. Exclusion criteria were standard MR exclusion criteria, cardiovascular diseases, recent heart or head surgery, current pregnancy, history of psychiatric or neurological disorders and current use of any psychoactive medication. The study was conducted according to the latest version of the Declaration of Helsinki. The full procedure and purpose were explained to each subject in detail as approved by the institutional review boards before they gave written informed consent to enter the study.

2.2 Tasks

2.2.1 EMOBACK task

The EMOBACK task **[28]** is an emotional 2-back task that uses verbal stimuli selected from the Berlin Affective Word List (BAWL; **[29]**). Subjects were required to monitor a series of words and to respond every time a word was presented that was the identical to the one presented 2 trials previously. They were instructed to respond as quickly and as accurately as possible. The stimuli were categorized as either positive, negative, or neutral and were matched with regard to length, imageability, emotional arousal and frequency of appearance. Stimuli were presented in 15 blocks, 5 for each valence category (positive, negative, or neutral). Between the block a fixation cross appeared for 10–14 s. Each block contained 15 words presented for 500ms each. The interstimulus interval was 1500ms long. A brief training of the task outside the scanner preceded the scanning session. The task lasted for 12 minutes.

2.2.2 FACES task

In the faces task, participants were shown pictures from the Warsaw Set of Emotional Facial Expression Pictures (WSEFEP, **[30]**). The block design task consisted of 12 blocks with 6 negative emotional faces displaying sadness, fear, and disgust (in randomized order) and 12 blocks with scrambled faces (control condition). In total, 72 negative faces of 24 actors (50% female) were shown for 3 seconds each. The inter-trial interval was jittered between 10±1seconds. During the inter-trial-interval (ITI), participants viewed

a white fixation cross on a black background. To ensure attention, participants were asked to indicate by button press whether the person was female for the portraits or for the scrambled faces whether the colored frame around the picture was blue (compared to green). The paradigm lasted 13 minutes. A brief training of the task outside the scanner preceded the scanning session.

2.2.3 IAPS task

The IAPS task consisted of 80 photographs (40 positive and 40 negative) from the International Affective Picture System **[31]** presented in a block-design. Five pictures were shown during a block of 20s duration. To ensure attention, after participants were presented a question after each block regarding the content of one of the five pictures for 8s (e.g., 'Was there a cat in the picture?'). After the rating a fixation cross was shown for 20s to serve as a baseline condition. The fMRI-paradigm was composed of 16 blocks (8 positive and 8 negative) with an overall duration of 13 min.

2.2.4 OASIS task

The OASIS task is a passive picture viewing task with attentional control. During the task, scenes from the OASIS picture set **[32]** with negative valence and high arousal rating were presented in a block-design. Scrambled pictures were used in a neutral control condition. There were 14 negative and 14 neutral blocks, each lasting 18 seconds. Within each block, three picture stimuli were presented consecutively for 6 seconds each, resulting in a set of 42 negative pictures and 42 scrambled pictures in total. The order of the blocks was semi-randomized. The inter-trial-interval was jittered within a range of 10±1 seconds to ensure reduced predictability of picture onset and optimized sampling of the BOLD signal **[33]**. During the ITI, participants saw a fixation cross. To ensure attention, participants were asked to indicate by button press whether there was a person present in the picture or for the scrambled pictures whether the bounding box was blue or green. A brief training of the task outside the scanner preceded the scanning session. The experiment lasted 15 minutes.

Supplementary Table 2 gives an overview of all task characteristics for the four tasks and Supplementary Figure 1 shows example stimuli from each task. All tasks were presented via MRI compatible video goggles (VisuaStim digital, Resonance Technology, Inc., Los Angeles, CA, USA) using Presentation® (Neurobehavioral Systems, Inc., Albany, CA, USA). Participants responded by pushing a fiber-optic light sensitive key press.

2.3 Data collection

Imaging was performed using 3T MR systems at three study sites (Berlin Center for Advanced Neuroimaging (BCAN), Center for Cognitive Neuroscience Berlin (CCNB) and University of Zurich (UZH). The exact scanner type and sequence parameters at each site can be found in Supplementary Table 3. For each sample, scanning consisted of functional imaging by an T2-weighted echo planar imaging sequence and one anatomical reference image using a 3-dimensional T1-weighted scan. The Faces and OASIS tasks were assessed in one session, following a 3D scan. For the two other tasks, subjects completed a 3D scan and one task-based functional scan (EMOBACK and IAPS, respectively). Imaging for all 4 tasks was collected in one run.

2.4 Data analysis

For behavioral data, accuracy was defined as accuracy= #correct responses/#trials for the FACES, OASIS and IAPS tasks and as accuracy = (#hits-#false alarms)/#targets in the EMOBACK task. A threshold of 80% accuracy for FACES, OASIS and IAPS tasks and 50% accuracy for EMOBACK task was defined for participants to be included in data analysis.

FMRI data were analyzed using MATLAB 2020a (The Mathworks Inc., Natick, MA, USA) and SPM12 revision 7771 (Statistical parametric mapping software, SPM; Wellcome Department of Imaging

Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk). The first five volumes of each run were discarded to allow for T1 stabilization. The following pre-processing steps were realized: realignement according to the first volume for motion correction, normalization to a standard stereotactic space template from the Montreal Neurological Institute (MNI) and spatial smoothing using a 6 mm FWHM Gaussian kernel. The time series were high-pass filtered (filter width 128s) to eliminate low-frequency components and adjusted for systematic differences across trials. We checked for artifacts and set a cut-off for motion parameters at 3mm or 3°; all volumes of all subjects passed this check. Statistical analysis on the subject level was performed by modeling the different conditions convolved with a hemodynamic response function as explanatory variables within the context of the general linear model on a voxel-by-voxel basis **[34]**. Realignment parameters were included as additional regressors in the statistical model. A fixed-effect model was performed to create images of parameter estimates, which were then entered into a second-level random-effects analysis. For the fMRI data group analysis, the contrast images from the analysis of the individual participants were analyzed using one-sample t-tests.

For each subject, contrasts testing response to emotional stimuli relative to baseline or neutral stimuli were calculated. Specifically, for the four tasks, these were: 1. EMOBACK: emotional stimuli versus fixation condition (Emotional > break); 2. OASIS: emotional stimuli versus control condition (Emotional > scrambled) 3. IAPS: emotional stimuli versus fixation condition (Emotional > break) 4. FACES: emotional stimuli versus control condition (Emotional > scrambled).

Regions-of-interest (ROIs) were defined to examine emotion related brain activations. Specifically, the following ROIs previously linked to emotion processing **[1,11]** were selected (abbreviation and MNI coordinates in brackets): the bilateral dorsolateral prefrontal cortex (l/rdlPFC; ±40 36 32), the bilateral amygdala (l/rAM ±24 -2 -20), the bilateral anterior insula (l/rAI ±34 20 0) and the pregenual anterior cingulate cortex (pgACC; 0 42 2). Spherical ROI templates with a diameter of 10 mm were built with automated term-based meta-analyses on neurosynth.org or based on own previous studies (for pgACC; **[28]**). All ROIs are illustrated in Fig. 1. The mean parameter estimate of each ROI was extracted using the REX Toolbox (https://www.nitrc.org/projects/rex/). Significance tests for the ROI analyses were conducted with an α-level Bonferroni adjusted for the number of ROI of p<.05/7=p<.0071

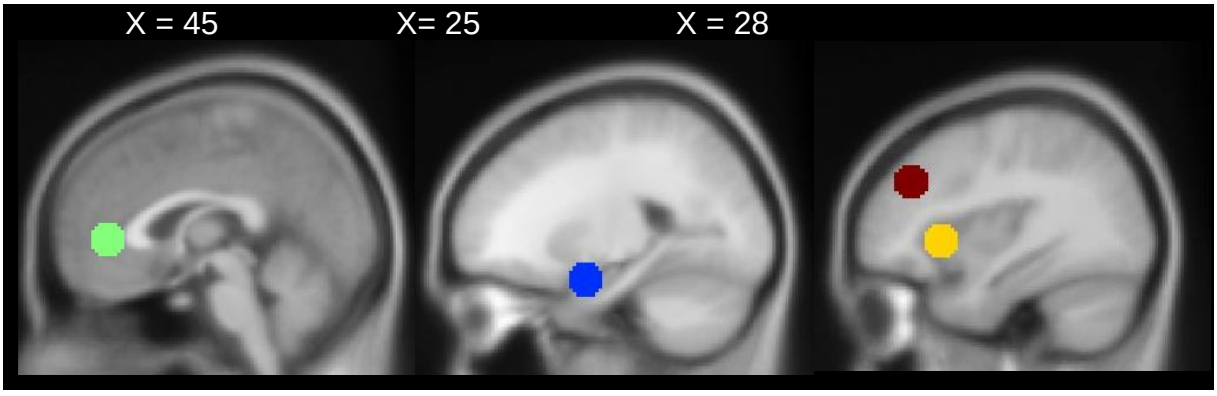

Figure 1. Region of interest (ROI) templates were spheres with 10mm diameter. Red = dorsolateral prefrontal cortex, yellow=anterior insula, green = pregenual anterior cingulate cortex, blue = amygdala.

Paired and independent sample t-tests were conducted to compare activation in the ROI between the tasks that have been collected in the same and different samples, respectively. As exploratory analyses these are reported at an uncorrected α-level of p=.05.

3. Results

Figure 2 shows an overview of the activations in our regions of interest for all 4 tasks. Activations in response to the emotional working memory condition compared to break in the EMOBACK task were found in bilateral anterior insula, right dorsolateral prefrontal cortex along with a significant decrease in activity in the pgACC (pgACC: mean β=-0.681 95% CI [-0.512, -0.849] t(14) = -8.666 p<.00001;

lAI: mean β=1.004 95% CI [0.810,1.199] t(14) = 11.110 p<.00001; rAI mean β=0.910 95% CI [0.686,1.135] t(14) = 8.713 p<.00001; rdlPFC: mean β=1.310 95% CI [1.010,1.611] t(14) = 9.341 p<.00001;). There was also noticeable activation in the left dlPFC that was, however, not significant to a Bonferroni corrected alpha-level (ldlPFC: mean β=0.320 95% CI [0.046, 0.593] t(14) = 2.505 p = .0252).

The FACES task elicited significant activation in the bilateral amygdala (lAM: mean β=.469 95% CI=[.296,.644] t(14)=5.783 p=.00005; rAM: mean β =0.466 95% CI [0.278, 0.652] t(14) = 5.365 p = .00001).

The IAPS task elicited activation in the bilateral amygdala and bilateral anterior insula during presentation of emotional stimuli (activation in the left amygdala and bilateral anterior insula was not significant to an Bonferroni adjusted alpha-level of p=.007; rAM: mean β=0.898 95% CI [0.454,0.631] t(14) = 4.33 p = .0007; lAM: mean β = 0.646 95% CI [0.186,1.106] t(14) = 3.015 p = .009, lAI: mean β=0.404 95% CI = [0.026,0.781] t(14) = 2.295 p=.038 rAI: mean β=0.366 95% CI = [0.108,0.624] t(14) = 3.043 p = .009).

Activation elicited by emotional stimuli in the OASIS task was found in the bilateral amygdala as well as in the bilateral anterior Insula (Bonferroni-corrected significance not met for rAI; lAM: mean β=0.431 95% CI [.278,.584] t(14) = 6.063 p = .00003; rAM: mean β = 0.422 95% CI [0.245,0.601] t(14) = 5.103 p = .00016; lAI: mean β = 0.299 95% CI=[0.133,0.465] t(14) = 3.882 p = .002; rAI: mean β = 0.163 95% CI [.050,.276] t(14) = 3.091 p=.008).

As data for the FACES and the OASIS task stem from the same subjects we further conducted exploratory paired t-tests to directly compare activation patterns between the two tasks. No significant difference arose except for the right anterior insula where activation in the OASIS task exceeded that in the FACES task (OASIS: M = 0.163±0.041 FACES: M =0.002± 0.027, Cohen's d = .633, p=.028).

Further, we also conducted exploratory independent t-tests comparing activation elicited in each of the regions of interest between the tasks that were run in different samples. In the right DLPFC, the activation elicited by EMOBACK was found to be significantly stronger than that under any other task (EMOBACK: M= 1.310±.525 IAPS M=.245±.673 FACES: M=.094±.159 OASIS: M = .031±.270 Cohen's d >1.7 all p<.001 for all comparisons of EMOBACK with other tasks). In the left DLPFC the only significant difference that arose was between EMOBACK (M= .320±.477) and FACES task (M:.030±.162; Cohen's d=.982 p=.015).

In both the left and right amygdalae, the EMOBACK elicited significantly less activation than the other tasks (EMOBACK lAM: M=-.185±.255 rAM=-.210±.347 Cohen's d>1.4 p<.001 for all comparisons with other tasks), in the right amygdala the activation elicited by IAPS was also significantly stronger than that in the OASIS task. (IAPS: M=.898±.775 OASIS M=.422±.310 Cohen's d=.805 p=.042)

In the anterior insula the activation elicited by the EMOBACK was found to be significantly greater bilaterally than that by any other task (EMOBACK rAI: M=.910±.404 lAI: M=1.004±.350 Cohen's >1.1 p<.006 for all comparisons). For the right anterior insula, a significant difference was found also between the IAPS and the FACES task, (IAPS: M=.365±466 FACES: M= -.003±.158 Cohen's d=1.094 p=.007) with greater activation elicited by the IAPS task.

In the pgACC, no significant difference was found between the de-activations elicited by EMOBACK or IAPS task, however both differed significantly from the other two tasks, FACES and OASIS (EMOBACK M:-0.681±.294 IAPS: M=-0.331±.606 FACES: M= .033±.219 OASIS: M=.082±.301 Cohen's d>.75 p<.05 for all comparisons of EMOBACK or IAPS task with OASIS and FACES task).

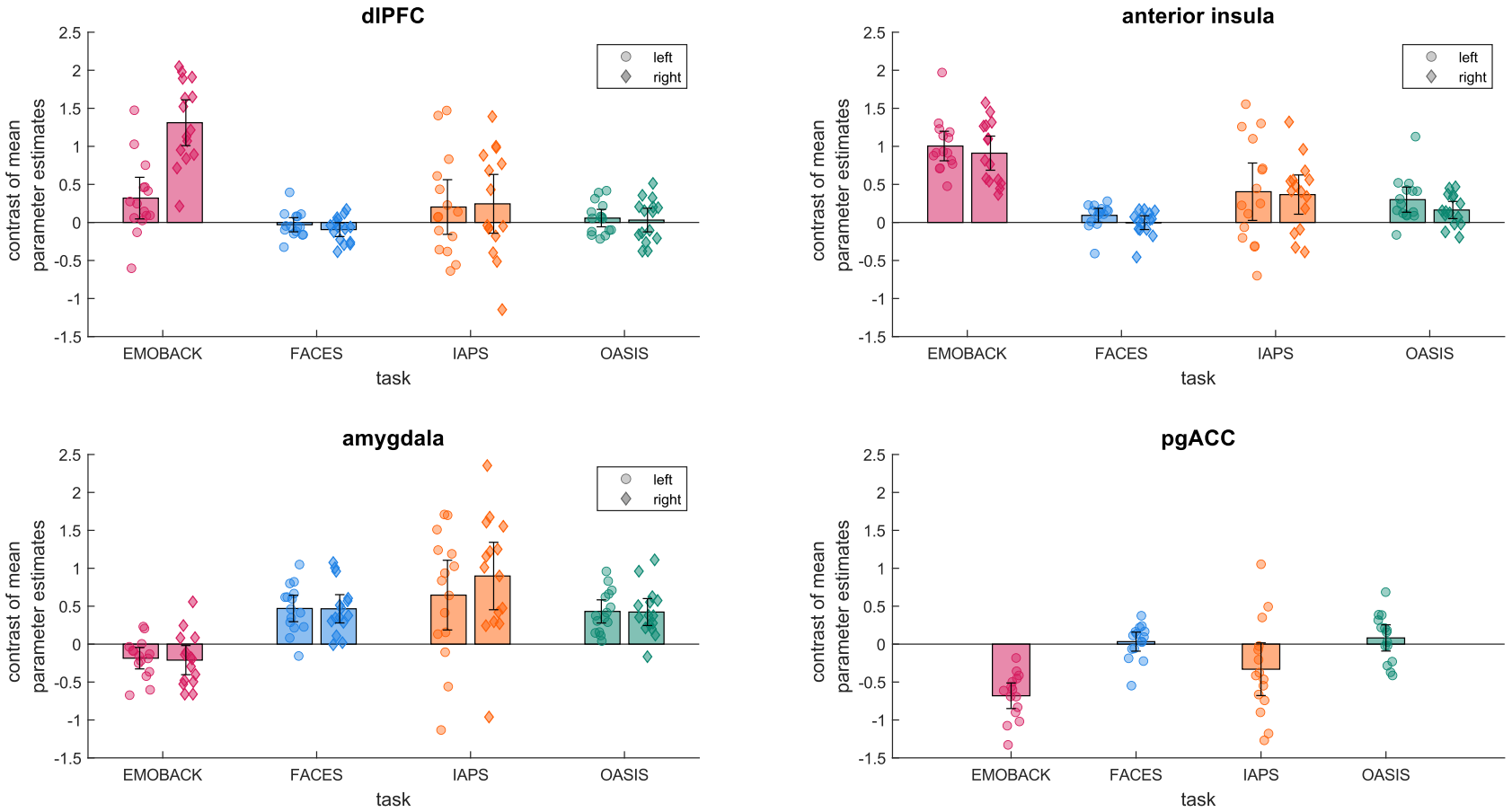

Figure 2. Mean parameter estimates of neuronal activation in the prespecified regions of interest on the group (bars) and individual (dots) level. Error bars represent the 95% confidence interval. Colors represent the four tasks; pink: EMOBACK (Emotional > break), blue: FACES (Negative > scrambled), orange: IAPS (Emotional > break), green: OASIS (Negative > scrambled).

4. Discussion

We compared four fMRI paradigms, that are often applied in the Affective Neurosciences, regarding their potential of eliciting activation in regions commonly associated with emotion processing. Our results indicate that the different fMRI paradigms elicit different neural activation patterns. The EMOBACK task elicited activation in the right dlPFC and the bilateral anterior insula and deactivation in the pgACC (but no significant change in amygdala activation). The FACES task induced activity selectively in the bilateral amygdala and the two tasks that use emotionally valenced scenes, OASIS and IAPS, both induced activity in the bilateral amygdala and insula. While the activations in right amygdala and anterior insula appeared stronger in the IAPS task, there was less variance in the OASIS task, that consists solely of negative emotional scenes, resulting in more statistically significant activations.

A meta-analysis of n-back tasks with neutral stimuli found activity in the bilateral middle frontal gyrus and left anterior insula (among other regions; [35]), pointing to the activation in the right anterior insula in our data being attributable to the emotional nature of the stimuli at use. The activation elicited by EMOBACK in our data is in line with previous research from our group that found activation in the bilateral dlPFC and anterior insula as well as deactivation in a region in the rostral anterior cingulate cortex [28]. While we observed some activation in the left dlPFC, it was much less pronounced and not statistically significant. Previous studies have also reported predominant involvement of the right compared to the left dlPFC in coping with emotional distractors in working memory tasks [26,36]. The exploratory independent sample t-tests between the tasks revealed that the EMOBACK task elicited significantly greater right dlPFC and bilateral anterior insula activity than any other of the studied tasks. This finding is plausible given that the EMOBACK is the only task of those studied here that has a working memory component on top of the emotional stimulation and also the one with the shortest stimulus duration, likely requiring greater attention. We did not find amygdala activation in response to the EMOBACK task. This is in line with previous results showing high cognitive effort in emotion-cognition-interference tasks reducing amygdala activation in response to emotional stimuli [36]. The EMOBACK also uses written words as stimulus material, which have consistently been shown to be associated with a lower probability of amygdala activation compared to emotional pictures [37], possibly due to greater stimulus complexity of the latter [38]. The pregenual ACC is part of the default mode network, which is characterized by deactivation during goal-directed tasks but is activated in autobiographical and self-referential thought and social cognition [19,39]. However, the pgACC is also implied in the cognitive regulation of affect [20]. The deactivation found here might thus represent an interaction of both reduced activity due to a cognitive process and involvement in the regulation of activity in emotion-reactive brain regions. A previous study from our group concordantly found the pgACC to deactivate less in an emotional compared to a neutral condition of the EMOBACK [28].

Our result regarding the FACES task eliciting amygdala activation distinctively is in line with meta-analytic findings on tasks using emotional faces [6,7], where several brain regions apart from the amygdala (e.g., fusiform gyrus) were significantly associated with viewing facial expressions of emotion, but none of the other ROIs studied here. Robust engagement of the bilateral amygdala has been found in response to facial stimuli regardless of valence [7]. However, the amygdala is routinely implicated in orienting responses to behaviorally relevant stimuli, suggesting it is especially sensitive to the emotional content in facial expressions [12].

The two tasks studied here that use pictures of naturalistic emotional scenes elicited activations in the anterior insula and amygdala. The tasks using naturalistic scene stimuli were found to elicit a wider set of neural activations than the FACES task, which is in line with a meta-analytic comparison of these two types of tasks [6]. While this meta-analysis did not find an association of scenic emotional stimuli with activation in the anterior insula, a later meta-analysis did establish a robust association of anterior insula activation and emotional stimulation [17]. Although in the direct comparison the IAPS task provoked a significantly greater activation in the right amygdala and right anterior insula, the OASIS task elicited more reliable (and significant) bilateral activation in both amygdala and anterior insula. This may be due to differences between the tasks: While the OASIS task shows only negative stimulus material to participants, the IAPS task uses both positive and negative scenes. The representation of positive and negative emotion in the brain seems to largely overlap [40], however, there have been reports

of negative emotions eliciting stronger activation in the amygdala [41] and the insula [42] compared to positive emotions, which might explain the different activation patterns between the two tasks. It further seems plausible that showing aversive content exclusively, as in the OASIS task, might more likely induce a negative affective state as compared to alternating between pictures of positive and negative valence as in the IAPS task, hence triggering a more consistent neuronal response. As we did not collect ratings of subjective emotional experience during the tasks, we can only speculate about this relation.

Our results from the direct comparison of the FACES and the OASIS tasks appear at odds with the only other study that compared passive viewing tasks of emotional facial expressions and scenes [43]. In this study, the anterior insula showed greater activity in response to emotional face stimuli compared to naturalistic scenes. The stimuli selection (a wider range of emotions including positive ones) and contrasts used (emotion – fixation), however, were different from the tasks studied here. It remains inconclusive, whether the activation profiles we report from the tasks studied here generalize to similar paradigms or are rather specific to the exact task.

Our results demonstrate that the different paradigms elicit different activation profiles and can be used to address different aspects of emotion processing. The pattern of activation elicited by the EMOBACK task suggests that it is well suited for the study of emotion-cognition interactions in the anterior insula, pgACC, and (right) dlPFC, as might be of interest for example in the study of depression and its treatment [44,45]. Investigators primarily interested in amygdala activations and its potential change in response to interventions could deduct from our results to employ the FACES task, whereas the OASIS task showed robust activation in amygdala as well as anterior insula, allowing for a broader study of brain regions involved in emotion processing. Our results are less conclusive about recommendations concerning the IAPS task. It might have the greatest face validity to assess emotion processing among the tasks studied here as it presents naturalistic scenes of both positive and negative valence. However, in our sample, there was substantial variability in the neural response during IAPS task performance and a statistically significant change in activation was found only in the right amygdala.

Currently, a big variety of fMRI paradigms are in use for the study of emotion processing, limiting comparability between studies and impeding concise meta-analyses [9]. Therefore, it can be difficult to extract from the literature which paradigm is best suited for a specific research question; especially, as it has become clear that analytic choices can heavily impact the results of fMRI studies [46,47]. To allow for a comparison between fMRI tasks, it is crucial that the data are studied using the same analysis pipeline, as we did here. We thus hope that the present results of activation elicited by different emotional fMRI paradigms in relevant pre-defined ROIs might provide guidance for planning studies on emotion processing.

Ultimately, the field of affective and clinical neuroscience would profit from standardized task protocols for the study of certain brain regions or mental processes as it would grant optimized comparability of results and meta-analytic synthesis. Recent studies have shown that the fMRI paradigms currently in use lack the reliability that would be needed for the use of fMRI as a biomarker in pathology and intervention research [48,49]. One potential remedy that has been discussed is increasing the amount of individual data collected (i.e., longer scan time) [50], which could be achieved relatively easily by collecting several runs of the tasks in question.

The present study has limitations that need to be considered when interpreting the results. Although the region of interest approach does increase power compared to whole-brain analyses, the size of the available samples was quite small, especially considering that the effects reported for emotion perception tasks are at best of moderate size (.5< Cohen's d<.8; [47]). Our study thus had limited power to find 'true' effects and there is an increased likelihood of statistically significant results representing false positives. We did however apply Bonferroni-correction to account for multiple testing, limiting the risk of false positive results. Nevertheless, it is a limitation of the present study that acquisition site was not included in the statistical modelling of the data. The data analyzed for this study stem from different samples adding in-between subject variance and were collected on different MRI scanners (although with largely similar sequences). Therefore, we cannot rule out systematic variability in the data stemming from the acquisition set-up [51]. Studies investigating multi-site-reliability of task-based fMRI

found that a possible effect of site on the data is likely small [52,53]. Nevertheless, it is a limitation of the present study that acquisition site was not included in the statistical modelling of the data. We used a standard SPM12-based pre-processing pipeline relying on defaults. Although this approach is very common, there are now superior alternatives available, in particular fMRI prep, a robust pre-processing pipeline that combines optimal processing steps from different analytical software packages [54]. Our results might be weakened by the suboptimal pre-processing. The mean age of the samples studied differed notably, and although a recent meta-analysis [1] did not find an effect of age on neural activations during emotion processing, such effects have been suggested [55,56] and might have influenced the differences between activation pattern that we observed here. As all participants in this study were young to middle-aged, a possible impact of age differences on the data it is likely small. Lastly, the samples we analyzed for this study were confined to males. While they have been scrutinized [57], there have been reports of gender differences in neural processes in emotion processing (e.g.,[58]). Although the latest meta-analysis on the matter did not find a consistent difference in neural activation patterns in emotion processing tasks between men and women [1], previous meta-analyses found functional lateralization differences based on gender [41,59], such that a potentially limited generalizability of our findings should be considered.

5. Conclusions

The present study found that four common emotional fMRI paradigms elicit different profiles of neural activation. The results suggest that the FACES task is most useful for the selective study of the amygdala, whereas the OASIS task robustly activated the left anterior insula and bilateral amygdala. The EMOBACK task evoked activation in the right dlPFC, bilateral anterior insula, and deactivation of the pgACC. These results are valuable to inform the planning of future studies and the eventual development of functional MRI biomarkers.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Figure S1: Example Stimuli, Table S1: Demographic variables and scanning site for the three samples, S2 Task characteristics of the four emotion tasks, S3 MRI sequence parameters at the different sites, S4 Region of interest analyses for the four tasks.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, Corinna Hartling, Anne Weigand and Simone Grimm; methodology, Corinna Hartling, Sophie Metz, Corinna Pehrs, Milan Scheidegger, Rebecca Gruzman, Christian Keicher, Andreas Wunder, Anne Weigand, Simone Grimm; software, Corinna Hartling and Corinna Pehrs; validation, Corinna Hartling, Anne Weigand and Simone Grimm; formal analysis, Corinna Hartling; investigation, Sophie Metz, Milan Scheidegger, Christian Keicher, Andreas Wunder, Corinna Hartling, Rebecca Gruzman; resources, Simone Grimm, Milan Scheidegger, Christian Keicher, Andreas Wunder; data curation, Corinna Hartling; writing—original draft preparation, Corinna Hartling; writing—review and editing, Corinna Hartling, Sophie Metz, Corinna Pehrs, Milan Scheidegger, Rebecca Gruzman, Christian Keicher, Andreas Wunder, Anne Weigand, Simone Grimm; visualization, Corinna Hartling; supervision, Corinna Pehrs, Anne Weigand, Simone Grimm; project administration, Simone Grimm, Milan Scheidegger, Christian Keicher Andreas Wunder; funding acquisition, Simone Grimm. All authors have read and agreed to the published version of the manuscript."

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References

1. García-García, I.; Kube, J.; Gaebler, M.; Horstmann, A.; Villringer, A.; Neumann, J. Neural Processing of Negative Emotional Stimuli and the Influence of Age, Sex and Task-Related Characteristics. Neurosci. Biobehav. Rev. 2016, 68, 773–793.

2. Wu, M.; Kujawa, A.; Lu, L.H.; Fitzgerald, D.A.; Klumpp, H.; Fitzgerald, K.D.; Monk, C.S.; Phan, K.L. Age-Related Changes in Amygdala-Frontal Connectivity during Emotional Face Processing from Childhood into Young Adulthood. Hum. Brain Mapp. 2016, 37, 1684–1695, doi:10.1002/hbm.23129.
3. McTeague, L.M.; Rosenberg, B.; Lopez, J.M.; Carreon, D.; Huemer, J.; Jiang, Y.; Chick, C.; Eickhoff, S.; Etkin, A. Identification of Common Neural Circuit Disruptions in Emotional Processing Across Psychiatric Disorders. Am. J. Psychiatry 2020, 177, 411–421, doi:10.1176/appi.ajp.2019.18111271.
4. Outhred, T.; Das, P.; Felmingham, K.; Bryant, R.; Nathan, P.; Malhi, G.; Kemp, A. Impact of Acute Administration of Escitalopram on the Processing of Emotional and Neutral Images: A Randomized Crossover FMRI Study of Healthy Women. J. Psychiatry Neurosci. JPN 2014, 39, 267–75, doi:10.1503/jpn.130118.
5. Enneking, V.; Dzvonyar, F.; Dück, K.; Dohm, K.; Grotegerd, D.; Förster, K.; Meinert, S.; Lemke, H.; Klug, M.; Waltemate, L.; et al. Brain Functional Effects of Electroconvulsive Therapy during Emotional Processing in Major Depressive Disorder. Brain Stimulat. 2020, 13, 1051–1058, doi:10.1016/j.brs.2020.03.018.
6. Sabatinelli, D.; Fortune, E.E.; Li, Q.; Siddiqui, A.; Krafft, C.; Oliver, W.T.; Beck, S.; Jeffries, J. Emotional Perception: Meta-Analyses of Face and Natural Scene Processing. Neuroimage 2011, 54, 2524–2533.
7. Müller, V.I.; Höhner, Y.; Eickhoff, S.B. Influence of Task Instructions and Stimuli on the Neural Network of Face Processing: An ALE Meta-Analysis. Cortex 2018, 103, 240–255, doi:10.1016/j.cortex.2018.03.011.
8. Reisch L.M.; Wegrzyn M.; Kissler J.; Woermann F.G.; Bien C.G. Negative Content Enhances Stimulus-Specific Cerebral Activity during Free Viewing of Pictures, Faces, and Words. Hum. Brain Mapp. 2020, 41, 4332–4354, doi:10.1002/hbm.25128.
9. Riedel, M.C.; Yanes, J.A.; Ray, K.L.; Eickhoff, S.B.; Fox, P.T.; Sutherland, M.T.; Laird, A.R. Dissociable Meta-analytic Brain Networks Contribute to Coordinated Emotional Processing. Hum. Brain Mapp. 2018, 39, 2514–2531.
10. Villalta-Gil V; Hinton KE; Landman BA; Yvernault BC; Perkins SF; Katsantonis AS; Sellani CL; Lahey BB; Zald DH Convergent Individual Differences in Visual Cortices, but Not the Amygdala across Standard Amygdalar FMRI Probe Tasks. NeuroImage 2017, 146, 312–319, doi:10.1016/j.neuroimage.2016.11.038.
11. Lindquist, K.A.; Wager, T.D.; Kober, H.; Bliss-Moreau, E.; Barrett, L.F. The Brain Basis of Emotion: A Meta-Analytic Review. Behav. BRAIN Sci. 2012, 35, 121–143.
12. Whalen, P.J.; Davis, F.C.; Oler, J.A.; Kim, H.; Kim, M.J.; Neta, M. Human amygdala responses to facial expressions of emotion. In The human amygdala.; The Guilford Press: New York, NY, US, 2009; pp. 265–288 ISBN 978-1-60623-033-6.
13. Stuhrmann A; Suslow T; Dannlowski U Facial Emotion Processing in Major Depression: A Systematic Review of Neuroimaging Findings. Biol. Mood Anxiety Disord. 2011, 1, 10, doi:10.1186/2045-5380-1-10.
14. Gentili, C.; Cristea, I.A.; Angstadt, M.; Klumpp, H.; Tozzi, L.; Phan, K.L.; Pietrini, P. Beyond Emotions: A Meta-Analysis of Neural Response within Face Processing System in Social Anxiety. Exp. Biol. Med. 2016, 241, 225–237, doi:10.1177/1535370215603514.
15. Craig AD How Do You Feel? Interoception: The Sense of the Physiological Condition of the Body. Nat. Rev. Neurosci. 2002, 3, 655–66.
16. Zaki J; Davis JI; Ochsner KN Overlapping Activity in Anterior Insula during Interoception and Emotional Experience. NeuroImage 2012, 62, 493–9, doi:10.1016/j.neuroimage.2012.05.012.
17. Duerden, E.G.; Arsalidou, M.; Lee, M.; Taylor, M.J. Lateralization of Affective Processing in the Insula. NeuroImage 2013, 78, 159–175, doi:10.1016/j.neuroimage.2013.04.014.
18. Seeley WW; Menon V; Schatzberg AF; Keller J; Glover GH; Kenna H; Reiss AL; Greicius MD Dissociable Intrinsic Connectivity Networks for Salience Processing and Executive Control. J. Neurosci. Off. J. Soc. Neurosci. 2007, 27, 2349–56.
19. Raichle, M.E. The Brain's Default Mode Network. Annu. Rev. Neurosci. 2015, 38, 433–448.
20. Palomero-Gallagher, N.; Hoffstaedter, F.; Mohlberg, H.; Eickhoff, S.B.; Amunts, K.; Zilles, K. Human Pregenual Anterior Cingulate Cortex: Structural, Functional, and Connectional Heterogeneity. Cereb. Cortex 2019, 29, 2552–2574, doi:10.1093/cercor/bhy124.
21. Vogt BA Submodalities of Emotion in the Context of Cingulate Subregions. Cortex J. Devoted Study Nerv. Syst. Behav. 2014, 59, 197–202, doi:10.1016/j.cortex.2014.04.002.
22. Phan KL; Wager T; Taylor SF; Liberzon I Functional Neuroanatomy of Emotion: A Meta-Analysis of Emotion Activation Studies in PET and FMRI. NeuroImage 2002, 16, 331–48.
23. Tang, W.; Jbabdi, S.; Zhu, Z.; Cottaar, M.; Grisot, G.; Lehman, J.F.; Yendiki, A.; Haber, S.N. A Connectional Hub in the Rostral Anterior Cingulate Cortex Links Areas of Emotion and Cognitive Control. eLife 2019, 8, doi:10.7554/eLife.43761.

24. Ochsner, K.N.; Silvers, J.A.; Buhle, J.T. Functional Imaging Studies of Emotion Regulation: A Synthetic Review and Evolving Model of the Cognitive Control of Emotion. Ann. N. Y. Acad. Sci. 2012, 1251, E1.
25. Schweizer S; Satpute AB; Atzil S; Field AP; Hitchcock C; Black M; Barrett LF; Dalgleish T The Impact of Affective Information on Working Memory: A Pair of Meta-Analytic Reviews of Behavioral and Neuroimaging Evidence. Psychol. Bull. 2019, 145, 566–609, doi:10.1037/bul0000193.
26. Van Dillen, L.F.; Heslenfeld, D.J.; Koole, S.L. Tuning down the Emotional Brain: An FMRI Study of the Effects of Cognitive Load on the Processing of Affective Images. NeuroImage 2009, 45, 1212–1219, doi:10.1016/j.neuroimage.2009.01.016.
27. Kohn, N.; Eickhoff, S.B.; Scheller, M.; Laird, A.R.; Fox, P.T.; Habel, U. Neural Network of Cognitive Emotion Regulation—an ALE Meta-Analysis and MACM Analysis. Neuroimage 2014, 87, 345–355.
28. Grimm, S.; Weigand, A.; Kazzer, P.; Jacobs, A.M.; Bajbouj, M. Neural Mechanisms Underlying the Integration of Emotion and Working Memory. NeuroImage 2012, 61, 1188–1194, doi:10.1016/j.neuroimage.2012.04.004.
29. Melissa L. H. Võ; Markus Conrad; Lars Kuchinke; Karolina Urton; Markus J. Hofmann; Arthur M. Jacobs The Berlin Affective Word List Reloaded (BAWL-R). Behav. Res. Methods 2009, 41, 534–538, doi:10.3758/BRM.41.2.534.
30. Olszanowski, M.; Pochwatko, G.; Kuklinski, K.; Scibor-Rylski, M.; Lewinski, P.; Ohme, R.K. Warsaw Set of Emotional Facial Expression Pictures: A Validation Study of Facial Display Photographs. Front. Psychol. 2015, 5, 1516.
31. Lang, P.J.; Bradley, M.M.; Cuthbert, B.N. International Affective Picture System (IAPS): Technical Manual and Affective Ratings. NIMH Cent. Study Emot. Atten. 1997, 1, 39–58.
32. Kurdi, B.; Lozano, S.; Banaji, M.R. Introducing the Open Affective Standardized Image Set (OASIS). Behav. Res. Methods 2017, 49, 457–470, doi:10.3758/s13428-016-0715-3.
33. Price CJ; Veltman DJ; Ashburner J; Josephs O; Friston KJ The Critical Relationship between the Timing of Stimulus Presentation and Data Acquisition in Blocked Designs with FMRI. NeuroImage 1999, 10, 36–44.
34. Friston, K.J.; Holmes, A.P.; Price, C.J.; Büchel, C.; Worsley, K.J. Multisubject FMRI Studies and Conjunction Analyses. NeuroImage 1999, 10, 385–396, doi:10.1006/nimg.1999.0484.
35. Wang, H.; He, W.; Wu, J.; Zhang, J.; Jin, Z.; Li, L. A Coordinate-Based Meta-Analysis of the n-Back Working Memory Paradigm Using Activation Likelihood Estimation. Brain Cogn. 2019, 132, 1–12, doi:10.1016/j.bandc.2019.01.002.
36. Erk S; Kleczar A; Walter H Valence-Specific Regulation Effects in a Working Memory Task with Emotional Context. NeuroImage 2007, 37, 623–32.
37. Costafreda, S.G.; Brammer, M.J.; David, A.S.; Fu, C.H.Y. Predictors of Amygdala Activation during the Processing of Emotional Stimuli: A Meta-Analysis of 385 PET and FMRI Studies. Brain Res. Rev. 2008, 58, 57–70, doi:10.1016/j.brainresrev.2007.10.012.
38. Schlochtermeier LH; Kuchinke L; Pehrs C; Urton K; Kappelhoff H; Jacobs AM Emotional Picture and Word Processing: An FMRI Study on Effects of Stimulus Complexity. PloS One 2013, 8, e55619, doi:10.1371/journal.pone.0055619.
39. Spreng RN The Fallacy of a "Task-Negative" Network. Front. Psychol. 2012, 3, 145, doi:10.3389/fpsyg.2012.00145.
40. Lindquist, K.A.; Satpute, A.B.; Wager, T.D.; Weber, J.; Barrett, L.F. The Brain Basis of Positive and Negative Affect: Evidence from a Meta-Analysis of the Human Neuroimaging Literature. Cereb. Cortex 2016, 26, 1910–1922, doi:10.1093/cercor/bhv001.
41. Wager TD; Phan KL; Liberzon I; Taylor SF Valence, Gender, and Lateralization of Functional Brain Anatomy in Emotion: A Meta-Analysis of Findings from Neuroimaging. NeuroImage 2003, 19, 513–31.
42. Aldhafeeri FM; Mackenzie I; Kay T; Alghamdi J; Sluming V Regional Brain Responses to Pleasant and Unpleasant IAPS Pictures: Different Networks. Neurosci. Lett. 2012, 512, 94–8, doi:10.1016/j.neulet.2012.01.064.
43. Britton JC; Taylor SF; Sudheimer KD; Liberzon I Facial Expressions and Complex IAPS Pictures: Common and Differential Networks. NeuroImage 2006, 31, 906–19.
44. Korgaonkar, M.S.; Grieve, S.M.; Etkin, A.; Koslow, S.H.; Williams, L.M. Using Standardized FMRI Protocols to Identify Patterns of Prefrontal Circuit Dysregulation That Are Common and Specific to Cognitive and Emotional Tasks in Major Depressive Disorder: First Wave Results from the ISPOT-D Study. Neuropsychopharmacol. -N. Y.- 2013, 38, 863–871.
45. Phillips, M.L.; Chase, H.W.; Sheline, Y.I.; Etkin, A.; Almeida, J.R.; Deckersbach, T.; Trivedi, M.H. Identifying Predictors, Moderators, and Mediators of Antidepressant Response in Major Depressive Disorder: Neuroimaging Approaches. Am. J. Psychiatry 2015, 172, 124–138.

46. Botvinik-Nezer, R.; Holzmeister, F.; Camerer, C.F.; Dreber, A.; Huber, J.; Johannesson, M.; Kirchler, M.; Iwanir, R.; Mumford, J.A.; Adcock, R.A.; et al. Variability in the Analysis of a Single Neuroimaging Dataset by Many Teams. Nature 2020, 582, 84–88, doi:10.1038/s41586-020-2314-9.
47. Poldrack RA; Baker CI; Durnez J; Gorgolewski KJ; Matthews PM; Munafò MR; Nichols TE; Poline JB; Vul E; Yarkoni T Scanning the Horizon: Towards Transparent and Reproducible Neuroimaging Research. Nat. Rev. Neurosci. 2017, 18, 115–126, doi:10.1038/nrn.2016.167.
48. Elliott ML; Knodt AR; Ireland D; Morris ML; Poulton R; Ramrakha S; Sison ML; Moffitt TE; Caspi A; Hariri AR What Is the Test-Retest Reliability of Common Task-Functional MRI Measures? New Empirical Evidence and a Meta-Analysis. Psychol. Sci. 2020, 31, 792–806, doi:10.1177/0956797620916786.
49. Frohner J.H.; Smolka M.N.; Kroemer N.B.; Teckentrup V. Addressing the Reliability Fallacy in FMRI: Similar Group Effects May Arise from Unreliable Individual Effects. NeuroImage 2019, 222, 174–189, doi:10.1016/j.neuroimage.2019.03.053.
50. Nee, D.E. FMRI Replicability Depends upon Sufficient Individual-Level Data. Commun. Biol. 2019, 2, 1–4, doi:10.1038/s42003-019-0378-6.
51. Jovicich, J.; Czanner, S.; Han, X.; Salat, D.; van der Kouwe, A.; Quinn, B.; Pacheco, J.; Albert, M.; Killiany, R.; Blacker, D.; et al. MRI-Derived Measurements of Human Subcortical, Ventricular and Intracranial Brain Volumes: Reliability Effects of Scan Sessions, Acquisition Sequences, Data Analyses, Scanner Upgrade, Scanner Vendors and Field Strengths. Neuroimage 2009, 46, 177–192, doi:10.1016/j.neuroimage.2009.02.010.
52. Gee, D.G.; McEwen, S.C.; Forsyth, J.K.; Haut, K.M.; Bearden, C.E.; Addington, J.; Goodyear, B.; Cadenhead, K.S.; Mirzakhanian, H.; Cornblatt, B.A.; et al. Reliability of an FMRI Paradigm for Emotional Processing in a Multisite Longitudinal Study. Hum. Brain Mapp. 2015, 36, 2558–2579, doi:https://doi.org/10.1002/hbm.22791.
53. Forsyth, J.K.; McEwen, S.C.; Gee, D.G.; Bearden, C.E.; Addington, J.; Goodyear, B.; Cadenhead, K.S.; Mirzakhanian, H.; Cornblatt, B.A.; Olvet, D.M. Reliability of Functional Magnetic Resonance Imaging Activation during Working Memory in a Multi-Site Study: Analysis from the North American Prodrome Longitudinal Study. Neuroimage 2014, 97, 41–52.
54. Esteban, O.; Markiewicz, C.J.; Blair, R.W.; Moodie, C.A.; Isik, A.I.; Erramuzpe, A.; Kent, J.D.; Goncalves, M.; DuPre, E.; Snyder, M. FMRIPrep: A Robust Preprocessing Pipeline for Functional MRI. Nat. Methods 2019, 16, 111–116.
55. Cacioppo, J.T.; Berntson, G.G.; Bechara, A.; Tranel, D.; Hawkley, L.C. Could an aging brain contribute to subjective well-being? The value added by a social neuroscience perspective. In Social neuroscience: Toward understanding the underpinnings of the social mind.; Oxford series in social cognition and social neuroscience.; Oxford University Press: New York, NY, US, 2011; pp. 249–262 ISBN 978-0-19-531687-2.
56. MacCormack, J.K.; Stein, A.G.; Kang, J.; Giovanello, K.S.; Satpute, A.B.; Lindquist, K.A. Affect in the Aging Brain: A Neuroimaging Meta-Analysis of Older Vs. Younger Adult Affective Experience and Perception. Affect. Sci. 2020, 1, 128–154, doi:10.1007/s42761-020-00016-8.
57. Bluhm, R. New Research, Old Problems: Methodological and Ethical Issues in FMRI Research Examining Sex/Gender Differences in Emotion Processing. Neuroethics 2013, 6, 319–330.
58. Wrase, J.; Klein, S.; Gruesser, S.M.; Hermann, D.; Flor, H.; Mann, K.; Braus, D.F.; Heinz, A. Gender Differences in the Processing of Standardized Emotional Visual Stimuli in Humans: A Functional Magnetic Resonance Imaging Study. Neurosci. Lett. 2003, 348, 41–45, doi:10.1016/S0304-3940(03)00565-2.
59. Stevens JS; Hamann S Sex Differences in Brain Activation to Emotional Stimuli: A Meta-Analysis of Neuroimaging Studies. Neuropsychologia 2012, 50, 1578–93, doi:10.1016/j.neuropsychologia.2012.03.011.

X Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

XI Publikationsliste

Eine kontinuierlich aktualisierte Liste findet sich unter: https://orcid.org/0000-0002-6312-0232

Peer-reviewed articles

Hartling, C., Metz, S., Pehrs, C., Scheidegger, M., Gruzman, R., Keicher, C., Wunder, A., Weigand, A. & Grimm, S. (2021). Comparison of Four fMRI Paradigms Probing Emotion Processing. *Brain Sciences*, *11*(5), 525.

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Hartling, C., Fan, Y., Weigand, A., Trilla, I., Gärtner, M., Bajbouj, M., Dziobek, I., Grimm, S. (2019). Interaction of HPA axis genetics and early life stress shapes emotion recognition in healthy adults. *Psychoneuroendocrinology*, 99, 28-37.

Impact factor: 4.732 (2020)

Carstens, L., Hartling, C., Stippl, A., Domke, A. K., Herrera-Mendelez, A. L., Aust, S., Gärtner, M., Bajbouj, M. & Grimm, S. (2021). A symptom-based approach in predicting ECT outcome in depressed patients employing MADRS single items. *European Archives of Psychiatry and Clinical Neuroscience*, 1-10.

Impact factor: 5.270 (2020)

Castens, L., Hartling, C., Aust, S., Domke, A. K., Stippl, A., Spies, J., Brakemeier, E.L., Bajbouj, M. & Grimm, S. (2021) EffECTively treating depression: A pilot study examining manualized group CBT as follow-up treatment after ECT. *Frontiers in Psychology*, 12.

Impact factor: 2.990 (2020)

Demir, Z., Böge, K., Fan, Y., Hartling, C., Harb, M. R., Hahn, E., Seybold, J., Bajbouj, M. (2020). The role of emotion regulation as a mediator between early life stress and posttraumatic stress disorder, depression and anxiety in Syrian refugees. *Translational Psychiatry*, *10*(1), 1-10.

Impact factor: 6.222 (2020)

Poster presentations

Hartling, C., Fan, Y., Weigand, A., Trilla, I., Gärtner, M., Bajbouj, M., Dziobek, I., Grimm, S. HPA-axis genetics modulate the effect of early life stress on emotion recognition in healthy adults. Poster presented at 48th International Society for Psychoneuroendocrinology Annual Conference 2018, Sep 6-8, Irvine, CA, USA

Hartling, C., Carstens, L., Stippl, A. Bajbouj, M., Grimm, S. Mechanisms of anti-depressant treatment response (MATTER): rationale and study protocol. Poster presented at 28th European Congress of Psychiatry, 2020, July 4-7, virtual

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