Non-verbal working memory: A functional near-infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI) comparison

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NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

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Abstract

Different brain networks seem to be activated for verbal and non-verbal visual and spatial information in working memory. There exists a broad range of research on visual-spatial working memory. However, an approach which uses objects with multiple integrated features and a clear specification on the verbal dimension, has been less applied. Non-verbal working memory for visual-spatial information has been more neglected than verbal working memory. Hence, this study sought to address the neural networks that are utilized for non-verbal working memory performance. Brain activity was measured from 12 participants, in total, while they performed on a newly composed non-verbal working memory task. Both functional near-infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI) were used for the purpose. Results indicated that non-verbal working memory involves right-lateralized brain activations, where frontoparietal networks and visual pathways are recruited for performance. These findings serve as important input to the neural network model of the non-verbal working memory system. Thus, the task appears to effectively test the concept. fNIRS and fMRI were used for resting-state measurements on the same participants as well. They were measured for five minutes before and after the working memory task with both measurement tools. Results yielded differences between the two sessions in both fMRI and fNIRS. The connectivity changes may reflect effects of the task on the resting-state.

Keywords: *Non-verbal working memory, Visual-spatial, fMRI, fNIRS, Resting-state*

Sammendrag

Ulike hjernenettverk virker å bli aktivert for verbal og ikke-verbal visuell og romlig informasjon i arbeidsminnet. Det finnes et bredt spenn av forskning på det visuell-romlige arbeidsminnet. Likevel, har en tilnærming som benytter seg av objekter med flere integrerte egenskaper og en klar spesifikasjon på den verbale dimensjonen blitt mindre anvendt. Det ikke-verbale arbeidsminnet for visuell-romlig informasjon har blitt mer oversett enn det verbale arbeidsminnet. Derfor søker denne studien å adressere de nevrale nettverkene som utnyttes for ikke-verbal arbeidsminneprestasjon. Hjerneaktivitet ble målt fra totalt 12 deltagere mens de utførte en nylig komponert ikke-verbal arbeidsminneoppgave. Både funksjonell nær-infrarød spektroskopi (fNIRS) og funksjonell magnetisk resonans avbildning (fMRI) ble benyttet for formålet. Resultatene indikerte at det ikke-verbale arbeidsminnet involverer høyre-lateraliserte hjerneaktiveringer, hvor frontoparietale nettverk og visuelle traséer ble benyttet for prestasjon. Disse funnene tilbyr viktig tilførsel til den nevrale nettverksmodellen av det ikke-verbale arbeidsminnet. Dermed virker oppgaven å teste konseptet effektivt. fNIRS og fMRI ble også brukt for å måle resting-state fra de samme deltagerne. Resultatene uttrykket forskjeller mellom de to øktene ved både fMRI og fNIRS. Endringene i konnektivitet kan reflektere effekter av oppgaven på resting-state.

NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

Preface

The current project was initially inspired by an essay that I wrote on the differentiation of verbal and non-verbal working memory for a methods course in the Spring semester last year (2022). Also, I had an interest in methodology. Professor Karsten Specht was the one who suggested that we could investigate non-verbal working memory further with both fMRI and fNIRS. To investigate non-verbal working memory would be intriguing in itself. However, what especially piqued my interest was the opportunity to investigate the concept with a newly arrived measurement tool (fNIRS). Thereby, my master's thesis was determined to involve an investigation of non-verbal working memory with the use of both fMRI and fNIRS.

Due to some apparent shortages in the field of non-verbal working memory, a task for the Autumn became to develop new ways of testing the concept. Therefore, I thoroughly investigated what had been applied in experiments before, both regarding tasks and materials. The features that seemed to be used most frequently and reliably were put together into multi-featured objects. After the project was approved by the Regional committees for medical and health research ethics, late winter to early May consisted of data collection.

I am thankful for receiving the opportunity that I was given by Professor Karsten Specht, who allowed me to be highly involved in the making of a new research project. Furthermore, I am thankful that I got to be involved in every aspect of the research processes, from the very beginning to the end. I would also like to thank Ryan Douglas Mccardle for helping me to finalize the making of the stimuli sample that were used for this present project.

Table of content

Memory is a fundamental capacity for human beings. However, the concept "*memory*" comes with several facets. In its essence, memory can be seen as the capacity that allows us to both keep and connect experiences we have made. There are three major classifications of memory: sensory memory, short-term memory (STM), and long-term memory (LTM) (Camina & Güell, 2017). Sensory memory involves the initial processes where extrinsic information is captured and stored shortly by our senses and perceptual system, which makes it possible for this information to be further processed (Camina & Güell, 2017). The short-term memory refers to the processes that comes after sensory encoding and memory, where information is held in a short period of time (seconds). "*Working memory*" (WM) is a conceptualized capacity of processes that occur during the short-term memory window. It has been conceptualized to be differentiated from short-term memory by defining STM as only involving non-attention aspects for short memory storage, whereas WM performance involves attention for storage and/or processing (Cowan, 2008; Engle et al., 1999; Kane et al., 2001). Even though that may be the case, whether to use the term "short-term memory" or "working memory" has been a matter of semantics and taste (Cowan, 2008). The concept of WM represents at least a functional unit of memory, which involves our abilities to capture information, hold representations of the information in mind in an accessible state, and use it for a cognitive task (Cowan, 2014). Long-term memory, on the other hand, involves the processes that make us able to store information for longer periods of time. Long-term memory involves multiple types of information, multiple storages, and may be retrieved consciously or unconsciously (Camina & Güell, 2017). However, to describe and discuss this memory-puzzle much further would exceed the scope of this thesis. The thesis will mainly be concerned with working memory. Nevertheless, it is worth to keep the concepts of sensory memory and long-term memory in mind as working memory typically operates with the input from these systems.

The need for working memory is omnipresent in our daily life and has been studied extensively. Without the ability to take in and hold information so that we can respond quickly to challenges we encounter, we would not get much done. The fact that the concept is a strong predictor of performance on a wide range of complex cognitive tasks, highlights the importance of working memory (Emch, von Basian, & Koch, 2019). The term "working memory" has widespread use in psychology, and is often related to other concepts, such as intelligence, executive function, and learning (Cowan, 2014).

Furthermore, it works on different levels and in many different situations. For example, a person may be asked to listen to a text and sort out all the verbs from the sentences or listen to a song and remember the title based on the melody and lyrics. It can also involve such as remembering the digits from car plates that you need to report shortly afterwards, to plan for future events, and even abstract ideas. These examples are meant to highlight how flexible the working memory needs to be for us to be able to perform across several types of tasks and settings. Furthermore, sometimes, we only need to sort out a few defining features from the complete set of features that certain information contains (Cowan, 2014). A classic example is that of a child that does not yet know what is or is not a tiger. The concept of tiger involves a big cat with stripes. However, the child cannot only focus on the feature "cat" or "stripe" without combining them. Furthermore, to focus on other features of the set of information that comes with a tiger, such as ears, nose, tail, etc., would not be an effective strategy. Thus, to grasp what a tiger is, the child must be able to keep in mind what "cat" involves simultaneously as it also keeps in mind the notion of stripes. Interestingly, the learning of the concept of "tiger" probably starts with working memory but has great potential to be learned and transferred to long-term memory (Cowan, 2014). What this indicates is that working memory is effective on tasks when we effectively reduce information so that only the necessary components are held "in mind".

Working memory has been defined widely. In a compilation of descriptions, it can be described as a multi-component and task-specific online storage which holds information for a few seconds or minutes to manipulate it, with the use of an activated portion of long-term memory, executive attention, and goal-directed cognitive functions (Cowan, 2008, 2014). Thus, the content of working memory processes can be highly diverse. It is the time- and task-specific nature of the operation that defines it as a working memory operation. However, it seems to be multiplex in time, where the brain weights and moves the information in network-like manners and combines new information with prior knowledge. So, the information is almost "juggled" and "packed" during encoding and delay, and then reactivated in a manner that sometimes appears pseudo-random and at other occasions very goal-specific. What that really means, is that when new information is processed, it seems to activate certain networks that might tap into associated knowledges we already have stored so that we can perform efficiently and rapidly on the current cognitive task. However, the performance may or may not *appear* efficient for the specific task (Lundqvist, Herman, & Miller, 2018). This highlights that even though working memory processes occur, it does not mean that they will be or appear effective.

Working memory storage only holds a small amount of information. Miller (1956) introduced the article "*The magical number seven plus or minus two ...*" and the notion that our short-term memory, which is the information we can hold in our minds, is limited to a capacity of about 7 "chunks" of information. That is, for example, "1 0 0 0 0" are five items, but if you put them together into "10000" (i.e., ten thousand) they function as one piece of information rather than five separate ones. This can be done with several types of information, and one "chunk" in itself could be quite complex. This is generally agreed upon. The basic finding is that participants' effective performance is limited to about 5 to 9 categories or chunks of information. However it is often suggested that discrepancies easily can occur,

depending on such as object and task features and familiarity, feedback, and circumstances (Cowan, 2015). These findings typically report a limitation of three or four items or chunks. Thus, the number might not be as fixed as 7 +/- 2 but rather more fluid depending on how the attention needs to be allocated. The limit seems to be reduced to a range of about 3 for adults when the attention needs to be focused on an ensemble of items all at once (Cowan, 2015). For non-verbal visual working memory, it has also been suggested that it is only possible to retain about 4 pieces of the same feature (e.g., color) but it could be coupled with about 4 of another feature (e.g., orientation) in conjunction. Thus, it might be that visual working memory stores integrated objects rather than individual features (Cowan, 1998; Luck & Vogel, 1997). However, it has also been suggested that the limitations to working memory storage rather reflects how well attentional control is deployed than storage capacity per se (Adam et al., 2015; Kane and Engle, 2002).

Content can range from abstract stimuli that are hard to choose between and describe with words, to stimuli that can easily be chosen and described with words (Cowan, 2014). We have a "control system" that guides selection so that we can decide rather quickly which stimuli to act upon. This can be seen as an important part of the task coordination and updating function of working memory and is often referred to as the "*executive system*" or "*executive functions*" (Vandierendonck, 2014). Selective attention processes are seen as essential building blocks for the success of these functions (Eriksson et al., 2015). This involves the orientation of attention that allows for selection and suppression of information. Effectively, the selection and suppression of information should be driven by its task relevance. The selected material is what executive functions use to drive meaningful and task-appropriate actions. Thus, it may seem that both executive and selective functions of attention have a symbiotic relationship within working memory (Vandierendonck, 2014). Often, this involves shifts in *"top-down"* and "*bottom-up*" attention, which means that the environment

and task may demand back-and-forth changes from goal-directed focus to behaviorally relevant sensory events that often are salient and unattended. Novelty and unexpectedness can affect this dynamic interplay as well (Corbetta & Shulman, 2002).

What we can draw from this is that working memory depends on dynamic interactions between the nature of the task, the resources of the performing individual, and the environment the individual is meant to perform in. What has been presented so far is the basis for how the concept "working memory" will be treated in the present thesis.

State-based and multi-store models

When environments change, executive functions are necessary to detect these changes and to make decisions about whether the changes are relevant or irrelevant to the task at hand. In Cowan's (1988) "*embedded-process model*" of working memory, it is postulated that the mind forms a neural model of the processed stimuli, and that incoming stimuli that match this model become habituated, whereas stimuli that clash with the neural model will become dishabituated, in the sense of affecting attentional orientation. A dual mechanism of voluntary executive control and involuntary orienting responses is suggested as well, and may cause some struggle (Cowan, 2014). This suggests that the neural model is affected both by our goals and intentions (i.e., voluntary executive control) and confirming or conflicting information from the external environment, where stimulus salience may cause involuntary shifts of attention.

Where involuntary orienting responds to impressions from the environment can interfere with task performance, restraints in time and capacity may do the same. Working memory operations can become fallible because of these restraints. How much and how well we are able to encode, hold, and use information can be affected by multiple factors related to

the person (e.g., genetic inheritance, coding strategy, cognitive load, former experience), the properties of the surroundings, and how much time we have at hand.

Cowan (1988, 2001) has discussed the nature of working memory limitations and has shed light on two different perspectives (see Figure 1): The first perspective states that working memory can be limited because the focus of attention (FoA) is limited in capacity. Thereby, working memory may lose its effectiveness on a task if the amount or complexity of information exceeds what the focus of attention can encompass. The second perspective of working memory limitations is concerned with how different types of stimuli might interfere with task performance. Within this view, it is suggested that working memory utilizes an activated portion of LTM ("*activated LTM*"). It is assumed to be less accessible than attended representations but more than LTM representations in general. The capacity limitation is suggested to occur when items are no longer rehearsed or refreshed in working memory because of stimuli interferences, which causes the activated LTM to be lost. What these perspectives highlight, is that working memory can become influenced by the capacity of attention, and that it may be affected by both external (i.e., stimuli interferences) and internal (i.e., activated LTM) inputs.

Figure 1

The modified theoretical modeling framework of working memory by Cowan (1998, 2008)
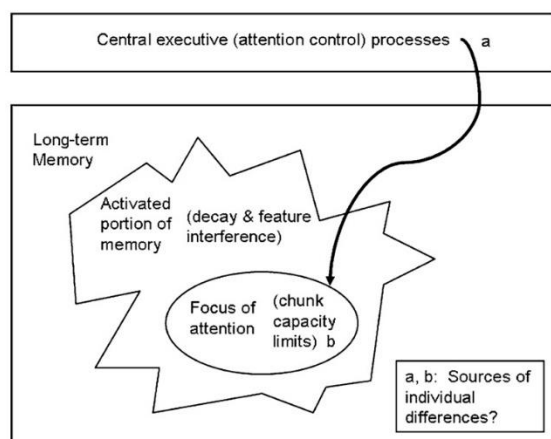
The existence of activated LTM is argued for through the finding that already existing synapses and ion channels implicated in perceptual object representations are recruited on tasks demanding working memory (Eriksson et al., 2015). However, neuroimaging studies have suggested that activated LTM is not really active, but rather that the representations are latent short-term representations (Eriksson et al., 2015). What that means is that the aid does not come from a continuous active state of LTM representations, but is rather a product of transient, short-term changes in synaptic weights. These latent representations are believed to be built up from focus of attention and retained in an activity-silent manner that allows for larger storage capacity than active working memory can provide alone (Lewis-Peacock et al., 2012; Nikolaev & van Leeuwen, 2019) That is, it can provide a larger storage capacity in the sense that previously attended information receives a neural signature (i.e., as a memory) that can be reactivated quickly with a refocus of attention toward the information (Lewis-Peackock et al., 2012).

Notwithstanding the discussion of whether activated LTM really is active or not, the model of Cowan emphasizes that working memory operates conjointly with attentional mechanisms, and that these might make working memory vulnerable to limitations. However, it is worth to note that attentional mechanisms do not only provide ground for limitations but are essential for the *optimal* function of working memory as well. In general, models emphasizing collaborations between LTM and WM are often called *embedded process models*.

When novel a stimulus is introduced, LTM cannot easily support working-memory maintenance. Furthermore, the complexity of the task may affect utilization of LTM, and time may intervene with how much utilization is affected by the complexity. Differences in complexity may involve different stimulus properties within the same perceptual system (e.g., vision) and/or across different modalities (e.g. vision and hearing). High stimulus-complexity

affects both the ability to use the information after encoding and the precision of the encoding itself (Fougnie, Suchow, & Alvarez, 2012; Van den Berg et al., 2012). That is, both complexity of the information and the time at hand affects the pool of resources available to use the information effectively and accurately on working memory tasks. Interestingly, it is suggested that it is the deployment of attentional control, and not the storage capacity per se, that differentiate individuals the most (Adam et al., 2015; Kane & Engle, 2002).

Baddeley and Hitch (1974) have attempted to model the multicomponent nature and organization of working memory (see Figure 2). One of their main contributions was the illumination of the diversity of short-term memory involved in working memory processes, which initially was neglected in Cowan's model (Cowan, 2014). At first, they postulated two short-term storages: a phonological storage of verbal information, called the *"phonological loop"*, and a visual-spatial storage, called the *"visuo-spatial sketchpad"*. One reason for the inclusion of qualitatively different storages comes from the finding that performance was most interfered with if similar information was presented. However, in the context of the visuo-spatial sketchpad storage, irrelevant visual material has been found to affect visual imagery but not visual storage. Thus, it is argued that image generation and visual short-term memory are dissociated (Baddeley, 2012; Borst, Niven & Logie, 2012; Klauer & Zhao, 2004; Logie, 1986). Despite of this, Cowan (2014) highlights that generality testing of the dissociation is needed.

Figure 2

The initial three-component model of working memory by Baddeley and Hitch (1974;

Baddeley, 2000)
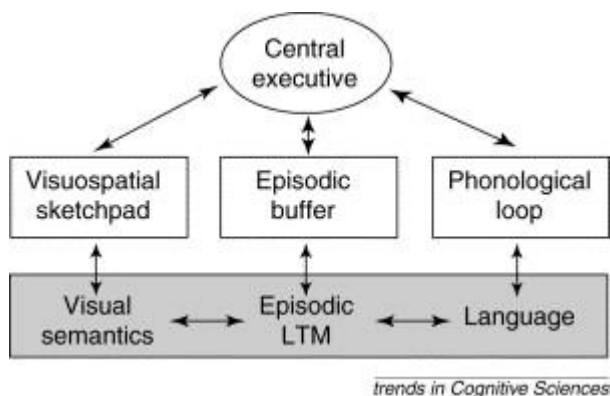
A "*central executive*", equivalent to an "executive system", was hypothesized to

control the information that is processed in either of the two short-term storages, where it is

kept in an active state. Later, a *"episodic buffer"* was also added, which is thought to be

responsible for short-term holding of semantic information and integration of phonological

and visual-spatial information (Baddeley, 2000; Cowan, 2014). This can be seen as a

multimodal hub for maintenance and storage, which can draw from all working memory

subcomponents and LTM.

The episodic buffer solves the binding problem, which refers to the fact that

information is received through separate channels but experienced as a coherent event

(Gathercole, 2008). The idea is that the central executive controls the allocation of

information from different modalities into the buffer. Evidence for an episodic buffer comes,

for example, from findings where patients with reduced short-term memory for sequences of

words and sentences still show the normal pattern for better memory of meaningful over

meaningless material (i.e., intact semantic information evaluation) (Gathercole, 2008).

Generally, the separation of executive and storage mechanisms, and of verbal and non-

verbal, visuospatial storage is supported by neurophysiological findings (Daniel, Katz, &

Robinson, 2016; Eriksson et al., 2015). However, the regional activity of WM overlaps with

that of perception and LTM of the same content, implicating common locations for WM, LTM, and perceptual processes (Eriksson et al., 2015).

Even though there exist other models of working memory than those of Cowan's "*state-based*" and Baddeley and Hitch's "*multi-store*" models, they are probably the models with the most pronounced influence. Most theories include overlapping concepts but weights them differently and have different approaches for WM investigations. For example, Kane and Engle (2003) and Unsworth and Engle (2007) suggest that attentional control is the main contributor of individual differences in working memory; Oberauer provides a theoretical modification of Cowan's model, with a narrower FoA (Oberauer & Hein, 2012); and Logie (2011) suggests a modification of Baddeley's visuospatial sketchpad, with a clearer distinction between visual and spatial storage and rehearsal components.

Other types of models focus on the underlying neural mechanisms of working memory. More precisely, they postulate conceptualizations from findings regarding the neural spiking activity that underlies working memory. Some suggest that persistent spiking activity, especially in the prefrontal cortex (PFC), maintains information during short-term delays between encoding and utilization. Support has been provided through findings showing that neurons in lateral PFC (LPFC) have persistent activity after stimulus presentation has been discontinued, suggesting sustained WM representation (Sreenivasan & D'Esposito, 2019). Sustained activity in PFC has been proposed to protect information maintenance during WM tasks, and thus, overdrive the potential vulnerability of maintaining information in the same sensory regions that process incoming information (Eriksson et al., 2015). Clearly, the central focus of "*persistent-activity*" models is on the online nature of the memory system.

"*Activity-silent*" models of WM are partially at odds to "persistent-activity" models. Their perspective is that there exist both "online" representations in WM that are kept in a stable and active state after stimulus offset, and "offline" representations in LTM that can be

sustained without persistent neural activity (Stokes, 2015). This may be the case as WM processes can show multiple signatures of retrieval from LTM (Foster, Vogel & Awh, 2019). The medial temporal lobe (MTL), which often is reported to be involved in LTM, seems to be kept active in WM operations during longer delays, when load exceeds WM capacity, and with novel associations (Eriksson et al., 2015). This may be especially true for visual and less verbal WM performance (Olson et al., 2006). The "offline" representations are suggested as stored memories that are held "in mind" in the prefrontal cortex (PFC) but show no neural activity before an attentional shift rapidly reactivates its neural signature (Lewis-Peacock et al., 2012; Lundqvist et al., 2018). That is, information does not necessarily need to be kept in a continuous active state in order to be available. It is believed that transient bursts of spiking and asynchronous synaptic firing could provide the basis for this function. Thus, asynchronous firing might allow more flexible independent control over different items in WM, as they are kept "in mind" but do not demand continuous energy supply. Rather, they are reactivated by refocus of attention to task-relevant/unattended content.

The models presented above provide understandings of different segments of working memory through variations in conceptual weightings. In sum, working memory is a complex system that includes multiple cognitive components and integrates multimodal representations during encoding, maintenance, and utilization of information so that we can perform on tasks with a relatively short time frame.

Neurocognitive architecture of working memory

Cowan's model does not require explicitly and exclusively that working memory performance is decided by the transfer success of information from brain areas involved in encoding to areas dedicated to maintenance. Furthermore, a prediction of the model is that neural substrates of encoding, maintenance and recollection share similarities. It appears

agnostic to stimulus-specific network activation and task-phase differences (Habeck et al., 2012). Rather, it emphasizes that information exists "in mind" as heightened state of activity. Baddeley's model, on the other hand, distinguishes between encoding, maintenance and recollection phases and stimulus-specific storage units.

The three working memory stages are seen as emerging from ongoing brain activity and can thereby be measured through instruments meant to capture that. Critical activity linked with top-down, executive control-like functions that guides and directs behavioral responses have been traced to the prefrontal cortex, parietal cortices, and basal ganglia (Eriksson et al., 2015).

Habeck et al. (2012) investigated the relationship between verbal (i.e., letter task) and non-verbal (i.e., shape task) and found that load-related rehearsal patterns in the brain associated with the two tasks shared some similarities. Thus, stimulus of different qualities might employ similar brain regions. Some phonological-loop-associated brain areas were found to be involved in both the verbal and non-verbal stimuli task. The cross-applicability between modalities may give support for an episodic buffer to de-emphasize contributions from processing in modality specific network units.

Despite the findings that stimuli of different qualities can trigger activation in similar brain areas, the "executive brain regions" seem to allocate information through stimulus-specific networks, where the particular representations are held over a delayed period of time before potentially being retrieved and manipulated to be acted upon (Eriksson et al., 2015). To put it differently, brain areas may be activated similarly between different modalities, but their connectivity is modality-specific.

Prefrontal regions have been connected to every aspect of WM processes – that is, encoding of stimuli, maintenance, and response (Constantinidis & Procyk, 2004). The prefrontal brain regions project back to the areas from which they receive sensory output,

however indirectly to the primary motor cortex. Despite of the indirect communication, transfer of information or control from prefrontal regions to the premotor cortex has been suggested to bridge instruction and motor control (Constantinidis & Procyk, 2004). In the context of premotor- and motor cortex activation, it is worth mentioning that a suggested task of designing working memory tests involves the ability to discern the processes that happen in the maintenance of information from those associated with motor preparation and action planning (Lundqvist et al., 2018). Thus, it might be preferable to vary the period of maintenance (i.e., delay period) so that the responding individual cannot fully predict and prepare for appropriate motor response. Furthermore, to provide feedback of correct/wrong responses may serve as a type of action specification.

Even though PFC activation during WM tasks has been shown to represent abstract functions, such as rules, categories, and numerical quantities, it is not unique for the region; abstract functions are also associated with activity in the inferior temporal cortex (ITC) and parietal cortices. During working memory tasks, the PFC and parietal cortices exhibit similar activity, suggesting parallel functional systems and a functional integration between these regions. These are indirectly connected via the anterior cingulate gyrus as well (Goldman-Rakic, 1988). The direct and indirect functional connectivity between frontal and parietal cortices are seen as central for monitoring, maintaining, and resisting interference from competing information (i.e., *executive control*), in working memory (Biswal, 2010).

However, some differences have been implicated: the posterior parietal cortex (PPC) neurons respond to and encode the location of the most recent stimulus, whether relevant or not, whereas PFC neurons encode *combinations* of cued and relevant information and responds to them in a task-related manner: – thus, suggesting selection processes in PFC and possibly a higher abstraction level than in the PPC (Constantinidis & Procyk, 2004; Rigotti et

al., 2013). ITC and the PFC also show mutual influence, likely because of cortico-cortical connections (Gazzaley, Rissman, & D'Esposito, 2004).

When it comes to stimulus-specific activity, the same sensory brain regions that process the information are believed to store sensory information during delay periods and working-memory task performance (Eriksson et al., 2015). An indication that the brain stores stimuli differently depending on their properties comes from lesion studies: Lesions to the temporal cortex affect visual WM but not spatial WM, whereas patients with parietal lesions show the opposite pattern (Eriksson et al., 2015). Furthermore, lesions to the lateral temporal lobes and temporoparietal cortex, which are areas associated with semantic storage, affects verbal working-memory performance negatively (Binder et al., 2009; Bormann et al., 2015).

There seem to exist some differences in the organization of the PFC when it comes to stimulus processing: Left, ventral PFC is suggested to be more involved in verbal WM tasks, whereas right, dorsal PFC is suggested to be more involved in spatial WM tasks. Also, increased dorsal PFC activation is found during encoding and manipulation or monitoring, whereas ventral PFC seems to mediate maintenance. However, neural activity during maintenance of visual working memory has been associated with activations over the PFC, PPC, and early visual areas (Li, O'Sullivan, & Mattingley, 2022). The fact that information might be stored in both frontoparietal regions and/or sensory regions, may suggest that content-specific information can be flexibly maintained in multiple cortical regions (Li et al., 2022).

Furthermore, the complexity and memory load of the working memory operation seem to affect dorsal/ventral and left/right or selectivity in activation: increased memory load has been associated with increased right hemispheric activation, whereas studies have reported that more complex working memory tasks cause more bilateral PFC activation (Rypma & D'Esposito, 1999). Similarly to the PFC organization, a dorsal/ventral and left/right

lateralization is found in the parietal cortex depending on the content of the task and is suggested to reflect such as attention orientation and reorientation (i.e., top-down/bottom-up switches) (Corbetta & Shulman, 2002; Corbetta, Patel, & Shulman, 2008; Sack, 2009).

Not only the dorsal and ventral areas of the PFC are implicated in working memory with a possible selectivity in activation depending on the content of the task. Central regions of the PFC are involved as well: on a spatial location task, the middle frontal gyrus (MFG) was more activated in the right hemisphere, whereas on a nonspatial shape task, the MFG was bilaterally activated, while the cingulate gyrus showed left lateralized activation following the nonspatial task. The right MFG activation for the spatial task may reflect high executive demand as this seems to increase right lateralization in the frontal cortex for spatial WM (Wager & Smith, 2003). The MFG activation occurred closer to task onset rather than offset of the task (McCarthy et al., 1996). Also, the MFG (including rostral and dorsolateral PFC) is seen as a core region in the lateral frontoparietal network (L-FPN). One of the main tasks of this network is to exert control of information flow in the brain (thereof the names "*control network*", "the central executive network", or "executive control network") (Uddin, Yeo, & Spreng, 2019).

The meta-analysis of Nee et al. (2013) did not find a dissociation of multiple distinct functions in the PFC, but they did suggest a dorsal "where" / ventral "what" framework of PFC organization across diverse executive demands. A similar distinction is found with visual processing pathways: a dorsal pathway from the primary visual cortex (V1) to the posterior parietal cortex and superior regions of the parietal cortex has been found for spatial locations and control of actions, whereas a ventral pathway from V1 to the inferior temporal cortex (ITC) has been found for object recognition and visual memory of objects and patterns, with high selectivity to complex object shapes (Lehky & Sereno, 2007; Milner, 2012). It is suggested that the functional divisions found in frontal regions, may reflect continued streams

from occipital areas. Despite of this, there seems to be cross-talk between the two pathways, and multiple brain regions have been reported as sites of interaction (e.g., van Polanen & Davare, 2015).

Furthermore, a rostral-to-caudal organization seems to exist in the PFC, which relates to the abstraction level of the information. Rostral areas are thought to stand for executive functions and peak activity level for abstract goals and task rules. The rostral regions have widespread and diffuse connections to other parts of the brain, which are thought to allow for flexible projections to more caudal areas based on task demands (D'Esposito & Postle, 2015).

It is worth mentioning that ascending dopaminergic neuromodulatory signals from striatal regions to the PFC account for the "control of the controller". Dopamine is seen as crucial for maintenance of physiological processes and balancing of activity (i.e., neuromodulation) (Klein et al., 2019). Interestingly, the PFC and parietal regions are normally least active during the maintenance stage of WM, whereas higher striatal activity has sometimes been found in this period. It has been suggested that increased striatal activity and dopamine input to the PFC made the representations more rigid (i.e., more resistant to distractive information). This increased activity is postulated to function as a gating mechanism for maintenance/updating of representations in PFC and can possibly improve stimulus selection for response (Cools et al., 2010).

Interestingly, it has been suggested that prefrontal and parietal systems may be sufficient for maintenance of familiar stimuli, whereas the prefrontal-parietal system may need help from parahippocampal regions (e.g., entorhinal and perirhinal cortex) for working memory processes that involve novel items (Hasselmo & Stern, 2006). This notion receives support from impairments found in working memory for conjunctions, complex non-verbal stimuli and novel visual objects with parahippocampal lesions (Hasselmo & Stern, 2006).

When dopaminergic neurotransmission to the PFC is altered in individuals, hyperactivity has been seen in dorsolateral PFC (DLPFC) during maintenance condition in contrast to manipulation condition. It is worth to mention that the DLPFC is often a functionally defined region rather than reflecting an anatomic structure (Hertrich et al., 2021). It is a region of the middle frontal gyrus (MFG), and comprises Brodmann areas 46 and 9 (Hoshi, 2006; Jung, Ralph, & Jackson, 2022). Interestingly, this hyperactivation pattern was found in schizophrenia patients on a verbal working-memory (vWM) task, whereas an opposite pattern (i.e., hypoactivation) was found during a non-verbal working-memory (n-vWM) task. This suggests differently activated systems, depending on how verbalizable the stimulus is (as described above). Also, it shows that the PFC is highly dependent on input from and interplay with other regions to perform properly.

Regarding attentional control, the superior parietal cortex is associated with executive aspects of WM and the implementation of selective attentional control (Eriksson et al., 2015). Furthermore, dorsal parietal cortex (DPC), superior parietal lobule (SPL) and inferior parietal lobule (IPL) are associated with top-down attentional control mechanisms as well (Ganis, Thompson, & Kosslyn, 2004; Shomstein, 2012). Shifts in SPL and IPL seem to provide basis for brief attentional control of attentive states in top-down-like ways (Shomstein, 2012) Inferior frontal gyrus (IFG) and inferior frontal junction (IFJ) are believed to serve as convergence areas for stimulus-driven and top-down control of attention (Shomstein, 2012). Furthermore, regions in dorsal parietal and frontal cortex, which makes up a dorsal frontoparietal network, have been suggested to be involved in processing of top-down signals for visual and spatial stimulus features (e.g., shape, color, direction) or object attention (Corbetta & Shulman, 2002). Interestingly, the dorsal frontoparietal attention system seems to maintain a "salience map" so that bottom-up and top-down information can be combined during visual search (Corbetta & Shulman, 2002). That is, our expectations for the visual

search may influence the sensory salience of objects and enhance their chances of being selected and acted upon (Corbetta & Shulman, 2002). Ventral regions of the frontal cortex and the frontal eye fields (FEF) are recruited as well for visual top-down/bottom-up attentional allocation. Superior portions of the parietal lobule have been reported to be involved in goal-directed attentional orientation, whereas inferior portions are involved in stimulus-driven attentional orientation, reorientation, and selection (Gillebert et al., 2011; Shomstein, 2012). However, this distinction is not inherently independent.

The distribution of attention can both be controlled by the intentions of the person and of the salience of the stimulus. Stimuli that share feature similarities will demand more top-down attentional control and make people more vulnerable for capture (i.e., attention to task-unrelated stimulus). If this happens, activity in the temporo-parietal junction (TPJ) is expected (Shomstein, 2012). The TPJ cortex has been suggested as a core region of the ventral network (Corbetta et al., 2008).

Regarding vWM, left hemispheric laterality is usually found, and involves mostly parietal and temporal language-associated regions (Rothmayr et al., 2007; Habeck et al., 2012; Emch et al., 2019). However, it is not completely a left-hemisphere concept, as bilateral frontal activation and right-lateralization of cerebellum is found (Emch et al., 2019). With verbal information, differences in reaction time are associated with differences in left medial frontal gyrus and left precentral gyrus activity, whereas differences in load are associated with activation across the PFC, fusiform gyrus, parietal cortex, and parts of the cerebellum (Emch et al., 2019). Buchsbaum and D'Esposito (2008) reported superior temporal, ventral prefrontal regions, and left inferior parietal cortex as especially critical for vWM.

Non-verbal information might include spatial and visual information that is complex, abstract, and unfamiliar to the perceiving individual. The n-vWM has been linked with multiple regions and typically with a right-lateralization. Among other regions, it is associated

with right frontal activity. For example, non-verbal rehearsal was associated with activity in the right DLPFC and medial prefrontal regions (Rothmayr et al., 2007). Higher-level occipital, ventral temporal, and superior parietal areas are also linked with more complex aspects of visuospatial processing (Gotts et al., 2013). Several of these regions are associated with a dorsal frontoparietal network, which is also called "*attention network*" for its broad role in visuospatial attention (Corbetta and Shulman, 2002; Uddin et al., 2019). Furthermore, superior temporal gyrus showed positive loadings in a non-verbal shape task (Habeck et al., 2012). Also, the left medial frontal, middle frontal, and right precentral gyrus, the left and right SPL and PCu, and the right fusiform gyrus have all been associated with non-verbal information as well (Daniel et al., 2016). Differences between verbal and non-verbal information have been reported in the left PCu, the right MFG, and the left inferior frontal gyrus (Daniel et al., 2016). Thus, frontoparietal regions may be core regions for the differentiation of verbal and non-verbal WM.

However, research that specifically aims to investigate visual non-verbal WM is relatively scarce, despite more focus in recent years, and should be further explored. That is not to say that the research on visual-spatial capacities in humans is scarce per se, because it is rather rich and fruitful, but what appears as a remaining issue is how different forms of visual-spatial information affect processing mechanisms when they are integrated into the same object. To do that would have clear benefits for a comprehensive understanding of visuospatial working memory. Furthermore, studies on working memory would benefit from focusing on the integration of visuospatial information with different properties *together* with specifications on the verbal dimension, with non-verbal information being more neglected up to this date.

Patients with right MTL lesions made more vivid recollective judgments of encoded material, likely because they had to rely on left-hemisphere verbal encoding strategies.

Patients with left MTL lesions made more vague familiarity judgements, likely because they had to rely more on right-hemispheric perceptual processing (Goldby et al., 2001). Frontal lobe lesions often follow the same left/right verbal/non-verbal distinction but depends more on nature of stimulus and task demands than with MTL lesions (Goldby et al., 2001). It seems that laterality in prefrontal cortex may be influenced both by process-specific (encoding/retrieval) and material-specific (verbal/non-verbal) task demands. However, in a "global" perspective of vWM versus n-vWM, it seems that vWM involves more left-hemisphere activity, whereas n-vWM involves more right-hemisphere activity. Thus, WM might fit a "*material-specific*" model.

All that has been presented so far provides input to the specific landscape, fingerprints, and concerted functions of subserving working-memory modules. That is, the building blocks of working memory, and the constellations of the brain that make up the differentiated processes that still go under the concept of "working memory". Also, the fact that there still are unexplored pieces of working memory serves as an impetus to find new ways to vary both demands and properties of information so that more facets of the concept can be mapped. This present project will aim to investigate the modules of working memory that involves non-verbal, visual-spatial information with a new approach.

Resting-state

Another subject of the project that has not received attention so far concerns resting-state (R-S). This is a brain concept that stems from observations of deactivation in brain regions relative to passive viewing (Fransson, 2005; Shulman et al., 1997). During a task-free period where a person is resting or "doing nothing", it is normal to find spontaneous neural activity from remote regions that appear synchronized (Lu et al., 2010). This is referred to as resting-state functional connectivity (RSFC) (White et al., 2009). That is, spontaneous low-

frequency fluctuations in the frequency range of 0 to 0.1 Hz between multiple voxels and regions are interpreted as functionally connected brain activity (e.g., Biswal et al., 1995; Biswal, 2010; Chen et al., 2017; Cordes et al., 2000; Guye, Barolomei, & Ranjeva, 2008; He et al., 2008). SFLs are found both within and across hemispheres. The reason why these fluctuations are termed "spontaneous" is because they appear independent of cardiac and respiratory fluctuations (Biswal, 2010).

The term "*functional connectivity*" in itself can have multiple meanings, such as correlations across subjects, runs, blocks, individual time points, etc. (Fox & Greicius, 2010). The term refers essentially to the temporal correlations that remote brain regions show between each other. However, it does not indicate *how* the observed correlations are mediated (Friston, 1994). The notion behind this is that the regions are consistently coupled during the same behavior/task. Thus, it provides a direct approach and an operational definition of relatedness and functional relationships in the brain. When using the term, some choose to add specifications in coherence with the measurement instrument: for example, resting-state functional connectivity MRI (rs-fcMRI). Regardless of that, there exist some consistent observations from resting-state measurements that utilize fluctuations in blood oxygenation and flow. They have shown that functionally related brain regions exhibit correlations of low frequency fluctuation and has been found for multiple regions. These include such as correlations of cognitive networks between left and right hemisphere motor cortices and sensorimotor cortices in the absence of movement (e.g., Biswal et al., 1995; Cordes et al., 2000; Lowe, Mock, & Sorenson, 1998; Xiong et al., 1999), in visual networks (e.g., Cordes et al., 2000; Hampson et al., 2002; Lowe et al., 1998), auditory and language networks (e.g., Cordes et al., 2000; Hampson et al., 2002), and, motor areas and association areas (e.g., anterior and posterior cingulate cortices) that are involved in attention, as well (Greicius et al., 2004). A "default mode network" (DMN) has also been proposed from the findings that

certain regions routinely decrease during attention demanding tasks and exhibit greater activity during rest (Fox & Greicius, 2010; Fransson, 2005). Some of the regions associated with the DMN includes medial frontal and posterior cingulate regions and the inferior parietal and medial temporal lobe. These are the most typically characterized regions that make up the medial frontoparietal network (M-FPN) (Uddin et al., 2019). This is in contrast to the hypothesized *"central executive network"* (CEN) that operates during cognitively and emotionally challenging activities. These regions are typically anticorrelated with the DMN (Braunlich, Gomez-Lavin, & Seger, 2015). However, some DMN (or M-FPN) regions need not be task-negative but could be engaged during goal-directed cognition as well, depending on the nature of the task (Uddin et al., 2019; Zhao et al., 2016). This underscores the suggestion of Chang and Glover (2010) that the M-FPN and other frontoparietal networks should rather be viewed as dynamic rather than static. Indeed, the DMN is especially associated with such as imagination, future-thinking, mind-wandering, spontaneous thought, etc., but is also likely involved in processes of reconfiguration, recollection, and association of internal and external stimuli based on current goal-states (Uddin et al., 2019). This may be worth to keep in mind while assessing RSFCs.

Resting-state before and after specific tasks has been investigated, and it is indicated that the resting networks might reflect a dynamic image of the current cognitive state, indicated by dynamic regulations of regional cerebral blood flow (CBF) (Waites et al., 2005). That is, despite of being in a state free of any externally imposed task, the intrinsic brain activity might reflect prior stimulus exposure (Fransson, 2006). There has been discussions on whether the observed changes indicate biophysiological regulations to a fixed baseline brain network or cognitive and/or behavioral changes associated with the setting, task, and subjective feelings around the setting and task (Waites et al., 2005). It might be that, within functional connectivity networks, some brain regions are more constantly involved than

others that might be more susceptible to alterations in activity during rest, depending on exposure (Waites et al., 2005).

Effective-state connectivity (ESC), which is the influence regions or systems have on each other during task performance, might provide insight to this issue (Friston, 1994). Measurements of effective connectivity are often on a different and shorter time scale than that of functional connectivity (milliseconds vs. seconds and hemodynamic vs. spike trains) (Friston, 1994). However, in multiple cases, researchers have found that low-frequency physiological fluctuations observed at rest are enhanced during task performance (Biswal, 2010). It has been suggested that this points to functionally active networks being chronically active at rest as well (Biswal, 2010). That is, it might be a phenomenon where the RSFC is analogous to the effective connectivity. However, it has been emphasized that functional connectivity do not need to be due to effective connectivity (Friston, 1994). It does at least seem convincing that there are occurrences of meaningful functional activity during periods of rest.

Goals and implications

The present project have multiple goals. One goal is to investigate further the usage of functional near-infrared spectroscopy (fNIRS) in neurocognitive purposes by comparing it and functional magnetic resonance imaging (fMRI) data derived from participants performing on the same non-verbal working memory task.

The reason why these two measurement instruments are suited for comparison, is because they share similar basis for their brain-signal acquisition. Both draw information about the brain activity from local changes in hemoglobin with oxygen ("*oxyhemoglobin*", *oxy-Hb*) and without oxygen (*"deoxyhemoglobin", deoxy-Hb*). These local changes come as consequences of changes in CBF due to active neurons' increased energy demand. Active

brain regions are supplied with a larger amount of oxygen than the rate of oxygen consumption by the neurons (a response called "*hyperemia*"). This produces a high local increase in oxy-Hb and a strong signal that can be associated with performance on a task (Boas, Dale & Franceschini, 2004a; Buxton, 2013; Ferrari & Quaresima, 2012; Logothetis, 2008; Pinti et al., 2018). However, it is worth mentioning that even though the two instruments essentially measure the same activity, it is with two different approaches: Functional MRI utilizes the different magnetic properties of oxy-Hb and deoxy-Hb (e.g., Logothetis, 2008; Buxton, 2013), whereas fNIRS utilizes the different optical properties of oxy-Hb and deoxy-Hb (i.e., they absorb near-infrared light at different frequencies) (e.g., Cai et al., 2021; Cai et al., 2022; Hoshi, 2007; Lu et al., 2010; Tak & Ye, 2014).

Comparable results between these measurement instruments would strengthen the position of fNIRS as a tool that can be deployed as a cheaper and more easily applicable alternative to fMRI. The instrument is also easier to deploy for research on vulnerable groups and can be applied flexibly in different settings. What has been great with fMRI is that it has driven profound advances about brain functions under well-controlled conditions. However, a new step for brain research is to seek a richer understanding of how these functions work in dynamic and complex real-world environments. This is something that fNIRS might contribute to.

A second issue that will be addressed concerns the differentiation between verbal and non-verbal working memory. The research on non-verbal working memory is scarcer than that on verbal working memory. Also, experimental structures and stimuli used to measure non-verbal working memory seems less uniform, possibly because it is more difficult to define what is *not* verbalizable compared to what *is* verbalizable. By combining multiple features that have previously been applied to measure visuospatial and non-verbal working memory (i.e., color, shape/patter, field positioning) we aim to increase the understanding of

the concept, and to possibly come closer to a task that can be used more consistently to measure and capture it.

Furthermore, we aim to investigate resting-state in fMRI and fNIRS. Few studies have measured resting-state with fNIRS, and fewer have combined fNIRS resting-state measurement with other complementing instruments. Both instruments have previously been used to measure RSFC and are deemed to be able to capture the concept. Despite the fact that fNIRS might not supply much more insight compared to fMRI when it comes to brain coverage, there are some reasons for using fNIRS as well: for example, (1) it can be flexibly applied to different settings and conditions that fMRI cannot match; (2) it can be used more easily on almost all human subjects; (3) it can provide additional information on metabolic changes compared to the blood-oxygen-level-dependent (BOLD) fMRI; and (4) it has a higher temporal sampling rate than fMRI (Lu et al., 2010). These benefits are believed to produce a more reliable RSFC estimate than that from fMRI. Furthermore, it has been suggested that within-subject assessment in addition to group examinations could be an important ingredient to uncover fully dissociable networks (Braga & Buckner, 2017; Braga et al., 2019). However, fNIRS can only capture outer cortex signals, and, in this case, it will not cover the whole brain either.

There are multiple advantages of using both fMRI and fNIRS for RSFC measurement. One clear advantage is that effects of different settings during resting period can be measured. This will probably involve differences in both biophysiological states (e.g., blood pressure, respiration), that comes from laying down during fMRI versus sitting during fNIRS, and cognitive states, that comes from focusing on a fixation cross in a rigid environment in the MR-machine versus being able to look around in a regular seminar room and out of a window with both nature and city view during fNIRS measurement. Furthermore, since the

participants perform on the same task in both experimental settings, task-related variables such as task expectations and familiarity may alter RSFC from the first to the second trial.

That is, the interests of this project involves collecting data on brain activity and behavioral responses from two comparable neuroimaging instruments (i.e., fMRI and fNIRS) while participants perform on a non-verbal, visuospatial working memory task, to see whether they capture any differences in the neurological and behavioral domains. However, we expect the results to be similar between them, as they, in their essence, collect information about neural activity from the same source (i.e., blood oxygenation levels). This expectation is not only limited to the data derived from task performance but is the same for the resting-state measurements as well. However, we are aware that some variables, such as differences in settings and time and order of task performance, could affect the results.

Hypotheses

First and foremost, we expect that fMRI and fNIRS yield comparable results of brain activity in the corresponding regions that are captured by both of them (Hypothesis 1, H1). Globally, we expect more right than left hemispheric activity because of the non-verbal and visuospatial nature of the task (Hypothesis 2, H2). We expect prefrontal regions to be involved in every aspect of the working memory performance (Hypothesis 3, H3). We also expect to see a frontoparietal network activation (Hypothesis 4, H4).

Also, since the information is assumed to be unfamiliar to the participants, we do not expect much MTL activation as they probably have no stored LTM information that can support the working memory. Thus, the expectation is that the participants need to rely more purely on perceptual representations, which should give higher activity in the visual perception system. Therefore, it is expected that visual pathways are activated during the trials, with both dorsal and ventral processing pathways to be activated: Ventrally, from the

occipital lobe to the inferior temporal cortex, which is associated with object recognition and visual memory of objects and patterns, with high selectivity to complex object shapes (Hypothesis 5A, H5A) (Lehky & Sereno, 2007). Dorsally, the activity is expected to progress from the occipital lobe to superior regions of the parietal cortex, which is associated with spatial locations and selection of shapes (Hypothesis 5B, H5B) (Lehky & Sereno; 2007; van Polanen & Davare, 2015). At last, we expect that resting-state measurements reveal DMN activations (i.e., M-FPN activity), however, with effects of the task from the first session to the second session (Hypothesis 6, H6).

Methods

Measurement Instruments

The study will aim to further develop understandings of the brain processes behind the theoretically conceptualized working memory system, with a special focus on the non-verbal working memory. To examine this, fMRI and fNIRS will be used.

fMRI is a tool for measuring hemodynamic changes that comes with enhanced neural activity (Logothetis, 2008). What makes fMRI *functional* is the association that is made between localization of where brain activity takes place and the performance on a task and/or a behavior. For the investigation of brain functionality, some of the profound advantages that fMRI have are the (1) noninvasive nature of the tool, (2) relatively high spatiotemporal resolution, and (3) capacity to demonstrate complete brain networks during task performance (Logothetis, 2008).

fMRI provides direct measurements of tissue perfusion, blood-volume changes, or changes in oxygen concentration. However, it can only provide an indirect measurement of neuronal activity. The blood-oxygen-level-dependent (BOLD) contrast mechanism is the most common tool in human neuroimaging (Logothetis, 2008). As noted earlier, the fMRI (BOLD)

signal is derived from a paradoxical scenario, where venous blood is more oxygenated despite of the increased metabolic usage of oxygen, because the CBF increases in a larger scale than the metabolic rate (Buxton, 2013; Pinti et al., 2018). That is, the BOLD signal reflects a local increase as a result of reduced oxygen extraction factor (OEF) during increased neural activity (Buxton, 2013).

The tool takes advantage of the differential magnetic properties of hemoglobin saturated with oxygen ("*oxyhemoglobin", oxy-Hb*) and hemoglobin lacking oxygen ("*deoxyhemoglobin*", *deoxy-Hb*). In short, the MRI machine can be used to introduce an external magnetic field so that their magnetic properties can become evident. Brain areas with more oxyhemoglobin will give higher signal and appear brighter than deoxyhemoglobin. The brighter areas are utilized to indicate more brain activity. It is worth mentioning that it is only the relative change between oxy- and deoxyhemoglobin that causes signal changes. Therefore, a region with 100% oxy-Hb would not be seen as active.

The physiological variables that affects the BOLD-effect are combined changes in CBF, cerebral metabolic rate of oxygen ($CMRO_2$), and the cerebral blood volume (CBV), which drives changes in local deoxyhemoglobin concentration (Buxton, 2013). All these variables tends to increase with increased neural activity, but they have conflicting effects on the BOLD response (Buxton, 2013). That is, increased CBF "washes" out deoxyhemoglobin; increased $CMRO_2$ increases local production of deoxyhemoglobin; and increased *venous* CBV increases total deoxyhemoglobin content, which partially offsets the effects of the OEF change, whereas increased *arterial* CBV pushes out extravascular fluid and increases the measured signal through volume exchange. Thus, increases in arterial CBV typically produce a larger fMRI signal as it adds a positive signal change to the oxygenation-dependent change associated with deoxyhemoglobin changes (Buxton, 2013). Changes in these factors are mostly affected by changes in the neuronal excitation-inhibition balance (Logothetis, 2008).

Even though fMRI has clear advantages, there exists some shortcomings as well: (1) It is an expensive tool; (2) the testing environment may cause some discomfort and stress to participants; (3) the participant often needs to lay very still for a relatively long period of time, which impedes naturalistic behavior; (4) because it provides quantitative measures of physiological variables, it can be difficult to interpret the data in terms of underlying physiology; and (5) there is a hemodynamic response sensitivity to the size of activated neuron population, which can cause possible confusions about function-specific processing, bottom-up/top-down signals, and excitation and inhibition when interpreting data (Logothetis, 2008).

Despite of these shortcomings, fMRI is an important tool for making testable hypotheses about the functional organization of the whole brain, which can be tested through specialized experimental designs. In relation to working memory, it is an advantage that it allows for global testing of large-scale neuronal populations, as content-specific activity can be measured across the brain, and as important properties of WM probably emerge from large-scale network activity (Foster et al., 2019).

fNIRS aims to measure functional activation through tissue oxygenation and regional hemodynamic changes (Ferrari & Quaresima, 2012). Thus, what is measured with fNIRS is equivalent with that of fMRI. Both are noninvasive, but fNIRS can only capture activity in the cerebral cortex and uses near-infrared light in the range of 650-950 nm (λ). This tool takes advantage of the properties of the different abilities oxygenated and deoxygenated hemoglobin has when it comes to absorption and scattering of near-infrared (NIR) light. Oxygenated hemoglobin absorption is higher for $\lambda > 800$ nm, whereas deoxygenated hemoglobin absorbs better the NIR light at $\lambda < 800$ nm. This leads to changes in light attenuation, which can be measured by fNIRS. These differences are quantified through spectroscopic measurements. It is worth to mention that previous studies have shown that the

most sensitive indicator of changes in regional CBF in fNIRS measurements is oxy-Hb (Hoshi, 2007; Lu et al., 2010).

Optodes (emission and detection probes) are placed on the scalp of the head where near-infrared light is sent in, whereas photodetectors are placed nearby (1-3cm) to detect scattering and backscattering of the light. The goal is to gain information about brain tissue activity through the relative transparency of the optical window the light can reach through (Pinti et al., 2018) An issue with the method has been to develop detector systems that can distinguish cerebral tissue activity from extracerebral tissue activity, as the signals are detected from the scalp. Furthermore, the data from fNIRS does not provide anatomical information on the brain cortex (Cai et al., 2021). Thus, there might exist some uncertainties about which brain regions are sampled by fNIRS (Hoshi, 2007). However, quite precise geometric points of scalp surface locations and underlying cortical regions can be obtained from scalp-cortex correlations of light propagation (Cai et al., 2021). What this discussion essentially highlights is that fNIRS provides *functional*, rather than *structural*, information of the brain.

A clear advantage of fNIRS is that it is less restraining than fMRI, which makes it easier to apply on populations who will struggle under restrained conditions (e.g., children and individuals with neurodevelopmental disorders such as autism and attention-deficit hyperactivity disorder). It can be deployed more naturalistically than fMRI because it is portable and has relatively low sensitivity to body movements (Pinti et al., 2018). However, both fNIRS and fMRI can become corrupted by measurement noise, motion artifacts, and a multitude of physiological noise of non-neural origin, such as cardiac pulsation, respiration, and blood pressure Mayer waves (Boas et al., 2004a; Boas et al., 2004b; Caballero-Gaudes & Reynolds, 2017; Tak & Ye, 2014). These noise signals can be due to several reasons, but can occur with such as head movements, natural fluctuations in respiration and blood flow that

interfere with the signal, and the instrumentation (i.e., field strength and measurement wavelengths) (Boas et al., 2004a; Caballero-Gaudes & Reynolds, 2017). These issues can, however, be denoised and improved through statistical techniques. After applying these techniques to the fNIRS or fMRI data, the hemodynamic response to a task (or resting-state) should be larger in magnitude than non-neural fluctuations or other noise contributions if it shows to a true effect. An advantage of fNIRS is that it can provide a nonlinear and more direct measurement of blood-oxygen changes than the BOLD signal in fMRI. This offers the possibility of disentangling blood flow and oxygen consumption changes (Hoge et al., 1999; Tak & Ye, 2014). Thus, a more precise map of functional connectivity can possibly be drawn.

Participants

12 normal volunteers (7 males, 5 females) participated on the fMRI part of the study. 11 of the same 12 participants took part on the fNIRS part (7 males, 4 females). Only one of the participants performed on the fNIRS part first and the fMRI second. All the others performed on the fMRI part first. One of the males was left-handed, whereas the other participants reported right-handed dominance. None of them had any history of neurological disease. They were compensated with 200NOK for their participation on the fMRI part and 100NOK for their participation on the fNIRS part. The total compensation of 300NOK was separated between the two trials so that they would gain something from participating on each of the parts.

Before their first performance, all of the participants were introduced to the n-vWM task. All of the participants received the opportunity of both verbal and visual instructions of the task and the material. Most of the participants received the opportunity to run a trial version of the task through E-prime Go, as well. However, that was not possible to offer for all. As a compensation, those who did not test the trial version received a more thoroughly written

description of the task design and the material. The fMRI trials always occurred on Thursdays between 8:00 to 11:00 AM, with two possible slots (i.e., 8:00-9:30 or 9:30-11 AM). The fNIRS trials occurred on relatively consistent times as well: they took place on Fridays, where the times mainly ranged from 14:00 to 18:00 PM.

Ethics

The project was approved by *Regional Committees for Medical and Health Research Ethics* (Ref: REK-Vest, 536776). All the participants received the same information about the project and signed a consent form. This involved information about the purpose of the project, what they would go through during participation, possible advantages and disadvantages of participation, duration, that it would be voluntary and that they could leave and/or withdraw at any point without being questioned about why, how the information would be handled so that privacy and anonymity would be respected and safeguarded, their rights to view the data, and about insurance, approvals and contact information. Furthermore, it was informed that the information would be treated according to the EU's General Data Protection Regulation (GDPR), article 6a and 9 nr. 2a. Thus, the participants gained clear information about both what their own role in the project would involve, and how the researcher's code of conduct would be. These ethical considerations serve as means for securing respectful treatment of the participants themselves and the information derived from them. Furthermore, they function as critical principles for the researcher's actions during the entire project.

Regarding the role of the researcher, there are some neuroethical considerations that follow neuroimaging data. At a scientific level, there are several challenges surrounding the integration of knowledge and meaningful interpretations. This may involve influences from such as social, cultural, and financial perspectives, and results may influence these aspects as well (Illes & Racine, 2005). Neuroimaging research has expanded extensively to several

aspects of our everyday life. With this in mind, it is crucial to be aware of not only the integration of prior knowledges and interpretations with new findings but also of how it is framed. Researchers should as well be familiar with what the data look like. For example, if the data is shared and pathology is discovered unexpectedly by those who receive the data, then it raises a great question of who is responsible and how it should be handled (Illes & Racine, 2005). In the end, the brains and data that are used for neuroimaging purposes come from living human beings.

Materials

Measurement of non-verbal working memory was operationalized through two-dimensional Gabor filters, which are sinusoidal grating patches commonly used for visuospatial purposes in neurophysiological, psychophysical, and clinical studies (e.g., Foley et al., 2007; Ringach, 2002; Syväjärvi, Näsänen & Rovamo, 1999; Westheimer, 1998). Typically, these are greyscaled and involve variations in tilting/rotations and frequencies/dilations. Depending on the frequency of the patterns, different receptive fields of the retina with different spatial sensitivities are likely to contribute to detection (Foley et al., 2007).

In this study, they were manipulated with green color nuances and field positions as well. The visuospatial features of Gabor patches, color, and changes in field position were combined to increase the complexity of the fields and possibly make the stimuli more distinctive from verbal operations.

In this study, we followed the example of Wu et al. (2020) who used 64 variants that were manipulated in tilting, from left to right from 105° to 255° in equally spaced intervals, and stripe frequency from 1.5 to 15 log intervals (see Appendix A). These were combined with green color nuances with the use of python. The nuances involved variations in

brightness (0.3-1.8), sharpness (1.0-5.0), saturation (0.2-0.4), and temperature (0.1-0.6) (i.e.,

variations in chroma and value within the hue) (see Appendix B). These alterations were

deemed to make the stimuli more complex and demanding for visual perception, and, thus,

more difficult to verbalize.

Thus, visual non-nameable objects with different features codes have been applied in

this project. This varies how easy/difficult it will be both to release prior stimuli from memory

and refresh capacity for the coming ones. The stimuli should have a broad range of feature

similarity and dissimilarity. For this reason, a stimulus sample of 3840 Gabor filters were

created. That is, for each of the 64 Gabor patterns, 60 color nuances were made. It is also

worth to note that the positions in the presentation field were manipulated as well. These are

all the variations in the "perceptual set" of the task.

Procedure: Working memory task

The experimental task draws inspiration from the Wisconsin Card Sorting Test

(WCST). Both involve set-shifts and a change-detection paradigm. However, there are some

clear contrasts to the WCST with this task: (1) only one stimulus is shown at the time during

change-detection; (2) the participant receives instructions about the "rule" they are supposed

to track changes in; and (3) the participants do not receive signals about whether their

response was correct or incorrect according to the rule. One reason for not providing feedback

about correct/false responses to the participants is to reduce the participant's certainty of

learning and providing as little means as possible for action planning during the task.

The specific structure of the task involves a question about one of the three

stimulus/field features (i.e., "Same color?", "Same pattern?", or "Same position?") or whether

everything is identical (i.e., they need to track color, pattern, and position simultaneously).

That is, there are four conditions in this task: (1) Color, (2) pattern, (3) position, and (4) all

three of them at the same time. The study design followed a block-design. Despite of some neurophysiological drawbacks of block-designs, they have some advantages as well: they produce robust results, have increased statistical power compared to, for example, event-related designs, and show relatively large BOLD signal change related to baseline (Amaro & Barker, 2006). The task consisted of eight trials per condition and was repeated four times. This represents the ON-blocks of the study. These questions make up the "attentional sets", as they function to aid and drive detection. The question was followed by a reference symbol, then a delay period with time variations ranging from 500ms to 6000ms, and, lastly, a target symbol. A "Relax" period (OFF-block) that lasted 20s was introduced after the end of each ON-block. The task is to evaluate and respond rapidly whether the target symbol is identical to the reference symbol, or not, in correspondence with the question at hand (see Figure 3 for illustration). To assure that the task had a variation of similar/unsimilar reference and target symbols, E-prime was set to a 50% probability of similarity across the four repetitions of each condition. That is, within a block of trials, the probability could be higher or lower. Half of the participants used right hand for "Yes" / "Same" and left hand for "No"/ "Not the same", whereas the responses were flipped for the other half.

Figure 3

Example of how one trial of the task could look like
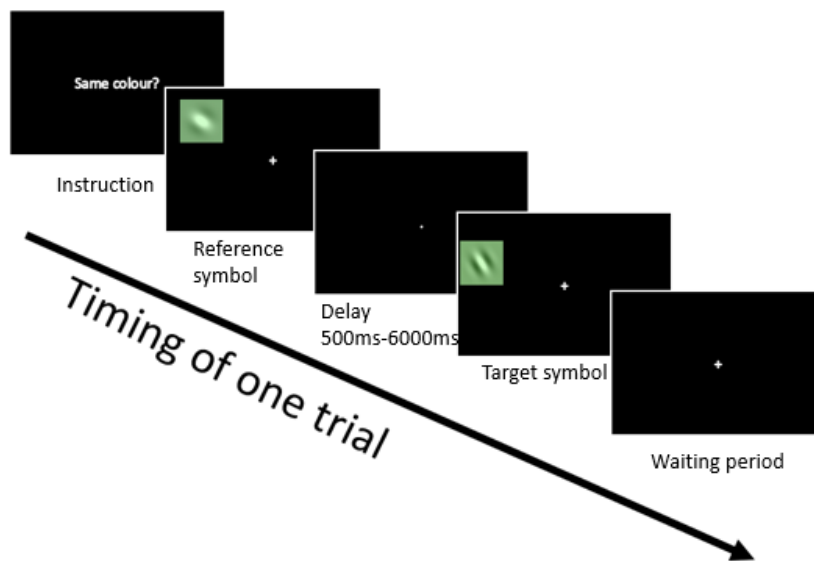
Earlier, it has been reported that similarity between probe and target stimulus affect WM performance more than the complexity of the item itself (Cyr et al., 2016; Foster, Vogel, & Awh, 2019). That is, the stimulus discernability, which at least reflects the difficulty of the task, heightens the loading more than what the feature complexities of a single stimulus does. Therefore, it makes more sense to ask for change-detection in features between a reference stimulus and a target stimulus rather than remembering features of a single stimulus.

The fact that the other properties of the stimulus than that of questioning could be varied and still be seen as identical according to the "rule" at hand, makes the task more naturalistic. The task can be seen as naturalistic as well if the aforementioned point is coupled with the function of varied delay period time. That is, in the real world, the environment may involve information that shares many feature similarities, and on many occasions, we have to respond to it quickly. Often, we have some notions for the prediction of when something will occur and how it will look. However, we cannot always be certain of *exactly* when or how it takes shape. Therefore, to match real world events, the delay between reference and target

stimulus and the difficulty level of stimulus discernability should be varied sufficiently (Barch et al., 1997; Lundqvist et al., 2018; Rothmayr et al., 2007). This task was taken seriously, as indicated by the random delay variation (1s-6s) and a large stimulus sample.

In its essence, the task is a working memory discrimination and recognition test for novel, visual items and spatial positions, where performance depends on the ability to identify and hold them in mind and respond quickly to new information. It fits the pattern of many visuospatial short-term memory tasks, in contrast to verbal auditory tasks, which rely more on identification of order or remembering of serial order position/time of presentation (Davis, Rane, & Hiscock, 2013). Since the task involves variations in both color and form, as well as position, it tests both non-verbal visual *and* spatial processing and storing capacities. Logie (1986) showed that imagery tasks could be visual rather than spatial. Later, multiple cases have supported the distinction between visual and spatial STM (Klauer & Zhao, 2004; Baddeley, 2012; Borst et al., 2012). Thus, it is an advantage that the task should tap well into both.

Procedure: Resting-state design

Resting-state was measured with both fMRI (rsfMRI) and fNIRS (rsfNIRS). During both fMRI and fNIRS, there were two resting-state sessions: One before the WM task and one after the task. Both sessions lasted five minutes. However, the setting of the two measurements were qualitatively different. During the rsfMRI sessions, the participants were laying in the MR-machine and instructed to look at a fixation cross. On the other hand, for the rsfNIRS sessions, the participants were sitting in a regular seminar room with window view of both nature and city.

A great practical question to resting-state measurement concerns how much data to acquire. Time of measurement in the current study was of 5 minutes, which matches the time

perspective most research of fcMRI have been using (Birn et al., 2013). Also, test-retest rs-fcMRI studies have mainly focused on scans between 3 and 11 minutes in length, which have shown to provide relatively stable estimates (Birn et al., 2013). It has been suggested that longer resting-periods would be more appropriate for capture of the phenomenon, but the current time of the resting-state measurements is suited for comparison with the majority of resting-state-measuring studies (Birn et al., 2013). Also, the decision of using 5 minutes, and not more, is related to the already long duration of the experimental task.

Data analysis: fMRI (n-vWM)

A 3T Siemens PRISMA scanner was used to perform functional MR imaging of the 12 subjects at the Radiological department of the MR-section at Haukeland University Hospital. The anatomical scans consisted of 192 sagittal slices, a 256 x 256 matrix, repetition time (TR) of 1.8s, time to echo (TE) of 2.3ms and high-resolution isotropic voxels of 1 x 1 x 1mm. For the fMRI scans, echo planar imaging (EPI) was performed. Also, both the working memory fMRI and rsfMRI were measured with a TR of 2s, a TE of 30ms, 36 axial slices, a 64 x 64 matric, and voxel size of 3.6 x 3.6 x 4.4mm. However, they differed in volumes, with 650 on the working memory task and 160 on resting-state measurements.

The fMRI-data were first pre-processed and analyzed with the SPM12 software package (https://www.fil.ion.ucl.ac.uk/spm/). Standard SPM parameters were applied through MATLAB (MathWorks Inc., Natick, MA, USA).

Each participant was analyzed with a standard SPM routine, starting with corrections of head movements. Motion corrections have the important function of regulating that voxels provide information from the specific locations they initially had. Also, motion may produce confounds as it produces signal. It does not solve every aspect of the movement-magnetic

field interactions, but it is an important tool for making the images more defined and increase our chances of securely stating where the signal came from.

The corrections of head movements were followed by co-registration of anatomical image and fMRI, segmentation and normalization of the anatomical image. These steps involves registering together different structural images (i.e., T1 anatomical scan and the mean image, produced during the realignment procedure), translating, rotating, and scaling of each subjects' brains so that they are warped into a so-called "*standardized space*", and spatial averaging. This was followed by application of the normalization on the fMRI images. The preprocessing ended with an applied Gaussian kernel of 8-mm for smoothing. The smoothening is meant to cancel out noise and enhance signal, which in turn increases the possibility of more overlap between clusters of signal during group analyses. In sum, these techniques are applied to secure as little disparity between the fMRI and the anatomic data as possible.

After this was done, the fMRI time series was analyzed with a General Linear Model (GLM). The GLM analysis and design matrix contained six movement parameters. The design matrix matches the block design. Contrasts was defined for each condition. That is, for color [1 0 0 0], pattern [0 1 0 0], position [0 0 1 0], and all [0 0 0 1]. These generated "*con-images*", one for each person and task condition. A high-pass filtering (640s) was applied, however, with adjustments due to relatively long blocks. Without the adjustments, much of the true signal would have been filtered out. What the high-pass filter does is removing low frequency components that can be seen as noise. Ideally, the choice of cut-off would maximize the signal/noise ratio. The procedure was equal for each participant.

The resulting contrast images were used as input for a SPM second-level analysis of the con-images, which followed an ANOVA model so that results from the 4 conditions could be compared across using t-tests. All comparisons were made with a family-wise error (FWE)

corrected significance threshold of 0.05. That is, the threshold was set with a probability of $p_{FWE} < 0.05$ from wrongly concluding that a family of voxels are significantly modulated during the active state. So, in its essence, FWE is merely a term for the false positives you "allow" in a test. The FWE-correction approach has the benefit of controlling the alpha error across every voxel and is believed to correct for the "multiple comparisons problem" (MCP) (also called the "multiple *testing* problem"). The problem stems from the fact that when the number of tests increases the number of false alarms increases too. With fMRI data, information about brain activity is gained from thousands of voxels, and in this case 212548 voxels. A voxel-wise analysis would run a separate hypothesis test for each voxel. Thus, the number of potential alpha errors would be massive, even with a significance level of 5% ($p < 0.05$). Therefore, it is an advantage to run multiple hypothesis tests with *clusters* of voxels. With $p < 0.05$ (FWE), the expected number of voxels per cluster was 3.845. This provides a dramatic decrease of the possibility of wrongly deeming activity as significant compared to what a voxel-wise analysis would.

The underlying idea is that activation is zero *everywhere*. Thus, a significant finding would indicate that the noise fluctuations in a cluster of voxels strongly differs from zero and shows an effect that is not merely random noise, but rather reflect true differences in the data. In this case, several clusters showed a high significance level. Thus, a FWE corrected p-value of $p < 0.005$ (i.e., $\alpha = 0.005$) was implemented to find those areas of activation that would "survive" with a higher threshold (T = 4.82).

The t statistic is essentially testing the null hypothesis that there exists no linear relationship between the conditions of interest and the voxel values. It is an index of how far the slope differs from zero, while accounting for the error of it. Even though it is clear that our measurement will be subject to error when we only have a few observations (12 respectively with fMRI, and 11 with fNIRS) and that the SPM statistics still carry a multiple comparison

problem, t-values that exceed the threshold of α = 0.005 seems unlikely to come by chance. However, that needs to be interpreted with caution; *"unlikely"* does not exclude the possibility that the distribution would support the null hypothesis with a larger sample and different group of participants.

Full Width at Half Maximum (FWHM) of the Gaussian Kernel represents smoothness of data, and with 3-D data, it is represented as a 3-vector. In this case, it was 10.1_X mm, 10.4_Y mm, 9.6_Z mm; 5.0, 5.2, 4.8 in voxels. The Gaussian spatial filter tends to be larger for multi-subject analyses, typically 6-8 mm. The FWHM is not the *applied* smoothness of the data. Rather, it reflects a combination of the intrinsic smoothness of the data that is fed into the GLM. The applied smoothness was, as mentioned above, of 8mm.

Data analysis: rsfMRI

The fMRI resting-state analysis was performed using the CONN-Toolbox. Data were processed using the standard pipeline, which includes correction of head movement, coregistration of the anatomical scan with the fMRI scans, segmentation, and normalization. Further, the CONN standard routines for denoising of the data and removal of artefact were implemented. Using the implemented standard atlas, ROI-ROI seed-based analyses were performed. Connectivity measures for the two resting-state scans, before and after the WM task, were statistical compared.

Data analysis: fNIRS (n-vWM)

The fNIRS setup consisted of 42 measurement channels, with an inter-optode distance of 1-3mm. Positioning of the array was in accordance with the international 10-10 system, with guidance from the fNIRS Optodes' Location Decider (fOLD) Toolbox (Morais, Balardin, &

Sato, 2018). The regions that were covered consisted mainly regions the of parietal cortex, temporal cortex, and the ventral PFC.

Standard settings for filtering was applied, which involved the removal of discontinuities, using a band-pass filter, and corrections of heartbeat and respiration. Furthermore, a high-pass filter of 160s was applied. For each of the participants, the entire time series was clipped to a total length of 1250s to remove potential disturbances that would come with each time we entered the room. In contrast with fMRI, the onsets of all four conditions were collapsed into one condition due to limitations in the available analysis software. As with fMRI, the data was analyzed with a specified GLM model on a subject-by-subject basis. However, a regular group analysis was not possible in the provided software.

Data analysis: rsfNIRS

fNIRS resting-state analysis was performed as a simple correlation analysis. After preprocessing of the fNIRS data, including removal of discontinuities and filtering, as described above, correlation matrices were estimated for each subject and the two sessions separately. For technical reasons, only 10 subjects could be analyzed since there was a missing resting-state dataset for one of the 11 subjects. Also, the correlation values were not normally distributed. Thus, to perform linear statistics, they needed to be transformed. Therefore, each correlation matrix was transformed into Z-scores using Fisher's Z-transformation.

Two analyses were performed. The first involved estimating the averaged correlation across subjects and sessions, which was evaluated with a one sample t-test. The second involved estimating differences in correlation coefficients between session 1 and 2 (i.e., before and after the n-vWM task), and the difference scores were subjected to a one-sample t-test, as well. Since this was only an explorative analysis, and resting-state fNIRS hasn't

become a standard routine so far, results were explored with a p-value of $p<0.05$, not corrected for multiple comparisons.

Results

fMRI (n-vWM)

SPM analyses showed no significant differences between the four conditions. Thus, a conjunction analysis of all conditions was implemented. This allowed joint analyzation of all the conditions. The analysis showed significant activations in a cluster of the right and left precuneus (PCu), and left superior parietal lobule (SPL), with peak x, y, z mm coordinates at 12, -72, and 58. Furthermore, significant activations were found in right supramarginal gyrus (SMG), with peak voxel coordinates at 40, -34, and 40. In addition, significant activity was revealed in right precentral gyrus (PrG), with peak at 46, 2, and 32. All conditions also produced significant activations in right middle frontal gyrus (MFG), supplementary motor cortex (SMC), and left superior occipital cortex (SOC), with peak x, y, z mm coordinates respectively at 44, 32, and 36 in the MFG, at 2, 6, and 54 in the SMC, and at -26, -76, and 26 in the SOC (see Table 1 and Figure 4 below for statistics and visualizations).

Table 1

SPM statistics from a conjunction analysis of activation effects from all conditions

Activation from the participants on all conditions							
Non-verbal working memory							
Statistical values			**Coordinates**			**Anatomical location**	
Cluster level		Peak-level					
Ke	pFWEcorr	*T*	*x*	*y*	*z*	Hemisphere	Structure
2125	**<0.001**	**9.92**	**12**	**-72**	**48**	**Right**	**PCu**
	<0.001	9.03	-8	-70	46	Left	PCu
	<0.001	8.15	-34	-60	56	Left	SPL
252	**<0.001**	**8.74**	**40**	**-34**	**40**	**Right**	**SMG**
	<0.001	7.54	48	-30	42	Right	SMG
	<0.001	6.53	46	-42	52	Right	SMG
410	**<0.001**	**8.56**	**46**	**2**	**32**	**Right**	**PrG**
	<0.001	6.67	50	6	44	Right	PrG
100	**<0.001**	**7.65**	**44**	**32**	**36**	**Right**	**MFG**
33	**<0.001**	**6.03**	**2**	**6**	**54**	**Right**	**SMC**
36	**<0.001**	**5.54**	**-26**	**-76**	**26**	**Left**	**SOG**

Note: Ke = cluster size. pFWEcorr = p-value corrected for family wise error. PCu = Precuneus. SPL = Superior parietal lobule. SMG = Supramarginal gyrus. PrG = Precentral gyrus. MFG = Middle frontal gyrus. SMC = Supplementary motor cortex. SOG = Superior occipital gyrus. Lines printed in bold denote the most significant voxel. The labels of the activated brain regions have been identified with SPM12 neuromorphometrics. The labels are defined from their respective x, y, z values (mm).

Figure 4

3D heatmap models of the brain from all the conditions of the n-vWM task conjoined.
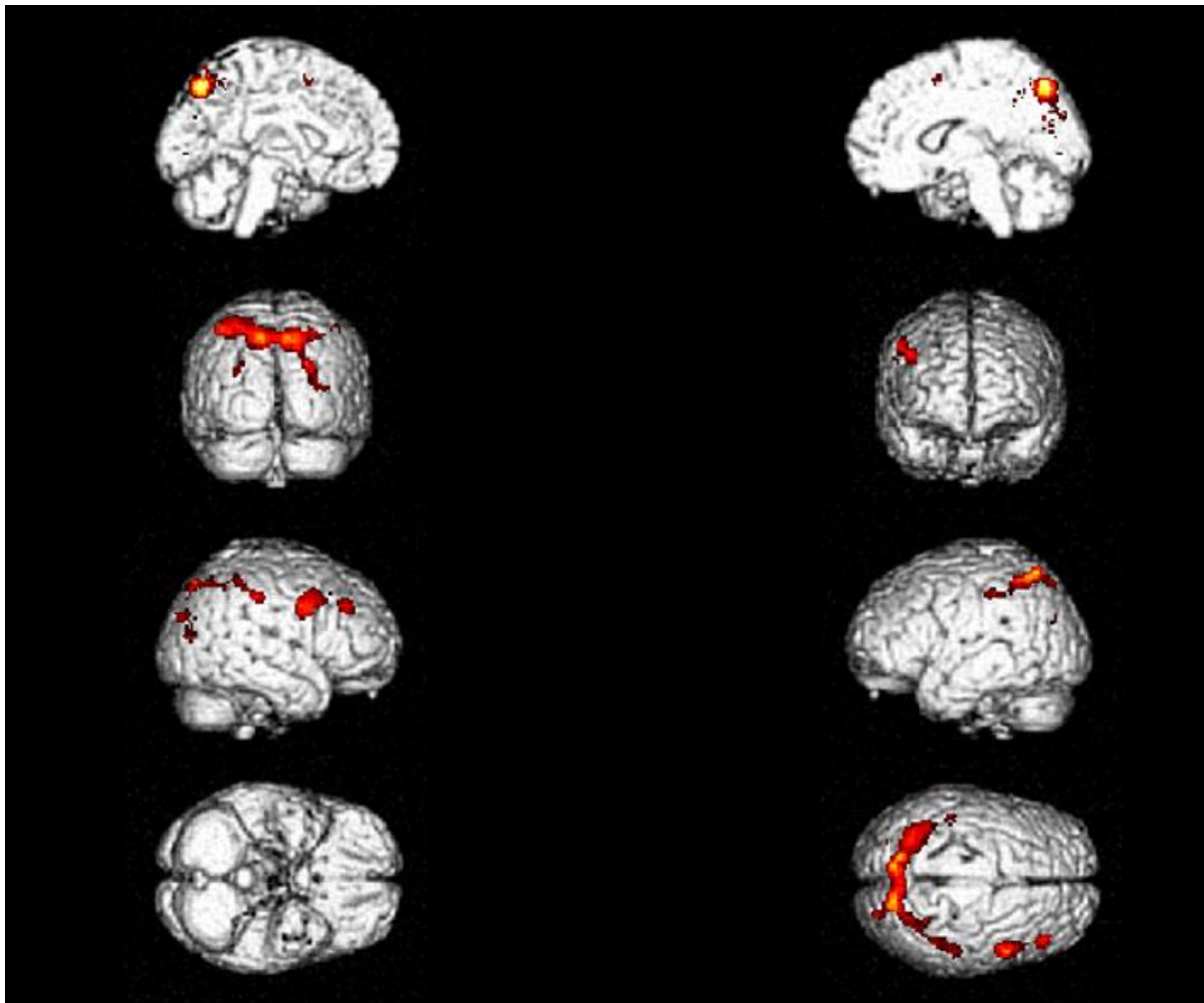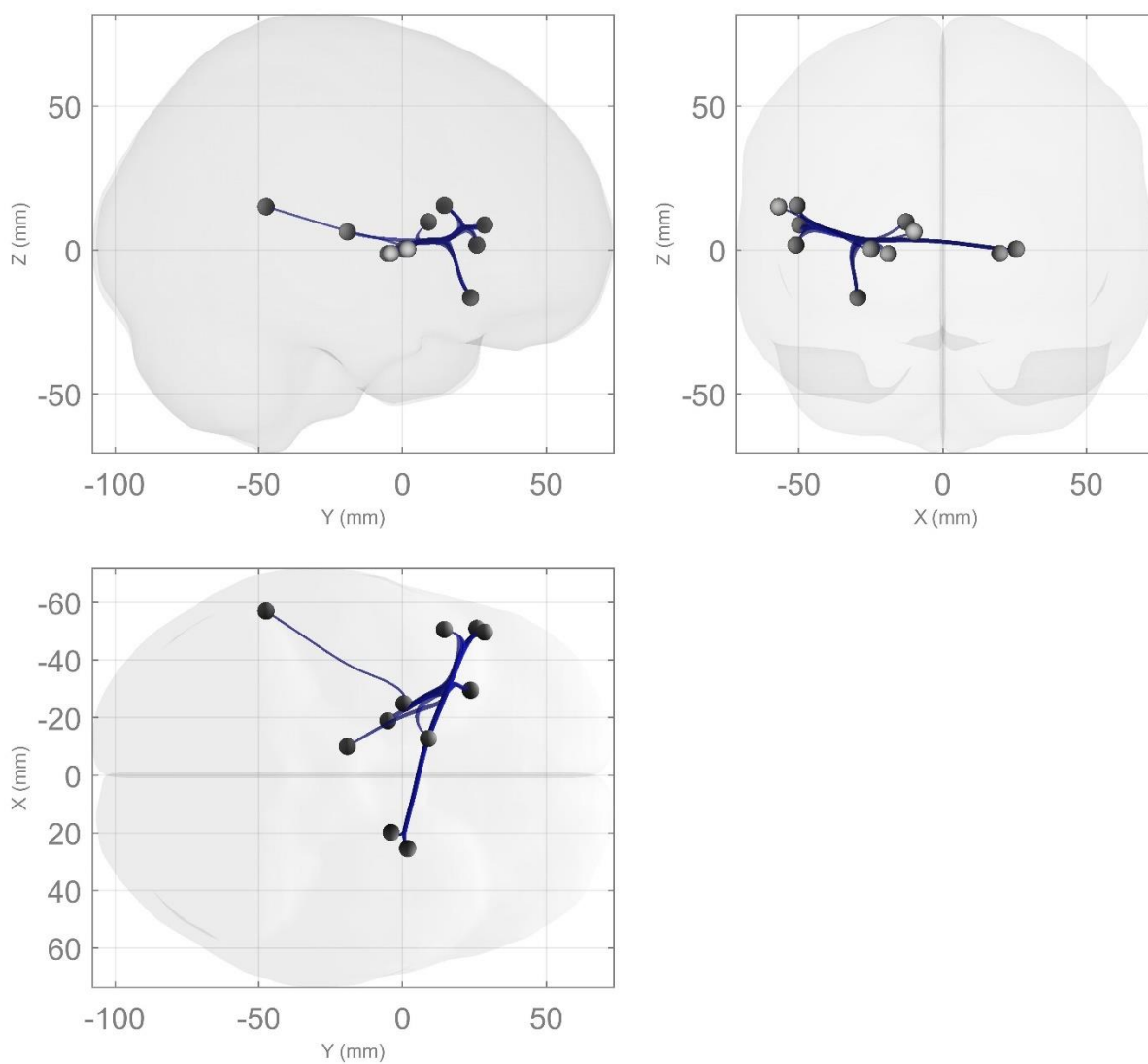

rsfMRI

Only one cluster of connections showed a significant difference between the two sessions. This cluster circumscribes the connections between the putamen and pallidum to left frontal areas (see Figure 5 and Figure 6).
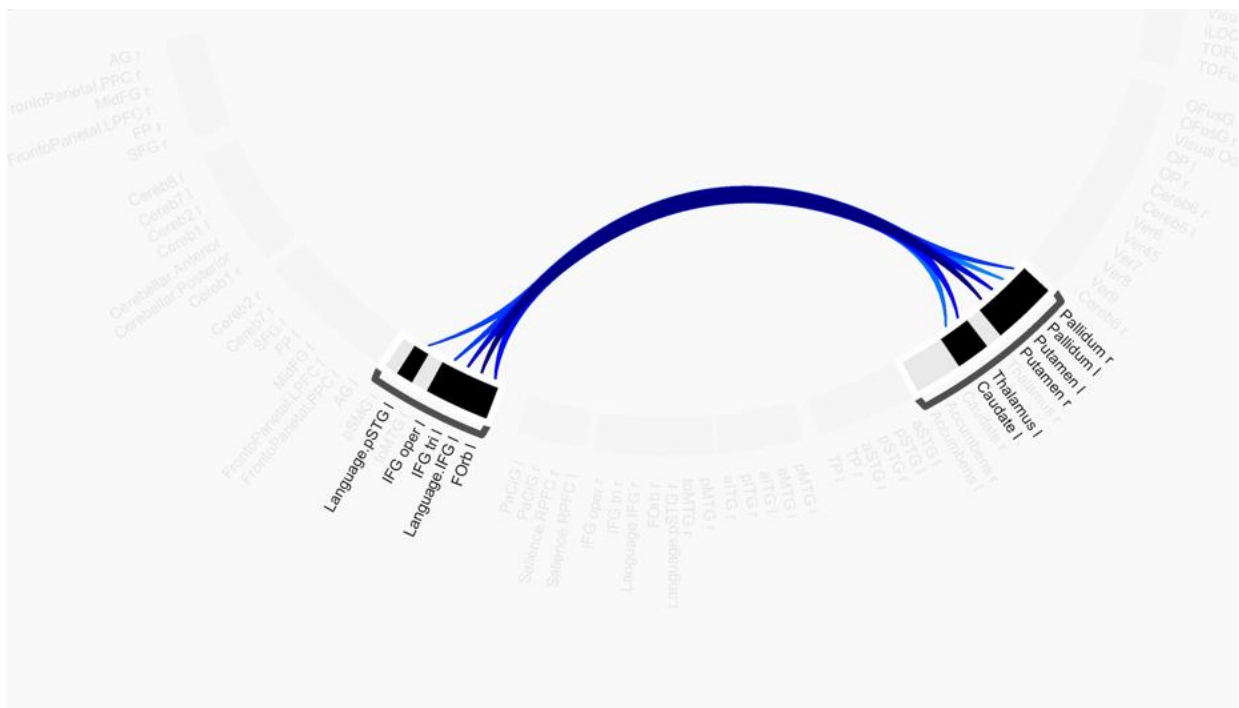
Figure 5

Brain regions with significant differences in resting-state from first to second WM session.

NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

Figure 6

Visualization of regions that show higher R-S functional connectivity between the sessions.


fNIRS (n-vWM)

There was no significant finding on group level for the non-verbal working memory task. It must be emphasized that the data suffers from high variability. This can clearly be seen in the matrix below, showing t-statistics from all subjects for every channel (Figure 7), and in the examples of two subjects, where one showed little activity (Figure 8), whereas the other mainly showed negative activity (Figure 9).
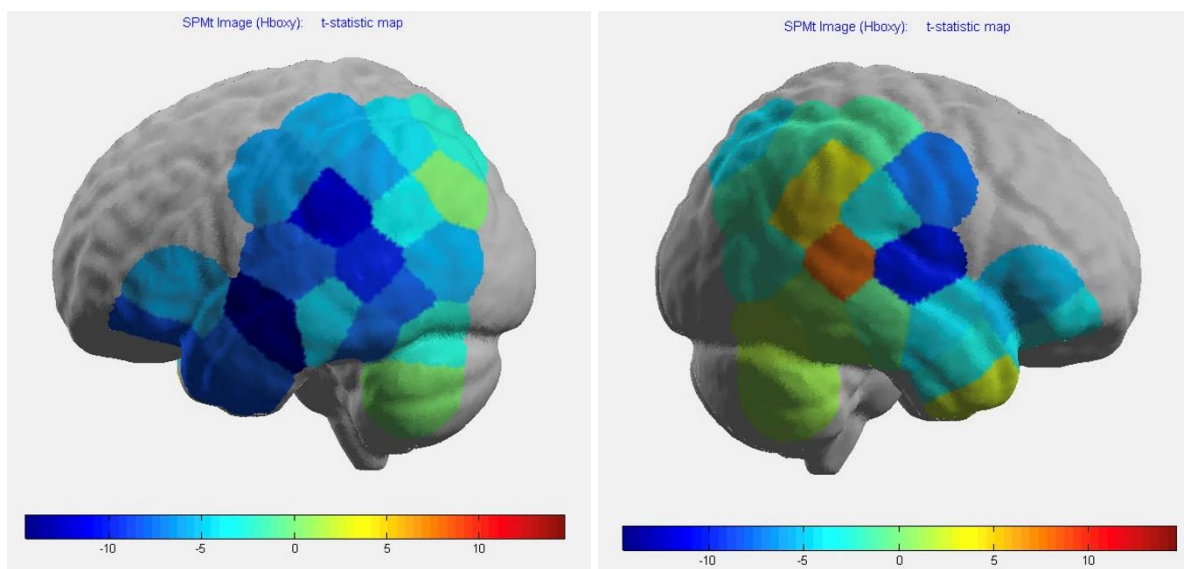
Figure 7

A matrix showing t-statistics from all subjects (rows) for every channel (columns)
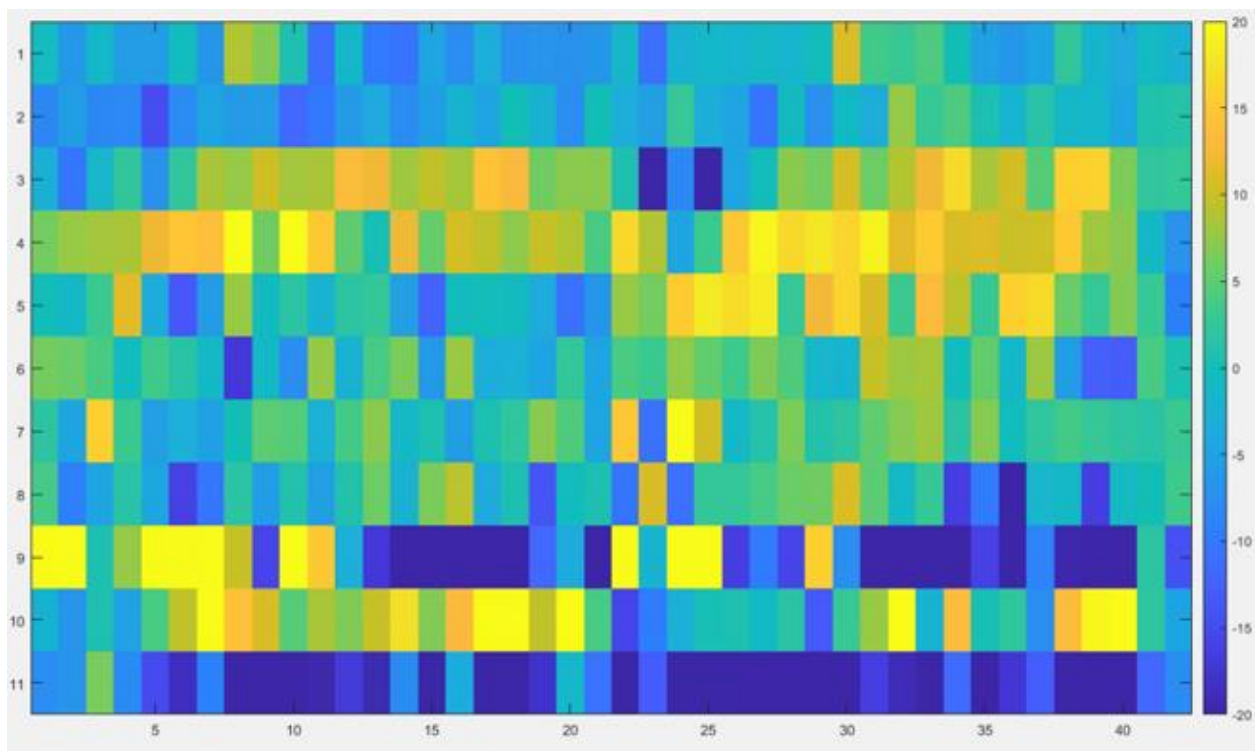
Figure 8

A subject showing little left hemispheric activity, but some right sided activity during the task.

Figure 9

A subject showing negative activity during the task.
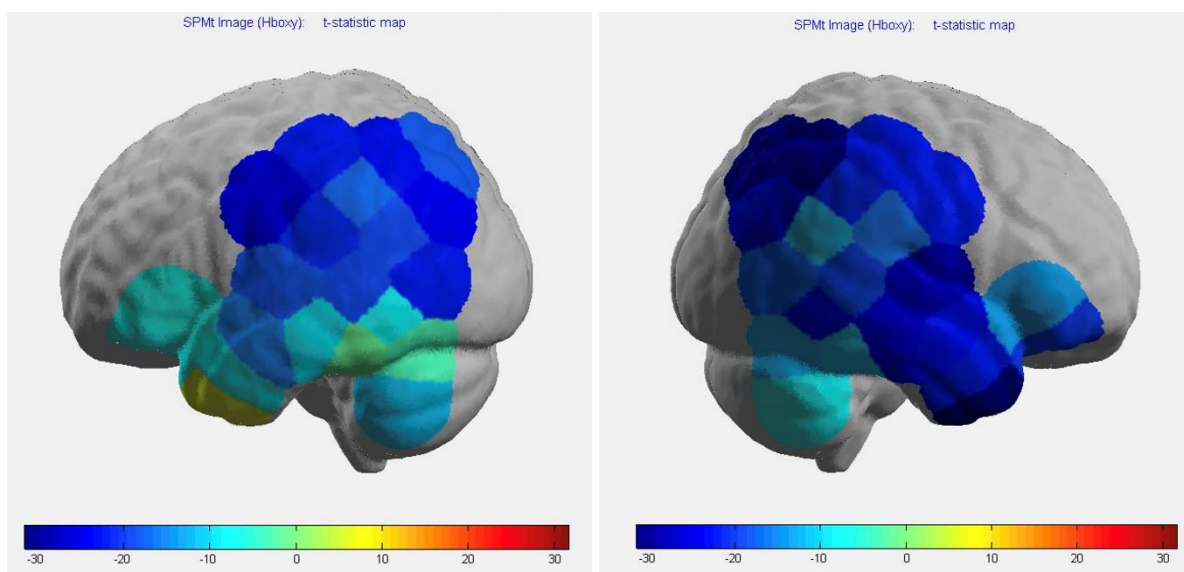
rsfNIRS

The results show clusters of high positive correlations for channels 1-7 and 8-19, covering frontal and mostly parietal areas. Further, these channels correlated also with their homologues channels of the other hemisphere (Figure 10, left panel). However, only the correlations around 10-15, i.e. the left parietal areas, became significant on a $p<0.05$ level (Figure 10, central panel). Interestingly, the same channels also showed the strongest difference between session 1 and 2 (Figure 10, right panel).

NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

Figure 10

Matrices showing t-statistics of resting-state measurements from all subjects.
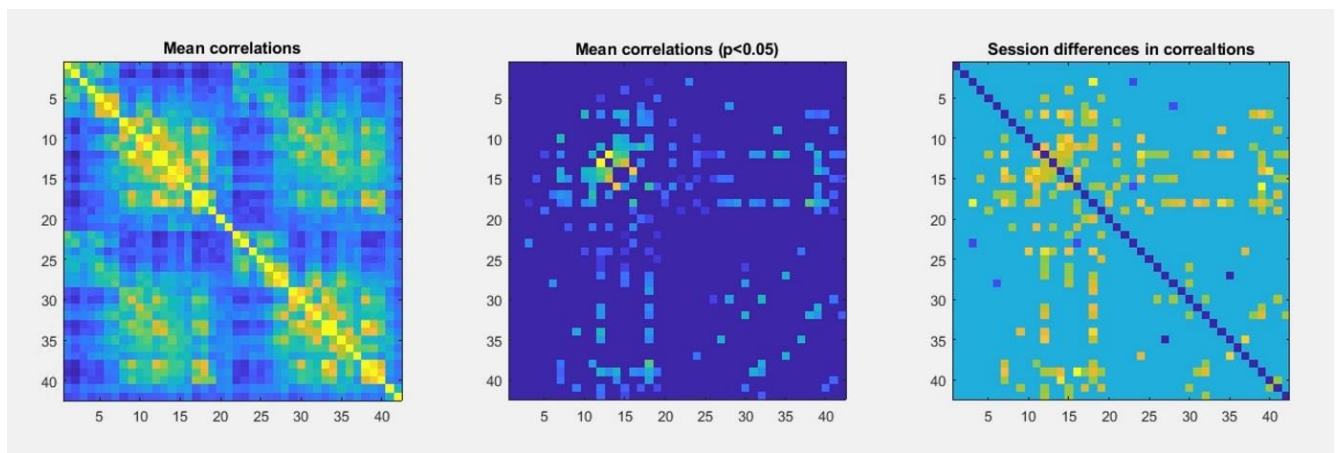
Discussion

In this study, patterns of neural responses were measured with fMRI and fNIRS while 12 (11 with fNIRS) participants performed on a non-verbal visual-spatial working memory task. Resting-state was investigated before and after the task with both measurement instruments as well. The basic notion for investigating n-vWM is that different brain networks are recruited for information that easily can be put words to versus information that cannot be easily put words to. This seems to be the case (e.g., Daniel et al., 2016; Goldby et al., 2001; Habeck et al., 2012; Rothmayr et al., 2007). We aimed to further explored this dissociation, with a strong emphasis on making the visual and spatial information as difficult to verbalize as possible. The resting-state measurements before and after the n-vWM task was implemented to investigate whether the task had any effects on resting-state activity. Also, the different setting during fNIRS measurements compared to fMRI measurements provided an interesting facet to the comparison of the data from the two instruments.

It was hypothesized that fMRI and fNIRS should yield similar results (H1). Furthermore, it was expected that the n-vWM task would produce more right-sided

activations (H2). The PFC was hypothesized to be involved in every aspect of the working

memory performance (H3). We expected to see FPN activations during the n-vWM task (H4).

Also, both ventral and dorsal visual pathway streams were hypothesized to be activated by the

task (H5A and H5B, respectively). At last, it was expected that the resting-state would yield

DMN-like activations, however, with influences of the task (i.e., difference between the two

sessions) (H6).

H1 was not supported by the fMRI and fNIRS data. However, the high variability of

the data derived from fNIRS negated any possible effects on group level that could have been

compared with the fMRI data. That is, essentially, the fNIRS data should be considered with

great caution. So, because there was no significant finding on group level for the fNIRS data

of the n-vWM task, we must rely on the fMRI data for H2-5B.

More right-sided activations were yielded by the fMRI data (see Table 1 and Figure 4

above). Thus, H2 was supported. Regarding H3, we did find support for PFC activity during

the n-vWM task, from the right MFG activation, close to Brodmann area 9, which overlaps

with the DLPFC (Hoshi, 2006; Jung et al., 2022; Zhao et al., 2016). H4 was supported by our

findings, with the right MFG and PPC regions being important sites of FPN activations.

Right-lateralized dorsal areas of the MFG and the SPL are associated with the D-FPN. This

network is thought to have a broad role in visuospatial attention; thereof the name "attention

network" (Uddin et al., 2019). Also, the MFG (including rostral and dorsal parts) has been

associated with the L-FPN, which seems to execute, direct, and control information flow in

WM; thereof the name "central executive network" (Uddin et al., 2019). Regarding H5A, it is

not apparent in our results that the WM task elicited ventral visual pathway activations.

However, SMG activity has previously been associated with a ventral salience network that

operates in a bottom-up attentional manner. Thus, the activity might reflect attentional

orienting processes of the ventral pathway needed for the complex information (Corbetta et

al., 2008). Even though we did not find significant activity in the PVC, we did find activations of superior parietal cortex regions that might reflect dorsal visual pathway streams. This might yield evidence in support of H5B.

Concerning H6, fNIRS resting-state did provide results that could resemble DMN-like activations. However, due to the low spatial resolution and weak values, it is difficult to differentiate whether the significant parietal channels belong to CEN or DMN, or both. Therefore, what we *can* state, is that there seems to be a difference between the two sessions, occurring in the parietal areas, around central areas for CEN and DMN (Fox & Greicius, 2010; Fransson, 2005; Uddin et al., 2019; Zhao et al., 2016). In conclusion, rsfNIRS showed a correlation between channels that could be expected from the fMRI literature. Regarding the rsfMRI, the significant cluster of connections between the putamen and pallidum to left frontal areas, was not directly expected. The putamen and pallidum (or globus pallidus) are parts of the basal ganglia. The basal ganglia is not unknown for projecting to frontal areas and has been suggested to be involved in a resting-state network (Robinson et al., 2009). The resting-state network involvement of basal ganglia has been found in both eyes closed and fixation conditions. The putamen has been associated with constitution of activation focus (Robinson et al., 2009). This could be interesting in this context, since the putamen was part of a cluster of connections that were significantly more activated between session one and two of resting-state. That is, it might suggest alterations in activation focus due to the task performance. However, what we most securely can state is that there existed differences in the RSFC before and after the WM task. This provides at least partial support for H6.

All the significantly activated brain regions from the conjoint analysis of all the n-vWM conditions can, in light of previous findings, be interpreted as functioning parts of the WM system. Interestingly, the MFG has been found to play a role in delay activity, with greater activation during longer delays (Barch et al., 1997). This MFG involvement

corresponded to DLPFC activity, which is assumed to play a central role in maintenance of information. Unfortunately, we have so far failed to perform an analysis of the delay activity. Because of that, we can only speculate that portions of the MFG activation in our study reflects active maintenance in the delay period. Despite of that, our findings do seem to include several of the areas that have previously been associated with delay activity for non-verbal stimuli: Daniel and colleagues (2016) found that non-verbal stimuli-based tasks activated the left medial frontal, bilateral middle frontal, and right precentral gyrus, the left and right SPL and PCu, and the right fusiform gyrus. Also, they found the most significant differences between verbal and non-verbal information in the left PCu (i.e., parietal), the right MFG (i.e., frontal), and the left inferior frontal gyrus (i.e., frontal). The PCu and the right MFG yielded higher activations for non-verbal information, whereas the left inferior frontal gyrus yielded higher activations for verbal information. As mentioned earlier, this indicates that frontoparietal regions are core regions for the differently activated networks depending on the verbalizability of information. Our findings do provide support for these non-verbal network activations.

Further on the role of the MFG, the accuracy of spatial WM has been linked to the strength of the functional connectivity between the right DLPFC and right MFG (Ren et al., 2019). The latter functional connectivity suggests essentially that central upper parts of the right frontal cortex can be associated with the accuracy of spatial WM. The PrG has, on the other hand, been associated with the accuracy of object WM. The SMC has been implicated in the accuracy of object WM, as well. Furthermore, both of these regions have been found to be functionally connected to the right intraparietal sulcus (IPS) (Ren et al., 2019). Thus, these regions seem to operate in functional proximity with the IPS, which has been associated with selection of competing stimuli and reorienting of attention to spatial information (Gillebert et al., 2011). The IPS has also been suggested to function as an interface between visual

perception and motor operations (Grefkes & Fink, 2005). Interestingly, the PrG has been linked to more general aspects of visual tasks: it exhibited late phasic activation that were associated with the generation of motor response, rather than visual imagery or perception per se (Ganis et al., 2004). This makes sense in light of its connectivity to the IPS, and one could perhaps speculate that the PrG (and the SMC) is involved in the manipulation of object information in WM.

The activation of the right SMG could be associated with motor operations, as well. The right SMG has been implicated in multiple bodily-related functions, such as operating with sensory information for proprioception and motor control (Ben-Shabat et al., 2015). The activity we found could be related to this. For example, using handles for response on the fMRI n-vWM trials could have been an unusual experience for the participants. Also, responding while laying down without seeing their hand- and finger movements could increase the sense of self-movement and awareness of body position (i.e., proprioception). However, as noted above, the activation of the SMG could be more closely linked to working memory as well. The SMG has been implied in the ventral network, where it forms connection with the ventral PFC. It is associated with bottom-up attention to information that is important for task performance, even if not it is not salient or distinctive (Corbetta et al., 2008). However, activations of the SMG can be linked with identification of salient information, as well (Uddin et al., 2019). The bottom-up-involvement of the SMG makes sense as the ventral part of the SMG operates in close proximity to the TPJ cortex, which is suggested to be especially involved in attentional switches between top-down and bottom-up (Corbetta et al., 2008; Shomstein, 2012). Thus, the activity might reflect important attentional orienting processes of the ventral pathway needed for processing of complex information. Also, that the SMG was significantly active in the right hemisphere does not come as a surprise since the ventral frontoparietal network (or ventral attention system/network)

typically appears as a right lateralized system (Corbetta & Shulman, 2002; Uddin et al., 2019).

Both the PCu and the SPL have been associated with top-down attention and selective attentional control of WM (Eriksson et al., 2015; Shomstein, 2012). These regions are involved in visual perception and are thought to play important roles in networks that include frontal cortices (i.e., D-FPN and L-FPN) (Ganis et al., 2004). They have been associated with processes underlying attention, spatial working memory, and have been linked with complex aspects of visuospatial processing (Courtney et al., 1996; Ganis et al., 2004; Gotts et al., 2013). Furthermore, the SPL has been suggested to be involved in all types of executive functions in WM (Wager & Smith, 2003). That the current n-vWM seems to have activated top-down related brain regions does not come as a surprise. Stimuli with high feature similarity tend to demand more top-down attentional control and parietal regions are typically activated when tasks and stimuli are heterogeneous. Thus, it is not surprising since most of the trials in the n-vWM task would involve materials with high feature similarity (Sack, 2009; Shomstein, 2012).

Lastly, in regard to the activated regions, the right superior occipital gyrus (SOG), a small convolution on the dorsal margin of the occipital lobe, was significantly active during all conditions. It was not specifically covered by the hypotheses but is a part of the operating visual pathways. The occipital lobe is the area of the brain that is specialized for visual processing, and among many functions, it is associated with visuospatial processing, color determination, and object recognition. Activation in the occipital cortex seems stronger for perception than imagery (Ganis et al., 2004). Similar to our finding, Ganis et al. (2004) found an activation of the left SOG during visual perception. The SOG has been shown to be involved in the direction of attention to visual-spatial information. This has been found with both unimodal and multimodal visual-spatial information (Macaluso et al., 2003).

The fact that the activation across the different conditions appeared similar, provides support to the notion that working memory functions in degrees of participation of different regions that might vary with the nature of the information, rather than in discrete parcellation. Furthermore, it indicates that objects that are varied along featural dimensions at the same time will make them more integrated. That is, performance on one task condition (e.g., color) does not seem to come without being affected by other features of the object. This matches the finding of Luck and Vogel (1997), which shows that visual working memory rather work with features of objects in concert rather than with individual features. However, that does not undermine arguments for functional network activations. Our findings mirror closely frontoparietal networks that have previously been reported in WM studies. Thus, it may rather suggest that objects with integrated features evoke interactions between networks and pathways.

Strengths and limitations

One of the most important strengths of this study comes from the fact that the newly composed n-vWM task appears to be effective in its testing of the concept. Furthermore, the material and the task appears to have been effective in integrating visuospatial features. The fMRI findings have contributed to the distinction of verbal vs. non-verbal working memory, in the sense that regions that have previously been implied in n-vWM, were yielded in our results as well. Thus, the findings serve as important input to the neural network model of the n-vWM system. Also, both the fMRI and fNIRS resting-state data indicated intriguingly a difference between session one and session two, which suggests that RSFC may be altered by current cognitive states. However, the fNIRS results should be considered with some caution since they are the product of an explorative correlational analysis that was not corrected for

multiple comparisons. As mentioned above, this is due to the lack of a standard procedure for fNIRS resting-state data analysis.

Despite the promising basis for fMRI and fNIRS comparison, the results did not match our expectations for it. The fMRI measurements were seemingly successful, however, that cannot be said about the fNIRS measurements. Because of the large variability between the participants in the fNIRS data, a larger sample size could possibly solve some of the issues on group level. However, we found fNIRS signals to be surprisingly vulnerable to dense and long hair. We knew that it could produce some signal difficulties, but we believe that it largely affected the results for some of the participants. Researchers that aim to use fNIRS should be aware that this could complicate measurements. Of course, some of the issues we had with this could stem from lack of experience with the measurement tool. Inasmuch as the experience could contribute to poor results, the optodes could potentially benefit from being improved, as well (not that there has not been attempts to improve this matter, see e.g., Khan et al., 2012). Also, since the testing of the participants occurred in a seminar room, with closed doors, we could not view whether some of the participants moved more than others. Thus, we cannot state whether the results could have been affected by movement artifacts outside of what was removed by the pre-processing. Furthermore, the negative or small activities shown by some of the participants during the n-vWM task could be due to other factors as well. For example, it might be that the late time of day and the fact that it occurred on a Friday, the beginning of the weekend, could have made some less alert and focused. Also, some participants could have been less engaged in the task since they had performed on it on an earlier occasion during the fMRI part. Lastly, participants could have been affected by the setting: being alone in a seminar room, with a window view, and few other potential stressors surrounding the performance compared to the fMRI part. It is possible that factors

such as these provided a fertile ground for more variable results compared to the fMRI measurements.

It might be that signals from some of the participants or from certain channels should have been excluded from subsequent analyses. However, with a small sample, it is difficult to make such decisions on terms that could be viewed as somewhat arbitrary and subjective.

Future directions

Researchers who find themselves interested in conducting a similar project in the future should be aware of multiple factors from our study that call for attention: A larger sample size would be beneficial. Also, measurements should occur at matching times during the day. Future studies should use a 50-50 distribution of measurement: That is, the order of fMRI and fNIRS measurements should involve half of the participants starting with fMRI and ending with fNIRS, whereas the other half is measured the other way around.

Furthermore, researchers should pay sufficient attention to the signal processing and filtering steps that should be performed and the order of execution for fNIRS data. In a commentary to Pinti and colleagues (2019) regarding pre-processing steps within a GLM framework, Bizzego, Balagtas, and Esposito (2020) highlighted that there currently is a high heterogeneity in the type of signal processing sequences. This is something that researchers should be aware of for future fNIRS purposes. That is not to say that we did not have awareness of these factors regarding the pre-processing. However, it serves as a note to other researchers, which stresses the attention to signal processing steps and other aspects when using fNIRS, so that reliable results can be produced and used for comparison.

Regarding the n-vWM task study design, event-related or mixed block/event-related designs have many benefits compared to block-designs and should be explored in the future. A reason is that it would allow capture of transient dynamic changes of activations during the

different WM stages, and between and within trials. However, for the purpose of this study, a block design was suiting. A block design has the advantage of having high power, and tends to produce robust results, which could be beneficial for a small sample size and the exploration of the effectiveness of the n-vWM task and the conditions (Amaro & Barker, 2006).

Conclusion

Here, GLM analyses were conducted on human neuroimaging data from both fMRI and fNIRS of a non-verbal working memory task. Resting-state data was collected with both measurement tools, as well. The explorative fNIRS resting-state analyses revealed differences between first and second sessions, with possible effects related to the task between the two sessions. Also, parietal areas showed significant activations around central areas for DMN and CEN. The resting-state fMRI did also show differences between the sessions; however, the brain regions between rsfNIRS and rsfMRI were not overlapping. The GLM analysis on the fMRI data yielded supporting results for a non-verbal working memory system. This involved frontoparietal network activations that have previously been observed to be important for both attentional operations and executive control of non-verbal information during working memory performances. Also, regions related to both dorsal and ventral visual pathways were significantly activated. These brain regions seem to play key roles in the non-verbal working memory system. Unfortunately, the fNIRS data suffered from high variability. Thus, the comparison of fMRI and fNIRS was not as successful as we had hoped. However, that should not create hindrances for future investigations with fNIRS alone, or in combination with fMRI. A larger sample size could possibly neutralize some of the issues.

NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

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NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

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NON-VERBAL WORKING MEMORY: fNIRS AND fMRI

Appendix A

Illustration of the Gabor patterns used in the present study.
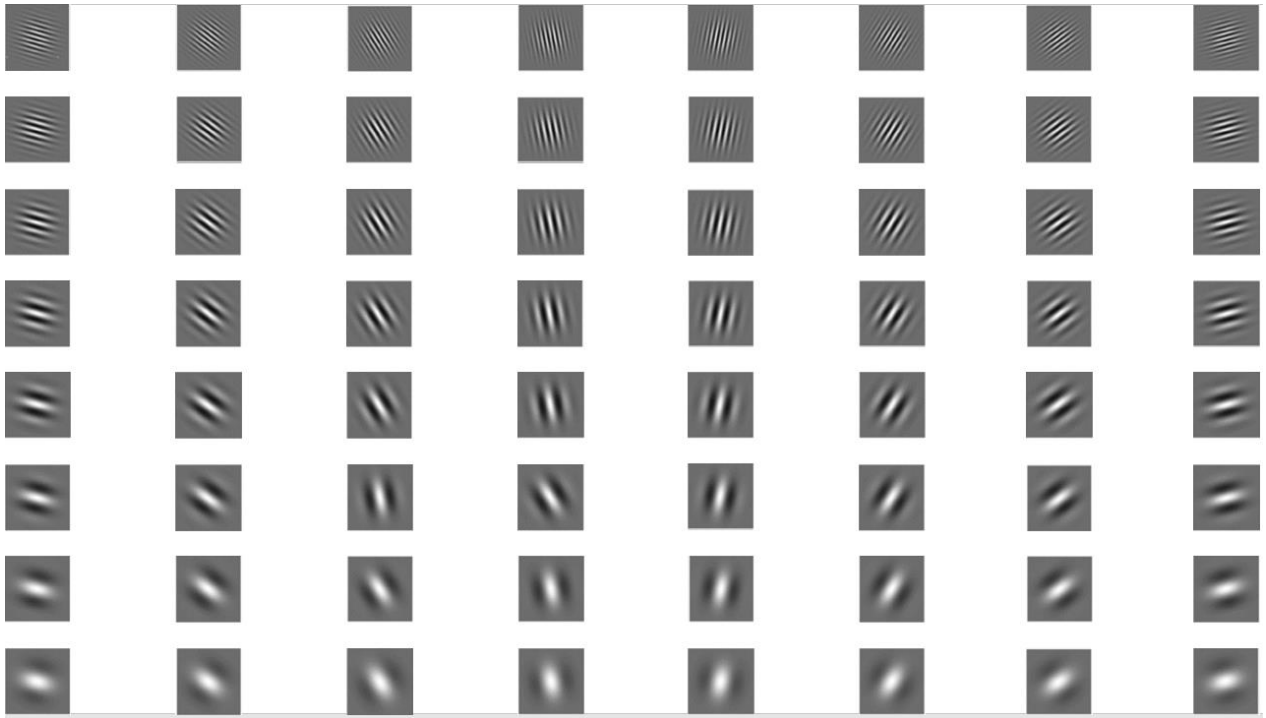
Appendix B

Illustration of color nuances with a example pattern in the centre