Decoding working memory and perceptual choice during tactile information processing

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Abbreviations

BOLD	blood oxygen level dependent
EEG	electroencephalogram
FEF	frontal eye fields
fMRI	functional magnetic resonance imaging
IFG	inferior frontal gyrus
IPL	intraparietal lobule
IPS	intraparietal sulcus
LIP	lateral intraparietal area
MEG	magnetoencephalograohy
MVPA	multivariate pattern analysis
NHP	nonhuman primate
PFC	prefrontal cortex
PMd	dorsal premotor cortex
PMv	ventral premotor cortex
S1	primary somatosensory cortex
S2	secondary somatosensory cortex
TMS	transcranial magnetic stimulation
WM	working memory

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Abstract

Working memory and decision-making are two building blocks of human cognition that are involved in most goal-directed behaviors. Exposing the neural underpinnings of these mental functions has been a central goal of cognitive and systems neuroscience. Critically, most models and theories have emerged from empirical findings in the visual domain, leaving open the question of whether they hold for other sensory domains.

In this dissertation, I aimed at studying the neural correlates of working memory and decision-making during tactile information processing. In particular, I conducted four fMRI studies to address the question of which brain regions represent the contents of working memory and perceptual choices. We found parametric working memory representation of vibrotactile frequencies distributed across sensory, posterior parietal, and frontal cortices. This finding was also replicated in the visual and auditory modalities. Perceptual choices are represented in the prefrontal and oculomotor regions, even when decoupled from saccade plans.

These results support the view that the loci of mental representations depend critically on task requirements and content types.

Zusammenfassung

Arbeitsgedächtnis und Entscheidungsfindung sind zwei Bausteine der menschlichen Kognition, die für zielgerichtetes Handeln von Bedeutung sind. Die Erforschung der neuroalen Grundlagen dieser mentalen Funktionen ist ein zentrales Ziel der kognitiven und systemischen Neurowissenschaften. Allerdings ist die überwiegende Mehrheit aktueller Modelle und Theorien aus empirischen Befunden von visuellen Experimenten hervorgegangen. Dies lässt die Frage offen, ob sie auch für andere sensorische Modalitäten gelten.

In dieser Dissertation untersuchte ich die neuronalen Korrelate von Arbeitsgedächtnis und Entscheidungsfindung während der taktilen Informationsverarbeitung. Ich führte vier fMRT-Studien durch, um die Frage zu beantworten, welche Hirnregionen den Inhalt des Arbeitsgedächtnisses und das Treffen von Entscheidungen repräsentieren. Im Ergebnis zeigte sich, dass eine Speicherung von Information über vibrotaktile Frequenzen im Arbeitsgedächtnis auf parametrische Weise stattfand und dieser Code über sensorische, posterior-parietale und frontale Kortex verteilt ist. Dieser Befund wurde auch in der visuellen und auditiven Modalität repliziert. Wir fanden außerdem, dass die vom Arbeitsgedächtnis informierten Entscheidungen in präfrontalen und okulomotorischen Regionen repräsentiert sind, auch wenn sie von Sakkadenplänen unabhängig sind.

Diese Ergebnisse unterstützen die Ansicht, dass die Loci mentaler Repräsentationen kritisch von Aufgabenanforderungen und Inhaltstypen abhängen.

List of original research articles

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1. Introduction

A defining feature of intelligence is the ability to flexibly coordinate thoughts and behaviors to achieve internal goals. That is, humans and animals do not just reflexively react to information from the environment, but carry out a sequence of mental operations to process the received information in order to initiate behaviors most beneficial for an internal goal (Miller and Cohen, 2000; Miller, 2001).

Among a range of mental operations, working memory (WM) and decision-making are two fundamental cognitive functions involved in most goal-directed behaviors. Working memory refers to the ability to mentally maintain and manipulate information that is not present in the immediate environment (Baddeley, 2012). This ability is a prerequisite for performing complex behaviors based on time-extended goals and contextual contingencies (Wolff et al., 2015). Decision-making, on the other hand, is a deliberative process in which a categorical judgement based on the available information (either in the physical environment or WM) is made toward a course of actions in accord with an internal goal (Gold and Shadlen, 2007). Given their paramount importance for flexible, intelligent behavior, understanding the neural underpinnings of WM and decision-making has been a central goal of cognitive and systems neuroscience.

In this dissertation, I investigate the neural correlates of WM and decision-making in the context of tactile information processing. Using fMRI and well-established

memory-guided decision-making paradigms (Romo and Salinas, 2001; 2003), I ask how the human brain represents the contents of WM and perceptual choices in particular behavioral contexts.

In the following section of the introduction, I give an overview on some of the most influential concepts and key findings that have shaped our current understanding of WM and decision-making. In particular, I place emphasis on reviewing empirical evidence and implications derived from extracellular recordings in nonhuman primates (NHP) using vibrotactile frequency discrimination tasks (Romo and de Lafuente, 2013). This NHP work has initiated some of the greatest progress in elucidating the neurobiology of tactile information processing and inspired the research questions of this dissertation. After the introduction I report the main results from four experiments, in which I investigated WM and perceptual choice representations by means of multivariate pattern analysis (MVPA) of human fMRI data and summarize the implications drawn from each experiment individually. In the last part of the dissertation I provide a broader discussion of the insights gained from the experiments and finish with future perspectives.

1.1 The study of working memory

The modern conceptualization of WM has been significantly influenced by two independent developments that date back to the 1970s. The first one was the landmark findings of two independent research groups (Fuster and Alexander, 1971; Kubota and Niki, 1971) using single-unit recordings in NHPs. They identi-

fied individual neurons in the prefrontal cortex (PFC) as exhibiting sustained activity throughout the retention interval of a delayed response task, bridging the temporal gap between stimulus presentation and the subsequent contingent response. This discovery led to the view that prefrontal sustained delay activity is the neural basis of WM and has made the PFC to the most investigated cortical region in the context of WM (Postle, 2006). The second development came from cognitive psychology with the introduction of the multicomponent model by Baddeley and Hitch in 1974. In their initial version of the model, Baddeley and Hitch (1974) proposed that WM is constituted by three components: a phonological loop and a visuospatial sketchpad as two independent storage buffers for verbal and visuospatial information; and a central executive, which exerts attentional control over individual storage systems. The idea that WM is processed by a central executive and multiple specialized storage compartments was seminal and has significantly guided neuroscientists' efforts to dissociate the neural mechanisms and brain structures implementing each of these functions.

1.1.1 Debate on the locus of working memory storage storage

Converging evidence from studies using a variety of methodologies in the last decades has reached the consensus that the PFC is crucially involved in WM processes (Curtis and D'Esposito, 2003). There is, however, still a lively debate about its role in the maintenance function (Sreenivasan et al., 2014; D'Esposito and Postler, 2015; Riley and Constantinidis, 2016; Leavitt et al., 2017; Xu, 2017).

Corroborated by findings from her own lab that prefrontal sustained delay spiking activity in NHPs is selective to spatial information without being contaminated by sensory and motor processes (Funahashi et al., 1989), Goldman-Rakic (1991) posited that prefrontal sustained delay spiking activity is the physiological manifestation of the storage buffer in the multicomponent model (Baddeley and Hitch, 1974; Baddeley, 2012). This proposal has proven to be enormously influential, in part because of the innovative idea of integrating concepts from psychological and neurophysiological research, which up until then, had taken place on two largely independent paths (Postle, 2006); and in part because the selective property of prefrontal sustained delay spiking activity generalizes across a variety of information, such as color (Buschman et al., 2011); numerosity (Nieder et al., 2002); objects and natural images (Miller et al, 1996; Meyer et al., 2011), spatial location (Funahashi et al., 1993; Rainer et al., 1998), tactile vibration (Romo, 1999; Hernandez, 2010), and visual motion (Zaksas and Pasternak, 2006; Mendoza-Halliday et al., 2014). Supported by a large body of evidence, Goldman-Rakic's proposal became the most prominent model of WM at that time (Postle, 2006).

However, there are multiple sources of empirical evidence in favor of the so-called sensory recruitment models (Pasternak and Greenlee, 2001), which emphasize regions engaged in perception as the primary locus of WM storage, and PFC as a source of top-down executive control to support memory storage (Postle, 2006; Sreenivasan et al., 2014; D'Esposito and Postler, 2015). First, stimulus-selective sustained delay activity observed in NHPs is not a specific prefrontal property. In fact, it has been reported across a widely distributed brain

network, including the auditory (Gottlieb et al., 1989), posterior parietal (Constantinidis and Steinmetz, 1996), somatosensory (Zhou and Fuster, 1996; Hernández et al., 2010), and visual cortices (Super et al. 2001, Van Kerkoerle et al., 2017). Second, prefrontal sustained activity is well-known for reflecting a variety of higher-order task information, such as abstract categories (Freedman, 2001) and task rules (Warden and Miller, 2010), which is thought to be crucial for any contexts requiring flexible behavior (Fuster, 1990; Miller and Cohen, 2001). This has given rise to the question of whether prefrontal sustained activity primarily subserves a general support mechanism rather than WM storage itself. Third and probably the strongest argument for sensory recruitment models, human fMRI studies using MVPA have succeeded in decoding a variety of sensory features such as color (Serences, 2009), orientation (Harrison and Tong, 2009), color pattern (Christophel et al., 2012), motion (Riggall and Postle, 2012), and tactile layout (Schmidt et al., 2018) from activity patterns in the visual or posterior parietal cortices in the absence of sustained, elevated activation. However, most of the studies using this technique failed to extract memorized information from the PFC, even in the presence of an elevated activity level (Christophel et al., 2012; Riggall and Postle, 2012; Emrich et al., 2013). Moreover, results from two fMRI studies using MVPA suggest that the precision of the neuronal representation in visual cortex reflects the fidelity of the mental representation. In one study, Ester and colleagues (2013) showed that the precision of the tuning curve of fMRI voxel populations was predictive to the behavioral performance. In another study by

Emrich and colleagues (2013), a load-dependent modulation in decoding accuracy was highly correlated with the load-dependent modulation in behavioral performance.

Taken together, there is a great body of evidence for both Goldman-Rakic's model and sensory recruitment models. Support for Goldman-Rakic's model mainly originates from extracellular recordings in NHPs (reviewed in Leavitt et al., 2017), while arguments for sensory recruitment models build primarily on evidence coming from human fMRI studies using MVPA (reviewed in Lee and Baker, 2013; Christophel et al., 2017). One should, however, be cautious in evaluating the evidence used to argue for one or the other view for several reasons. First, there might be a sampling bias regarding the recording sites in NHP studies, as it is not uncommon that researchers focus on neurons known for exhibiting specific response properties (Leavitt et al., 2017). Second, arguments against Gold-Rakic's model often rely on interpretations of negative findings in fMRI-MVPA studies. And lastly, because extracellular recordings and fMRI measure two totally different types of signals, interpretation of contrasting findings between these two recording modalities may be difficult (Riley and Constantinidis, 2016; Leavitt et al., 2017).

Recently, suggestions for a reconciliation of opposing findings favoring specific models have been made (Lee and Baker, 2013; D'Esposito and Postle, 2015; Christophel et al., 2017). In particular, Christophel and colleagues posit that the location of the stored information depends on the level of abstraction required for

the task or the strategies used. For instance, Lee et al. (2013) reported in a human fMRI study that object identity could be decoded from visual, but not PFC if subjects were asked to memorize visual properties of the objects, while a reversed pattern is found when subjects have to memorize the categories of the objects. These findings suggest that WM storage sites for the same stimulus may vary as a function of the required level of abstractness. When low-level sensory details are required, information tends to be represented in the hierarchically lower regions in the posterior area. When the stimulus need to be memorized as an abstract feature, it tends to be represented in higher association areas.

1.1.2 Empirical evidence for vibrotactile working memory

WM in the tactile domain has been extensively studied with the vibrotactile discrimination task, which was first introduced by Mountcastle and colleagues (1972, 1990). In the standard version of this task, the subject receives two vibratory stimulation, separated by a short retention interval, on their fingertip and indicates whether the frequency of the second vibration (f2) is higher or lower than the frequency of the first vibration (f1). This task is extremely versatile as it allows investigators to examine multiple cognitive operations: 1) encoding the first stimulus and extracting the relevant feature, 2) maintaining the feature in WM, 3) encoding the second stimulus and extracting the relevant feature, 4) comparing the feature of the second stimulus with the memory trace left by the first, and 5) communicating the outcome of comparison to the motor apparatus in order to produce an appropriate behavior (Romo and Salinas, 2001; Fassihi et al., 2013). This task

is often referred to as the parametric WM task as it requires the maintenance of a scalar analog value (frequency of the vibration) and an ordinal comparison with a second scalar analog value (Romo et al., 1999). This section mainly focuses on reviewing findings related to the WM component of this task, while a more detailed review of other components of the task can be found in section 1.2.3.

Extracellular recordings in nonhuman primates

The starting point of vibrotactile WM research dates back to 1999 with seminal work by Romo and colleagues, which showed that the firing rates of individual right PFC neurons in NHPs were parametrically modulated by the memorized frequencies throughout the entire retention interval, with different neuron populations either positively or negatively tuned to the frequencies maintained in WM. This work is remarkable because in addition to the finding of stimulus-specific modulation of prefrontal neurons, it also characterizes the parametric nature of the WM representation, which is directly linked to the stimulus attributes. This finding was subsequently replicated in a series of studies (Brody et al., 2003; Machens et al., 2005; 2010; Barak et al; 2010; Hernandez et al., 2010; Jun et al., 2010). The PFC was not the only brain structure showing such parametric representations of frequencies. As revealed by multiple studies, neurons in the premotor structures, including the dorsal premotor cortex (PMd), the ventral premotor cortex (PMv), and the supplementary motor area (SMA), as well as neurons in the secondary somatosensory cortex (S2) responded in a similar manner (Sa-

linas et al., 2000; Romo et al., 2002). However, about 60% of the premotor neurons exhibited frequency-selective responses only at the late stage of the retention interval (Romo and de Lafuente, 2013).

Notably, modulatory effects of frequencies were already observable during the stimulus presentation period in all the reported regions. This indicates that prefrontal and premotor cortices are, along with somatosensory cortices, involved in sensory processing. However, it is not clear what functions these frontal sensory representations might take. In contrast, frequency-selective responses of neurons in the primary somatosensory cortex (S1) were only evident during the stimulus presentation, but absent in the retention interval (Salinas et al., 2000; Romo et al., 2004; Hernández et al., 2010; Lemus et al., 2010).

Taken together, extracellular recordings in NHPs showed that frequencies held in WM are represented throughout the cortical hierarchy. Frequency-selective delay activity in S2 was only observable at the early stage of the retention interval, while prefrontal frequency-selective delay activity persisted across the entire retention interval. Finally, frequency-selective delay activity in premotor structures was most conspicuous at the late stage of the retention. These findings generally support the notion proposed by Goldman-Rakic (1991) that PFC is the primary WM storage. However, they do not necessarily undermine sensory recruitment models (Pasternak and Greenlee, 2001) as several regions involved in sensory processing were also found to carry information during the retention interval.

Non-invasive studies in humans

The initial vibrotactile WM study in humans was carried out with TMS, in which impulses were delivered to S1 at different stages of the retention interval of a vibrotactile discrimination task (Harris et al., 2002). These authors showed that behavioral performance decreases significantly when TMS is applied to S1 contralateral to the stimulus in the early part of the retention interval, and concluded from this finding that the memory trace resides in the contralateral S1. They argued that the disagreement with the findings referenced above of S1 neurons not engaged in WM maintenance might arise from the difference in the amount of training between NHP and human subjects. Note, however, that this TMS study did not investigate any cortical regions outside S1.

The first evidence for parametric WM coding of vibrotactile frequencies in humans comes from EEG experiments (Spitzer et al., 2010; Spitzer and Blankenburg, 2011). Analogous to the extracellular recordings referenced above, these authors observed parametric modulation of upper beta band power (20-25 Hz) as a function of the memorized frequency. Moreover, the right inferior frontal gyrus (IFG) in the PFC has consistently been identified as the most likely source of such a content-specific modulation, even with increased spatial acuity using MEG (von Lautz et al., 2017). However, prefrontal beta band power modulation does not persist throughout the entire retention interval and might reflect short beta bursts rather sustained activity (Stokes, 2015; Lundqvist et al., 2016). Moreover, beta band temporal dynamics seem to depend on task demands (Spitzer and Haegens, 2017). That is, prefrontal beta power modulations tend to occur at a relatively late

stage of the retention interval when the memorized information needs only to be (re)activated for the preparation of an upcoming comparison (Spitzer et al., 2010). On the other hand, when subjects need to prioritize one of the many previously presented frequencies for further maintenance, prefrontal beta activity modulations tend to take place at the early stage of the retention interval (Spitzer and Blankenburg, 2011). Thus, the parametric modulation of beta power oscillations might subserve a different function than that of the sustained parametric WM codes observed in NHPs (see Spitzer and Haegens, 2017 for a review of beta oscillation functions).

There are only few fMRI studies focusing on the exploration of brain regions involved in vibrotactile WM processes (Preuschhof et al., 2006; Kostopoulos et al., 2007; Li Hegner et al., 2010; Spitzer et al., 2014). In line with neurophysiological data derived from NHPs, these studies consistently found sustained, elevated BOLD delay activity in the ventrolateral PFC (vlPFC), premotor cortices, or S2, suggesting the engagement of a similar cortical network between NHPs and humans. In addition, results of human fMRI studies also indicate intraparietal lobule (IPL) and intraparietal sulcus (IPS), as a part of the vibrotactile WM network (Preuschhof et al., 2006; Kostopoulos et al., 2007; Li Hegner et al., 2010). Note, however, that all the fMRI studies referenced above used univariate activation-based analyses and, therefore do not provide information on whether the sustained delay activity in the identified regions is content-specific. Thus, it is not clear whether the contrasting results between species typically observed in other domains will also apply in the vibrotactile domain.

Domain-general parametric WM coding

Evidence from NHP and human studies broadly suggest that vibrotactile frequency information held in WM is primarily reflected by the parametric modulation of prefrontal neuronal firing rates. However, it is also conceivable that such a parametric WM code is not specific to vibrotactile information, but is a general mechanism for the maintenance of scalar quantity information from a range of sensory modalities. To test this idea, Spitzer and Blankenburg (2012) asked participants to perform a discrimination task which required the maintenance of frequencies of auditory, tactile, or visual flutter during EEG recordings. As well as replicating of previous findings of parametric modulations of prefrontal beta activity as a function of the vibrotactile frequencies, they were also able to show similar effects across sensory modalities. Likewise, Vergara et al. (2015) demonstrated that pre-SMA neurons use analogous parametric code in firing rates to represent memorized frequencies, regardless of whether they were extracted from touch or audition. These results indicate that at least some aspects of parametric WM are represented in an abstract, supramodal scalar format (Spitzer and Haegens, 2017), providing important empirical support for the notion that emphasizes levels of abstraction as one of the fundamental principles for the topographic organization of WM storage (Christophel et al., 2017).

1.2 The study of perceptual decision-making

Perceptual decision-making is a process in which sensory information is gathered and used to make a categorical judgement. To understand the neural underpinning of this process, neuroscientific research on perceptual decision-making has typically focused on questions like how choice-relevant sensory information is represented or how decisions are computed from these representations (Gold and Heekeren, 2014). Much of the progress has been achieved by the application of approaches from statistical decision theory, such as signal detection theory or sequential sampling models, to neural data (Gold and Shadlen, 2007; O'Connell et al., 2017). These approaches have provided a set of methodological and theoretical principles for many studies and are seminal in shaping the current understanding of perceptual decision-making. Below I illustrate briefly how these frameworks are used to identify neural signals that support the generation of perceptual choices.

1.2.1 Signal detection theory

Signal detection theory (SDT) was developed to provide a mechanistic account of the detection of weak sensory signals (Green and Swets, 1966; Macmillan and Creelman, 2004). The basic idea is that perceptual performance not only depends on the sensitivity of the decision-maker but also on how the decision-maker uses the perceived information to reach a decision.

In SDT, the decision-maker infers the identity of a stimulus (h_1 vs h_2) from sensory information, which is represented by the neural responses elicited by experimental manipulations (typically measured in quantities like the spike count of a single neuron or a pool of neurons). These neural responses constitute a sample of evidence, which is corrupted by internal and external noises. Thus, the evidence can be described as a random variable from a distribution with parameters (e.g. the mean, dispersion) set by h_1 or h_2. To solve this inference problem, the decision-maker evaluates the likelihood of the evidence being drawn from distributions underlying h_1 and h_2, and computes the ratio of the two likelihoods: $p(evidence \mid h_1) / p(evidence \mid h_2)$. The decision-maker then applies a criterion to the likelihood ratio to reach a choice, such as choose h_1, if the likelihood ratio is ≥ 1. Using this framework, it is possible to determine whether and to which extent responses of individual neurons are sensitive to stimulus identities. More importantly, it also enables investigators to infer quantitative relationships between responses of individual neurons and the subject's choice behavior (Parker and Newsome, 1998).

Successful applications of SDT can, for instance, be found in a number of experiments in which the extent to which motion-selective neurons in the medial temporal area (MT) support NHPs' percept in a random dot-motion (RDM) task was investigated (Newsome et al., 1989; Salzman et al., 1990; Britten et al., 1992; 1996). In this task, the subject observes a cloud of moving dots, with a certain proportion of dots moving coherently in one of two opposite directions, while the remaining dots meander randomly. The subject judges the direction of the coherently moving dots by making a saccade to one of two targets. The amount of

sensory evidence favoring a particular motion direction is controlled by the experimenters by varying the proportion of dots moving coherently.

Strikingly, the sensitivity of optimally tuned MT neurons is on average as high as that of the NHPs themselves (Newsome et al., 1989; 1992). This has been interpreted as supporting MT neurons' contribution to perceptual discrimination. This view is further strengthened by a study demonstrating that microstimulation of neurons tuned to a given motion direction systematically increased the probability that NHPs will choose that same direction (Salzman et al., 1990), indicating that the choice behavior may be causally linked to the responses of individual MT neurons. Moreover, Britten et al. (1996) showed that the trial-by-trial variability in the firing rates of individual MT neurons was subtly but reliably correlated with NHPs' choices. These results suggest that MT activity represents sensory information used by the NHPs to perform the task. However, the relatively low correlation between the activity of single neurons and NHPs' choices also indicates that a direct read-out of information from single neurons might not be sufficient to account for NHPs' performance. This led to the proposal that perceptual decisions might be based on information integrated from neuron populations with opposite tuned properties for motion directions (Shadlen et al., 1996; Shadlen and Newsome, 1998; Gold and Shadlen, 2001).

Taken together, using analytical tools based on the SDT framework, Newsome and colleagues have established the link between the activity of MT neurons and behavioral choice, and significantly facilitated our understanding of perceptual decision-making. As I will elaborate later, SDT-based approaches have also been

successful in describing the relationship between behavioral choice and the activity of sensory neurons in the somatosensory system (Romo and Salinas, 2003).

1.2.2 Sequential-sampling models

Sequential sampling models can be regarded as a dynamic extension of SDT, which also takes into account a key variable in many decision-making situations, time (Ratcliff, 1978; Wagenmakers et al., 2007). In contrast to SDT, which typically assumes that decisions are formed based on a single sample of evidence, the essence of sequential sampling models is that decisions are formed by repeatedly sampling, accumulating evidence, and withholding commitment over time until a criterion amount of evidence favoring one of the choices is obtained (Ratcliff and Smith, 2004; O'Connell et al, 2017). The main component of sequential sampling models for a decision process are the rate of accumulation and the decision criterion (Ratcliff et al., 2016). A low accumulation rate indicates poor quality of information and results in longer response latencies and more errors than if the accumulation rate is high. A low decision criterion, on the other hand, implies that the decision is made based on little accumulated evidence, facilitating fast decisions at the cost of a higher error rate. Sequential-sampling models were developed under the premise that accumulating multiple samples of evidence will improve the reliability and minimize the effects of noises (Smith and Ratcliff, 2004). This concept is closely related to the sequential probability ratio test (SPRT), a mathematical procedure for obtaining a given rate of accuracy with minimum amount of evidence (Wald, 1945). In fact, if samples are independent,

some sequential sampling models are statistically equivalent to SPRT and can be viewed as models that accumulate a log likelihood ratio derived from every sample of evidence in time until a stopping point (Gold and Shadlen, 2001; 2007; Radcliff et al., 2016).

Models within this framework may differ in their assumptions about how evidence is accumulated (cf. Smith and Ratcliff, 2004; Ratcliff et al., 2016). For instance, random walk or diffusion models employ relative evidence criteria, meaning that evidence in favor of one choice alternative is evidence against the other alternative. In contrast, accumulator models use absolute evidence criteria. That is, evidence favoring each of the two alternatives is accumulated separately. The decision is determined by the first accumulator to reach it is respective bound (Usher and McClelland, 2001).

Sequential-sampling models have become extremely popular in various research fields because they provide a straightforward, quantitatively precise way to account for speed and accuracy in behavioral tasks in various contexts (Smith and Ratcliff, 2004). Furthermore, there is also a great body of evidence concerning how and where evidence accumulation is implemented in the brain.

The earliest evidence comes from studies using RDM tasks: After having established MT neurons role as the “sensors” for visual motion directions, Newsome and colleagues shifted their focus to identifying brain regions that integrate information over space and time (Shadlen et al., 1998). Given that decisions in their task were conceptualized as a problem of action selection (choice favoring a rightward motion direction is the same as choosing a rightward saccade and vice

versa), they focused on regions implicated in the selection and preparation of eye movements, such as the lateral intraparietal area (LIP), frontal eye fields (FEF), and superior colliculus (SC).

This approach has turned out to be very successful. Schadlen and Newsome (1998; 2001) observed a gradual increase in LIP firing rates during the stimulus presentation, when sensory evidence favored a saccade toward the target inside a neuron's receptive field. When the target outside the receptive field was preferred, they observed a leveling-off or a slight decrease in the neuron's activity. Importantly, this ramp-like activity is thought to reflect more than the usual motor build-up signals during saccade preparation (Wurtz et al., 2001), because it possesses unique characteristics which are consistent with what one would expect from evidence accumulation. First, the rate of the ramp activity scales with the coherence level of the moving dots (Shadlen and Newsome, 1996; 2001). Second, when allowing subjects to report their decisions as soon as possible, the ramp activity reaches a common peak level shortly before saccade initiation independently of the degree of motion coherence (Roitman and Shadlen, 2002), supporting the idea that evidence accumulation terminates after reaching a criterion. Third, quantitative models suggest that the average firing rate in LIP approximates the temporal integral of differential activities of MT neurons with distinct motion direction preferences (Mazurek, 2003), corroborating the idea that sensory evidence is integrated across different pools of MT neurons (Shadlen and Newsome, 1996; Shadlen et al., 1998). Similar findings have also been reported in other oculomotor regions, such as the FEF (e.g., Hanes and Schall, 1996; Kim

and Shadlen, 1999; Ding and Gold, 2012) and the SC (e.g., Horwitz and Newsome, 1999; Ratcliff et al., 2003).

In sum, the results referenced above make a strong case for oculomotor regions' involvement in representing evidence accumulation underlying perceptual decisions. These findings have given rise to the view that decisions are formed in an intentional framework, that is, directly in effector-specific motor planning signals (Gold and Shadlen, 2007; Cisek and Kalaska, 2010). Moreover, these findings have paved the way for an extremely fruitful marriage between neurophysiology and quantitative modeling in decision-making research and made sequential-sampling models the most important theoretical framework for generating and testing tractable hypotheses about the neural computation for a variety of types of decisions across species (Hanks and Summerfield, 2016).

However, some recent findings have cast doubts on LIP and other oculomotor regions' role in decision formation in tasks with saccadic responses. These studies showed that LIP activity during the decision phase was multiplexed with information of a range of sensory, task, and motor-related variables (Bennur and Gold, 2011; Meister et al., 2013; Park et al., 2014), leading to the hypothesis that LIP may only exhibit ramp-like activity mirroring evidence accumulation when heterogeneous responses are averaged together (Meister et al., 2013; Park et al., 2014; see also Hanks and Summerfield, 2015). Moreover, the idea that decisions are directly formed in the effector-specific circuit may only apply to contexts in which the perceptual choice is rigidly mapped to a particular action. Results from

human neuroimaging suggest the presence of a domain-general evidence accumulation mechanism in prefrontal and parietal regions (e.g. Heekeren et al., 2006; Ho et al., 2009; O'Connell et al., 2012; see Heekeren et al., 2008; Kelly and O'Connell, 2015 for comprehensive reviews). In addition, evidence accumulation over time is likely only one of many ways to account for the neural signals observed during the decision phase. Likewise, it is well conceivable that there are situations, in which evidence accumulation over time is not required for reaching a choice.

1.2.3 Empirical evidence from vibrotactile frequency discriminations

Aside from the RDM tasks which require subjects to make perceptual judgements of a single visual stimulus, another very popular approach to studying decision processes is the vibrotactile frequency discrimination task (Mountcastle et al. 1972). As introduced in the previous section, this task requires subjects to compare the frequencies of two sequentially presented vibrotactile stimuli and indicate whether the frequency of the second stimulus (f2) is higher or lower than the frequency of the first (f1), typically with a manual response. In other words, subjects decide between f2 < f1 or f2 > f1. One intriguing feature of this task is that the decision is based on the evaluation of a stimulus in comparison to a percept held in WM. In the previous section I reviewed empirical evidence for brain activity representing frequency-specific information held in WM. Here I continue with findings from NHP and human studies that have shed light on how such memory-guided decisions may be implemented in the brain.

Extracellular recordings in nonhuman primates

Single-unit recordings in the S1 contralateral to the stimulus have shown that vibrotactile frequencies during the discrimination task are encoded by the rapidly adapting neurons in Brodmann area 3b and 1 with two different coding schemes (Mountcastle, 1990; Salinas et al., 2000; Hernández, 2002; 2010; Lemus et al., 2010). One sub-population of S1 neurons responds periodically, phase-locked to stimulus frequencies (temporal code), whereas a second sub-population encodes stimulus frequencies by means of a rate code, meaning that the average firing rates increases monotonically with increasing frequency. Results from SDT-based analyses indicate that NHPs' behavioral performance is better explained by S1 neurons exhibiting a rate code (Hernández et al., 2000; Salinas et al., 2000). For instance, the discriminability of neurons employing a rate code closely matched behavioral sensitivity. Neurons employing a temporal code, on the other hand, discriminated vibrotactile frequencies significantly better than the NHPs themselves did, suggesting that NHPs do not exploit the temporal information to solve the task. Likewise, behavioral choice could be better predicted by the average firing rates than the periodic spike activities. These findings have led to the conclusion that the average firing rates represent the sensory evidence used to perform this task (Romo and Salinas, 2003; Romo and de Lafuente, 2013).

Neurons in a number of downstream regions to S1, including S2, PFC, PMv, PMd, and SMA, have also been observed to represent stimulus frequencies with a rate code (Romo et al., 1999; 2004; Hernández, 2002; 2010; Barak et al., 2010; Jun et al., 2010), with the shortest response latency in S1, followed by S2, then by

PFC and PMv, and finally by PMd and SMA (Hernández et al., 2010). In contrast, the temporal code is absent in these downstream regions. In addition, firing rates of about a half of the S2 and frontal neurons (PFC, PMv, PMd, and SMA) are positively modulated by the stimulus frequency, whilst the other half show an opposite preference and are negatively modulated by the stimulus frequency. f1 appears to be encoded by such a dual code in S2 and frontal neurons at multiple stages of the task, including the f1 presentation, during the retention interval, in which NHPs had to maintain their percept of f1 in WM (please see section 1.1.2 for more details), and f2 presentation. Neurons in S1, on the other hand, encodes f1 exclusively with a positive rate code during f1 presentation (e.g. Hernández et al., 2000; 2010; Lemus et al., 2010).

The core of the discrimination task – the comparison between f1 and f2 – takes place during the presentation of f2. At the early stage of this period, the activity of individual neurons in S2, PFC, PMv, PMd, and SMA are either modulated by f2 or by f1, presented few seconds before (Romo et al., 2002; 2004; Hernández et al., 2002; 2010; Jun et al., 2010). Over the course of f2 presentation, however, the activity of these neurons starts to reflect the choice made by the subjects, namely f2 < f1 or f2 > f1. Moreover, Romo and colleagues (Romo et al., 2002; 2003; 2004; Hernández et al., 2002; 2010) showed that firing rates to choices scale with the difference between the activities of neuron populations that encode f1 and f2 with opposite tuning properties (positive vs negative), with premotor cortices exhibiting the strongest effect. This indicates that decisions are formed by a subtraction operation of f2 – f1 in these regions and the sign resulting from

this subtraction operation reflects the choice (Romo and de Lafuente, 2013). Interestingly, in the context of RDM tasks, a similar mechanism has also been suggested to read out activities from different neuron populations (Gold and Shadlen, 2002), hinting at a general principle for neural coding.

Contrary to other regions, S1 neurons have only been reported to encode f1 and f2 during stimulus periods. Thus, it is unlikely that S1 is involved in the decision formation. Notably, choice signals are also found in the primary motor cortex (M1) during f2 presentation (Romo et al., 2002), however, with a longer response latency than all other regions. This has led to the suggestion that M1 may be involved in converting of the result of the comparison process elaborated in other brain regions into the final motor response (Salinas and Romo, 1998).

Premotor cortices' involvement in the comparison process is further corroborated by a recent study investigating oscillatory dynamics of local field potentials in NHPs. Haegens and colleagues (2011) revealed that the beta band power in the LFPs recorded from PMd and SMA are categorically modulated by the choices, suggesting that the comparison process is also supported by neural dynamics at a larger scale.

The findings of premotor structures exhibiting signals that reflect the comparison between f1 and f2 aligns well with the idea of an intentional framework from the RDM context, positing that decisions are formed in regions involved in action selection. However, because perceptual choice in these studies was directly mapped to a particular manual response, there remains the question of whether

the observed decision signal was rather related to the motor preparation than to decision formation per se.

Non-invasive human studies

The number of human studies of the vibrotactile decision-making is rather small. The initial attempts to elucidate the mechanisms of human vibrotactile decisions were carried out with fMRI. Preuschhof et al. (2006) reported a broad brain network including prefrontal, posterior parietal and sensorimotor regions showing elevated BOLD activity during the comparison period. Moreover, Pleger et al (2006) revealed that BOLD signals in the left dorsal lateral PFC (dlPFC), anterior cingulate gyrus, and insula scale with task difficulties. These findings are broadly consistent with fMRI findings from the visual domain which implicate the left dlPFC (Heekeren et al., 2004; 2006), IFG (Liu and Pleskac, 2011; Filimon et al., 2013) and insula (Ho et al., 2009; Liu and Pleskac, 2011) in the temporal integration of sensory evidence, irrespective of the response modality. However, due to the sluggish nature of the BOLD signal, it can be difficult to interpret what components of decision formation the observed elevated activities reflect (see Mulder et al., 2014).

Only recently, the field has started to study human vibrotactile decisions by means of EEG. In line with the study focusing on LFP oscillatory activities in NHPs (Haegens et al., 2011), Herding and colleagues revealed that the differential power of upper beta band oscillation reflects subjects' perceptual choices, with the SMA as the most likely source for manual responses (2016) and the FEF for

saccadic responses (2017). Note, however, analogous to the above-mentioned studies using NHPs, the perceptual choice in these EEG studies was also implemented as a choice between two alternative manual responses. Thus, it remains unclear whether the effector-specific premotor regions would still encode perceptual choice under conditions in which choice and action selection are dissociated from each other.

1.3 Aims of the thesis

To date, a large part of our knowledge of the neural mechanisms underlying working memory and decision-making in the tactile domain comes from the extraordinary body of NHP research by Romo and colleagues (reviewed in Romo and de Lafuente, 2013). In spite of a steady growth in the number of human studies recently, the body of human literature is still sparse. Hence, the primary goal of this thesis is to investigate the neural correlates of tactile WM and decision-making in the human brain.

In particular, together with my colleagues, I used fMRI and MVPA to address two current questions in the literature: First, motivated by the recent controversy over the primary storage location of WM, we sought to directly test for brain regions that represent the frequency of vibrotactile stimulation held in WM. To get more in-depth insights into the nature of the WM representation, we also probed for brain regions showing selective activity to the frequencies of visual and auditory stimulation during the retention interval. Second, I aimed to investigate the representation of perceptual choices when choices are independent of action selection.

Compared to extracellular recordings in NHPs and human EEG, methods frequently used in earlier related studies, the fMRI MVPA approach has the crucial advantage of providing a system-level perspective over the entire network engaged in the representation of information. Thus, the use of this approach will not only bridge the gap between human and NHP research, but also complement and extend previous findings.

2. Summary of the experiments

In the following I summarize the four empirical studies presented in this dissertation. For each of them, we employed a frequency discrimination task that was specifically adapted to the particular research questions in the given study. The essence of the task remains the same across all four studies. Moreover, all stimulus frequencies used in these studies lay well within the flutter range between 5 and 50 Hz (Romo and Salinas, 2003). Three published papers and one manuscript under review are attached.

2.1 Study 1: Parametric vibrotactile working memory representation in frontal regions

As reviewed in the introduction, evidence from single-unit recordings in NHPs and human EEG suggests that vibrotactile frequencies held in WM are represented by a parametric code in the right lateral PFC (Romo et al., 1999; Spitzer et al., 2010). These findings are well in line with a large body of NHP work across different sensory domains and corroborate an influential WM framework proposing a leading role of PFC in the coding of memorized contents (Goldman-Rakic, 1991). Recently, this view has been seriously challenged by findings from multiple human fMRI studies using MVPA, predominantly from the visual domain, showing that memorized sensory features could be decoded from the activity in

sensory cortices, but not from the PFC (reviewed in Sreenvasan et al., 2014). These fMRI-MVPA findings in humans conflict with a large body of evidence from NHP research and favor the idea that WM contents are represented in the sensory cortices. In the vibrotactile domain however, existing fMRI studies using univariate analysis were restricted to investigating which brain regions are activated during the retention interval. Direct evidence from human fMRI data for brain regions representing the memorized vibrotactile frequencies was still missing.

In this study, we sought to bridge the gap between NHP and human research. To this end, we recorded fMRI data from 24 participants while they performed a variant of the vibrotactile frequency discrimination task. In this version of the task, two sample frequencies were presented in a random order to subjects, followed by a visual retro-cue instructing which of the two frequencies had to be memorized. After a 12 s retention interval, subjects performed a two-alternative forced choice task to indicate which of the two probe frequencies was identical to the memorized sample. The use of the retro-cue enabled the dissociation of WM-related activity from stimulus-driven signals (Harrison and Tong, 2009).

We used multivariate decoding techniques to identify brain regions that exhibit frequency-selective activity patterns during the 12 s retention interval. While most existing MVPA studies employed classification algorithms such as linear discriminants or a support vector machine, we applied support vector regression (SVR) to decode the memorized frequencies. It was of particular relevance because it treated the memorized frequencies as a continuous rather than a categorical variable, and thus allowed us to assess whether locally distributed activity patterns

reflect the parametric change in the memorized frequencies (Kahnt et al., 2011). Moreover, we employed a searchlight protocol, which enabled the detection of parametric WM representations across the whole brain without a priori assumptions about where to expect them (Kriegeskorte et al., 2006).

Our findings suggest that frontal regions including the bilateral premotor cortices, SMA and, the right IFG represent the memorized frequencies in a parametric fashion. Strikingly, these regions overlap highly with those reported in the single-cell recordings in NHPs reviewed above (e.g. Romo et al., 1999, Hernández et al., 2010). Thus, our results establish a direct link between the parametric WM codes found in NHPs and humans and highlight the pivotal role of the human PFC in information storage during WM. Contrary to many previous fMRI-MVPA studies, we did not find content-specific information in the sensory cortical region (e.g. Christophel et al., 2012; Riggall and Postle, 2012; Emrich et al., 2013; Schmidt et al., 2018). The difference in results is likely due to the different requirements across tasks: while most of the previous studies required the maintenance of low-level sensory information, our study emphasized the retention of scalar quantity information rather than the sensory details of the to-be-memorized stimuli. This interpretation is well in line with a recent account of topographic organization of WM storage (Christophel et al., 2017), proposing that sensory cortices encode the memorized information in a low-level sensory format, while higher association cortices encode it in a more abstract format.

2.2 Study 2: Overlapping frontoparietal networks for tactile and visual parametric working memory

In study 1 we showed that parametric WM representations in the PFC reflect the maintenance of scalar quantity rather than the sensory qualities of vibrotactile stimulation. One way to further test and extend this finding is to investigate whether the PFC represents memorized frequencies regardless of the sensory modality used for the stimulus presentation and the generalizability of such a WM representation across sensory modalities.

We asked 20 subjects to perform a cross-modal retro-cue discrimination task with vibrotactile and visual flicker stimulation, while lying in an fMRI scanner. At the start of each trial, tactile and visual samples with different frequencies were presented simultaneously. A retro-cue instructed subjects to either maintain the tactile or the visual frequency, followed by a visuo-tactile mask. After a 6 s retention interval, either a visual or a tactile probe frequency was delivered and participants had to judge whether its frequency was lower or higher than the memorized one. The sensory modality of the probes was independent of the sample stimulus, so that subjects could not anticipate whether the impending comparison would be within or across sensory modalities. We applied the analogous searchlight protocol with SVR as used in study 1 to explore (i) which brain regions represent memorized frequencies of both the vibrotactile and the visual flicker and (ii) whether mnemonic representations of tactile and visual frequencies rely on a supramodal WM code. Based on the findings from study 1 and previous electrophysiological recordings in humans and NHPs (Spitzer and Blankenburg, 2012; Vergara et al.,

2015), we expected to observe such a supramodal WM code in the right IFG and/or preSMA.

We were able to replicate our previous findings from study 1 of vibrotactile parametric WM representations in the PFC and premotor cortices (Schmidt et al., 2017). Moreover, parametric WM representations were evident in several posterior parietal regions including IPL and IPS. When applying the same analysis to visual WM conditions, we observed a highly similar pattern of informative brain regions in frontoparietal cortices with overlaps in the right IFG, preSMA, and IPL, suggesting that the parametric WM coding property of the frontoparietal regions goes beyond a specific sensory modality. Interestingly, contrary to the first study, we also found that somatosensory and visual cortices carried information about the memorized frequencies from their principal sensory modalities. The additional recruitment of sensory cortices may result from the higher demand of a cross-modal task compared to a unimodal task. In a further step, we used cross-classification to test whether tactile and visual WM representations rely on a supramodal code. That is, SVRs were trained with data from one sensory modality and tested on how well they were able to predict the data from the other modality. An above-chance prediction accuracy at a given brain region would indicate that this region used a similar multivariate code to represent tactile and visual memoranda. However, we did not find empirical support for such a modality-independent WM code. This was somewhat surprising as the overlapping frontal regions comprised exactly those regions which have been implicated in processing memorized frequencies in a supramodal fashion (Spitzer and Blankenburg, 2012; Ver-

gara et al., 2015). One possible reason for the absence of evidence for a supramodal multivariate code may be the limited sensitivity of fMRI to information that is represented at a high level of granularity (Dubois et al., 2015).

In sum, the results suggest that tactile and visual parametric WM representations are distributed throughout the cortical hierarchy. We identified a common frontoparietal network that represents memorized frequencies regardless of whether the information is derived from touch or vision, while sensory cortices carry only information that is provided by their principal sensory modalities. Despite the lack of evidence for a supramodal multivariate code, our findings underpin the general role of frontoparietal cortex in maintaining quantitative information across sensory modalities.

2.3 Study 3: Parametric working memory representation for auditory flutter stimulation

To further elucidate the modality-independent and modality-specific aspects of the mnemonic representation of frequencies, we extended our investigations to the auditory domain. Except the auditory flutter stimulation, we kept the experimental design, analysis strategies, and sample size in this study identical to those in study 1 in order to make a valid comparison between the results from both studies.

Similar to study 2, we reported multiple frontoparietal regions as carrying frequency-specific information during the retention interval. Furthermore, we also

observed frequency-selective activity patterns in the bilateral posterior superior temporal gyrus, which constitutes the auditory belt areas. A conjunction analysis including the data of study 1 revealed overlapping regions in premotor structures and the right IFG. The finding of the right IFG and the premotor structures as exhibiting frequency-selective activity patterns is not only consistent across studies 1 – 3, but also in remarkable agreement with the previous related NHP work, underscoring the key contributions of these regions in representing frequencies held in WM.

2.4 Study 4: Decoding vibrotactile choice independent of sensory and motor task components

In study 4, we shifted our focus from the representation of parametric WM to the representation of perceptual choice in the context of frequency discrimination tasks. Converging evidence from previous extracellular recordings in NHPs and EEG in humans suggest that perceptual choice is encoded a sensorimotor network including S2, PFC and premotor structures (Haegens, 2011; Herding et al., 2016; 2017; see Romo and de Lafuente, 2013 for a review). However, these studies used experimental settings in which perceptual choices were correlated with the sensory and motor components of the task. That is, the first frequency (f1) was typically set as the reference against which the second frequency (f2) was compared. Thus, subjects typically decided “higher” if frequencies were presented in an increasing order (f1 < f2) and “lower” if they are presented in a de-

creasing order (f1 > f2). Furthermore, perceptual choice in these studies was directly mapped to a movement toward a specific spatial target. These correlations preclude a clear dissociation between choice-related signals and signals involved in sensory and motor processing, thus complicating the interpretation of the findings.

To overcome this limitation, we devised a specific version of the vibrotactile frequency discrimination task: A visual cue at the beginning of each trial instructed subjects to use either f1 as the comparison stimulus (compare f1 against f2) or f2 as the comparison stimulus (compare f2 against f1), thereby decoupling the choice from the stimulus order. This visual cue was followed by two vibrotactile stimuli with different frequencies separated by a 1 s retention period. To disentangle choice from the saccade response direction, a visual matching cue indicating either a higher or a lower comparison frequency was presented 2 s after the f2 offset. Subjects compared their choice (f1 > f2 vs f1 < f2) with the visual matching cue and reported a match or mismatch with a saccade to one of the two color-coded targets presented after the matching cue offset. The matching cues and the locations of the color-coded target were orthogonal to each other and pseudo-randomly presented so that subjects could neither anticipate the target color nor the saccade direction. Notably, in this study we combined the vibrotactile frequency discrimination task with saccade responses, a commonly used response modality in the RDM task. This yielded a more direct comparison between findings from vibrotactile frequency discrimination task and the RDM task

We applied the searchlight protocol with support vector machines to distinguish locally distributed activity patterns that were associated either with the choice “f1 > f2” or “f1 < f2”. As the result, we identified the left inferior prefrontal cortex and the oculomotor system, including the bilateral frontal eye fields (FEF) and intraparietal sulci, as representing perceptual choices. Moreover, we showed that the decoding accuracy of choice information in the right FEF is strongly linked to subjects’ behavioral performance. Not only are these findings in remarkable agreement with evidence from previous NHP studies (see Gold and Shadlen, 2007; Romo and de Lafuente, 2013), they also provide novel fMRI evidence for choice coding properties in human oculomotor regions, which are not limited to saccadic decisions, but pertain to conditions where choices are taken from an more abstract context.

3. General discussion

The goal of my empirical work in the present dissertation was to investigate how the human brain represents the contents of WM and perceptual choices during tactile information processing. To this end, together with colleagues, I conducted four fMRI MVPA studies with the well-established frequency discrimination paradigm (Mountcastle et al., 1990; Romo and de Lafuente, 2013). In study 1, we addressed the question of which human brain regions carry information about the frequencies of vibratory stimuli held in WM (Schmidt et al., 2017). To get insights into the modality-specific and modality-independent aspects of the frequency-specific representations, we tested for brain regions that exhibit WM representations for frequencies induced by the visual or auditory stimulation in study 2 and 3 (Uluc et al., 2018; Wu et al., 2018a). Finally, in study 4 we aimed to find representations of perceptual choices that are not contaminated by sensory and motor processing (Wu et al., under review). Here, I discuss the most important findings and implications from our empirical work in a broader context.

3.1 Parametric working memory distributed throughout the cortical hierarchy

3.1.1 Working memory representation in frontoparietal cortices

One of the major findings from WM studies presented here is that a network of frontal regions, including the right IFG and bilateral premotor structures, exhibits a multivariate parametric WM representation of vibrotactile frequencies (Schmidt et al., 2017; Wu et al., 2018a). The identified frontal network closely resembles the network reported in NHP studies (Romo and de Lafuente, 2013), as well as encompasses regions reported in human M/EEG studies (Spitzer et al., 2010; Spitzer and Blankenburg, 2011; 2012; von Lautz et al., 2017). The results thereby extend for the first time this parametric WM code in the vibrotactile domain to multivariate fMRI activity patterns. Interestingly, and yet to be explored in the NHP and human EEG literature, we also identified posterior parietal regions including the IPL and IPS as exhibiting parametric WM representation of vibrotactile frequencies (Wu et al., 2018a). Finally, we found that the parametric coding property of these frontoparietal regions is not limited to the retention of vibratory stimuli, but generalizes to memorizing frequencies of visual flicker and acoustic flutter (Uluc et al., 2018; Wu et al., 2018a).

Our finding of frontal content-specific WM codes is in contrast to several recent fMRI MVPA studies in which sensory features could be reliably decoded from activity patterns in sensory cortex, but not from frontal cortices (e.g. Christophel et al., 2012; Riggall and Postle, 2012; Emrich et al, 2013). This discrepancy can be reconciled with a recent WM account proposed by Christophel and colleagues

(2017). They suggest a gradient of abstractness of the mental representations as the organizational principle of WM contents, which spans sensory cortices encoding low-level sensory information and prefrontal regions representing more abstract, categorical WM contents. In contrast to previous MVPA studies requiring subjects to memorize sensory details, subjects in our studies were asked to memorize scalar quantity information derived from tactile/visual/acoustic sensation (Romo et al., 1999). This type of information is inherently more abstract in the sense that the same information can be conveyed by different sensory modalities. Thus, frequencies are likely stored in a more abstract, quantitative format in higher associative cortices (Christophel et al., 2017; see also Spitzer and Blankenburg, 2011; 2012; Spitzer Blankenburg et al., 2013). In line with this interpretation, we have shown that the SVR performance depends critically on the linear ordering of the stimulus frequencies, supporting the quantitative nature of the frequency representation.

In addition to the prefrontal and premotor regions, we also found intraprietal regions to carry frequency-specific information during the retention interval (Uluc et al., 2018; Wu et al., 2018a). Among a variety of cognitive functions ascribed to intraparietal regions, their crucial involvement in number cognition appears to be closely related to frequency discrimination performance. This is because both numbers and frequencies can be viewed as quantitative features that are ordered along a continuum (Nieder, 2017, see also Jacob et al., 2012; Nieder 2016 for comprehensive reviews). The putative link between these two concepts is supported by some parallel findings. For instance, results from human fMRI studies indicate that both number (Arsalidou and Taylor, 2011) and frequency

discrmination (Kostopoulos et al., 2007) activate a frontoparietal network constituted by the vlPFC, SMA, and intraparietal regions. These findings are corroborated by NHP studies showing that numerical and frequency-specific information is encoded by the above-mentioned frontal areas, with individual neurons representing numerical or frequency information in a supramodal fashion (Nieder, 2012; Vergara et al., 2015). Here, we draw another parallel between frequency and number cognition by reporting intraparietal regions as representing the memorized frequencies (Uluc et al., 2018; Wu et al., 2018a). Given the close link between number and frequency coding and the high correspondence between the frontoparietal network found in our studies and the well-established number network including the lPFC, SMA, and intraparietal regions (Nieder, 2016), it is conceivable that these common regions may play a general role in the coding of quantitative information.

3.1.2 Working memory representation in sensory cortices

Apart from the above-mentioned regions in frontoparietal cortices, we also found that somatosensory, visual, and auditory cortices carry information about the frequencies held in WM (Uluc et al., 2018; Wu et al., 2018a). The crucial difference to frontoparietal regions is, however, that these sensory regions only show selectivity to memorized frequencies from their principal sensory modality. This indicates that these memory representations may be closer related to sensory properties of the input stimuli than those found in the frontal and parietal cortices.

Notably, the observation that sensory cortices carry frequency-specific information held in WM contradicts the typical null findings reported in studies using NHP subjects (e.g. Romo et al., 2004; Lemus et al., 2009; Lemus et al., 2010). As outlined in the introduction, this is a common contradiction between human fMRI and NHP extracellular recordings in the literature (Leavitt et al., 2017; Xu, 2017). One issue that may have contributed to this differential recruitment of sensory regions is that NHP studies usually employ relatively coarse discrimination, while human subjects have most often to perform more fine-grained discriminations. Also, the considerably longer training time of NHPs compared with humans is likely to play a role. Both the more coarse discrimination and the longer training are believed to lead to subjects memorizing stimuli in a more categorical fashion (Serences, 2016) so that a recruitment of high-fidelity memory representation in the sensory cortices may become dispensable.

An alternative, but less discussed possibility is that the content-specific BOLD activities observed in human sensory cortices may be mainly driven by non-spiking feedback signals from downstream regions, while most null findings reported in the NHP literature are based on the lack of content-selective spiking activity reflecting the feedforward signal. Evidence for this alternative explanation has been given by a recent study in which NHPs performed a delayed motion discrimination task (Mendoza-Halliday et al., 2014). The authors failed to find content-selective spiking activity in MT during the retention interval, but did find it in the lateral PFC. Strikingly, they found content-specific modulation of LFPs in MT that was most likely induced by top-down inputs from the lateral PFC. Given that

the BOLD signal has been shown to be primarily associated with LFPs (Logothetis et al., 2001; Bartolo et al., 2011), this finding has been used as evidence to argue that content-specific BOLD activity observed in human sensory cortices may reflect in large part the feedback-driven LFPs and consequently accounts for the varying results between NHP and human studies. Although this account has yet to be substantiated by further evidence, it has provided an important perspective for the interpretation of varying data from different recording modalities.

In sum, we found parametric WM representations of stimulus frequencies distributed throughout the cortical hierarchy. In particular, the identified frontal regions, including the right IFG and premotor structures, overlap with those reported in the previous related NHP studies (Romo and de Lafuente, 2013). This cross-species accordance provides compelling evidence that the PFC does not merely exert cognitive control over hierarchically lower regions, but also engages in the maintenance of WM contents. Our data clearly speak against a privileged role of either the PFC or the sensory cortices in the maintenance of WM contents. Instead, they support the idea of a distributed storage of memoranda across cortical areas (Lee and Baker, 2016; Christophel et al., 2017). The distributed representation also implicates a recurrent flow of task-relevant information across all cortical regions involved in the task (Klein-Flugge and Bestmann, 2012; Selen et al., 2012; Siegel et al., 2015). In view of these findings, WM may be better described as an integrated process of multiple brain regions with graded functional specializations rather than the simple interactions between a central executive and a specialized information storage (D'Esposito and Postle, 2015; Christophel et al., 2017).

3.2 Abstract choice representation in effector-specific regions

In study 4 (Wu et al., under review), my colleagues and I sought to identify neural correlates of vibrotactile choice that are neither confounded by the stimulus order nor by the preparation of saccadic movement. With a modified version of the vibrotactile frequency discrimination task, we identified the left prefrontal and oculomotor regions including the FEF and intraparietal structures as carrying information about vibrotactile choices made in a more abstract context. Furthermore, we found that the fidelity of the abstract choice representation in the right FEF is linked to subjects' choice behavior. That is, the higher the decoding accuracy, the better the discrimination performance.

The identification of oculomotor regions as carrying choice information is compatible with a vast amount of evidence from oculomotor decision tasks (e.g., RDM task) which suggests a major involvement of oculomotor regions in the temporal integration of sensory evidence (Gold and Shadlen, 2007). With this result, we have established a link between two major paradigms in perceptual decision-making (oculomotor decision-making vs. vibrotactile comparisons).

The finding of a behaviorally relevant abstract choice code in FEF, a region primarily associated with saccade movement selection is particularly intriguing. It indicates that the FEF is actively involved in the decision-making process even in situations when a saccade movement cannot be prepared. An important question that emerged from the results is what functional role the correlation between FEF decoding accuracy and choice behavior may reflect. In this respect, a recent

study by Hanks and colleagues (2015) is particularly revealing. These authors found evidence for behavioral performance in a decision task to be causally related to premotor structures' ability to categorize accumulated sensory evidence into discrete choices. Accordingly, one possible interpretation is that decoding accuracies in the FEF index the quality of such categorization processes and are therefore predictive of the behavioral performance.

One limitation of study 4 is that its design does not allow the testing of where abstract decisions are formed as such. We do not know whether the observed abstract choice information is directly computed in any of the identified regions or merely reflects feedback from a decision computation elsewhere in the brain. From the point of view of an intentional framework of decision making, abstract decisions are unlikely to be directly formed in brain structures involved in action selection, such as the FEF or intraparietal regions. This is because abstract choices reflect commitments to apply particular rules rather than actions and should therefore be formed in regions associated with abstract concept processing, such as the lateral PFC (Shadlen et al., 2008; Kiani and Shadlen, 2013). One should, however, take in to consideration that FEF and intraparietal neurons have been shown to be selective for a range of information types, such as sensory, abstract categorical, and motor information (e.g. Meister et al., 2013; Rigotti et al., 2013; Siegel et al., 2015). Therefore, they should not be excluded as potential candidate regions. In fact, I believe that intraparietal regions are a particularly promising candidate for the coding of abstract choice formation in vibrotactile frequency discrimination tasks. This is because, apart from their well-established

role in number coding (Nieder, 2016), intraparietal regions have also been indicated to play a key role in the coding of the relation between scalar quantities (Jacob et al., 2012). Unfortunately, our current understanding of intraparietal functions in frequency discrimination tasks is relatively limited compared to that of sensory and frontal regions. Future studies in NHPs and humans using different methods will complement our findings and provide more insights into the role of intraparietal regions in frequency discrimination.

Finally, as referenced in the introduction, there is a growing body of human neuroimaging studies focusing on the neural processes underlying the formation of abstract decisions (Heekeren et al., 2008; Kelly and O'Connell, 2015). However, one should consider that most of these studies were designed to trace neural responses reflecting evidence accumulation over time, which to date has only rarely been associated with decisions based on comparison between two sequentially presented stimuli. Thus, the extent to which sensory accumulation processes account for decisions based on sequential comparisons remains largely unknown. In this respect, there are on-going efforts, for example from our group, to link the presumed sensory accumulation process with sequential discrimination tasks, which may provide more insights into this question.

3.3 Outlook

The empirical work presented in this dissertation were designed to investigate the neural signature of either WM or decision-making. Results of these studies motivate further investigations of the link between these two fundamental functions of

human cognition. For instance, there is a high degree of local integration between WM and choice information (study 2 and 4) in the bilateral intraparietal and premotor regions. This observation aligns well with previous results in the NHP literature showing that neurons of multiple regions are capable of encoding WM content and choice across multiple task stages (Romo and de Lafuente, 2013). It further indicates that WM and decision-making might be supported by more integrated neural mechanisms within the brain network involved in the task (Singer, 2013).

Future research will benefit from a focus on the relationship between WM and decision-related representations, especially the transformation processes of how WM representations are used to accumulate evidence for a decision. This could, for example, be achieved by explicitly testing the covariation between WM and decision-related representations. In this context, it would also be important to address questions related to the interregional differences in information coding, such as: How do WM contents stored in the premotor cortex differ from those in intraparietal regions? Or what is the unique contribution of choice information in each individual brain region? Another important issue is the question of how multiple regions coordinate WM and decision-making. To address this topic, it would be crucial to explore the temporal dynamics of information across different regions. One possible way to do this is to use representational similarity analysis to combine measurements of independent fMRI and M/EEG datasets (Cichy et al., 2014). In this context, the application of laminar fMRI may provide deeper insights into how feedforward and feedback responses within a recurrent network give rise to mental representations and consecutive decisions (Lawrence et al., 2017).

References

Arsalidou M, Taylor MJ (2011) Is 2 + 2 = 4? Meta-analyses of brain areas needed for numbers and calculations. Neuroimage 54:2382–2393

Baddeley A (2012) Working Memory: Theories, Models, and Controversies. Annu Rev Psychol 63:1–29

Baddeley AD, Hitch G (1974) Working Memory. Psychol Learn Motiv 8:47–89

Barak O, Tsodyks M, Romo R (2010) Neuronal population coding of parametric working memory. J Neurosci 30:9424–9430

Bartolo MJ, Gieselmann MA, Vuksanovic V, Hunter D, Sun L, Chen X, Delicato LS, Thiele A (2011) Stimulus-induced dissociation of neuronal firing rates and local field potential gamma power and its relationship to the blood oxygen level-dependent signal in macaque primary visual cortex. Eur J Neurosci 34:1857–1870

Bennur S, Gold JI (2011) Distinct Representations of a Perceptual Decision and the Associated Oculomotor Plan in the Monkey Lateral Intraparietal Area. J Neurosci 31:913–921

Brody CD, Hernández A, Zainos A, Romo R (2003) Timing and neural encoding of somatosensory parametric working memory in macaque prefrontal cortex. Cereb Cortex 13:1196–1207

Britten KH, Newsome WT, Shadlen MN, Celebrini S, Movshon JA (1996) A relationship between behavioral choice and the visual responses of neurons in macaque MT. Vis Neurosci 13:87–100

Britten KH, Shadlen MN, Newsome WT, Movshon JA (1992) The analysis of visual motion: a comparison of neuronal and psychophysical performance. J Neurosci 12:4745 LP-4765

Buschman TJ, Siegel M, Roy JE, Miller EK (2011) Neural substrates of cognitive capacity limitations. Proc Natl Acad Sci U S A 108:11252–11255

Christophel TB, Hebart MN, Haynes J-D (2012) Decoding the contents of visual short-term memory from human visual and parietal cortex. J Neurosci 32:12983–12989

Christophel TB, Klink PC, Spitzer B, Roelfsema PR, Haynes J-D (2017) The Distributed Nature of Working Memory. Trends Cogn Sci 21:111–124

Cichy RM, Pantazis D, Oliva A (2014) Resolving human object recognition in space and time. Nat Neurosci 17:455

Cisek P, Kalaska JF (2010) Neural mechanisms for interacting with a world full of action choices

Gottlieb Y, Vaadia E, Abeles M (1989) Single unit activity in the auditory cortex of a monkey performing a short term memory task. Exp Brain Res 74:139–148

Curtis CE, D'Esposito M (2003) Persistent activity in the prefrontal cortex during working memory. Trends Cogn Sci 7:415–423

D'Esposito M, Postle BR (2015) The Cognitive Neuroscience of Working Memory. Annu Rev Psychol 66:115–142

Ding L, Gold JI (2012) Neural Correlates of Perceptual Decision Making before, during, and after Decision Commitment in Monkey Frontal Eye Field. Cereb Cortex 22:1052–1067

Dubois J, de Berker AO, Tsao DY (2015) Single-Unit Recordings in the Macaque Face Patch System Reveal Limitations of fMRI MVPA. J Neurosci 35:2791 LP-2802

Emrich SM, Riggall AC, LaRocque JJ, Postle BR (2013) Distributed patterns of activity in sensory cortex reflect the precision of multiple items maintained in visual short-term memory. J Neurosci 33:6516–6523

Ester EF, Anderson DE, Serences JT, Awh E (2013) A Neural Measure of Precision in Visual Working Memory. J Cogn Neurosci 25:754–761

Fassihi A, Akrami A, Esmaeili V, Diamond ME (2014) Tactile perception and working memory in rats and humans. Proc Natl Acad Sci 111:2331–2336

Filimon F, Philiastides MG, Nelson JD, Kloosterman NA, Heekeren HR (2013) How Embodied Is Perceptual Decision Making ? Evidence for Separate Processing of Perceptual and Motor Decisions. J Neurosci 33:2121–2136

Freedman DJ, Riesenhuber M, Poggio T, Miller EK (2001) Categorical Representation of Visual Stimuli in the Primate Prefrontal Cortex. Science (80-) 291:312 LP-316

Funahashi S, Bruce CJ (1989) Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. J Neurophysiol 61:331–349

Funahashi S, Chafee M V, Goldman-Rakic PS (1993) Prefrontal neuronal activity in rhesus monkeys performing a delayed anti-saccade task. Nature 365:753

Fuster JM (1990) Prefrontal Cortex and the Bridging of Temporal Gaps in the Perception-Action Cycle. Ann N Y Acad Sci 608:318–336.

Fuster JM, Alexander GE (1971) Neuron Activity Related to Short-Term Memory. Science (80-) 173:652 LP-654

Gold JI, Heekeren HR (2014) Neural Mechanisms for Perceptual Decision Making. Neuroeconomics:355–372

Gold JI, Shadlen MN (2001) Neural computations that underlie decisions about sensory stimuli. Trends Cogn Sci 5:10–16

Gold JI, Shadlen MN (2007) The Neural Basis of Decision Making. Annu Rev Neurosci 30:535–574

Goldman-Rakic PS (1991) Cellular and circuit basis of working memory in prefrontal cortex of nonhuman primates. Prog Brain Res 85:325–336

Gottlieb Y, Vaadia E, Abeles M (1989) Single unit activity in the auditory cortex of a monkey performing a short term memory task. Exp Brain Res 74:139–148

Green D, Swet J (1966) *Signal detectability and psychophysics.* Wiley, New York

Haegens S, Nácher V, Hernández A, Luna R, Jensen O, Romo R (2011) Beta oscillations in the monkey sensorimotor network reflect somatosensory decision making.

Hanes DP, Schall JD (1996) Neural Control of Voluntary Movement Initiation. Science (80-) 274:427 LP-430

Hanks TD, Kopec CD, Brunton BW, Duan CA, Erlich JC, Brody CD (2015) Distinct relationships of parietal and prefrontal cortices to evidence accumulation. Nature 520:220–223

Hanks TD, Summerfield C (2017) Perceptual Decision Making in Rodents, Monkeys, and Humans. Neuron 93:15–31

Harrison SA, Tong F (2009) Decoding reveals the contents of visual working memory in early visual areas. Nature 458:632–635

Harris JA, Miniussi C, Harris IM, Diamond ME (2002) Transient storage of a tactile memory trace in primary somatosensory cortex. J Neurosci 22:8720–8725

Heekeren HR, Marrett S, Ungerleider LG (2008) The neural systems that mediate human perceptual decision making. Nat Rev Neurosci 9:467–479

Heekeren HR, Marrett S, Bandettini PA, Ungerleider LG (2004) A general mechanism for perceptual decision-making in the human brain. Nature 431:859–862

Heekeren HR, Marrett S, Ruff DA, Bandettini PA, Ungerleider LG (2006) Involvement of human left dorsolateral prefrontal cortex in perceptual decision making is independent of response modality. Proc Natl Acad Sci U S A 103:10023–10028

Herding J, Ludwig S, Blankenburg F (2017) Response-Modality-Specific Encoding of Human Choices in Upper Beta Band Oscillations during Vibrotactile Comparisons. Front Hum Neurosci 11:1:11.

Herding J, Spitzer B, Blankenburg F (2016) Upper Beta Band Oscillations in Human Premotor Cortex Encode Subjective Choices in a Vibrotactile Comparison Task. J Cogn Neurosci 28:668–679.

Hernández A, Nácher V, Luna R, Zainos A, Lemus L, Alvarez M, Vázquez Y, Camarillo L, Romo R (2010) Decoding a perceptual decision process across cortex. Neuron 66:300–314

Hernández A, Zainos A, Romo R (2000) Neuronal correlates of sensory discrimination in the somatosensory cortex. Proc Natl Acad Sci U S A 97:6191–6196

Hernández A, Zainos A, Romo R (2002) Temporal Evolution of a Decision-Making Process in Medial Premotor Cortex. 33:959–972.

Ho TC, Brown S, Serences JT (2009) Domain General Mechanisms of Perceptual Decision Making in Human Cortex. J Neurosci 29:8675–8687

Horwitz GD, Newsome WT (1999) Separate Signals for Target Selection and Movement Specification in the Superior Colliculus. Science (80-) 284:1158 LP-1161

Jacob SN, Vallentin D, Nieder A (2012) Relating magnitudes: the brain's code for proportions. Trends Cogn Sci 16:157–166

Jun JK, Miller P, Hernández A, Zainos A, Lemus L, Brody CD, Romo R (2010) Heterogenous population coding of a short-term memory and decision task. J Neurosci 30:916–929

Kahnt T, Heinzle J, Park SQ, Haynes JD (2011) Decoding different roles for vmPFC and dlPFC in multi-attribute decision making. Neuroimage 56:709–715

Kelly SP, O'Connell RG (2015) The neural processes underlying perceptual decision making in humans: Recent progress and future directions. J Physiol 109:27–37

Klein-Flügge MC, Bestmann S (2012) Time-Dependent Changes in Human Corticospinal Excitability Reveal Value-Based Competition for Action during Decision Processing. J Neurosci 32:8373 LP-8382

Kim J-N, Shadlen MN (1999) Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. Nat Neurosci 2:176–185

Kostopoulos P, Albanese M-C, Petrides M (2007) Ventrolateral prefrontal cortex and tactile memory disambiguation in the human brain. Proc Natl Acad Sci U S A 104:10223–10228

Kriegeskorte N, Goebel R, Bandettini PA (2006) Information-based functional brain mapping. Proc Natl Acad Sci U S A 103:3863–3868

Kubota K, Niki H (1971) Prefrontal cortical unit activity and delayed alternation performance in monkeys. J Neurophysiol 34:337–347

Lawrence SJD, Formisano E, Muckli L, de Lange FP (2017) Laminar fMRI: Applications for cognitive neuroscience. Neuroimage

Leavitt ML, Mendoza-halliday D, Martinez-trujillo JC (2017) Sustained Activity Encoding Working Memories : Not Fully Distributed. Trends Neurosci 40:328–346

Lee S-H, Kravitz DJ, Baker CI (2013) Goal-dependent dissociation of visual and prefrontal cortices during working memory. Nat Neurosci 16:997–999

Lee S-H, Baker CI (2016) Multi-Voxel Decoding and the Topography of Maintained Information During Visual Working Memory. Front Syst Neurosci 10:2

Lemus L, Hernández A, Luna R, Zainos A, Romo R (2010) Do sensory cortices process more than one sensory modality during perceptual judgments? Neuron 67:335–348

Lemus L, Hernández A, Romo R (2009) Neural codes for perceptual discrimination of acoustic flutter in the primate auditory cortex. Proc Natl Acad Sci U S A 106:9471–9476

Li Hegner Y, Lee Y, Grodd W, Braun C (2010) Comparing tactile pattern and vibrotactile frequency discrimination: a human FMRI study. J Neurophysiol 103:3115–3122

Liu T, Pleskac TJ (2011) Neural correlates of evidence accumulation in a perceptual decision task. J Neurophysiol 48824:2383–2398

Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A (2001) Neurophysiological investigation of the basis of the fMRI signal. Nature 412:150

Lundqvist M, Rose J, Herman P, Brincat SL, Buschman TJ, Miller EK (2016) Gamma and Beta Bursts Underlie Working Memory. Neuron 90:152–164

Machens CK, Romo R, Brody CD (2005) Flexible control of mutual inhibition. Science (80-) 307:1121–1124

Macmillan N, Creelman C (2005) *Detection Theory*. New York: Psychology Press

Mazurek ME, Roitman JD, Ditterich J, Shadlen MN (2003) A Role for Neural Integrators in Perceptual Decision Making. Cereb Cortex 13:1257–1269

Meister MLR, Hennig JA, Huk AC (2013) Signal Multiplexing and Single-Neuron Computations in Lateral Intraparietal Area During Decision-Making. J Neurosci 33:2254 LP-2267

Mendoza-Halliday D, Torres S, Martinez-Trujillo JC (2014) Sharp emergence of feature-selective sustained activity along the dorsal visual pathway. Nat Neurosci 17:1255–1262

Meyer T, Qi X-L, Stanford TR, Constantinidis C (2011) Stimulus Selectivity in Dorsal and Ventral Prefrontal Cortex after Training in Working Memory Tasks. J Neurosci 31:6266 LP-6276

Miller EK (2000) The prefrontal cortex and cognitive control. Nat Rev Neurosci 1:59–65

Miller EK, Cohen JD (2001) An Integrative Theory of Prefrontal Cortex Function. Annu Rev Neurosci 24:167–202

Miller EK, Erickson CA, Desimone R (1996) Neural Mechanisms of Visual Working Memory in Prefrontal Cortex of the Macaque. J Neurosci 16:5154 LP-5167

Mountcastle VB, LaMotte RH, Carli G (1972) Detection thresholds for stimuli in humans and monkeys: comparison with threshold events in mechanoreceptive afferent nerve fibers innervating the monkey hand. J Neurophysiol 35:122–136

Mountcastle VB, Steinmetz MA, Romo R (1990) Frequency discrimination in the sense of flutter: psychophysical measurements correlated with postcentral events in behaving monkeys. J Neurosci 10:3032 LP-3044

Mulder MJ, van Maanen L, Forstmann BU (2014) Perceptual decision neurosciences - a model-based review. Neuroscience 277:872–884

Newsome WT, Britten KH, Movshon JA (1989) Neuronal correlates of a perceptual decision. Nature 341:52

Nieder A, Freedman DJ, Miller EK (2002) Representation of the Quantity of Visual Items in the Primate Prefrontal Cortex. Science (80-) 297:1708 LP-1711

Nieder A (2012) Supramodal numerosity selectivity of neurons in primate prefrontal and posterior parietal cortices. Proc Natl Acad Sci U S A 109:11860–11865

Nieder A (2016) The neuronal code for number. Nat Rev Neurosci 17:366–382

Nieder A (2017) Magnitude Codes for Cross-Modal Working Memory in the Primate Frontal Association Cortex. Front Neurosci 11:1–7

O'Connell RG, Dockree PM, Kelly SP (2012) A supramodal accumulation-to-bound signal that determines perceptual decisions in humans. Nat Neurosci 15:1729

O'Connell RG, Shadlen MN, Wong-Lin K, Kelly SP (2018) Bridging Neural and Computational Viewpoints on Perceptual Decision-Making. Trends Neurosci

Park IM, Meister MLR, Huk AC, Pillow JW (2014) Encoding and decoding in parietal cortex during sensorimotor decision-making. Nat Neurosci 17:1395

Parker AJ, Newsome WT (1998) SENSE AND THE SINGLE NEURON: Probing the Physiology of Perception. Annu Rev Neurosci 21:227–277

Pasternak T, Greenlee MW (2005) Working memory in primate sensory systems. Nat Rev Neurosci 6:97–107

Pleger B, Ruff CC, Blankenburg F, Bestmann S, Wiech K, Stephan KE, Capilla A, Friston KJ, Dolan RJ (2006) Neural Coding of Tactile Decisions in the Human Prefrontal Cortex. J Neurosci 26:12596–12601

Postle BR (2006) Working memory as an emergent property of the mind and brain. Neuroscience 139:23–38.

Preuschhof C, Heekeren HR, Taskin B, Schubert T, Villringer A (2006) Neural correlates of vibrotactile working memory in the human brain. J Neurosci 26:13231–13239

Ratcliff R (1978) A theory of memory retrieval. Psychol Rev 85:59–108.

Ratcliff R, Cherian A, Segraves M (2003) A Comparison of Macaque Behavior and Superior Colliculus Neuronal Activity to Predictions From Models of Two-Choice Decisions. J Neurophysiol 90:1392–1407

Ratcliff R, Smith PL, Brown SD, McKoon G (2016) Diffusion Decision Model: Current Issues and History. Trends Cogn Sci 20:260–281

Riggall AC, Postle BR (2012) The Relationship between Working Memory Storage and Elevated Activity as Measured with Functional Magnetic Resonance Imaging. J Neurosci 32:12990–12998

Rigotti M, Barak O, Warden MR, Wang X-J, Daw ND, Miller EK, Fusi S (2013) The importance of mixed selectivity in complex cognitive tasks. Nature 497:1–6

Riley MR, Constantinidis C (2016) Role of Prefrontal Persistent Activity in Working Memory. Front Syst Neurosci 9:1–14

Roitman JD, Shadlen MN (2002) Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. J Neurosci 22:9475–9489

Romo R, Brody CD, Hernández A, Lemus L (1999) Neuronal correlates of parametric working memory in the prefrontal cortex. Nature 399:470–473

Romo R, de Lafuente V (2013) Conversion of sensory signals into perceptual decisions. Prog Neurobiol 103:41–75

Romo R, Hernández A, Zainos A (2004) Neuronal Correlates of a Perceptual Decision in Ventral Premotor Cortex. Neuron 41:165–173.

Romo R, Hernández A, Zainos A, Salinas E (2003) Correlated Neuronal Discharges that Increase Coding Efficiency during Perceptual Discrimination. Neuron 38:649–657

Romo R, Salinas E (2001) Touch and Go: Decision-Making Mechanisms in Somatosensation. Annu Rev Neurosci 24:107–137

Romo R, Salinas E (2003) Flutter discrimination: neural codes, perception, memory and decision making. Nat Rev Neurosci 4:203–218

Salinas E, Hernández A, Zainos A, Romo R (2000) Periodicity and Firing Rate As Candidate Neural Codes for the Frequency of Vibrotactile Stimuli. J Neurosci 20:5503 LP-5515

Salinas E, Romo R (1998) Conversion of Sensory Signals into Motor Commands in Primary Motor Cortex. J Neurosci 18:499 LP-511

Salzman CD, Britten KH, Newsome WT (1990) Cortical microstimulation influences perceptual judgements of motion direction. Nature 346:174

Schmidt TT, Blankenburg F (2018) Brain regions that retain the spatial layout of tactile stimuli during working memory – A “tactospatial sketchpad”? Neuroimage 178:531–539

Schmidt TT, Wu Y, Blankenburg F (2017) Content-specific codes of parametric vibrotactile working memory in humans. J Neurosci 37:9771–9777

Selen LPJ, Shadlen MN, Wolpert DM (2012) Deliberation in the Motor System: Reflex Gains Track Evolving Evidence Leading to a Decision. J Neurosci 32:2276 LP-2286

Serences JT (2016) Neural mechanisms of information storage in visual short-term memory. Vision Res 128:53–67

Serences JT, Ester EF, Vogel EK, Awh E (2009) Stimulus-specific delay activity in human primary visual cortex. Psychol Sci 20:207–214

Shadlen MNN, Kiani R (2013) Decision making as a window on cognition. Neuron 80:791–806

Shadlen MN, Britten KH, Newsome WT, Movshon JA (1996) A computational analysis of the relationship between neuronal and behavioral responses to visual motion. J Neurosci 16:1486 LP-1510

Shadlen MN, Kiani R, Hanks TD, Churchland AK (2008) Neurobiology of Decision Making - An intentional Framework (Engel C, Singer W, eds). Cambridge: MIT Press.

Shadlen MN, Newsome WT (1998) The Variable Discharge of Cortical Neurons: Implications for Connectivity, Computation, and Information Coding. J Neurosci 18:3870 LP-3896

Shadlen MN, Newsome WT (2001) Neural Basis of a Perceptual Decision in the Parietal Cortex (Area LIP) of the Rhesus Monkey. J Neurophysiol 86:1916–1936

Siegel M, Buschman TJ, Miller EK (2015) Cortical information flow during flexible sensorimotor decisions. Science 348:1352–1355

Singer W (2013) Cortical dynamics revisited. Trends Cogn Sci 17:616–626

Smith PL, Ratcliff R (2004) Psychology and neurobiology of simple decisions. Trends Neurosci 27:161–168.

Spitzer B, Blankenburg F (2011) Stimulus-dependent EEG activity reflects internal updating of tactile working memory in humans. Proc Natl Acad Sci U S A 108:8444–8449

Spitzer B, Blankenburg F (2012) Supramodal parametric working memory processing in humans. J Neurosci 32:3287–3295

Spitzer B, Goltz D, Wacker E, Auksztulewicz R, Blankenburg F (2014) Maintenance and manipulation of somatosensory information in ventrolateral prefrontal cortex. Hum Brain Mapp 35:2412–2423

Spitzer B, Haegens S (2017) Beyond the Status Quo: A Role for Beta Oscillations in Endogenous Content (Re-) Activation. Eneuro 4:ENEURO.0170-17.2017

Spitzer B, Wacker E, Blankenburg F (2010) Oscillatory correlates of vibrotactile frequency processing in human working memory. J Neurosci 30:4496–4502

Sreenivasan KK, Curtis CE, D'Esposito M (2014) Revisiting the role of persistent neural activity during working memory. Trends Cogn Sci 18:82–89

Stokes MG (2015) "Activity-silent" working memory in prefrontal cortex: A dynamic coding framework. Trends Cogn Sci 19:394–405

Supèr H, Spekreijse H, Lamme VAF (2001) A Neural Correlate of Working Memory in the Monkey Primary Visual Cortex. Science (80-) 293:120 LP-124

Uluç I, Schmidt TT, Wu Y hao, Blankenburg F (2018) Content-specific codes of parametric auditory working memory in humans. Neuroimage 183:254–262.

Usher M, McClelland JL (2001) The time course of perceptual choice: The leaky, competing accumulator model. Psychol Rev 108:550–592.

van Kerkoerle T, Self MW, Roelfsema PR (2017) Layer-specificity in the effects of attention and working memory on activity in primary visual cortex. Nat Commun 8:13804

Vergara J, Rivera N, Rossi-Pool R, Romo R (2015) A Neural Parametric Code for Storing Information of More than One Sensory Modality in Working Memory. Neuron 89:54–62

von Lautz AH, Herding J, Ludwig S, Nierhaus T, Maess B, Villringer A, Blankenburg F (2017) Gamma and Beta Oscillations in Human MEG Encode the Contents of Vibrotactile Working Memory. Front Hum Neurosci 11:576

Wagenmakers E-J, Van Der Maas HLJ, Grasman RPPP (2007) An EZ-diffusion model for response time and accuracy. Psychon Bull Rev 14:3–22

Wald A (1945) Sequential Tests of Statistical Hypotheses. Ann Math Stat 16:117–186

Wolff MJ, Ding J, Myers NE, Stokes MG (2015) Revealing hidden states in visual working memory using electroencephalography.

Wu Y, Uluç I, Schmidt TT, Tertel K, Kirilina E, Blankenburg F (2018a) NeuroImage Overlapping frontoparietal networks for tactile and visual parametric working memory representations. Neuroimage 166:325–334

Xu Y (2017) Reevaluating the Sensory Account of Visual Working Memory Storage. Trends Cogn Sci 21:794–815

Zaksas D, Pasternak T (2006) Directional Signals in the Prefrontal Cortex and in Area MT during a Working Memory for Visual Motion Task. J Neurosci 26:11726 LP-11742

Zhou YD, Fuster JM (1996) Mnemonic neuronal activity in somatosensory cortex. Proc Natl Acad Sci U S A 93:10533–10537

A. Original research articles

Study 1

For copyright reasons the original publication is not included in this PDF. Please access the publication via the DOI provided below.

Schmidt TT, **Wu Y-h**, Blankenburg F (2017) Content-Specific Codes of Parametric Vibrotactile Working Memory in Humans. J Neurosci 37:9771–9777. DOI: https://doi.org/10.1523/JNEUROSCI.1167-17.2017

Study 2

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Wu Y-h*, Uluç I*, Schmidt TT, Tertel K, Kirilina E, Blankenburg F (2018) Overlapping frontoparietal networks for tactile and visual parametric working memory representations. Neuroimage 166:325–334. DOI: https://doi.org/10.1016/j.neuroimage.2017.10.059

Study 3

For copyright reasons the original publication is not included in this PDF. Please access the publication via the DOI provided below.

Uluç I, Schmidt TT, **Wu Y-h**, Blankenburg F (2018) Content-specific codes of parametric auditory working memory in humans. Neuroimage 183:254–262. DOI: https://doi.org/10.1016/j.neuroimage.2018.08.024

Study 4

The manuscript attached below is a pre-refereeing version and does not correspond exactly to the final published version.

Wu Y-h, Velenosi LA, Schröder P, Ludwig S, Blankenburg F (under review) Decoding vibrotactile choice independent of stimulus order and saccade selection during sequential comparisons.

HUMAN BRAIN MAPPING

Decoding vibrotactile choice independent of stimulus order and saccade selection during sequential comparisons

Journal:	*Human Brain Mapping*
Manuscript ID	HBM-18-1032
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Date Submitted by the Author:	25-Sep-2018
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Keywords:	Vibrotactile frequency, perceptual decision-making, perceptual choice, fMRI, multivariate pattern analysis MVPA

Title: Decoding vibrotactile choice independent of stimulus order and saccade selection during sequential comparisons

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Short running title: Decoding vibrotactile choices in humans

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Conflicts of interest

The authors declare no competing financial interest.

Abstract

Decision-making in the somatosensory domain has been intensively studied using vibrotactile frequency discrimination tasks. Results from human and monkey electrophysiological studies from this line of research suggest that perceptual choices are encoded within a sensorimotor network. These findings, however, rely on experimental settings in which perceptual choices are inextricably linked to sensory and motor components of the task. Here, we devised a novel version of the vibrotactile frequency discrimination task with saccade responses which has the crucial advantage of decoupling perceptual choices from sensory and motor processes. We recorded human fMRI data from 32 participants while they performed the task. Using an assumption-free, whole-brain searchlight multivariate classification technique, we identify the left inferior prefrontal cortex and the oculomotor system, including the bilateral frontal eye fields (FEF) and intraparietal sulci, as representing vibrotactile choices. Moreover, we show that the decoding accuracy of choice information in the right FEF is strongly linked to the behavioral performance. Not only are these findings in remarkable agreement with previous work, they also provide novel fMRI evidence for choice coding property in human oculomotor regions, which is not limited to saccadic decisions, but pertains to contexts where choices are made in a more abstract form.

Keywords

decision-making, perceptual choice, vibrotactile frequency, fMRI, multivariate pattern analysis

Introduction

A perceptual decision comprises multiple stages converting sensory inputs via a categorical judgement about the perceived information into an appropriate behavior. One of the main aims of perceptual decision making research has been to identify, characterize, and dissociate brain activities directly linked to the decision from other signals that accompany this chain of processes.

In the somatosensory domain, neural mechanisms underlying perceptual choices have been extensively studied with electrophysiology in monkeys using vibrotactile frequency discrimination tasks (Romo and de Lafuente, 2013). In these studies, monkeys compare two sequentially presented vibrotactile stimuli and indicate whether the frequency of the second stimulus (f2) is higher or lower than the first (f1) with a manual response. The findings suggest that the comparison process and the resulting perceptual choice are encoded within a sensorimotor network, including prefrontal, premotor, motor and sensory cortices (Haegens et al., 2011; Hernández, Zainos, & Romo, 2002; Hernández et al., 2010; Romo, Hernández, & Zainos, 2004).

In humans, the initial attempt to identify neural correlates of vibrotactile decision making was conducted with fMRI (Pleger et al. 2006; Preuschhof, Heekeren, Taskin, Schubert, & Villringer, 2006). These authors revealed that multiple regions, particularly the dorsolateral prefrontal cortex and the insula are involved in decision-making (see also Kelly & O'Connell (2015) for a review of fMRI studies in the broader field of visual decision making). However, due to the sluggish nature of BOLD signal, the question of how the observed changes in BOLD amplitude are related to different decision processes, such as sensory evidence accumulation, remains a matter of debate (Mulder, van Maanen, & Forstmann, 2014), rendering it difficult to ground these studies within a greater context. Further evidence from

human data has been recently reported in EEG studies. In line with research focusing on the oscillatory activity in monkeys (Haegens et al., 2011), Herding and colleagues found that choices are encoded by differential power of upper beta band oscillations in premotor structures. Notably, the most likely source of the beta band modulation moved according to the response effector: the medial premotor cortex for manual responses (Herding, Spitzer, & Blankenburg, 2016) and the frontal eye field for saccades (Herding, Ludwig, & Blankenburg, 2017). Taken together, the electrophysiological findings across species suggest a pivotal role of sensorimotor regions in computing and representing vibrotactile choice. Moreover, the findings align well with results from monkey studies in the visual domain, which suggest that perceptual decisions are mainly formed in brain regions involved in guiding motor responses (Cisek & Kalaska, 2010; Gold & Shadlen, 2007).

The vibrotactile frequency discrimination task has been a powerful tool for exploring the neural underpinnings of somatosensory decision-making. However, in the standard versions of this task, perceptual choices are inextricably linked to the sensory and motor components of the task. That is, f1 is typically set as the reference frequency against which f2 is compared. Thus, participants will typically decide “higher” if frequencies are presented in an increasing order (f1 < f2), and “lower” if they are in a decreasing order (f1 > f2). Furthermore, each perceptual choice is most often directly mapped to a movement toward a specific spatial target. The resulting correlations preclude a clear dissociation between choice-related signals and signals involved in sensory and motor processing (Huk, Katz, & Yates, 2017). Additionally, there is a growing body of evidence suggesting that abstract, motor-independent choices are represented by brain regions beyond the sensorimotor system (Hebart, Donner, & Haynes, 2012; Filimon, Philiastides, Nelson, Kloosterman, & Heekeren, 2013).

With the present fMRI study, we aimed to identify human brain regions that represent vibrotactile choice independent of the sensory and motor components of the task. We

modified the vibrotactile frequency discrimination task so that the choice is disentangled from the preceding stimulus order and the succeeding saccade movement direction. Importantly, we employed a searchlight multivariate pattern analysis (Kriegeskorte, Goebel, & Bandettini, 2006) which allowed the identification of choice-selective activity patterns across the whole brain without a priori assumptions about where to expect such a representational code.

Materials and Methods

Participants

32 healthy, right-handed volunteers with normal or corrected-to-normal vision participated in the experiment (22 female, mean age = 27 years, range = 22 – 39). All participants gave written informed consent prior to the experiment. The experimental protocols were approved by the local ethics committee of the Freie Universität Berlin. Data from two participants were discarded due to excessive head motion (> 8 mm), leaving 30 participants for further analyses.

Experimental procedure and stimuli

Participants compared frequencies of two vibrotactile stimuli sequentially administered to their left index finger and decided whether the comparison frequency was higher or lower than the reference frequency by making a saccade toward a color-coded target (Figure 1). To decouple perceptual choice (higher vs lower) from stimulus order (f1 < f2 vs f1 > f2), f1 and f2 alternately served as the comparison frequency based on the rule presented at the beginning of each trial. In half of the trials, participants indicated whether f1 was higher or lower than f2 (rule 1) and in the other half, they indicated whether f2 was higher or lower than f1 (rule 2).

Furthermore, instead of pre-assigning a choice to a specific spatial target or target color, participants reported a match or mismatch between their perceptual choice and the proposition indicated by a matching cue. Importantly, the matching cue and the following target screen were presented after the decision phase so that participants could neither anticipate the target color nor prepare a motor response towards the spatial target.

Each trial began with a fixation period of variable duration (3, 4, 5, or 6 s). A rule cue (square or diamond) was shown at the center of the presentation screen for 500 ms and instructed participants which of the subsequently presented vibrotactile stimuli served as the comparison stimulus. The specific association between cue symbols and rules was counterbalanced across participants. The rule cue was followed by two vibrotactile stimuli with different frequencies (each 500 ms), which were separated by a 1 s retention period. After a decision phase of 2 s, an equilateral triangle, serving as a visual matching cue, was centrally presented for 500 ms. An upward-pointing triangle indicated a comparison stimulus of higher frequency, whereas a downward-pointing triangle indicated a comparison stimulus of lower frequency. The matching cues were pseudo-randomly interleaved across trials. Participants compared their perceptual choice with the matching cue and reported a match or mismatch by making a saccade to one of the two color-coded targets (blue vs yellow dot) presented in the periphery along the horizontal meridian after the matching cue offset. The color code was counterbalanced across participants and the location of the blue and yellow dots on the target screen alternated pseudo-randomly across trials. Participants were instructed to respond as fast as possible. A response later than 1.5 s after the target screen onset was considered a missed trial.

Vibrotactile stimuli were delivered to participants' left index fingers by a piezoelectric Braille display with 16 pins (4 x 4 quadratic matrix, 2.5 mm spacing), controlled by a programmable stimulator (QuaeroSys Medical Devices, Schotten, Germany). The frequency of the first

stimulus (f1) varied between 16, 20, 24, and 28 Hz. Each f1 was paired with an f2 that was either 4 Hz higher or lower, resulting in a total of eight stimulus pairs (16 vs 12 Hz, 16 vs 20 Hz, 20 vs 16 Hz, 20 vs 24 Hz, 24 vs 20 Hz, 24 vs 28 Hz, 28 vs 24 Hz, and 28 vs 32 Hz). All stimuli lay well within the flutter range (~5 – 50 Hz; Romo & Salinas, 2003).

A functional run consisted of 64 trials. Each of the stimulus pairs was presented eight times, each time with a different combination of rule cues (square vs diamond), matching cues (upward-pointing vs downward-pointing), and target screens (blue-left, yellow-right vs blue-right, yellow-left, Figure 1). The variable durations of the fixation period were balanced across rules and stimulus pairs. Trials lasted 11.5 s on average and were presented in a randomized order. The duration of a functional run was ~12.5 min. Participants were instructed to fixate throughout the entire duration of the run except for when they made saccadic responses.

Prior to the fMRI session, participants completed a training session to become familiar with the experimental procedure. The training session consisted of 64 to 128 trials and lasted a maximum of 45 min.

Importantly, the use of such a balanced design enabled the decoupling of choice-related signals from those related to stimulus order and preparation for a specific saccade response direction without requiring the temporal jittering of event onsets. This is because, due to the balanced design, each specific choice was expected to have approximately the same number of trials associated with each stimulus order and each saccade direction respectively (Hebart et al., 2012). This further ensured an equal estimability of all conditions of interest and minimized the possibility of classifying choices using the difference in the variability of the beta weight estimates (Hebart & Baker, 2017).

Data acquisition.

Saccadic eye movements were recorded using an MRI-compatible eye-tracker with a sampling rate of 500 Hz (Eyelink 1000, SR Research Ltd, Mississauga, Ontario, Canada). MRI data were recorded with a 3 T Tim Trio scanner (Siemens, Erlangen) equipped with a 12-channel head coil at the Center for Cognitive Neuroscience Berlin. For each participant, we collected 378 functional volumes per run (T2*-weighted gradient-echo echo-planar images, TE: 30 ms, TR: 2000 ms, flip angle: 90°, FOV: 192 mm, matrix size: 64x64, 3x3x3mm^3, 0.6mm gap, 37 slices, ascending sequence). In addition, anatomical images (T1 weighted MPRAGE, TE: 2.52 ms, TR: 1900 ms, flip angle: 9°, FOV: 256 mm, matrix size: 256x256, 176 slices, 1x1x1 mm^3) were collected for co-registration and spatial normalization purposes. Of the 30 participants whose data was analyzed, 28 completed six functional runs, while the remaining two completed five functional runs.

Data analyses.

Preprocessing. fMRI data preprocessing and analyses based on general linear models (GLM) were performed using SPM12 (Wellcome Trust Centre for Neuroimaging, www.fil.ion.ucl.ac.uk/spm). Possible artifacts in individual slices of the functional volumes were corrected via an interpolation approach as implemented in the SPM ArtRepair toolbox (Mazaika, Hoeft, Glover, & Reiss, 2009). Preprocessing steps prior to multivariate pattern analysis (MVPA) included slice-time correction and spatial realignment to the mean functional image. MVPA was performed using The Decoding Toolbox (Hebart, Goergen, & Haynes, 2015). We used the SPM Anatomy toolbox (Eickhoff et al. 2005) for cytoarchitectonic reference. In addition, we used probabilistic maps of visual topography in

human cortex as reference to identify brain regions that can be classified as the frontal eye fields (FEF, Wang, Mruczek, Arcaro, & Kastner, 2014; www.princeton.edu/~napl/vtpm.htm).

Decoding perceptual choices. We used a searchlight decoding analysis to identify brain regions that carry information about the perceptual choice during decision phases. Prior to the decoding analysis, we fit a GLM (192 s high pass filtered) to each participant's preprocessed data to obtain run-wise beta weights for each voxel. Each perceptual choice (higher vs lower) was modelled as a stick regressor at the onsets of decision phases in correct trials and convolved with the canonical hemodynamic response function. Incorrect and missed trials were modelled with a separate regressor of no-interest. Additionally, ten principal components accounting for the variance in the white matter (WM) and cerebrospinal fluid (CSF) signal time courses (Behzadi, Restom, Liau, & Liu, 2007) were included in the GLM alongside six head motion parameters as nuisance regressors. Finally, constant terms were included to account for run-specific effect, resulting in 20 regressors per run. Note that we only included data from correct trials in the subsequent decoding analysis based on the reasoning that incorrect trials were likely accompanied by indecisions during the time window of interest and would diminish the decodability of choice information.

For each participant, we employed a searchlight decoding analysis with linear support vector machine classifiers (SVM) in the implementation of LIBSVM (c = 1; Chang & Lin, 2011) and a leave-one-run-out cross-validation scheme. Beta weights for the choice regressors from each functional run were used as samples, yielding a total of twelve samples for participants who completed six runs and ten samples for participants who completed five runs. Beta weights of each voxel were normalized across samples before they were forwarded to the classification.

In each searchlight step, we extracted beta weights from all voxels within a 4-voxel radius sphere (maximal 251 voxels) at a given location of the brain to create pattern vectors. An

SVM classifier was trained to distinguish between the pattern vectors of different choices with the data from all but one run and tested for its generalizability on the data from the remaining run. The performance of the classifier was indicated by the decoding accuracy on the test run, that is, the percentage of correctly classified samples. This training-testing procedure was iterated so that every run had been used as the test data once. We averaged decoding accuracies across all iterations and assigned the mean decoding accuracy to the center voxel of the searchlight. The described searchlight procedure was repeated for every voxel in the brain, yielding a continuous brain map of mean decoding accuracies which was considered to reflect the amount of information about a participant's choice across the whole brain.

For the group inference, the decoding accuracy map of each participant was normalized to MNI space, resliced to 2 mm^3 voxel size, and smoothed with a full width at half maximum Gaussian kernel of 5 mm. We computed a one-tailed one-sample t-test to assess whether the observed decoding accuracies were significantly higher than chance level (50%) across the whole brain. Voxels showing significant decoding accuracies indicated that the local activity patterns carried information about perceptual choices. We further assessed whether there was a correlation between decoding accuracies in the identified regions and the behavioral performance using a one-tailed one-sample t-test with the behavioral performance as a covariate.

Decoding task rule. We were also interested in whether any brain regions represent information about the task rule during the decision phases. To test this, we used a GLM with regressors modelling the task rules at the onsets of decision phases. Again, we modelled correct and incorrect/missed trials in separate regressors and included the WM/CSF signal and motion parameters as nuisance regressors. Furthermore, the analogous procedure for the searchlight decoding analysis and the group inference was applied to the resulting beta

weights, with the difference that the pattern vectors corresponded to activity patterns evoked by the different task rules.

Control analyses

To ensure the thoroughness of the present study, we conducted further analyses to verify that the informative brain regions detected in the choice decoding analysis were indeed driven by choice representation and not confounded by stimulus order or saccade direction. To this end, we performed two sets of decoding analyses. For the first set, we employed a GLM with regressors modelling participants' perceptual choices (higher vs lower) for trials of each stimulus order (f1 < f2 vs f1 > f2) separately. Beta weights corresponding to the resulting four regressors were subjected to two searchlight decoding analyses, one for each stimulus order, using the identical parameters as in the main analysis. This way, local activity patterns associated with "higher" and "lower" choices were ensured to be independent of stimulus order. The resulting decoding accuracy maps from the two analyses were then averaged, resulting in an averaged decoding accuracy map for choices controlling for stimulus order. Using the analogous procedure, we further obtained an averaged decoding accuracy map in which choice-related activity patterns were classified separately for each of the saccade directions. Finally, participants' averaged decoding accuracy maps from these two sets of decoding analyses were forwarded to group inferences in order to identify regions carrying choice information. These analyses fully controlled for confounds related to the stimulus order or the saccade direction at cost of a significantly reduced (50%) number of trials for the decoding analyses and accordingly, reduced power. Nonetheless, if the informative activity patterns identified by the main choice decoding analysis were indeed driven by perceptual choice, we would expect to observe similar results in the control analyses.

We further tested whether the observed choice-selective regions could be accounted for by overall changes in the BOLD activation in single voxels. For this purpose, we ran an analogous searchlight decoding analysis, but reduced the number of voxels within the local searchlight to one. If the observed choice information was mainly represented in a multivariate code, this analysis based on a single voxel should not be able to detect choice-related information.

Results

Behavioral results

The average proportion of correct responses across 30 participants was 0.877 (SD: ±0.057, range: 0.726 – 0.966). To assess effects of different task components on behavioral performance, we computed a three-way ANOVA with task rule (rule 1 vs rule 2), stimulus order (f1 > f2 vs f1 < f2), and magnitude of f1 (16, 20, 24, and 28 Hz) as within-subject factors. This analysis did not reveal main effects of task rule ($F_{(1, 29)} = 0.256$, $p = 0.617$) or stimulus order ($F_{(1,29)} = 0.585$, $p = 0.451$), indicating that the cognitive demands were approximately equal across these factors. Furthermore, the analysis revealed a significant interaction between the stimulus order and the magnitude of f1 ($F_{(3,87)} = 17.046$, $p < 0.001$). For trials with f1 in the lower range, participants performed better when f2 was comparatively low (f1 > f2) than when f2 was comparatively high (f1 < f2). Conversely, the performance for trials with f1 in the higher range was better when f2 was higher than f1 compared to those with lower f2 (Figure 2). Such a behavioral pattern is a frequently observed phenomenon in studies using comparison tasks and is referred to as the time-order effect or contraction bias (Ashourian & Loewenstein, 2011; Fassihi, Akrami, Esmaeili, & Diamond, 2014; Herding et al., 2016; Preuschhof, Schubert, Villringer, & Heekeren. 2009). This effect suggests a biased

perception or memory trace of f1 toward the mean of the stimulus set. Importantly, this effect remains stable across the different task rules, as indicated by a non-significant three-way interaction ($F_{(3,87)} = 1.049$, $p = 0.375$).

To address the concern that the exclusion of incorrect and missed trials from fMRI analyses may result in a biased distribution of stimulus orders (f1 > f2 vs f1 < f2) and saccade directions (right vs left) across choices and thereby confound the fMRI choice decoding results, we computed two Pearson chi-square tests for each participants respectively. No systematic associations between the choice behavior and these two variables were revealed in any of the participants (stimulus order: all $p > 0.1$; saccade direction: all $p > 0.1$). We further explored whether participants' eye position during decision phases varied systematically across choices. Due to technical problems during data collection, we were only able to acquire eye movements along both the x- and y-axis for 20 participants', while the data of the remaining 10 participants consisted of only eye movements along the x-axis. For each participant, we extracted the average eye position along the x- and, when possible, y-axis across the two second decision phase of each trial. Next, we computed a two-tailed two-sample t-test to scrutinize systematic deviations between eye positions corresponding to different choices for the x- and y-axis respectively. No systematic relationship with choice was revealed in any of the participants (all $p > 0.05$, Holm-Bonferroni corrected across axes for each participant).

Collectively, the behavioral results suggest that participants' choice behavior was neither modulated by the stimulus order, nor by the eye movements during and after the decision phase. Thus, it is rather unlikely that these factors influenced the choice decoding results reported below.

Neuroimaging results

Choice-selective brain regions. To identify brain regions that carry choice information independent of stimulus order and saccade selection during the decision phase, we applied an assumption-free, searchlight MVPA across the whole brain. The results are shown in Figure 3A and Table 1 ($p < 0.05$, false discovery rate (FDR) corrected for multiple comparisons at the cluster level with a cluster-defining voxel-wise threshold of $p < 0.001$). As indicated by the significant above-chance decoding accuracies, this analysis revealed multiple clusters with distinguishable activity patterns for different choices. These clusters were located within the bilateral posterior parietal cortices (PPC) including the intraparietal sulci (IPS) and the inferior parietal lobules (IPL), the left lateral prefrontal cortex (lPFC), including the inferior and middle frontal gyrus (IFG, MFG), as well as the bilateral precentral gyri (PreCG) encroaching into the caudal-most part of the superior frontal sulci (SFS) which are known as the FEF (identified with probabilistic maps by Wang et al. 2014; cf. also Amiez, Kostopoulos, Champod, & Petrides, 2006; Kastner et al., 2004).

Furthermore, an additional t-contrast with the percentage of correct responses included as a covariate, revealed that, amid the identified regions, the behavioral performance was significantly correlated with the decoding accuracy in the right FEF (Figure 3B: x = 34, y = 0, z = 52, $t_{(28)} = 5.73$, $p < 0.05$, peak-level family wise error (FWE) corrected for small volume within the detected choice-selective regions). The decoding accuracy at the peak voxel and the behavioral performance across participants were positively correlated with a Pearson correlation coefficient of $r = 0.736$ ($R^2 = 0.542$, $df = 29$, $p < 0.001$). To preclude that the correlation was primarily driven by the participant with the lowest values in both variables (see Figure 3B), we repeated the correlation coefficient estimation without that participant's data. The correlation coefficient of the reduced sample size decreased slightly to $r = 0.683$, however, it remained statistically significant ($R^2 = 0.467$, $df = 28$, $p < 0.001$).

Rule-selective brain regions. Next, we investigated whether information about the task rule was represented during the decision phase. Rule-selective activity patterns were observed in the prefrontal regions of both hemispheres including the left MFG and bilateral IFG, PPC including the bilateral superior parietal lobules (SPL), and the left supramarginal gyrus (SMG) in the IPL. We further computed a "null" conjunction of the choice and the rule contrasts and found that a cluster centered around the left inferior frontal sulcus (IFS) was the only brain region to code both choice and rule ($p < 0.001$, cluster corrected at $p_{FDR} < 0.05$; Figure 3C, D and Table 1).

Control analyses

To further ensure that the results from the choice decoding analysis were mainly driven by choice-related BOLD signals, we conducted two additional sets of decoding analyses. These analyses controlled for effects related to stimulus order and saccade direction. The results are displayed in Figure 4 ($p < 0.001$, uncorrected at voxel level due to significantly reduced amount of data). As expected, both sets of analyses yielded highly similar decoding results to the main results, with overlapping clusters in bilateral IPS, FEF, and the left lPFC. This result demonstrates that our paradigm has effectively disentangled choice representation from stimulus order and saccade selection and confirms that the results derived from the main analysis are choice-specific.

Finally, to assess whether overall changes in the activity level of single voxels within a cluster could account for the observed choice information, we ran a decoding analysis with a single voxel searchlight. The analysis did not reveal any significantly informative brain regions ($p < 0.001$, cluster corrected at $p_{FDR} < 0.05$), indicating that choice-related information was indeed represented by patterns of local activity rather than a univariate code.

Discussion

In the present study we employed a modified version of the vibrotactile frequency discrimination task to explore brain regions that carry information about perceptual choice independent of stimulus order and saccade selection. Using MVPA on human fMRI data, we found vibrotactile choice-selective brain activity patterns in oculomotor regions including bilateral FEF and intraparietal regions, as well as the left lPFC. We thereby provide novel fMRI evidence for brain regions representing abstract choice in somatosensory decision-making.

The identification of choice information distributed across effector-specific premotor (FEF) and lateral prefrontal structures aligns well with previous electrophysiological studies in monkeys using the vibrotactile frequency discrimination task (Haegens et al., 2011; Hernandez et al., 2002; 2010; Romo et al., 2004). Most interestingly, and yet to be explored in the monkey literature, we also observed vibrotactile choice-selective activity patterns in intraparietal regions (IPS and IPL), which constitute, alongside the FEF and subcortical structures, the oculomotor system. This finding is compatible with a vast amount of evidence from monkey research using saccade responses in visual random-dot motion (RDM) tasks suggesting a major involvement of monkey FEF and LIP (homologous to human IPS) in sensory evidence accumulation toward a decision (Ding & Gold, 2012; Kim & Shadlen, 1996; Roitman & Shadlen, 2002; Shadlen & Newsome 2001). With these results, we establish an important link between researches from two influential perceptual decision-making paradigms and thereby promote the notion of supramodal decision making mechanisms.

Note however, that previously reported decision-related signals in the FEF and LIP were mainly observed in studies in which perceptual choice was directly mapped to a specific,

predictable saccade direction. A significant portion of decision-related signals in the FEF or LIP disappeared when saccade directions were decorrelated from perceptual choices (Bennur & Gold, 2011; Gold & Shadlen, 2003; reviewed in Huk et al. 2017). Similarly, recent human fMRI studies also failed to capture decision-related signals in the FEF or IPS when there was no fixed mapping between choice and saccade direction (Filimon et al. 2013; Herbart et al. 2012; Li Hegner, Lindner, & Braun, 2015). From these results one might conclude that oculomotor regions may merely represent the motor decisions. Crucially, there are several aspects of our study which render this interpretation unlikely: The current experiment was designed so that choice-related signals could be separated from sensory and motor components of the task. Moreover, we further validated the effectiveness of this experimental protocol with control analyses on behavioral and fMRI data. Thus, we are confident that the distinctive activity patterns observed in oculomotor regions were mainly driven by the choice information. In this light, our data provide novel evidence for choice selectivity in human oculomotor regions, which is not confined to saccadic decisions, but pertains to contexts where choices are made in a more abstract form.

One question emerged from our findings is why oculomotor regions represent perceptual choice despite its independence from the ensuing saccade direction? In fact, there is an increasing body of monkey literature showing that LIP and FEF are selective for various kinds of task-relevant information during a decision process (reviewed Huk et al. 2017; Stokes Buschman, & Miller, 2017). For instance, the intraparietal choice selectivity in our study is consistent with the well-established role of the PPC in representing abstract categorical information (Freedman & Assad, 2011; 2016). Indeed, these authors have proposed a common neural mechanism underlying abstract decision-making and categorization. Likewise, in line with our findings in the FEF, several studies have demonstrated that the functionality of premotor structures goes beyond the coding of motor-

related information and extends to sensory and task information (Ferrera, Yanike, &, Cassanello, 2009; Mante, Sussillo, Shenoy, & Newsome, 2013; Nakayama, Yamagata, Tanji, & Hoshi, 2008; Siegel, Buschman, & Miller, 2015; Yamagata, Nakayama, Tanji, & Hoshi,. 2009; 2012). Intriguingly, we show that the differentiability of choice representations in the right FEF is linked to participants' choice behavior. That is, the higher the decoding accuracy, the better participants performed the task. It is not immediately apparent from our data what functional role this observed correlation may reflect. Nevertheless, there is compatible evidence from recent studies in rats suggesting that the behavioral performance in a decision task is causally related to premotor structures' ability to categorize accumulated evidence into discrete choices (Erlich, Brunton, Duan, Hanks, & Body, 2015; Hanks et al., 2015). Accordingly, one possible interpretation is that decoding accuracies in the FEF index the quality of such categorization processes and are, hence, predictive of the behavioral performance. In concert with the implicated role of premotor structures in the transformation of abstract concepts into concrete motor commands (Nakayama et al., 2008; Yamagata et al., 2009; 2012), it is possible that choice information in the FEF reflects a temporary storage, waiting for additional information in order to be transformed into an appropriate saccade movement. This interpretation agrees with the growing body of evidence for a continuous flow of all task relevant information across a distributed brain network (Siegel et al., 2015). While this interpretation is appealing, future experiments may enable a temporal characterization of the information transformation from sensory processing to abstract choice and finally motor output.

In addition to the FEF and IPS, we found choice information in the left lPFC. This is consistent with previous monkey research using the vibrotactile frequency discrimination task, which shows that the lPFC computes perceptual choices (Hernandez et al., 2010; Jun et al 2010). Moreover, an involvement of lPFC is also compatible with previous human fMRI

studies suggesting lPFC's role in accumulating sensory evidence (Filimon et al., 2013; Heekeren, Marrett, Bandettini, & Ungerleider, 2004; Heekeren, Marrett, Ruff, Bandettini, & Ungerleider, 2006; Liu & Pleskac, 2011; Pleger et al., 2006). Notably, although choice-selective regions detected in the current study are compatible with those reported in previous studies, the fMRI-MVPA approach used here does not allow inference regarding the origin of choice information or where the sensory evidence is accumulated. With respect to this question, Shadlen and colleagues (Shadlen, Kiani, Hanks, & Churchland, 2008) suggest that abstract decisions are evolved by evidence accumulation toward the implementation of particular rules and that prefrontal regions are, due to their central role in the rule representation (Sakai, 2008), the most likely regions to host such a process. Considering that the left IFS has been identified to carry both the rule and choice information, it appears to be a promising candidate region for future studies to scrutinize the evolution of abstract vibrotactile decisions in humans. Indeed, there is evidence from a previous fMRI study in the visual domain highlighting left IFS' role in sensory evidence accumulation when choices are decoupled from specific motor commands (Filimon et al., 2013).

In addition to the left IFS, we suggest that intraparietal regions are, given their well-established role in magnitude processing (Jakob, Vallentin, & Nieder, 2012; Nieder, 2016), another potential candidate structure for deliberating decisions on the relation between two analog quantities, such as the vibrotactile frequencies. A shift to focusing on intraparietal regions and their interaction with other areas in monkey electrophysiology may provide substantial complementary insights into the neural mechanisms underlying vibrotactile decisions.

In conclusion, our results suggest that the human lPFC and oculomotor regions represent vibrotactile choice independent of stimulus order and saccade selection. These results are highly consistent with previous results from monkey electrophysiology and provide empirical

support for a pivotal role of human oculomotor regions in decision-making beyond the mere processing of saccadic movements.

References

Amiez, C., Kostopoulos, P., Champod, A., Petrides, M. (2006). Local Morphology Predicts Functional Organization of the Dorsal Premotor Region in the Human Brain. *Journal of Neuroscience*, *26*(10), 2724–2731. http://doi.org/10.1523/JNEUROSCI.4739-05.2006

Ashourian, P., & Loewenstein, Y. (2011). Bayesian inference underlies the contraction bias in delayed comparison tasks. *PLoS ONE*, *6*(5). http://doi.org/10.1371/journal.pone.0019551

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage*, *37*(1), 90–101. http://doi.org/10.1016/j.neuroimage.2007.04.042

Bennur, S., & Gold, J. I. (2011). Distinct Representations of a Perceptual Decision and the Associated Oculomotor Plan in the Monkey Lateral Intraparietal Area. *The Journal of Neuroscience*, *31*(3), 913–921. http://doi.org/10.1523/JNEUROSCI.4417-10.2011

Chang, C.-C., & Lin, C.-J. (2011). LIBSVM. *ACM Transactions on Intelligent Systems and Technology*, *2*(3), 1–27. http://doi.org/10.1145/1961189.1961199

Cisek, P., & Kalaska, J. F. (2010). Neural mechanisms for interacting with a world full of action choices. *Annual Review of Neuroscience*, *33*, 269–98. http://doi.org/10.1146/annurev.neuro.051508.135409

Cisek, P., & Kalaska, J. F. (2010). Neural mechanisms for interacting with a world full of action choices. *Annual Review of Neuroscience*, *33*, 269–98. http://doi.org/10.1146/annurev.neuro.051508.135409

Ding, L., & Gold, J. I. (2012). Neural Correlates of Perceptual Decision Making before, during, and after Decision Commitment in Monkey Frontal Eye Field. *Cerebral Cortex*, *22*(5), 1052–1067. http://doi.org/10.1093/cercor/bhr178

Erlich, J. C., Brunton, B. W., Duan, C. A., Hanks, T. D., & Brody, C. D. (2015). Distinct effects of prefrontal and parietal cortex inactivations on an accumulation of evidence task in the rat. *eLife*, *4*, 1–28. http://doi.org/10.7554/eLife.05457

Fassihi, A., Akrami, A., Esmaeili, V., & Diamond, M. E. (2014). Tactile perception and working memory in rats and humans. *Proceedings of the National Academy of Sciences*, *111*(6), 2331–2336. http://doi.org/10.1073/pnas.1315171111

Ferrera, V. P., Yanike, M., & Cassanello, C. (2009). Frontal eye field neurons signal changes in decision criteria. *Nature Neuroscience*, *12*(11), 1458–1462. http://doi.org/10.1038/nn.2434

Filimon, F., Philiastides, M. G., Nelson, J. D., Kloosterman, N. A., & Heekeren, H. R. (2013). How Embodied Is Perceptual Decision Making ? Evidence for Separate Processing of Perceptual and Motor Decisions. *The Journal of Neuroscience*, *33*(5), 2121–2136. http://doi.org/10.1523/JNEUROSCI.2334-12.2013

Freedman, D. J., & Assad, J. A. (2011). A proposed common neural mechanism for categorization and perceptual decisions. *Nature Neuroscience*, *14*(2), 143–146. http://doi.org/10.1038/nn.2740

Freedman, D. J., & Assad, J. A. (2016). Neuronal Mechanisms of Visual Categorization: An Abstract View on Decision Making. *Annual Review of Neuroscience*, *39*(1), 129–147. http://doi.org/10.1146/annurev-neuro-071714-033919

Gold, J. I., & Shadlen, M. N. (2003). The Influence of Behavioral Context on the Representation of a Perceptual Decision in Developing Oculomotor Commands. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *23*(2), 632–651.

Gold, J. I., & Shadlen, M. N. (2007). The Neural Basis of Decision Making. *Annual Review of Neuroscience*, *30*(1), 535–574. http://doi.org/10.1146/annurev.neuro.29.051605.113038

Haegens, S., Nácher, V., Hernández, A., Luna, R., Jensen, O., & Romo, R. (2011). Beta oscillations in the monkey sensorimotor network reflect somatosensory decision making. http://doi.org/10.1073/pnas.1107297108/-/DCSupplemental.www.pnas.org/cgi/doi/10.1073/pnas.1107297108

Hanks, T. D., Kopec, C. D., Brunton, B. W., Duan, C. A., Erlich, J. C., & Brody, C. D. (2015). Distinct relationships of parietal and prefrontal cortices to evidence accumulation. *Nature*, *520*(7546), 220–223. http://doi.org/10.1038/nature14066

Hebart, M. N., & Baker, C. I. (2017). Deconstructing multivariate decoding for the study of brain function. *NeuroImage*, (April), 1–15. http://doi.org/10.1016/j.neuroimage.2017.08.005

Hebart, M. N., Donner, T. H., & Haynes, J. D. (2012). Human visual and parietal cortex encode visual choices independent of motor plans. *NeuroImage*, *63*(3), 1393–1403. http://doi.org/10.1016/j.neuroimage.2012.08.027

Hebart, M. N., Goergen, K., & Haynes, J.-D. (2015). The Decoding Toolbox (TDT): a versatile software package for multivariate analyses of functional imaging data. *Frontiers in Neuroinformatics*, *8*(88), 1–18. http://doi.org/10.3389/fninf.2014.00088

Heekeren, H. R., Marrett, S., Bandettini, P. A., & Ungerleider, L. G. (2004). A general mechanism for perceptual decision-making in the human brain. *Nature*, *431*(7010), 859–862. http://doi.org/10.1038/nature02966

Heekeren, H. R., Marrett, S., Ruff, D. A., Bandettini, P. A., & Ungerleider, L. G. (2006). Involvement of human left dorsolateral prefrontal cortex in perceptual decision making is independent of response modality. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(26), 10023–8. http://doi.org/10.1073/pnas.0603949103

Herding, J., Ludwig, S., & Blankenburg, F. (2017). Response-Modality-Specific Encoding of Human Choices in Upper Beta Band Oscillations during Vibrotactile Comparisons. *Frontiers in Human Neuroscience*, *11*(118), 1:11. http://doi.org/10.3389/fnhum.2017.00118

Herding, J., Spitzer, B., & Blankenburg, F. (2016). Upper Beta Band Oscillations in Human Premotor Cortex Encode Subjective Choices in a Vibrotactile Comparison Task. *Journal of Cognitive Neuroscience*, *28*(5), 668–679. http://doi.org/10.1162/jocn_a_00932

Hernández, A., Nácher, V., Luna, R., Zainos, A., Lemus, L., Alvarez, M., … Romo, R. (2010). Decoding a perceptual decision process across cortex. *Neuron*, *66*(2), 300–14. http://doi.org/10.1016/j.neuron.2010.03.031

Hernández, A., Zainos, A., & Romo, R. (2002). Temporal Evolution of a Decision-Making Process in Medial Premotor Cortex, *33*, 959–972.

Huk, A. C., Katz, L. N., & Yates, J. L. (2017). The Role of the Lateral Intraparietal Area in (the Study of) Decision Making. *Annual Review of Neuroscience*, *40*(1), 349–372. http://doi.org/10.1146/annurev-neuro-072116-031508

Jacob, S. N., Vallentin, D., & Nieder, A. (2012). Relating magnitudes: the brain's code for proportions. *Trends in Cognitive Sciences*, *16*(3), 157–166. http://doi.org/10.1016/J.TICS.2012.02.002

Jun, J. K., Miller, P., Hernández, A., Zainos, A., Lemus, L., Brody, C. D., & Romo, R. (2010). Heterogenous population coding of a short-term memory and decision task. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *30*(3), 916–29. http://doi.org/10.1523/JNEUROSCI.2062-09.2010

Kastner, S., DeSimone, K., Konen, C. S., Szczepanski, S. M., Weiner, K. S., & Schneider, K. A. (2007). Topographic Maps in Human Frontal Cortex Revealed in Memory-Guided Saccade and Spatial Working-Memory Tasks. *Journal of Neurophysiology*, *97*(5), 3494–3507. http://doi.org/10.1152/jn.00010.2007

Kelly, S. P., & O'Connell, R. G. (2015). The neural processes underlying perceptual decision making in humans: Recent progress and future directions. *Journal of Physiology-Paris*, *109*(1–3), 27–37. http://doi.org/10.1016/J.JPHYSPARIS.2014.08.003

Kim, J.-N., & Shadlen, M. N. (1999). Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. *Nature Neuroscience*, *2*(2), 176–185. http://doi.org/10.1038/5739

Kriegeskorte, N., Goebel, R., & Bandettini, P. A. (2006). Information-based functional brain mapping. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(10), 3863–8. http://doi.org/10.1073/pnas.0600244103

Li Hegner, Y., Lindner, A., & Braun, C. (2015). Cortical correlates of perceptual decision making during tactile spatial pattern discrimination. *Human Brain Mapping*, *36*, 3339–3350. http://doi.org/10.1002/hbm.22844

Mante, V., Sussillo, D., Shenoy, K. V., & Newsome, W. T. (2013). Context-dependent computation by recurrent dynamics in prefrontal cortex. *Nature*, *503*(7474), 78–84. http://doi.org/10.1038/nature12742

Mulder, M. J., van Maanen, L., & Forstmann, B. U. (2014). Perceptual decision neurosciences - a model-based review. *Neuroscience*, *277*, 872–884. http://doi.org/10.1016/j.neuroscience.2014.07.031

Nakayama, Y., Yamagata, T., Tanji, J., & Hoshi, E. (2008). Transformation of a virtual action plan into a motor plan in the premotor cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *28*(41), 10287–97. http://doi.org/10.1523/JNEUROSCI.2372-08.2008

Nieder, A. (2016). The neuronal code for number. *Nature Reviews. Neuroscience*, *17*(6), 366–82. http://doi.org/10.1038/nrn.2016.40

Preuschhof, C., Heekeren, H. R., Taskin, B., Schubert, T., & Villringer, A. (2006). Neural correlates of vibrotactile working memory in the human brain. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *26*(51), 13231–9. http://doi.org/10.1523/JNEUROSCI.2767-06.2006

Preuschhof, C., Schubert, T., Villringer, A., & Heekeren, H. R. (2009). Prior Information biases stimulus representations during vibrotactile decision making. *Journal of Cognitive Neuroscience*, *22*(5), 875–887. http://doi.org/10.1162/jocn.2009.21260

Roitman, J. D., & Shadlen, M. N. (2002). Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *22*(21), 9475–89. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12417672

Romo, R., & de Lafuente, V. (2013). Conversion of sensory signals into perceptual decisions. *Progress in Neurobiology*, *103*, 41–75. http://doi.org/10.1016/j.pneurobio.2012.03.007

Romo, R., Hernández, A., & Zainos, A. (2004). Neuronal Correlates of a Perceptual Decision in Ventral Premotor Cortex. *Neuron*, *41*(1), 165–173. http://doi.org/10.1016/S0896-6273(03)00817-1

Romo, R., & Salinas, E. (2003). Flutter discrimination: neural codes, perception, memory and decision making. *Nature Reviews. Neuroscience*, *4*(3), 203–18. http://doi.org/10.1038/nrn1058

Sakai, K. (2008). Task Set and Prefrontal Cortex. *Annual Review of Neuroscience*, *31*(1), 219–245. http://doi.org/10.1146/annurev.neuro.31.060407.125642

Shadlen, M. N., Kiani, R., Hanks, T. D., & Churchland, A. K. (2008). *Neurobiology of Decision Making - An intentional Framework*. (C. Engel & W. Singer, Eds.)*Better Than Conscious?: Decision Making, the Human Mind, and Implications for Institutions*. Cambridge: MIT Press.

Shadlen, M. N., & Newsome, W. T. (2001). Neural Basis of a Perceptual Decision in the Parietal Cortex (Area LIP) of the Rhesus Monkey. *Journal of Neurophysiology*, *86*(4), 1916–1936. http://doi.org/10.1152/jn.2001.86.4.1916

Siegel, M., Buschman, T. J., & Miller, E. K. (2015). Cortical information flow during flexible sensorimotor decisions. *Science (New York, N.Y.)*, *348*(6241), 1352–5. http://doi.org/10.1126/science.aab0551

Stokes, M. G., Buschman, T. J., & Miller, E. K. (2017). *Dynamic Coding for Flexible Cognitive Control*. (T. Egner, Ed.)*The Wiley Handbook of Cognitive Control*. Wiley-Blackwell. http://doi.org/10.1002/9781118920541

Wang, L., Mruczek, R. E. B., Arcaro, M. J., & Kastner, S. (2015). Probabilistic Maps of Visual Topography in Human Cortex. *Cerebral Cortex*, *25*(10), 3911–3931. http://doi.org/10.1093/cercor/bhu277

Yamagata, T., Nakayama, Y., Tanji, J., & Hoshi, E. (2009). Processing of visual signals for direct specification of motor targets and for conceptual representation of action targets in the dorsal and ventral premotor cortex. *Journal of Neurophysiology*, *102*(6), 3280–94. http://doi.org/10.1152/jn.00452.2009

Yamagata, T., Nakayama, Y., Tanji, J., & Hoshi, E. (2012). Distinct information representation and processing for goal-directed behavior in the dorsolateral and ventrolateral prefrontal cortex and the dorsal premotor cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *32*(37), 12934–49. http://doi.org/10.1523/JNEUROSCI.2398-12.2012

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Tables

Table 1 Brain regions identified as containing information related to choice, task rule, and both.

Anatomical regions	Cluster size	MNI (x,y,z)			*t-value*	Mean accuracy
Choice						
R. IPL (PFm), IPS (hIP2, hIP3), SPL	953	32	-64	50	5.28	59.28
L. IFG, MFG, PreCG, SFS (FEF)	1137	-58	18	32	5.28	53.52
L. IPL (PF, PFm), IPS (hIP1, hIP2)	661	-52	-42	36	4.66	56.92
R. PreCG, SFS (FEF)	249	34	4	52	4.58	57.95
Task rule						
L. MFG, PreCG	1001	-52	8	38	5.25	58.97
R. IFG, PreCG	512	58	12	32	5.21	58.24
L. SPL	567	-4	-70	48	4.99	59.84
L. IPL/supramarginal gyrus (PFm, PF, PGa, PGp)	422	-60	-50	34	4.97	57.88
R. SPL	249	20	-74	64	4.65	52.43
Conjunction						
L. IFG, IFS, MFG, PreCG	377	-56	16	34	4.54	

All results are reported at a cluster corrected statistical level of $p_{FDR} < 0.05$ with an initial voxel-wise threshold of $p < 0.001$. MNI coordinates, t-values and the mean accuracies refer to the peak voxel within each cluster.

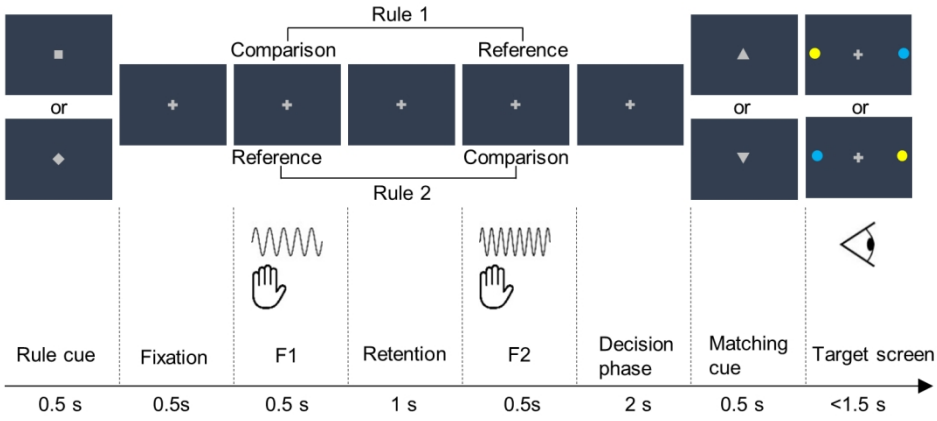
Figure legends

Figure 1. Experimental paradigm. A rule cue informed which of the two rules applied (pseudo-randomized across trials and counterbalanced across participants). Rule 1 indicated that participants had to compare f1 against f2, while rule 2 indicated a comparison in the reversed direction. This was followed by f1 and f2 presented to the participants' left index finger. After the decision phase, participants compared their perceptual choice with a visual matching cue (an upward-pointing triangle indicated "higher", while a downward-pointing triangle indicated "lower") and reported a match or mismatch with a saccade to either the blue or the yellow dots on the target screen. The spatial locations of the colored dots switched across target screens and the color code were counterbalanced across participants. The matching cues and target screens were orthogonal to each other and pseudo-randomly interleaved across trials so that participants were not able to anticipate the appropriate saccade directions during the decision phase.

Figure 2. The average behavioral performance across participants. The performance was modulated by the contraction bias (see text), irrespective of what rule was applied. Error bars represent SEM of the mean.

Figure 3. Neuroimaging results. (A) Brain regions carrying choice information independent of the stimulus order and the direction of the ensuing saccade (cluster corrected at $p_{FDR} < 0.05$). (B) A significant correlation between participants' behavioral performance and choice decoding accuracy was observed in the right FEF ($p_{FWE} < 0.05$, small volume corrected within the brain regions shown in A). (C) Brain regions containing information about the task rule. (D) Results from the conjunction analysis showing brain regions that represent both the choice and the rule information (C and D cluster corrected at $p_{FDR} < 0.05$). The unthresholded statistical maps are available at https://neurovault.org/collections/PTJKPIWY/

Figure 4. Comparisons between choice-selective regions identified in the main analysis with regions detected in the additional analyses controlled for effects related to the stimulus order (A, B) and the saccade selection (C, D). Results of the main analysis are displayed in green, while results from the control analyses are depicted in magenta. (A) Except the right FEF, all other clusters found in the main analysis (the bilateral intraparietal regions, the left lPFC, and the left FEF) overlap partially with those from the analysis controlled for the stimulus order. (B) Detail of the left prefrontal regions (cf. A) showing partial overlaps. (C) In addition to the overlapping regions shown in A, an overlap in the right FEF is also evident between the main analysis and the analysis controlled for saccade selection. (D) The left panel depicts the detail of overlaps in the left frontal regions, while a detailed view of the right FEF is displayed in the right panel (cf. C). Results are shown at a cluster corrected threshold of $p_{FDR} < 0.05$ for the main analysis and at uncorrected voxel-wise threshold of $p < 0.001$ for the control analyses. The unthresholded statistical maps are available at https://neurovault.org/collections/PTJKPIWY/



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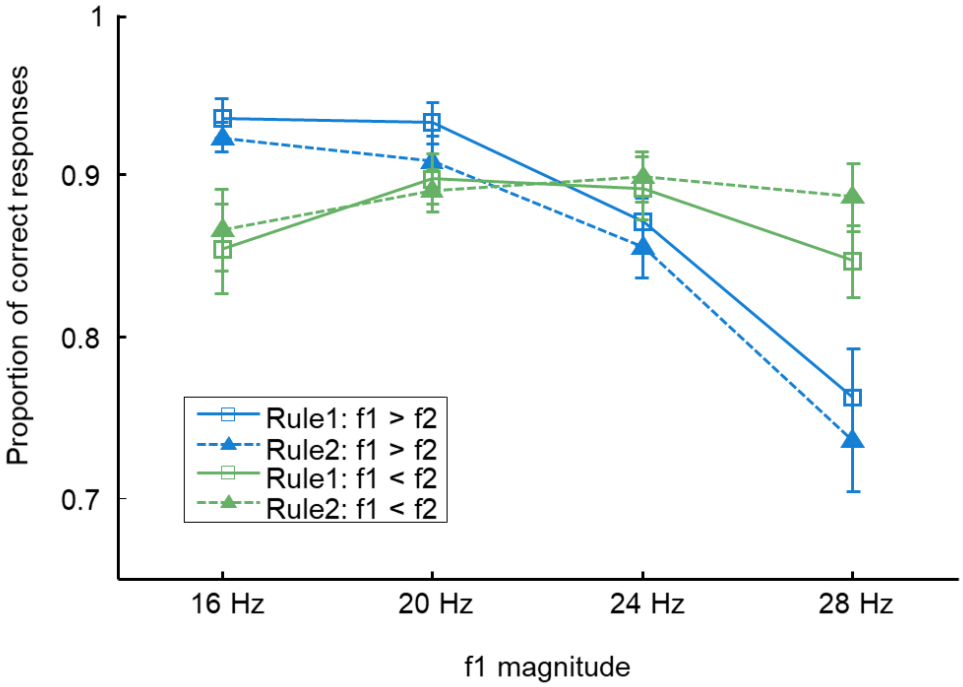

Figure 2. The average behavioral performance across participants. The performance was modulated by the contraction bias (see text), irrespective of what rule was applied. Error bars represent SEM of the mean.

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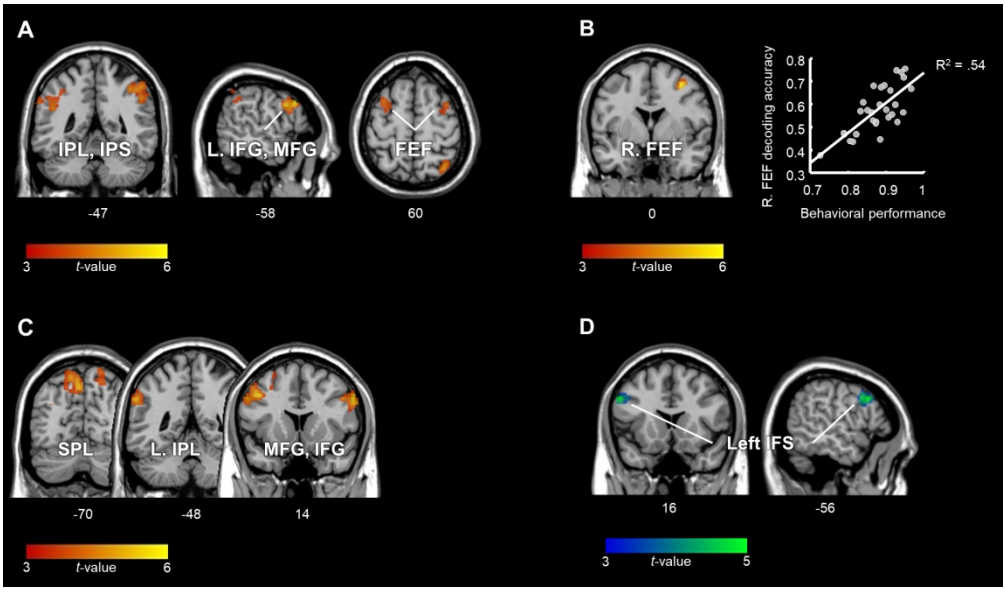

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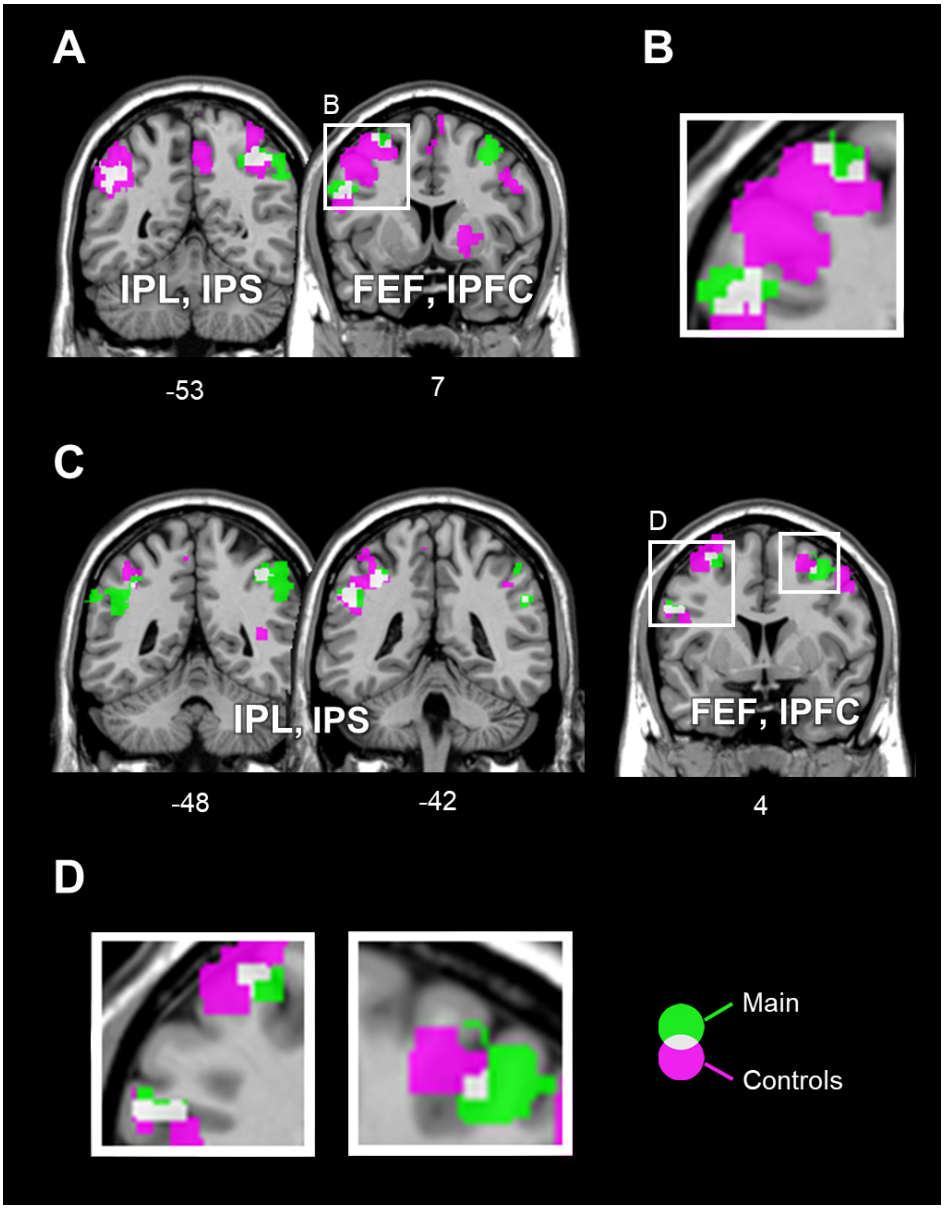

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86x109mm (300 x 300 DPI)

B. Supplement

Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

- dass ich die vorliegende Arbeit eigenständig und ohne unerlaubte Hilfe verfasst habe,
- dass Ideen und Gedanken aus Arbeiten anderer entsprechend gekennzeichnet wurden,
- dass ich mich nicht bereits anderwärtig um einen Doktorgrad beworben habe und keinen Doktorgrad in dem Promotionsfach Psychologie besitze, sowie
- dass ich die zugrundeliegende Promotionsordnung vom 08.08.2016 anerkenne.

Ort, Datum Unterschrift

Erklärung gemäß § 7 Abs. 3 Satz 4 der Promotionsordnung über den Eigenanteil an den veröffentlichten oder zur Veröffentlichung vorgesehenen eingereichten wissenschaftlichen Schriften im Rahmen meiner publikationsbasierten Arbeit

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II. Nummerierte Aufstellung der eingereichten Schriften (Titel, Autoren, wo und wann veröffentlicht bzw. eingereicht):

1. Schmidt TT, **Wu Y-h**, Blankenburg F (2017) *Content-specific codes of parametric vibrotactile working memory in humans.* Journal of Neuroscience, 37(40):9771-9777.

2. **Wu Y-h***, Uluç I*, Schmidt TT, Tertel K, Kirilina E, Blankenburg F (2017) *Overlapping frontoparietal networks for tactile and visual parametric working memory representations.* NeuroImage 166:325-334.

3. Uluç I, Schmidt TT, **Wu Y-h**, Blankenburg F (2018) Content-specific codes of parametric auditory working memory in humans. NeuroImage 183:254-262.

4. **Wu Y-h**, Velenosi LA, Schröder P, Ludwig S, Blankenburg F (submitted September 2018) Decoding vibrotactile choice independent of stimulus order and saccade selection during sequential comparisons. Human Brain Mapping.

*shared authorship

III. Darlegung des eigenen Anteils der Schriften:

Die Bewertung des Eigenanteils richtet sich nach der Skala: “vollständig – überwiegend – mehrheitlich – in Teilen” und enthält nur für den jeweiligen Artikel relevante Arbeitsbereiche.

Zu II.1.: Konzeption (in Teilen), Versuchsdesign (mehrheitlich), Programmierung (überwiegend), Datenerhebung (mehrheitlich), Datenauswertung (überwiegend), Ergebnisdiskussion (mehrheitlich), Erstellen des Manuskriptes (in Teilen).

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Zu II.4.: Konzeption (überwiegend), Versuchsdesign (überwiegend), Programmierung (vollständig), Datenerhebung (überwiegend), Datenauswertung (vollständig), Ergebnisdiskussion (überwiegend), Erstellen des Manuskriptes (vollständig).

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Name: Evgeniya Kirilina Unterschrift: _____

Name: Simon Ludwig Unterschrift: _____

Name: Pia Schröder Unterschrift: _____

Name: Kathrin Tertel Unterschrift: _____

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