The effects of sleep deprivation on visual perception and metacognition

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Summary

Sleep serves fundamental functions for the human brain and lack of sleep leads to impairments in cognitive and behavioural tasks. Yet, the mechanisms that underlie such impairments as well as the extent of cognitive domains affected by sleep deprivation (SD) are still not completely understood. To address these gaps, this thesis aims to investigate the effects of SD on two important but previously overlooked cognitive functions: visual perception and metacognition - the ability to self-monitor performance.

Investigation of visual perception focuses on the perceptual processing hierarchy. In Chapter 3, I explore the effects of SD on low-level visual functions (e.g. orientation sensitivity), using four psychophysical tasks assessed before and after a night of SD. I find differential effects of SD on performance between tasks, revealing selective impact of sleep loss on low-level perceptual functions. Chapter 4 investigates the high-level perceptual ability to categorise objects (faces vs scenes). Using functional Magnetic Resonance Imaging (fMRI), I observe that brain activity in regions specialized in face and scene processing is altered by SD, in parallel to a reduction in categorisation performance. Another aim of this thesis is to assess the impact of SD on metacognitive ability. This is investigated in Chapter 5 using confidence ratings in perceptual judgements to measure the correspondence between response confidence and response accuracy. Results show that after SD individuals become less able to discriminate accurate from inaccurate temporal perceptual judgements, reflecting poorer self-monitoring capacity after sleep loss. Chapter 6 brings together results of this thesis and provides suggestions to tackle novel questions in future research.

Overall, this thesis shows novel and detrimental effects of sleep loss at different levels of the perceptual processing hierarchy as well as on metacognition, extending our comprehension of the range of cognitive deficits caused by sleep deprivation.

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Contributors

The experiments presented in this thesis were part of a larger study conceived and designed by Dr Chen Song and carried out in CUBRIC. I provided contribution to experimental design, preparation and execution, and originated the research questions that are assessed in Chapter 3, Chapter 4 and Chapter 5. Computer tasks were programmed by Dr Chen Song and myself. I analysed and interpreted all data presented in this thesis (with the exception of the calculation of metacognitive sensitivity index in Chapter 5 programmed by Dr Chen Song). The composition of this thesis is entirely my own.

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List of Acronyms

2F	2-Flash fusion task
AAS	Ascending Arousal System
AFC	Alternative-Forced-Choice
AUROC2	Area Under type 2 Receiver Operating Characteristic curve
BOLD	Blood Oxygen Level Dependent
CBF	Cerebral Blood Flow
CBV	Cerebral Blood Volume
CFF	Critical Flicker Frequency
CHARMED	Composite Hindered And Restricted Model of Diffusion
CMRO2	Cerebral metabolic rate of oxygen
CR	Confidence Rating
dHb	de-oxygenated Hemoglobin
DMN	Default Mode Network
EEG	Electro Encephalography
EPI	Echo-Planar Imaging
ESS	Epworth Sleepiness Scale
FFA	Fusiform Face Area
fMRI	functional Magnetic Resonance Imaging
FOV	Field Of View
FWER	Family-Wise Error Rate
GLM	General Linear model
Hb	hemoglobin
HDR	HemoDynamic Response
IFC	Interval Forced Choice
IFI	Inter-Flash-Interval
ISI	Inter Stimulus Interval
ITI	Inter Trial Interval
JND	Just Noticeable Difference
LFP	Local Field Potential
LOT	Line Orientation Task

MEG	Magneto EncephaloGraphy
MOCS	Method Of Constant Stimuli
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
NREM	Non-Rapid Eye Movement
OD	Orientation Discrimination
OFA	Occipital Face Area
OPA	Occipital Place Area
PF	Psychometric Function
PPA	Parahippocampal Place Area
PSE	Point of Subjective Equality
PSQI	Pittsburgh Sleep Quality Index
PVT	Psychomotor Vigilance Task
qMT	quantitative Magnetization Transfer
REC	Recovery (sleep)
REM	Rapid Eye Movement
RF	Radio-Frequency
ROC	Receiver Operating Characteristic
ROI	Region of Interest
RSVP	Rapid Serial Visual Presentation
RT	Response Time
SCN	Supra-Chiasmatic Nucleus
SD	Sleep Deprivation
SDT	Signal Detection Theory
SNR	Signal to Noise Ratio
TE	Time Echo
TI	Tilt Illusion
TR	Repetition Time
VD	Vernier Discrimination
VLPO	Ventro-Lateral Pre-Optic nucleus
VWM	Visual Working Memory
WFHR	Wrong Face and House Response
WFR	Wrong Face Response

WHR	Wrong House Response
WR	Well-Rested

Chapter 1.
General introduction

1.1 Background

Every day millions of people wake up feeling unrested. They have not had an adequate night of sleep and their daily functioning will be compromised by sleepiness, irritability, difficulty focusing and remembering things. Sleep deprivation causes a wide range of impairments to cognitive, emotional and bodily functions that have tremendous costs and consequences for individuals and society but that are still far from understood.

The World Sleep Society and the Sleep Research Society recommend sleeping a minimum of 7 hours per night (Liu et al., 2016; Watson et al., 2015), however more than 30% of individuals in the USA and the UK report an average sleep duration shorter than 7 hours (Liu et al., 2016; National Sleep Foundation Poll, 2013), with 10-20% individuals further reporting sleep disturbances such as long sleep onset latency and difficulty maintaining sleep (Grandner, 2017). Reasons of poor sleep include societal and lifestyle factors (shift-work, globalization, 24/7 society), ethnographic and environmental factors (religion, culture, noise and heat) and psychological, physical and clinical factors (depression, insomnia, sleep apnea, stress, rumination) (Grandner, 2017; Hafner et al., 2017). Furthermore, during the COVID-19 pandemic, the prevalence of sleep problems in the general population (e.g. insomnia and hypersomnia) increased to around 40%, affecting COVID-19 patients and healthcare workers particularly (Alimoradi et al., 2021).

On top of the adverse health outcomes associated with chronic sleep loss including mortality, cardiovascular disease, hypertension, type 2 diabetes, respiratory disorders, obesity and depression (Cappuccio et al., 2010; Grandner, 2017; Watson et al., 2015), sleep loss is linked to significant professional, personal and societal costs. In the workplace, insomnia symptoms and sleep deprivation are associated with reduced productivity, increased absenteeism and elevated workplace accidents (Hafner et al., 2017; Kucharczyk et al., 2012). Moreover, fatigued-driving due to insufficient sleep accounts for 20% of road accidents in the UK (Jackson et al., 2011). Many of these consequences can be linked to impairment in cognitive functions after sleep deprivation. Sleep deprived individuals are more tired and they have higher chance to get distracted or doze off while performing a task (Banks et al., 2017;

Durmer et al.,2005). Sleep deprivation impairs individuals' ability to focus and attend to stimuli, learning new and remembering old information, as well as the ability to assess accurately a context to decide upon the best path of action to take (Aloha and Polo-Kantola, 2007; Goel et al., 2009; Killgore, 2010). Altogether, sleep deprivation negatively affects performance in daily situations and can compromise social and personal relationships.

A thorough understanding of how sleep loss affects brain and cognitive functions can provide better insights into what aspects of daily tasks, professions and activities are more susceptible to the negative consequences of sleep deprivation and help develop potential countermeasures to improve performance and reduce the risk of accidents.

In this chapter, after briefly introducing how sleep and wakefulness are regulated, I review experimental evidence of the neurocognitive effects of acute total sleep deprivation and present the main theoretical frameworks that have been put forward to explain how sleep deprivation affects neurobehavioural performance. Finally, I explain the rationale for investigating visual perception and metacognition in sleep deprived individuals, and describe the main aims and research questions of this thesis.

1.2 Regulation of sleep and wakefulness

The cycles of human activities are tightly regulated by the time of the day. During daytime, most people get up to work, socialize, exercise, feed and complete a large amount of activities. Then, at night time, most people go to bed and enter a state of apparent unresponsiveness that lasts about one third of the 24-hour day. This alternating cycle of wakefulness and sleep repeats regularly day after day, year after year.

The regulation of sleep and wakefulness is governed by two opposing physiological processes. On the one hand, a *homeostatic process* "S" tracks duration of time awake by accumulating sleep pressure with extended wakefulness and dissipating it over a sleep interval (Borberly, 1982; Borberly et al., 2016). On the other hand, a

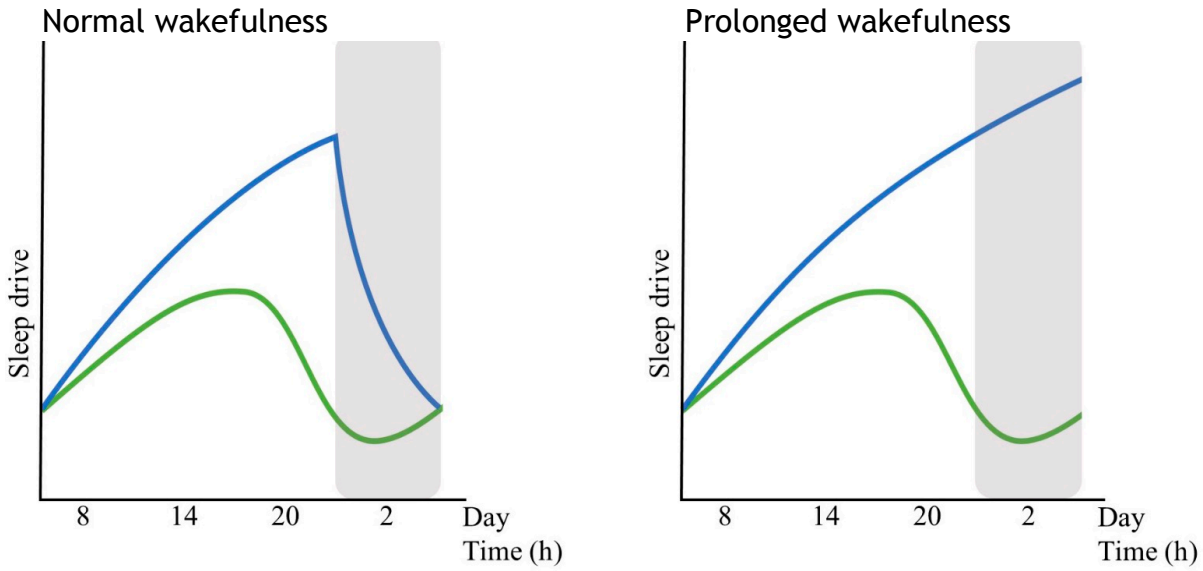

Figure 1.1: Regulation of sleep propensity. Sleep drive is determined by the interaction between the homeostatic process "S" (blue line) and the circadian process "C" (green line). The difference between the homeostatic and circadian processes determines the sleep propensity, which is highest when the circadian drive is lowest (i.e. during the night and early morning) and after a prolonged period of wakefulness. During the night (shaded area) homeostatic sleep pressure is dissipated if individuals sleep (left panel), otherwise it continues to build if individuals remain awake (right panel). Adapted from D'Ambrosio et al., 2019.

circadian process "C" tracks time of the day and fluctuates regularly over a 24 hour period, regulated endogenously but entrained with the external light/dark cycle (Achermann and Borberly, 1994; Daan et al., 1984). The interplay of these processes regulates the temporal dynamics of sleep and wakefulness periods, promoting wakefulness during the day and sleep during the night. The difference between the process S and C (Figure 1.1) determines *sleep propensity*, the readiness to transition from wakefulness to sleep. When sleep propensity accumulates beyond a certain threshold, sleep initiating mechanisms - triggered "top-down" by sleep-centres in the hypothalamus - inhibit cortical arousal and push global brain state towards sleep, during which sleep pressure can be progressively dissipated. If sleep is withheld, voluntarily or not, sleep pressure cannot be dissipated and progressively builds up (Figure 1.1, right). With prolonged wakefulness, homeostatic sleep pressure continues to elevate and sleep can be spontaneously triggered even when an individual is trying to resist it. For example, after a night of sleep deprivation, elevated sleep pressure can momentarily overcome the voluntarily and forced intent to remain awake, causing "microsleep" episodes, in which an individual falls asleep

for a few seconds and can no longer respond to the external environment. In many daily activity (e.g. driving) as well as safety critical operations (e.g. military, medical, flight control), this could have disastrous consequences. Sleep deprivation thus is a major contributor to errors and mistakes that greatly increase the risk of accidents.

1.3 Impact of sleep deprivation on cognitive and brain functions

Sleep deprivation is detrimental for brain and cognitive function, but a complete understanding of the range of impairments as well as the specific mechanisms that underlie them is still missing. Next, I review the most relevant evidence and theoretical frameworks about the impact of sleep deprivation on brain function, cognition and behavioural performance.

1.3.1 Vigilance, sustained attention and the state-instability hypothesis

Actively performing a task, from reading to maintaining a conversation, requires to be vigilant and attending the task at hand. Vigilance, also referred to as sustained or vigilant attention, is defined as the capacity to remain alert and responsive to external stimuli over a period of time (Oken et al., 2006; van Schie et al., 2021). Vigilance declines with increasing time awake and its reduction is characterized by fluctuations in behavioural performance (Lim and Dinges, 2008). Laboratory tasks such as the Psychomotor Vigilance Task (PVT, Dinges and Powell, 1985) assess vigilance by measuring how fast individuals respond to stimuli presented with irregular temporal interval (e.g. randomly between 2 and 9 seconds). With prolonged time awake, PVT performance is characterized by slowing of response times, more frequent attentional lapses - namely responses >0.5 seconds, and by a gradual increase in response time variability with prolonged task duration, known as time-on-task effect (Doran et al., 2001; Lim and Dinges, 2008). The large performance decrements in PVT reflect the high vulnerability of vigilant attention to sleep deprivation (Doran et al., 2001; Lim and Dinges, 2008; Van Dongen et al., 2003).

The pattern of vigilance impairment after sleep deprivation has been explained in terms of “state instability” (Doran et al., 2001; Dorrian et al., 2005). The state

instability hypothesis posits that sleep initiating mechanisms are triggered while individuals exert effort to remain awake and sustain attention on the task (Doran et al., 2001). These competing psychophysiological drives to sleep and to remain awake and alert manifest as stochastic fluctuations in vigilance, characterized by moments of apparently normal responsiveness, when vigilance is maintained, moments of attentional lapses, when vigilance falters but observer appears awake, and even microsleeps, when sleep initiating mechanisms overcome the effort to remain awake and lead to temporary unresponsiveness (Lim and Dinges, 2008). Physiologically, sleep initiating mechanisms occur as sleep-wake regulatory centres in hypothalamus (suprachiasmatic nucleus, SCN, and ventrolateral preoptic nucleus, VLPO) inhibit cholinergic and monoaminergic projections from subcortical nuclei (in basal forebrain, brainstem and hypothalamus - the Ascending Arousal System, AAS) to the neocortex that support global wakefulness (Saper, 2001; Van Dongen et al., 2011). Contrasting sleep initiating mechanisms in an effort to maintain wakefulness and remain vigilant are brain regions that support voluntary arousal and top-down attention such as thalamus, prefrontal, anterior cingulate and parietal regions (Corbetta, 1998; Fan et al., 2005; Kastner and Ungerleiden, 2000). These regions show compensatory increases in activity when sleep deprived subjects are able to maintain stable performance (Drummond et al., 2005; Drummond et al., 2004; Portas et al., 1998; Tomasi et al., 2009). Conversely, brain activity reduction in these frontal-parietal regions is associated to performance deficits across a variety of task including PVT (Drummond et al., 2005), visual short-term memory task (Chee and Chuah, 2007), object-selective attention task (Chee et al., 2008; Chee et al., 2011) and attentional orienting task (Tomasi et al., 2009).

The emerging picture is that, as increasing homeostatic sleep pressure with prolonged wakefulness trigger sleep-initiating mechanisms and reduce cortical arousal and attentional resources, compensatory increases in fronto-parietal circuits and thalamus allow to sustain attention and remain vigilant and engaged with the task, guaranteeing a stable level of performance. However, top-down attentional resources including vigilant attention progressively falter under increasing amount of sleep pressure, as evidenced by neural activity reductions in fronto-parietal and thalamic regions, leading to attentional lapses (Drummond et al., 2005),

performance variability (Chee et al., 2008; Dorrian et al., 2005), sensory processing reductions (Chee et al., 2011; Poh and Chee, 2017), increased distractibility (Chee et al., 2010; Kong et al., 2012) and disengagement from external stimuli (Killgore, 2010).

In sum, based on the state-instability hypothesis, the largest consequence of sleep deprivation is the fluctuation in vigilant attention due to the opposing wake and sleep drives (Balkin et al., 2008; Lim and Dinges, 2008). For this reason, some have suggested that performance impairments observed after sleep deprivation could be largely explained by decline in domain-general attentional capacities that impede sustained focus on the task and leads to lapses and errors (Balkin et al., 2008; Lim and Dinges 2008; Ma et al., 2015).

1.3.2 High-level cognitive functions and the prefrontal vulnerability theory

Although vigilance tasks like the PVT are considered the most susceptible to the effects of sleep deprivation (Lim and Dinges, 2010; Lo et al., 2012; Wickens et al., 2015), there is also an extensive literature on the impact of sleep deprivation on performance in high-level, executive functions tasks (Alohla and Polo-Kantola, 2007; Durmer and Dinges, 2005; Garcìa et al., 2021; Goel et al., 2009; Killgore et al., 2010). Executive functions are a set of cognitive functions including working memory, planning, task-switching, verbal fluency, inhibition and flexibility that rely on prefrontal cortex (Jurado and Rosselli, 2007).

A very influential framework developed to explain the effects of sleep deprivation was the prefrontal vulnerability hypothesis or neuropsychological theory (Harrison and Horne, 2000; Horne, 1993). Based on evidence of selective alterations in prefrontal activity relative to other regions after sleep deprivation (Finelli et al., 2000; Thomas et al., 2000), it was argued that prefrontal cortex was particularly susceptible to sleep loss and hence executive functions were more likely to be compromised (Harrison and Horne, 2000). The degree to which sleep deprivation affects executive functions however has been controversial. While some studies reported that performance in executive functions tasks is impaired after sleep

deprivation (Drummond et al., 2006; Harrison and Horne, 1998; Killgore, 2006; Nilsson et al., 2005), there have been many observations of preserved executive functions after sleep loss (Binks et al., 1999; Pace-Schott et al., 2009; Sagaspe et al., 2006). Part of the reasons why such inconsistencies have been observed depends on the nature of the tasks assessed. Cognitive tasks in general, and executive functions tasks in particular, rely on intertwined cognitive operations that are difficult to disentangle, the so-called "task impurity problem" (Jackson et al., 2013; Phillips, 1997; Whitney and Hinson, 2010). For example, executive tasks like Stroop or Wisconsin Card Sorting Test – commonly used in the sleep deprivation literature - include both executive (e.g. task switching, inhibition, working memory) as well as non-executive (e.g. sustained attention, stimulus encoding, motor response selection) components, so global measures of task performance like accuracy or response times reflect a mixture of all these components (Whitney and Hinson, 2010). As such, reduction in accuracy or slower response times in executive functions tasks *per se* do not provide valid evidence of selective impairments in executive functions, since they do not isolate different components (Whitney and Hinson, 2010). To tackle this point, Tucker and colleagues (2010) used a modified Sternberg memory task to address how sleep loss affects executive and non-executive components of verbal working memory. From the pattern of results they observed, Tucker and colleagues (2010) found no evidence of impairment in executive, working memory component. The authors concluded that much of the inconsistencies in previous results may likely be due to "focus on global performance outcomes that represent a mixture of different cognitive processes" (Tucker et al., 2010, pp56). In other words, non-executive components such as vigilance can explain much of the performance decrement in different executive tasks after sleep deprivation.

More recent studies following that of Tucker and colleagues (2010) have attempted to address this problem and disentangle task performance in multiple subcomponents to evaluate effects of sleep deprivation on specific cognitive processes. For example, Drummond and colleagues (2012), separately investigated the capacity and filtering efficiency of visual working memory (VWM). They found that VWM capacity was preserved after one night of total sleep deprivation, while the ability to filter irrelevant information was impaired and led to reduced

performance accuracy (Drummond et al., 2012). In a series of studies, Whitney and colleagues (Honn et al., 2019; Whitney et al., 2017; Whitney et al., 2015) identified cognitive flexibility as a high-level function that is selectively and particularly affected by sleep loss, independent of sustained attention impairments. Cognitive flexibility allows one to maintain task-relevant information in focus (stability*)* and then to update such information based on external demands (flexibility). Using a go/no-go task where the stimulus response contingencies had to be learned from feedback, authors found that sleep deprived people were not able to learn task rules as effectively as well-rested controls, neither were they able to adapt to rule-changes halfway through the task (Whitney et al., 2015; Honn et al., 2019). Yet, the two groups were equally able to remember presented probes, indicating preserved short-term memory as well as lack of attentional lapses after sleep deprivation (Honn et al., 2019). Similarly, Whitney and colleagues (2015) showed that the magnitude of cognitive flexibility impairment observed in the go/no-go task could not be accounted for by the frequency of attentional lapses observed in a parallel PVT task, further strengthening the selective impairment in cognitive flexibility and the lack of association between vigilance reduction and performance impairment.

Overall, task performance depends on attentional capacity to orient to and filter stimuli for prolonged time as well as executive functions to maintain goals in mind, adapt to changes in environment, and select the best strategy to achieve set goals. Sleep deprivation appears to impair basic attentional processes that are necessary for many different tasks, particularly when the task requires little engagement. However, sleep deprivation also has selective impairments to cognitive functions like cognitive flexibility that are not readily explained by state instability or prefrontal vulnerability hypotheses.

1.3.3 Task-specific impairments and local sleep theory

One limitation of both the prefrontal vulnerability and state instability theory is that they do not readily explain task-specific effects of sleep deprivation, namely why sleep deprivation affects the performance on some tasks but not others. If a reduced global modulation of sleep/wake state was responsible for the neurobehavioural effects of sleep deprivation, one would likely observe performance impairments in

all tasks, rather than task-specific effects (Hudson et al., 2020). Moreover, the prefrontal dysfunction hypothesis does not account for the selectivity of prefrontal cortex functions impairments by sleep deprivation.

One account that has been put forward to reconcile different findings is the occurrence of use-dependent local sleep in neuronal population involved in task execution (Hudson et al., 2020; Krueger et al., 2008; Van Dongen et al., 2011). Local sleep refers to the expression of Non-Rapid Eye Movement (NREM) sleep like activity in neuronal assemblies (i.e. synchronized slow oscillations characterized by brief periods of inactivity followed by short synchronized bursts) independent of the activity of adjacent neural populations (Krueger et al., 2008; Vyazovskiy et al., 2011). In other words, local sleep manifests as islands of sleep-like neural activity among regions exhibiting wake-like activity. *Use-dependent* refers to the spatial specificity of this phenomenon, in that the probability of exhibiting such sleep state depends on amount and intensity of previous activity of a specific neuronal population (Krueger and Tononi, 2011; Krueger et al., 2019). Interestingly, according to this view, sleep in local neuronal assemblies is triggered intrinsically possibly due to local accumulation of sleep regulatory substances (e.g. adenosine, Krueger et al., 2019; Krueger et al., 2008; or intra-cellular chloride, Alfonsa et al., 2022), rather than initiated "top-down" by sleep-regulatory centres. Evidence of local sleep has been demonstrated using implanted electrodes in the cortex of rats (Vyazovskyi et al., 2011) and humans (Nir et al., 2017), and there is also evidence of local electroencephalography (EEG) slowing in humans that support the hypothesis of local sleep (Andrillon et al., 2019; Bernardi et al., 2015; D'Ambrosio et al., 2019; Hung et al., 2013; Quercia et al., 2018). Critically, the functional importance of local sleep has been evidenced by the its temporal correspondence with attentional lapses and trial errors (Andrillon et al., 2019; Bernardi et al., 2015; Nir et al., 2017; Vyazovskyi et al., 2011).

But how could local sleep lead to decline and variability in task performance observed after sleep deprivation and with time on task? One possibility is that the occurrence of local sleep could cause neuronal assemblies to disengage from the coordinated activity with other neuronal populations that support optimal task

execution (Chee et al., 2011; Hudson et al., 2020; Van Dongen et al., 2011). As a result, information processing underlying task execution would be degraded, and if multiple assemblies expressed local sleep simultaneously, the circuit function may be compromised (Figure 1.2).

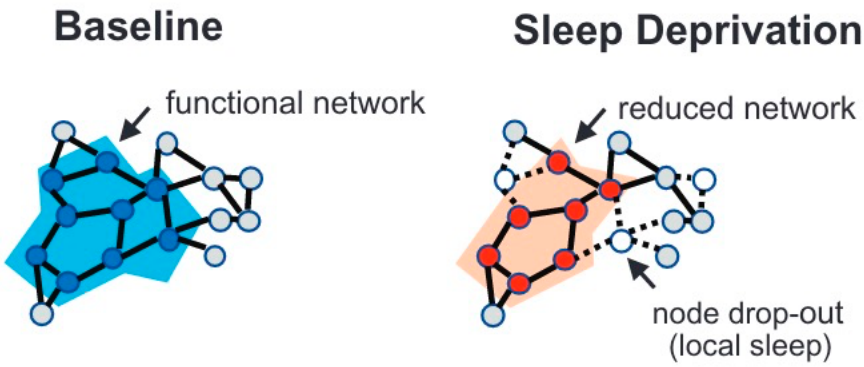

Figure 1.2: Effects of local sleep on neuronal circuits underlying task performance. A local sleep episodes is characterized by temporary disconnection of neuronal populations involved in task execution, which leads to interruption of information processing, with possible consequences for behavioural performance such as errors or slower responses. Adapted from Massar et al., 2019.

Local sleep could also explain the selectivity of sleep deprivation effects on different task. Since neural circuits express local sleep in a use-dependent manner, tasks more susceptible to sleep deprivation would be those relying on the neural circuits that have been most intensely used during the preceding awake period. A study by Bernardi and colleagues (2015) supported this by showing that impairments in executive functions tasks after 24 hours sleep deprivation were larger in a group that practiced a prefrontal task repeatedly for 24 hours relative to another group that practiced a visuomotor task, and vice versa. They also showed that the occurrence of local theta waves (an electrophysiological manifestation of local sleep, Nir et al., 2017) over task-relevant regions were more likely to occur during error trials than correct trials (Bernardi et al., 2015). Moreover, the reduced activation of fronto-parietal areas after sleep deprivation related to attentional lapses and other performance impairments (Chee et al., 2008; Drummond et al., 2005) may also be due to local sleep (Chee, 2015; Hudson et al., 2020). Fronto-parietal attentional network in fact represents a bottleneck of processing that is used in virtually any task requiring attention, hence the functional circuits that

underlie this cognitive ability are likely used extensively and may thus be more susceptible to manifest local sleep episodes.

Overall, the emerging picture is that homeostatic and circadian subcortical centres modulate the *propensity* for local sleep in cortical regions globally via AAS, but sleep is evoked intrinsically in local neuronal assemblies as a function of use-time and intensity (Hudson et al., 2020; van Dongen et al., 2011).

1.4 Sleep deprivation, perception and metacognition

Overall, although previous studies have characterized many of the neuro-behavioural impairments of sleep deprivation and have shed light on some of the mechanisms potentially involved, a complete understanding of the range of impairments of sleep deprivation and their underlying causes is still missing. One fundamental cognitive function that has been largely overlooked is visual perception. Perception is the seemingly effortless process whereby external sensory information are combined and processed to produce meaningful representations of the environment. Visual perception is built across a hierarchy of processing stages from low-level analysis of image contrast, luminance and boundaries, to higher-level analysis where the representation of complex shape and meaningful objects are generated (Grill-Spector and Malach, 2004; Groel, 2017). Perception represents a foundation for higher-order cognitive function like decision making, memory and action, so alterations in perceptual processes can potentially compromise the higher-order cognitive functions which rely on them.

Interestingly, occurrence of perceptual distortions and hallucinations with prolonged sleep deprivation common (Babkoff et al., 1989; Hurdiel et al.,2015; Waters et al., 2018) and suggests that perceptual processing may in fact be compromised by sleep deprivation. Moreover, considering the high reliance of brain processing on visual information – between 20-30% of the cerebral cortex is dedicated to processing visual information (Van Essen, 2004; Wandell et al., 2007), it is not unlikely that repeated, extensive use of the visual processing circuits would lead to functional fatigue and trigger local sleep episodes in visual processing circuits. In turn, these may affect perceptual processing and alter the formation of an accurate representation of the

external world. Given the complex hierarchy of perceptual processing stages, perceptual alterations could result from information processing failures at earlier or later stages or both. However, very few studies have looked at how sleep deprivation affects the perceptual processing hierarchy. Moreover, whether early, low-level perceptual processes or later, higher level ones are influenced by sleep deprivation is unclear.

Another possibility that may help understand the occurrence of perceptual alterations and hallucinations after sleep deprivation, is that sleep deprived individuals may become less able to distinguish reality from imagination. An inability to discriminate real from imaginary perception could reflect deficits in metacognitive abilities after sleep deprivation. Metacognition is the introspective ability that allows one to self-monitor performance and discriminate one's own correct from incorrect responses (Fleming et al., 2010). Previous studies that have investigated how metacognitive abilities are affected by sleep deprivation however provided contrasting results (Aidman et al., 2017; Baranski, 2007; Blagrove and Akehurst, 2000). Moreover, a recent review stressed that previous results are largely biased by the methodological limitations in task design and analysis performed, including not controlling for task performance (Boardman et al., 2021). As such, it is still largely unclear whether and how sleep deprivation affects metacognitive abilities.

1.5 Thesis aims and research questions

The impact of acute, total sleep deprivation on cognitive function and behavioural performance has been extensively investigated over the last century and functional neuroimaging has greatly improved the understanding of the mechanisms by which sleep loss affects brain activity (Chee and Chuah, 2008; Chee and Asplund, 2013; Krause et al., 2017; Ma et al., 2015). Nonetheless, research on the effects of sleep loss has overlooked critical aspects of cognition such as perception, which constitutes a fundamental cognitive function *per se* as well as a foundation for higher cognitive functions like decision making. Moreover, a valid and reliable assessment of metacognitive abilities before and after sleep deprivation is timely.

The overall aim of this thesis is thus to explore the effects of sleep deprivation on visual perception and perceptual metacognition. By characterizing the effects of sleep deprivation on visual perceptual properties and metacognitive abilities, this research can provide a significant contribution towards a complete and detailed understanding of the impact of sleep deprivation on cognition and brain. Moreover, results of this research will help to identify contexts and aspects of operations and activities in which sleep-deprivation-related accidents are more likely to occur following selective impairments to specific cognitive domains, and to discover potential targets for countermeasures to the selective sleep deprivation effects helpful to mitigate these effects.

More specifically, this thesis has three main aims.

Aim 1: assess how sleep deprivation affects low-level properties of visual perception.

In Chapter 3, I address how sleep deprivation affects low-level visual perception. Specifically, I measure perceptual sensitivity to line orientation (orientation discrimination task), to lines position (vernier discrimination task), to contextual elements (tilt-illusion task) and to temporal sequences of stimuli (two-flash discrimination task). These allow to assess how sleep deprivation affects orientation sensitivity, visual hyperacuity, contextual modulation and temporal resolution of visual perception. These properties represent building blocks of visual perception, critical to generate higher, complex perception of shapes and figures.

Aim 2: evaluate how sleep deprivation affects high-level perceptual discrimination and its underlying neural mechanisms.

In Chapter 4, I address the impact of sleep deprivation on high-level perceptual functions. I measure the ability to categorise noise-degraded stimuli in a novel face/house/blank discrimination task, and assess whether illusory perceptions increase with sleep deprivation. Moreover, using fMRI I measure neural activity in category-selective visual regions, and assess whether sleep deprivation degrades high-level perceptual processing.

Aim 3: investigate the impact of sleep deprivation on perceptual metacognition.
In Chapter 5, I investigate how sleep deprivation affects perceptual metacognition. I collect response accuracy and confidence ratings trial by trial in three different perceptual tasks designed to maintain a constant level of difficulty. Then, using specific analyses that allow dissociation of metacognitive sensitivity (ability to discriminate correct from incorrect decisions) from subjective measures of decision confidence and from objective measure of response accuracy, I evaluate whether sleep deprivation affects the metacognitive ability to discriminate correct from incorrect perceptions and whether individuals become more or less confident in their responses.

Chapter 2.
Sleep deprivation experiment and assessment of visual perception and metacognition

2.1 Sleep deprivation experimental protocol

All experiments presented in this thesis are part of one single, large, multimodal and multisession study aimed at investigating the effects of sleep deprivation on brain function, brain structure and microstructure, cognitive abilities and behavioural performance. All participants completed the same experimental protocol, which involved multiple sessions of cognitive-behavioural tasks and neuroimaging scans over 4 consecutive days including 36 hours of continuous wakefulness including one night of acute total sleep deprivation.

2.1.1 Participant selection, instructions and preparation

A total of 16 young healthy adults were recruited among Cardiff University staff and students and received financial compensation (£200) upon completion of the experiment as well as meal vouchers to order food during the experiment. Participants were recruited if they lived within 20 minutes' walk from Cardiff University Brain Research Imaging Centre (CUBRIC), where all tests took place. Volunteers read and signed a written informed consent before the beginning of the experiment. Out of 16 participants who took part in the study, only 14 volunteers completed it. One volunteer withdrew in the evening before starting the night of sleep deprivation. Another participant withdrew in the morning after the night of sleep deprivation. The final sample thus included 14 participants, aged 24.3 years old on average and ranging between 21 and 32 years old. 11 participants were female, 3 were males; 11 participants were right-handed and 3 were left-handed. For the remaining of this thesis, information presented refers to the final sample who completed the study, unless otherwise specified. The study was approved by the Ethics committee of Cardiff University, in accordance with the Declaration of Helsinki.

Participants first came to the laboratory for an initial screening and were given general instructions and information about the experiment. Before starting the experiment, participants completed a computerized version of the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) and the Epworth Sleepiness Scale (ESS; Johns, 1991).

The PSQI is a questionnaire measuring subjective sleep quality and is used to identify individuals who have experienced poor sleep quality during the preceding month. The questionnaire comprises 20 questions surveying different areas of sleep such as sleep efficiency, frequency of awakenings, sleep disturbances, medical treatments for sleep, etc. (Buysse et al., 1989). The maximum score of the PSQI is 21, with higher scores indicating poorer sleep quality. A score of 5 is considered a threshold separating good sleepers (<5) from poor sleepers (=>5). Specifically, score above 5 are considered indicative of severe sleep difficulties in two areas or moderate sleep difficulties in three areas. In this sample, median PSQI score of participants was 2 (IQR = 1.75), indicating very good sleep quality over the month preceding the experiment for the average participant. Only one volunteer had a PSQI score of 6. This confirms that 13/14 participants were healthy, regular sleepers and that one remaining volunteer experienced some moderate albeit not extreme sleep difficulties in the month before the experiment.

The ESS is a standard measure of daytime sleepiness, namely the propensity of falling asleep when required or intending to stay awake (Johns and Hocking, 1997). The ESS is a questionnaire including 8 questions related to the likeliness of falling asleep during various activities such as while reading or watching tv, while driving, while engaged in social conversation, etc. Responses are reported on a 4-point scale from 0 (no chance of falling asleep) to 3 (high chance of falling asleep). The ESS score is obtained by summing all response scores (maximum score is 24). A score >10 is indicative of excessive daytime sleepiness (Johns, 1991; Johns and Hocking 1997). In the sample included in this thesis, the average ESS score was 5.5 (IQR = 5). Only one volunteer reported daytime sleepiness >10 (ESS score of 14). This volunteer was different from the one identified as poor sleeper with the PSQI.

In preparation for the experiment, volunteers were instructed to refrain from drinking tea, coffee or caffeinated drinks, and not to consume other drugs and alcohol starting from one week prior to Day1 of the experiment. While most sleep and sleep deprivation studies opt to exclude caffeine for only 24 hours before experimental testing, here caffeine was removed starting one week before the testing sessions to allow for caffeine withdrawal effects (including fatigue, headache

Table 2.1: sleep habits of all volunteers who took part in the study. The bottom row shows mean (standard deviation) hours slept by participants and median (inter-quartile range) for bed time, wake time, PSQI score and ESS score of participants. P06 and P08 withdrew from the study and were excluded from all analyses.

	Sleep routine during the week preceding the experiment			**Screening questionnaires**	
ID	Bed time Mean (range)	Wake time Mean (range)	Hours slept Mean (range)	PSQI score	ESS score
P01	00:00 (23:45 - 00:15)	07:30 (06:30 - 09:00)	6.5 (6 - 7.5)	1	8
P02	23:45 (23:30 - 00:00)	08:00 (06:50 - 10:00)	7.4 (4.5 - 8)	2	3
P03	23:00 (22:00 - 00:00)	07:30 (07:00 - 10:00)	7.3 (5 - 10)	3	2
P04	22:40 (22:10 - 23:00)	06:45 (06:00 - 07:15)	8 (8 - 8.2)	1	2
P05	00:00 (23:30 - 01:00)	09:00 (08:30 - 09:40)	8.8 (7.5 - 9.5)	1	5
P07	23:00 (22:30 - 23:30)	07:45 (05:30 - 08:00)	7.4 (6 - 8.5)	6	6
P09	22:30 (22:00 - 00:00)	06:45 (06:00 - 08:00)	8.1 (8 - 8.5)	2	5
P10	23:30 (23:00 - 00:00)	08:30 (08:00 - 09:30)	8.5 (8 - 9.5)	2	6
P11	23:15 (22:15 - 00:15)	07:30 (04:10 - 09:00)	7.2 (5 - 8)	2	2
P12	23:00 (22:50 - 23:20)	08:00 (07:20 - 08:20)	8.7 (8 - 9.5)	3	8
P13	23:00 (22:30 - 00:00)	08:00 (07:00 - 09:00)	8.3 (8 - 9)	2	14
P14	00:30 (00:00 - 01.30)	06:00 (05:00 - 07:00)	6 (4.5 - 8)	1	3
P15	23:30 (23:00 - 00:45)	08:00 (06:30 - 09:00)	7.6 (7 - 9)	3	9
P16	23:15 (22:30 - 00:00)	07:30 (06:15 - 9:30)	8 (6 - 9)	0	10
all	/	/	7.7 (0.8)	2 (1.75)	5.5 (5)

and discomfort) to vanish and not interfere with the experimental measures (Alhola and Polo-Kantola, 2007). Finally, participants were instructed to maintain a regular sleep and wake time, and specifically to go to bed between 11PM - 12AM and to wake up between 7 – 8AM. This was aimed at regularizing participants sleep/wake schedule to the experimental schedule that was adopted during the experiment. To track participants sleep habits and check compliance with instructions, participants were asked to complete a morning and evening sleep diary online (<1 minute to complete) starting one week before the experiment and reporting the time they went to bed, time they woke up, amount of hours slept, naps duration, physical exercise and caffeine/alcohol intake. Participants also wore a portable actigraphy watch (MiBand) from one week before the experiment until the end of experimental sessions. Sleep habits collected from PSQI, ESS and sleep diaries are reported in Table 2.1.

2.1.2 Experimental procedure

One goal of this project was to generate a multimodal dataset including behavioural (response times and accuracy), cognitive (vigilance, selective spatial attention, perception and metacognition), physiological (heart rate, pupillometry) and neuroimaging (brain structure, microstructure and function) measures on the same individuals over a period of 36 hours sustained wakefulness and after a night of recovery sleep. The dataset would allow investigation of the impact of sleep deprivation on brain and behaviour as well as to assess the brain functional and structural mechanisms that underlie evolution of changes in behavioural performance and cognitive functions over sustained wakefulness. For this purpose, the experimental protocol was designed to include neuroimaging scans and cognitive tests at different timepoints. Morning, afternoon, evening and night tests were included to track the timecourse of performance decrement and brain structural and functional changes with increased time awake as well as to control for circadian rhythm influences at different times of the day and night.

The experimental protocol is illustrated in Figure 2.1. The experiment took place over 4 consecutive days and included a total of 8 distinct sessions. Participants arrived at the laboratory in the afternoon of Day1 and started the first testing

battery around 5PM (Day1PM session). At the end of the first session, they then went home to sleep in their own bed during Night1. The decision of allowing participants to sleep in their own house rather than in the laboratory was taken to maximise sleep quality and minimize disruption of volunteers' sleep and wake schedules. Volunteers returned to the laboratory for testing on Day2 morning at 7AM (Day2AM session) as well as on Day2 late afternoon at 5PM (Day2PM session). Day1 and Day2 sessions made up the Well-Rested, baseline sessions (WR). During Night2, volunteers remained awake in the laboratory under constant supervision and completed the battery of behavioural tasks at 1AM (Night2Early session) and again at 4AM (Night2Late session). In the morning and evening of Day3 they completed two further testing sessions starting at 7AM and 3PM respectively (Day3AM and Day3PM sessions). Night2 and Day3 sessions constituted Sleep Deprived (SD) sessions. Volunteers then went home around 10PM for one night of recovery sleep (Night3) and returned for testing the following morning between 7 and 9 AM (Day4AM session). Day4 session was the Recovery (REC) session.

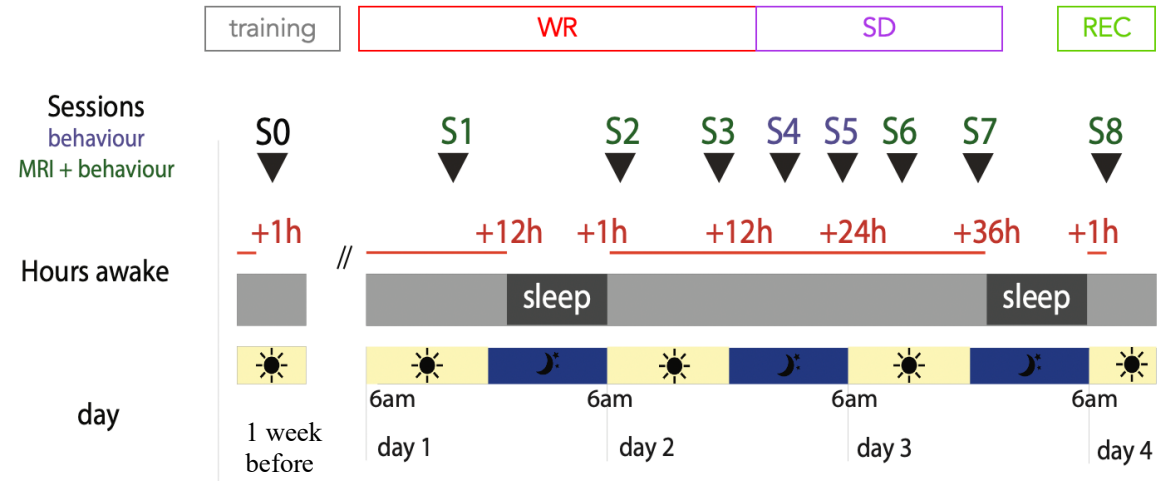

Figure 2.1: Sleep deprivation experiment protocol. All participants completed the same protocol including 6 behavioural + MRI sessions and 2 behavioural-only sessions over 4 consecutive days. From day 2 to day 3 participants remained awake continuously for 36 hours.

Between sessions, except during Night2, volunteers were free to leave the University premises to attend lectures, relax at home, shower, eat. Importantly, volunteers were instructed not to take any naps, consume caffeine or energy drinks and practice physical exercise until the end of the experiment. To ensure compliance with the instructions, participants wore a Philips SmartSleep Headband from Day1

until Day4, at all times except during the MR scans. The Philips SmartSleep Headband is equipped with a single frontal electrode and an amplifier that continuously record brain electrophysiological activity on the subject's forehead. A Philips proprietary algorithm analyses the frontal electrophysiological signal and identifies the sleep/wake state (NREM1-3; REM; Wake). Philips SmartSleep Headband was used only for confirmation that participants remained awake when they were supposed to stay awake, as well as a descriptive index of the amount of hours participants slept during Night 1 and Night3 (Table 2.2).

In each testing session, volunteers completed a battery of behavioural tasks (a total of 9 tasks including PVT, visual search task, attentional capture task, orientation discrimination task, vernier discrimination task, two-flash discrimination task, tilt-illusion task, face/house/blank discrimination task varying signal intensity and face/house/blank discrimination task varying noise intensity), 4 task functional MRI scans (PVT, attentional capture task, face/house/blank discrimination task with varying noise intensity and retinotopic mapping), 4 minutes resting state functional MRI, 2 quantitative MR sequences (Quantitative Magnetization Transfer - qMT, mcDESPOT) and 2 multi-compartment diffusion MR sequences (CHARMED, AxCaliber).

Behavioural tasks were divided into 4 blocks, each taking between 15 and 20 minutes to complete. The type of task within each block and their order were fixed, but blocks were counterbalanced between sessions in the same way across participants. MR scans were divided into 2 blocks, one taking 60 minutes to complete (and including all task-fMRI sequences) and the other 90 minutes to complete (including all other sequences). At the beginning of each block, participants were asked to rate their mood, vigilance and motivation on 7-point Likert-type scale and to complete a Stanford Sleepiness Scale (Shahid et al., 2011) – a 7-point Likert-type scale assessing subjective sleepiness. The total duration of a testing battery, including behavioural and neuroimaging parts, was 4 hours, including 10 minutes break every hour. At the very end of the experiment, participants were debriefed by an experimenter.

Table 2.2 shows sleep duration in Night1, Night2 and Night3 as recorded from the

Table 2.2: Hours of sleep measured by the Philips SmartSleep Headband.

ID	Night1	Night2 (sleep deprivation)	Night3 (recovery)
P01	6.5	0	5.5
P02	4.5	1	1.4*
P03	4	1.75	5.5
P04	7	0	9
P05	6.2	*Unavailable data***	7
P07	6.8	0	7
P09	8	0	9
P10	6	0	8
P11	6.2	0.5	7.5
P12	5.2	0	*Unavailable data***
P13	7.5	0	2.5***
P14	4.7	0	7
P15	6.2	1	8
P16	6.8	0	9
Mean (SD)	6.1 (1.1)	0.3 (0.5) †	7.5 (1.3) †

* recording stopped at 00:47AM

** recording did not start.

*** battery died at 01:47AM

† excluding subjects with incomplete data

Philips SmartSleep Headband. In night 1, participants sleep duration was on average 1.5 hours shorter than their self-reported sleep duration during the week before the experiment (see Table 2.1). Moreover, during Night2 – the sleep deprivation night, the headband detected non-zero hours of sleep in some participants. This appears in marked contrast with the overt display of sustained wakefulness (e.g. eyes open, talking to experimenter) by participants during the night of sleep deprivation and suggests that sleep data extracted from the headband be taken with caution. However, it points to the fact that participants started experiencing difficulty remaining awake, sleepiness and fatigue from the middle of the night of sleep deprivation. In fact, as reported by participants themselves and as noted by experimenters during behavioural tasks, participants had the tendency to close their eyes occasionally during tasks, evidencing fatigue and tiredness. To make sure that participants remained awake, experimenters kept close attention to participants responses, and, if they took too long to respond or missed two responses in a row,

experimenters probed participants by calling out their names and encouraging them to remain awake and keep their eyes open.

2.1.3 Performance training

Performance improves with practice (i.e. training or learning effect) and when repeatedly testing performance across WR and SD states, learning effects could interact with the effects of sleep deprivation. Here, participants completed between 3 and 4 training sessions before the main experiment to familiarise with the tasks and reach a stable level of performance. These training sessions took place between two weeks and one day before the experimental sessions (for most participants, these were scheduled starting one week before the experiment), over few consecutive days with one or two sessions per day. These sessions included practicing the battery of behavioural tasks that were later assessed in the experiment (listed above). Performance in these tasks improved over two or three training sessions, then reached a stable performance (Supplementary Figure S2.1).

2.2 Assessment of visual perception

2.2.1 Introduction to psychophysics

Psychophysics is the study of the quantitative relationship between external, objective physical stimuli and the internal, subjective perceptions they give rise to (Kingdom and Prins, 2016). Before the mid 1800s, the nature of subjective perception was deemed inaccessible and matter only to philosophical speculation. However, a few scientists contributed to the debunk this belief around the mid 1800s. Ernst H. Weber in 1834 conducted the first experiments attempting to identify how changes in physical stimulus intensities related to changes in perceptions. In 1860, Gustav Fechner, extended the previous work of Weber and formalized their observations into mathematical formulas relating perceived sensations to physical stimuli. Fechner proposed two important hypotheses: (1) that the change in physical stimulus intensity required to generate a just noticeable difference (JND) in perception is proportional to the absolute intensity of the stimulus (known as the Weber Law), and (2) that the perceived intensity of a stimulus is proportional to the logarithm of its physical intensity (known as the Fechner law) (Fechner, 1860; Gescheider, 1997). With these formulations Fechner

firstly quantified numerically how physical stimuli relate to internal sensations, laying the foundation of modern experimental psychology and the quantitative study of perception. Throughout the years, examination of perception with psychophysical methods has flourished and allowed systematic and quantitative assessment of perceptual processes and perceptual decision making.

2.2.2 Psychophysics and signal detection theory

The modern and widely accepted theoretical framework guiding interpretation of psychophysical data is Signal Detection Theory (SDT, Green and Swets, 1966). According to SDT, observers perceptual decisions are uncertain. When observers attend to a stimulus and are asked to report its presence or to discriminate one of its feature, the internal representation of the stimulus or stimulus feature takes a certain value on an internal *decision variable* dimension (for example the stimulus presence or its luminance) (Stanislaw and Todorov, 1999). The observer then compares whether the value of the *decision variable* is above or below an internal *decision criterion*, an abstract threshold separating the decision variable space in two parts, corresponding to the two decision outcomes (e.g. yes or no). If the decision variable value is above the criterion, the observer reports "yes" or "option A" (in detection or discrimination task respectively), whereas if the decision variable is below the criterion, the observer reports "no" or "option B". Across multiple trials where stimulus and noise (or stimulus A and stimulus B) are randomly intermixed and presented, stimulus trials will generate a distribution of decision variable *S* or S_A, while the noise or alternative stimulus trials will generate a distribution of decision variable *N* or S_B (Figure 2.2). Critically, the degree of overlap of the two distributions is inversely related to the sensitivity of the observer. A measure of sensitivity of SDT in fact is the distance between the means of the two distribution, a parameter known as *d'* (d-prime), or *discriminability index* (Green and Swets, 1966; Stanislaw and Todorov, 1999). Another measure is the response bias, which refers to the tendency of an observer to report one response over the other and corresponds to the location of the decision criterion. Importantly, the criterion determines the conditional probabilities that an observer reports either response (Yes or No; A or B) given the presented stimulus (stimulus or noise; stimulus A or stimulus B). One of the key points of SDT is that the sensitivity of the observer is

independent of the response criterion, or bias, so it can allow to estimate and compare sensitivity when people have different bias (Hautus et al., 2021).

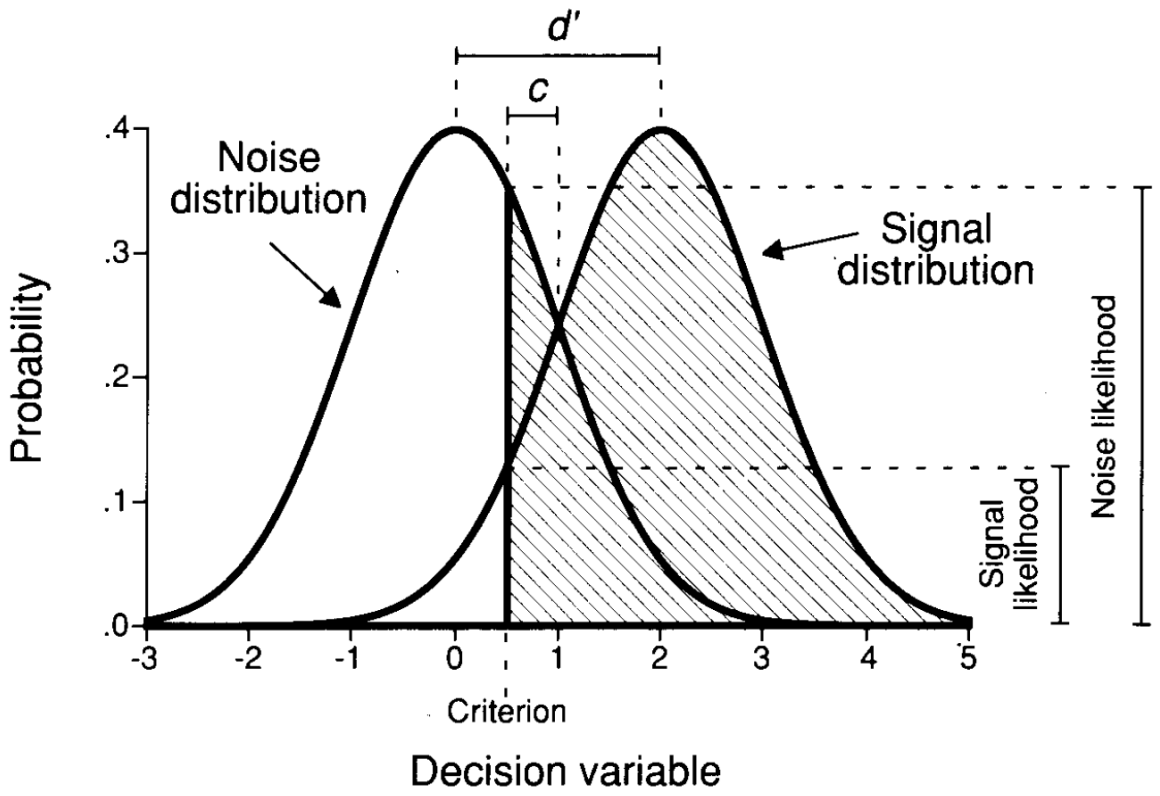

Figure 2.2: Schematic illustrating Signal Detection Theory. Probability distributions of the decision variable for signal trials (stimulus present or stimulus A) and noise trials (stimulus absent or stimulus B). In each trial, stimulus generates an internal decision variable which is compared to the observer's internal criterion. If the decision variable is greater than the criterion, the observer will report choice A (or Yes), otherwise they will report choice B (or No). Adapted from Stanislaw and Todorov, 1999.

2.2.3 Perceptual sensitivity and threshold

The main outcome of a psychophysical tasks is often an estimate of the observer's perceptual sensitivity, the ability to detect and discriminate sensory stimuli (Gescheider, 1997). For example, measures of sensitivity include *absolute threshold*, the minimal detectable physical stimulus, and *difference threshold*, or JND, which refers to the minimal detectable physical stimulus difference (Gescheider, 1997; Green and Swets, 1966; Hautus et al., 2021). On the one hand, absolute threshold can be identified via detection tasks, where an observer is asked to report whether they perceived a stimulus (e.g. a tone, or a flash) by reporting yes or no, while the magnitude of stimulus energy is varied trial by trial (e.g. tone

decibel or flash luminance). In such yes/no task, the absolute or detection threshold corresponds to the stimulus magnitude that produces a perception a certain proportion of time (e.g. the loudness or brightness at which participant perceive the tone/flash 50% of the times) (Gescheider, 1997). On the other hand, difference threshold is similarly estimated by varying stimulus magnitude trial by trial, but observers are asked to identify a difference in the stimuli presented, for example between a presented stimulus relative to a standard reference or between two consecutive (two-interval forced choice or 2IFC) or simultaneous (two alternative forced choice, or 2AFC) stimuli. The difference threshold is also identified as the stimulus magnitude that participant can correctly discriminate a given proportion of times (e.g. usually 50% or 75%, depending on the approach employed to model behavioural responses) (Gescheider, 1997; Kingdom and Prins, 2016).

2.2.4 Psychophysical procedures

Psychophysical tasks can vary depending on the procedure used to select and present stimuli (Kingdom and Prins, 2016). Two common psychophysical task procedures include the *Method of Constant Stimuli (MOCS*) and *adaptive staircase*. In MOCS task, a range of stimulus parameters (e.g. flash luminance values) are selected before the task begins. Several trials are then randomly presented for each stimulus parameter during the task. The choice of stimulus parameters usually ranges from very low to very high feature intensity. The wide range of stimuli allows to include stimuli that are easily detectable/discriminable (i.e. above threshold), stimuli that are undetectable/indistinguishable (i.e. below threshold) and stimuli that are sometimes detected/discriminated and sometimes not (i.e. around threshold). MOCS allows reliable and accurate estimation of perceptual sensitivity and threshold by modelling performance using the psychometric function (described below). It also allows to generate accurate estimation of performance at all stimulus parameters levels, generating a model of perceptual responses that can generalize beyond the specific stimuli presented (Waskom et al., 2019).

An alternative procedure is the *adaptive procedure* (Leek, 2001; Treutwein, 1995). In adaptive procedures, stimulus parameter is adjusted trial-by-trial depending on performance history of the observer. For example, in *two-up-one-down staircase*

procedure, stimulus difficulty parameter is increased by one step (i.e. it becomes more difficult to detect/discriminate) when observer responds correctly on two consecutive trials and is reduced by one step (i.e. easier to detect/discriminate) after one single incorrect trial. The critical characteristic of the staircase procedure is that stimulus parameter presentation will fluctuate closely around observer's perceptual threshold (Levitt, 1971), stabilizing performance around 71% accuracy.

2.2.5 Psychometric function

One common way to characterize performance and estimate perceptual sensitivity from a psychophysical task is to use the psychometric function (Kingdom and Prins, 2016; Wichmann and Hill, 2001). The psychometric function (PF) illustrates the relationship between stimulus and perception by plotting the response of the observer (yes/no or proportion correct, usually plotted on the Y axis) relative the stimulus parameter presented in a task (e.g. luminance or decibel, usually plotted on the X axis). Two types of PF are commonly used with the main difference being the response variable plotted on the Y-axis (Figure 2.3): proportion of choice A (or B) or performance accuracy (Gold and Ding, 2013). The choice of the PF to adopt depends on the type of task, number and type of stimuli presented and response options. The classic PF, originally employed in early yes/no detection experiments, relates the proportion of "yes" responses to the magnitude of the stimulus parameter. This PF is also commonly used in discrimination experiments with two response options, where the proportion of one of the two possible responses (A or B) is plotted on the Y-axis. In this "choice PF", perceptual sensitivity is reflected by

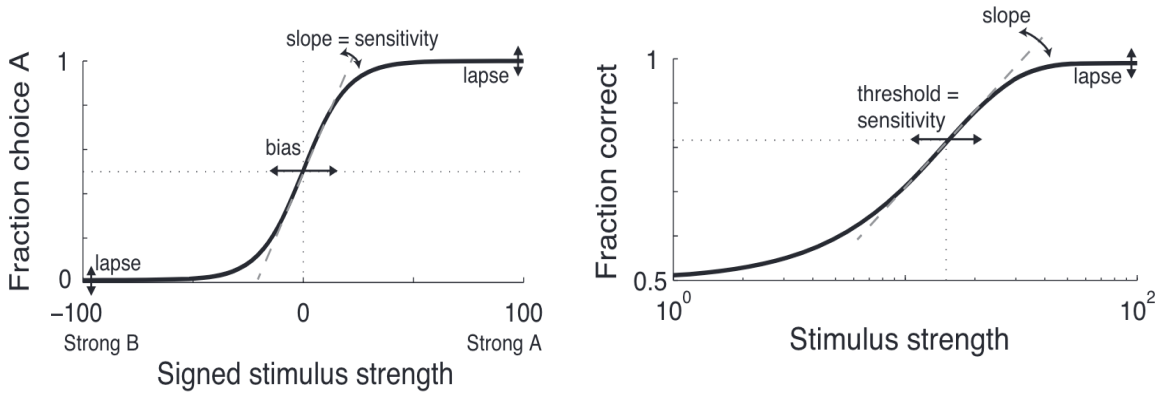

Figure 2.3: Psychometric functions. Two common versions of psychometric functions to model behavioural performance. Adapted from Gold and Ding, 2013.

the slope parameter of the PF, with steeper slope indicating higher perceptual sensitivity (Gold and Ding, 2013; Stanislaw and Todorov, 1999). In addition, the middle of the psychometric curve, or stimulus magnitude which observers report as yes or option A in 50% of the trials is known as the Point of Subjective Equality (PSE) in discrimination experiment or as the absolute threshold in detection experiments.

The other popular approach to characterize psychophysical performance is to plot the proportion of correct responses for each absolute stimulus parameter (Kingdom and Prins, 2016). If an appropriate range of stimuli is selected for presentation and a sufficient number of trials are completed, the PF which originates by joining the accuracy points (or by fitting a sigmoid function) ranges from the guess rate (1/number of response alternatives) at the minimum stimulus parameter to 100% correct at the maximum stimulus parameter. Perceptual sensitivity here is reflected by the psychophysical threshold, usually the stimulus magnitude at which performance is accurate in 75% of trials (Gold and Ding, 2013). This method adapts to different experimental paradigms and stimulus presentation modalities and is often used in 2AFC/2IFC discrimination tasks. Frequently performance is not 100% correct at highest stimulus intensities. In fact, even at high stimulus intensities participants sometimes make mistakes. The difference between actual performance and maximal performance accuracy (i.e. 100%) at the highest stimulus parameter is known as the lapse rate. In fact, the errors made at such high stimulus parameters are usually referred to as *lapses*, as they reflect non-sensory mechanisms at play and momentary lapses of attention such as erroneous button presses, blinks sneezes etc. (Kingdom and Prins, 2016).

In this thesis, the use of psychophysical tasks (e.g. Figure 3.2) was instrumental to characterise visual perception and to evaluate perceptual properties of sensitivity and bias. Specifically, by varying the stimulus physical parameters (e.g. horizontal lines offset in the vernier discrimination task) and asking participant to make the same perceptual judgement (e.g. whether the top one of two abutting vertical lines

is positioned rightward or leftward relative to the bottom one), I was able to probe the sensory mechanisms underlying perceptual decisions .

2.3 Assessment of metacognition

Chapter 5 includes a series of psychophysical staircase tasks aimed at assessing the impact of sleep deprivation on perceptual metacognition. Metacognition refers to the ability to correctly discriminate one's own accurate from inaccurate choices and can be referred to as a Type 2 task (relative to the Type 1 task which is the perceptual discrimination of the stimulus) (Galvin et al., 2003). It is an introspective ability inasmuch requires observers to evaluate their own responses, rather than the objective state of the world.

Accurate and valid assessment of metacognition requires a combination of objective (first-order) and subjective (second-order) measures of task performance during a cognitive task (Fleming and Lau, 2014). Objective measures such as performance accuracy provide an index of performance independent of subjective bias. Subjective measures such as confidence ratings (CR) in response accuracy provide a subjective estimate of performance based on individual introspection. In metacognition studies, observers provide subjective estimates of response accuracy after each trial, for example via Likert scale options that represent the level of confidence in response accuracy (Fleming et al., 2010). From the joint analysis of objective and subjective performance measures, it is possible to calculate *metacognitive sensitivity (*also known as metacognitive accuracy or metacognitive discrimination) (Fleming and Lau, 2014), which reflects how well an observer discriminates correct from incorrect decisions. For example, observers that give high confidence to correct decisions and low confidence to incorrect decisions have accurate evaluation of their own cognitive processes and are deemed to have high metacognitive sensitivity. Importantly, individuals can have different tendencies to report higher or lower confidence ratings on average, an index that reflects *metacognitive bias*, but this should not be confounded for the ability to discriminate correct from incorrect decisions. In other words, an observer who gives high confidence ratings across most trials reflects that they are certain about their perceptual decisions, but it reveals nothing about their metacognitive ability to

discriminate the accuracy of their own perceptual choices decisions. Figure 2.4 illustrates the difference between metacognitive bias and metacognitive sensitivity.

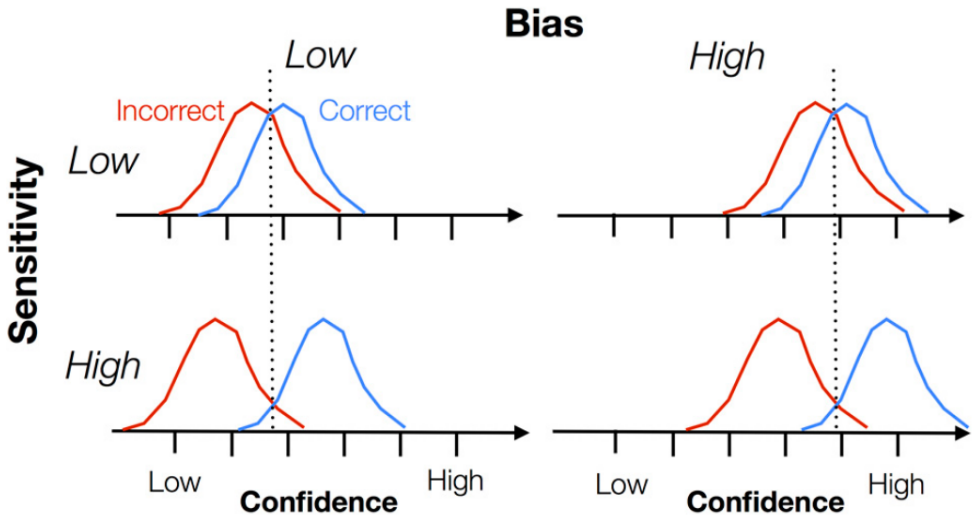

Figure 2.4: difference between metacognitive sensitivity and metacognitive bias. The probability density functions correspond to hypothetical distributions of confidence for correct (blue) and incorrect (red) decisions. Metacognitive bias (dotted vertical line) is expressed by the tendency to report high (right column) or low (left column) confidence ratings. Metacognitive sensitivity is reflected by the separation between the distributions of confidence ratings for correct and incorrect decisions. When the distribution largely overlap, (top row), discriminability of correct from incorrect decisions based on confidence ratings is low. When the distributions are well separated (bottom row), confidence ratings can discriminate well between correct and incorrect decisions. Adapted from Fleming and Lau, 2014.

One important aspect for valid and effective measurement of metacognitive sensitivity is the range of stimulus strength. When measuring metacognitive sensitivity, differences between levels of confidence ratings should map onto differences in internal representation of confidence rather than onto differences in external stimulus strength. Hence, it is crucial to adopt a method of stimulus presentation that minimizes differences in stimulus strength. Furthermore, the range of stimulus strength should be such to generate task performance between ceiling and chance, so that task performance is neither too easy – which would likely yield high metacognitive sensitivity values, neither too difficult, which would yield low or zero metacognitive sensitivity values. Staircase methods are ideally suited for these goals as they adapt stimulus strength trial-by-trial to keep performance level nearly-constant around a threshold value (e.g. 71% accuracy).

2.4 Assessment of brain function

In Chapter 4 of this thesis, I present results from a functional MRI experiment measuring Blood-Oxygenation-Level Dependent (BOLD) signal as an index of neural activity. In this section, I introduce some concepts relevant to understand how BOLD signal is generated from both the MR physics and neurophysiological standpoints.

2.4.1 Basis of MR signal

Inside a MR scanner lies a large and strong magnet, usually about 3 Tesla – 60,000 times stronger than the Earth's magnetic field. The magnet generates a strong magnetic field, B_0, which causes hydrogen nuclei to align parallel to it. As all nuclei align with the main magnetic field, they are in a state of equilibrium and the net magnetization is near zero. A set of radiofrequency (RF) coils are used to send brief RF impulses that generate another magnetic field, B_1, at a right angle to the static magnetic field B_0. B_1 perturbs the alignment of the atomic nuclei shifting them away from equilibrium and inducing a transverse magnetization. As soon as RF impulses cease, atomic nuclei rapidly return from perturbed state back to equilibrium, a process known as *relaxation*. During this time, some of the energy of the atomic nuclei is emitted as radiofrequency waves and can be detected by receiver coils of the MR scanner as MR signal. Relaxation of the atomic nuclei includes both decrease of the transverse magnetization ("decay") and increase of longitudinal magnetization (along the B0, "recovery"). The former is known as T2 and reflects the length of time required for the magnetization to decay from the transverse plane. The latter is known as T1 and reflects the length of time it takes for recovery of longitudinal magnetization back to its initial values. In addition, decay of transverse magnetization can be further amplified by the presence of local inhomogeneities in the magnetic field. This causes MR signal decay to be even faster, and to account for this variation it is referred to as T2*. In other words, T2* is the time it takes for the transverse magnetization to decay when there are local inhomogeneities.

Grey matter, white matter, cerebrospinal fluid and other brain tissues have different proportion of hydrogen nuclei so they exhibit differences in their magnetic properties and relaxation times. Crucially, such differences can be exploited to

design MRI sequences that are sensitive to different tissue types or to local variations in MR signal. For example, standard *functional* MRI BOLD sequence at 3Tesla is usually a T2*-weighted sequence to maximise sensitivity to local inhomogeneities driven by varying oxygen concentration in grey matter tissue that reflect changes in neural activity.

To map spatially specific information form MR images, the application of spatially varying magnetic field gradients **is required**. These gradients are created by introducing specific magnetic field variations across the region of interest within the scanner. Gradients ar produced by dedicated gradient coils, which generate additional magnetic fields along the x, y, and z axes. By applying different strengths and timing patterns to these gradients, the magnetic field becomes spatially dependent, allowing for the encoding of location-specific information.

2.4.2 Cerebral metabolism and neurovascular coupling

The brain requires oxygen and glucose to synthesise ATP and create energy to support metabolic activity. However, the brain cannot store glucose or oxygen locally and requires constant and quick supply of these nutrients for maintenance of its functions (Clarke & Sokoloff, 1999). Nutrients are transported and delivered locally via the neurovascular system including arteries, capillaries and veins. In addition, the brain has high metabolic costs: it consumes about 20-25% of the glucose used by the entire body and 20% of the oxygen supply despite weighting only 2% of body mass (Raichle and Gusnard, 2002; Shulman et al., 2004). To support this energy-thirsty organ, an efficient cardiovascular system is in place that regulates cerebral blood flow (CBF) according to energetic demands of local neuronal tissue. Specifically, when neuronal activity rises to support motor, sensory or cognitive function and the cerebral metabolic rate of oxygen ($CMRO_2$, i.e. the rate of oxygen consumption) of the local neural tissue also increases, the CBF rises to deliver oxygen-rich blood and nutrients to the demanding neural tissue to support its activity. Importantly, these changes in CBF and $CMRO_2$ are localized to the demanding regions, creating a map of local inhomogeneities that can be measured and imaged (Logothetis et al., 2001).

2.4.3 Hemodynamic activity and BOLD contrast

The increased energetic demands of the activated neurons lead to an increase of CBF and cerebral blood volume (CBV) that allows for delivery of more oxygenated blood and nutrients to the demanding region (Iadecola et al., 1997). Also $CMRO_2$ increases, but the amount of oxygen delivered by increased CBF exceeds the amount of oxygen needed by neuronal metabolism (Fox and Raichle, 1986). This mismatch leads to a local surplus of oxygenated blood in the region of neuronal activity, a condition that is exploited by BOLD contrast imaging (Figure 2.5).

BOLD contrast is an indirect measure of neuronal function since it is sensitive to changes in oxygen concentration in blood that depend on the neuronal activity demands. Oxygen in the blood is transported by haemoglobin, a protein contained in red blood cell that has magnetic properties. Specifically, oxygenated haemoglobin (Hb) is diamagnetic and weakly interferes with the surrounding magnetic field whereas deoxygenated haemoglobin (dHb) is paramagnetic and distorts the surrounding magnetic field. Since the MR signal is sensitive to magnetic distortions within its B0 field, the ratio of Hb and dHb determines the magnitude of the MR signal measured with BOLD-contrast MR imaging. Specifically, a greater fraction of Hb relative to dHb generates a larger magnitude of MR signal, since Hb is diamagnetic and interferes weakly with the magnetic field. Conversely, a greater fraction of dHb relative to Hb leads to a reduction in MR signal, since dHb is paramagnetic and increases the distortion of the magnetic field. As such, the BOLD activity is a relative rather than absolute index of the oxygenated blood and is usually interpreted in reference to a baseline, such as the average BOLD signal during the fMRI scan (Stark and Squire, 2001).

The local concentration of Hb and dHb in the brain varies quickly upon neuronal activation. As neurons activate, their increased oxygen consumption leads to an initial increase in dHb, which leads to a BOLD signal reduction (Ogawa et al., 1990). As soon as the local blood flow increases however, more oxygen remains in the blood than the neurons consume (Fox and Raichle, 1986), leading to an increase of Hb relative to dHb and an increase in MR signal.

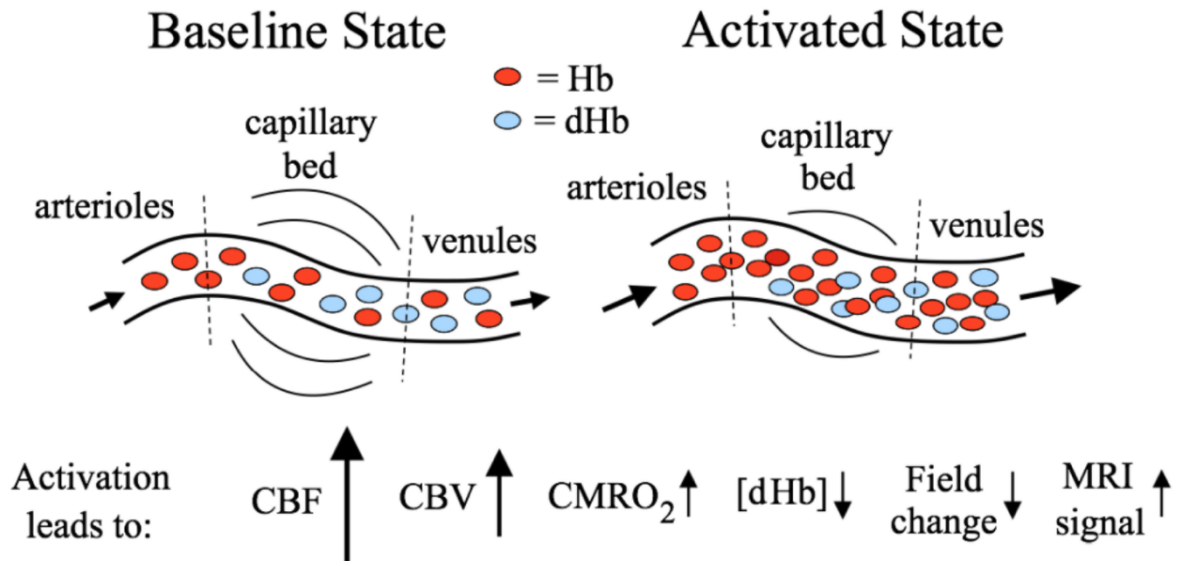

Figure 2.5: changes in neurovasculature upon neuronal activation underlie the basis of BOLD signal. Adapted from https://www.fmrib.ox.ac.uk/primers/appendices/mri_physics.pdf.

2.4.4 Neurophysiological correlates of BOLD signal

The BOLD signal is correlated with increased supply of oxygen-rich blood to support local neural tissue increased activity (Mandeville et al., 1998). However, which aspects of neural activity underlie the increased hemodynamic activity and increased BOLD responses are still not completely understood. A seminal study by Logothetis and colleagues (2001) measured simultaneously BOLD signal and electrophysiological activity in monkey neural tissue using depth electrodes and found that BOLD activity correlates with local field potential (LFP) better than with the spiking activity of single or multiple neurons. LFP is the low-frequency (usually below 250Hz) extracellular potential recorded from an electrode implanted in brain tissue. LFP is generated by synchronized oscillations in synaptic membrane potentials of neurons within a 3mm radius of an electrode tip implanted in neural tissue (Logothetis, 2008; Nunez and Srinivasan, 2005). This suggests that BOLD signal correlates with synaptic activity rather than with action potentials, although the two can be correlated (Logothetis et al., 2001). Moreover, while both synaptic activity and spiking activity increase local oxygen consumption, only synaptic activity has been shown to lead to increases in CBF (Mathiesen et al., 1998). Since CBF increases underlie BOLD signal, this further supports the idea that positive BOLD signal may reflect integrative, input-related neural activity rather than spiking,

output-related activity of local neuronal populations (Lauritzen et al., 2012; Logothetis, 2008; Logothetis et al., 2001).

2.4.5 The hemodynamic response

The stereotyped BOLD signal change evoked by a neuronal event is illustrated by the hemodynamic response (HDR) (Figure 2.6). The timecourse of the HDR is sluggish, lagging few seconds after the neural event originating it and lasting up to 20 seconds (Huettel et al., 2014). Firstly, an initial dip in BOLD signal, corresponding to the reduction in MR signal due to increased concentration of dHb relative to Hb, occurs briefly after neuronal activation (Menon et al., 1995). This initial dip is not always observed due to differences in magnetic field strength used, and spatial averaging that obscures the local, small-scale effect of the initial dip (Ances et al., 2004; Hu and Yacoub, 2012). 1-2 seconds after the neuronal response, CBF and CBV start to increase, and the higher proportion of Hb relative to dHb induces an increase in MR signal which peaks between 4 and 6 seconds after neuronal activation (Aguirre et al., 1998; Dale and Buckner, 1997; Huettel and McCarthy, 2000; Huettel et al., 2014). For prolonged stimuli, the peak extends into a plateau of variable duration. Then, as neural activation ceases, CBF and CBV slowly decrease, Hb and dHb levels slowly return to baseline and the BOLD response begins to fall. In this stage, the MR signal shows a reduction below baseline, known as undershoot, which could be explained by prolonged post-stimulus oxygen metabolism or by more rapid reduction in CBF relative to CBV which leaves increased concentration of dHb locally (van Zijl et al., 2012). Finally, the MR signal returns to baseline after about 20-30 seconds.

Overall, the HDR is a stereotyped BOLD response evoked by an isolated stimulus, but it is a crucial concept to understand the relationship between stimulus, neural response and measured BOLD signal (Buxton et al., 1998).

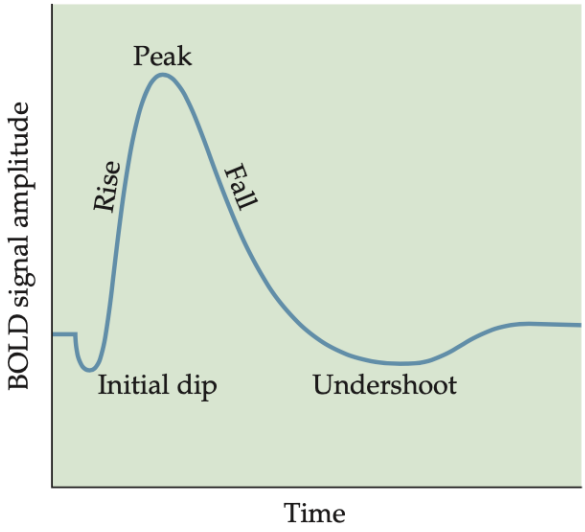

Figure 2.6: hemodynamic response characterizes the time course of BOLD signal evoked by a stimulus. BOLD response peaks about 4-6 seconds after stimulus onset corresponding to inflow oxygenated blood to the area of neural activation. Adapted from Huettel et al., 2014.

2.4.6 Linear properties of BOLD response

One of the key assumption of BOLD response is that it is linearly dependent on the underlying neural activity (Boynton et al., 2012). Linearity implies two key properties: scaling and additivity. Scaling means that the magnitude of the BOLD response is proportional to the magnitude of the underlying neural activity: stimuli that evoke greater neural activity also evoke larger-amplitude BOLD responses (Boynton et al., 2012; Boynton et al., 1996). Scaling is a fundamental property for interpretation of fMRI results that allows straightforward inference about neuronal activity from measures of BOLD signal in different conditions (i.e. if BOLD signal is higher in region A/group A than control, than neural activity is also higher) (Boynton et al., 2012; Huettel et al., 2014). Additivity, or superposition, implies that the output generated by two or more consecutive inputs equals the sum of the outputs generated by each input individually (Boynton et al., 2012; Huettel et al., 2014). Hence when two stimuli are presented in succession, the observed BOLD signal is a summation of the BOLD response evoked by each stimulus. Based on this property, one can estimate the BOLD response to closely presented stimuli, such as in event related designs and assume that the short inter-trial-interval does not influence the shape of the HDR (Dale and Buckner, 1997; Huettel et al., 2014) – although this is not always the case (see below).

Boynton and colleagues (1996) demonstrated scaling and additivity for blocked design (prolonged stimulus presentation). They showed that the BOLD response in primary visual cortex to black and white checkerboards was greater for stimuli with greater contrasts - known to evoke stronger neural response (e.g. Albrecht and Hamilton, 1982). They also showed that the BOLD response to a 12-second stimulus was similar to the BOLD response to two 6-second stimuli presented in succession (Boynton et al., 1996), demonstrating additivity. Dale and Buckner (1997) extended these findings to short-duration stimuli presented with variable inter-stimulus interval. They presented one, two or three identical stimuli with variable interval (2 or 5 seconds) and isolated the response to the second and third stimulus by means of subtraction. Comparison of the isolated BOLD responses revealed that they had roughly the same shape and amplitude as the BOLD response to the single stimulus (Dale and Buckner, 1997). This experiment was also a milestone in fMRI history as it validated the use of short-interval-trials and thus event-related design in fMRI experiments (Huettel et al., 2014).

Overall, the linear response function is a good approximation of the true underlying relationship between neural activity and BOLD response, but it is well documented that this linearity does not hold for short ISI (below 6 seconds) (Huettel and McCarthy, 2001; Robson et al., 1998; Vazquez and Noll, 1998). Specifically, a refractory period of up to 6 seconds (Huettel and McCarthy, 2001) leads to reduced BOLD response of a second stimulus presented less than 6 seconds after a first one. Critically, the refractory period depends on the sensitivity of a brain region to the observed stimulus, a characteristic that has been exploited by fMRI adaptation studies to assess functional selectivity of brain regions (Grill-Spector et al., 2004).

2.5 Supplementary material

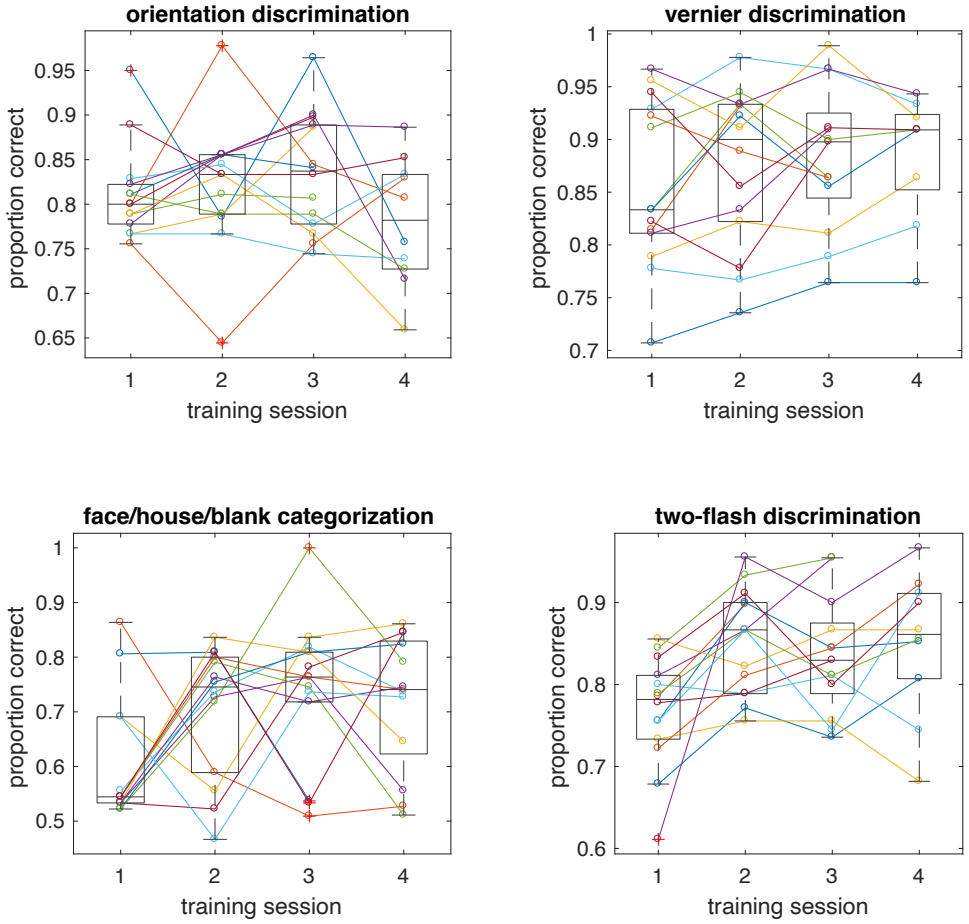

Figure S2.1: task performance training. Boxplot show median performance and inter-quartile range, lines show individual participant's accuracy in different training session. Overall, participants improved their accuracy over consecutive training sessions. This allowed to control learning effects that could have contrasted with the effects of sleep deprivation. Each training session included 90 trials (except the face/house/blank categorisation which included 110 trials per session). All tasks were 2IFC, except face/house/blank categorisation (3AFC).

Chapter 3.
Influence of sleep deprivation on low-level visual perception

3.1 Introduction

Humans are capable of perceiving incredibly small details in visual stimuli, such as minimal orientation differences in lines or misalignment between objects. These fine abilities contribute to generating rich and detailed contents that characterise our subjective conscious experience of the world.

Visual perception is the process that generates conscious representations from analysis of external physical stimuli. Visual perception occurs through stages, from the retina in the eye to high-level cortical regions in the brain (Grill-Spector and Malach, 2004). Early visual processing stages analyse local, low-level features of visual inputs, such as spatial contrast, colour and luminance (Carandini et al., 2005). Later stages compute high-level, abstract and holistic representations that guide classification and recognition (Groen et al., 2017). In this chapter I focus on perceptual discrimination of low-level visual features and investigate how it is influenced by sleep deprivation.

The early visual system is specialized in processing many low-level features of visual inputs, from edges and contours to contrasts and colours. A fundamental property of visual perception is spatial resolution. Spatial resolution, also known as visual acuity, can be defined as the minimal spatial separation between two elements that can be resolved (Westheimer, 1965). Visual acuity depends on the size of photoreceptors in the retina and is about 1 arc minute in the fovea (Hu et al., 2021; Westheimer, 1965). Yet, humans are able to resolve spatial details beyond this limit in certain scenarios. For example, humans can discriminate a positional offset of two abutting lines of just 5 arc seconds (more than 1/10 smaller than the visual acuity limit) (Westheimer, 1987). This ability is known as vernier acuity – or hyperacuity, since it is an order of magnitude finer than standard visual acuity (Westheimer, 1981). Vernier acuity contributes significantly to our fine ability to characterise the spatial positions of stimuli in the visual field.

Another hallmark property of visual system is orientation sensitivity (Carandini et al., 2005; Priebe et al., 2016). In a visual scene, elements are spatially defined by boundaries, edges and changes in luminance that have a certain orientation. Neurons

in primary visual cortex are sensitive to the orientation of these elementary visual features (Hubel and Wiesel, 1959; Tootell et al., 1998) and they provide a fundamental contribution to the construction of the spatial structure of a visual scene, including the forms of figures observed. Higher-level visual areas then use this visuo-spatial information to recognize and categorise figures as objects, faces, houses, etc. (Grill-Spector and Malach, 2004).

In a visual scene myriad of stimuli are present. Contextual elements are not ignored in visual processing but rather integrated and can influence the perception of other attended stimuli (Schwartz et al., 2007). For example, by the Gestalt law of proximity (Kofka, 1935), visual elements that are spatially adjacent are likely to be grouped together. Another example of this contextual modulation is the tilt illusion, in which the perceived orientation of a line is influenced by the orientation of a surrounding stimulus (Clifford et al., 2014). The strong illusion is a repulsion effect, in which a central grating surrounded by a grating tilted with up to 45° difference is perceived as tilted *away* from the surround grating (Clifford et al., 2002; Schwartz et al., 2009). There is also a weaker *attractive* illusion, when the surround grating is tilted more than 45° relative to the central grating, which is perceived as tilted towards the surround grating (Clifford et al., 2002; Clifford et al., 2000).

On top of the sensitivity to these typically spatial properties, another crucial property of visual perception is time. Discriminating temporal details is crucial in situations where visual information is presented rapidly such as when driving in traffic or in dynamic sports activities. Visual temporal resolution is the ability to resolve temporally consecutive stimuli (Levine, 2000), such as discriminating two flashes presented with a brief temporal interval (Reeves, 1996). Humans are capable of resolving temporal intervals around 30-40ms when stimuli are presented in the same location (Allan et al., 1971; Reeves, 1996).

Overall, visual perception is the product of specialized and integrated processing that contribute to generate a detailed, rich and accurate representation of reality. Whether sleep deprivation affects spatial or temporal properties of visual perception however has remained unclear.

After one night of total sleep deprivation, people commonly experience a range of cognitive impairments, such as reduced attention and increased sleepiness (Killgore, 2010, Krause et al., 2017), that are restored by subsequent recovery sleep (Belenky et al., 2003; Lamond et, 2007). Detection of visual stimuli has been shown to be less sensitive after sleep deprivation, as shown by increased response times and errors of omission (Rashid Izullah et al., 2021; Roge and Gabaude, 2009; Russo et al., 2005). However, whether sleep deprivation influences perceptual discrimination of low-level visual features such as orientation or line misalignment has been poorly investigated. In one study, Killgore and colleagues (2007) tested orientation sensitivity using a judgement of Line Orientation Test (LOT), requiring to match the orientation of a target line from a sample of various lines. After 23 hours awake, no change in task performance was observed, indicating preserved perception of line orientation in the sleep deprived state (Killgore et al., 2007). Another perceptual function, contrast sensitivity, was found to be slightly reduced after 48 hours of sleep deprivation in a study by Quant and colleagues (1992), but a more recent study failed to replicate this result (Koefoed et al., 2015). To assess temporal resolution in visual perception, studies have assessed the critical flicker frequency (CFF), the frequency at which a flickering light is perceived as a stationary light (Wells et al., 2001). Leonard and colleagues (1998) did not observe any difference in CFF before and after a 32 hours shift in medical doctors. Conversely, a study by Lee and colleagues (2002) found an increase in CFF after a night of total sleep deprivation, indicating poorer temporal resolution of visual perception (Lee et al., 2002). Consistent with the latter finding, sleep deprived subjects were less accurate at discriminating objects flashed at fast presentation rates in another study (Kong et al., 2014).

Overall, to the best of my knowledge, few studies have assessed the impact of sleep deprivation on discrimination thresholds of visual perceptual functions (e.g. Lee et al., 2002). Moreover, the studies presented above varied significantly with respect to task methodology, performance measures and duration of sleep deprivation adopted, and they provided inconsistent results. As such, the influence of sleep deprivation on perception spatio-temporal visual features remains unclear. Testing perceptual discrimination of multiple low-level visual features within the same

individuals can contribute to understanding how elementary properties of visual perception are influenced by sleep deprivation.

This chapter thus examines perceptual discrimination of low-level visual features over the course of 32 hours sustained wakefulness with the same participants. The aim was to evaluate the influence of sleep deprivation on visual perception of elementary visual features. In particular, I assessed four distinct visual properties: visual hyperacuity, orientation sensitivity, contextual modulation and temporal resolution. Using psychophysical tasks, I measured visual judgements as a function of different stimulus parameters and estimated the psychophysical threshold using a psychometric function as an index of perceptual sensitivity. Psychophysical tasks assessed were: vernier discrimination, orientation discrimination, tilt illusion task and two-flash discrimination task. The null hypothesis was that perceptual discrimination thresholds would not differ before and after a night of sleep deprivation and after a night of recovery sleep. Conversely, if visual hyperacuity and orientation sensitivity are influenced by sleep deprivation, perceptual threshold in the vernier discrimination and orientation discrimination tasks would be increased after one night of sleep deprivation, indicating that participants ability to resolve spatial details is reduced. Similarly, if sleep deprivation influenced how contextual elements modulate perception of a target in a visual scene, I expected to observed changes in the tilt-illusion magnitude (measured as the PSE of the psychometric function in the tilt-illusion task) after one night of sleep deprivation. Also, if sleep deprivation reduces temporal resolution of visual perception, I expected to observe increased two-flash discrimination threshold. Finally, if sleep recovers cognitive functions impaired by sleep deprivation, I also hypothesized that a night of recovery sleep after sleep deprivation would restore perceptual thresholds to the levels observed before sleep loss.

3.2 Methods

3.2.1 Participants

Fourteen volunteers (19-32 years old, 3 males) recruited among staff and students of Cardiff University took part in this study and received financial compensation.

The study was approved by ethical committee of Cardiff University. More details about the sample of participants are described in Chapter 2.

3.2.2 Experimental procedure

Participants completed the tasks as part of a larger multimodal experiment assessing the influence of sleep deprivation on brain, cognition and behaviour. The details of the complete experimental procedures are described in chapter 2. Briefly, before the experiment, participants completed training sessions to familiarize with the task and reach a stable level of performance (Supplementary Figure S2.1). During the experimental sessions, all participants completed tasks in the same order, which varied from session to session (Figure 3.1). Vernier discrimination and two-flash discrimination were completed as part of one block (which also included another version of the same tasks with confidence ratings of response accuracy to measure metacognitive abilities – see Chapter 5). Orientation discrimination and tilt illusion were part of another block (which also included a version of orientation discrimination task with confidence ratings and an object categorisation task). Between blocks, participants were allowed to rest for a maximum of 5 minutes.

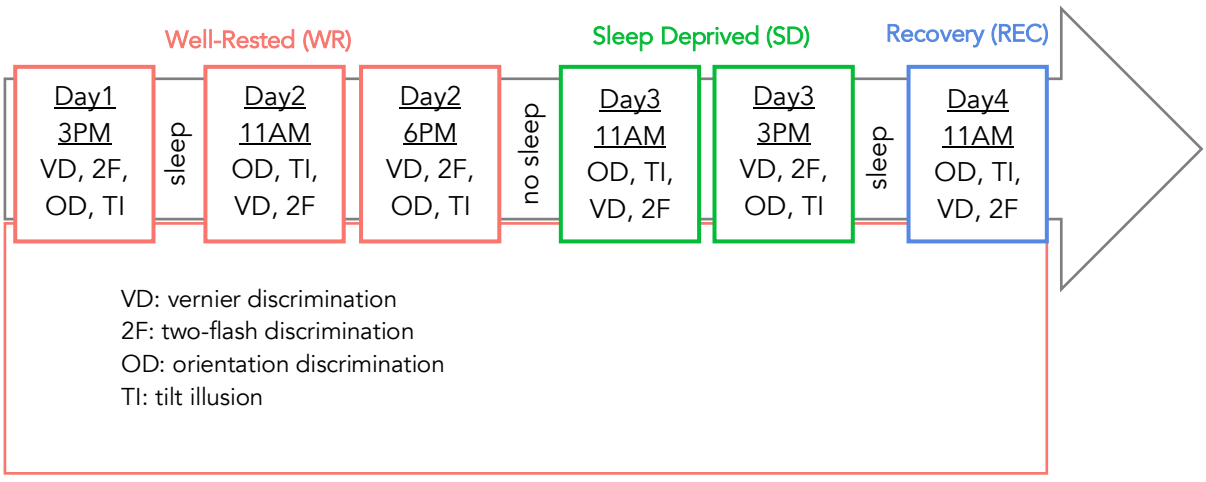

Figure 3.1: session times and task order employed in this experiment. Experiment lasted for 4 consecutive days, from the afternoon of Day 1 until the afternoon of Day4. Between Day1 and Day2, participants had a normal night of sleep at their house. Between Day2 and Day3 participants remained awake under constant supervision. Between Day3 and Day4 participants returned to their home to sleep in their own bedroom to minimise distress. To improve estimation of perceptual threshold from psychometric function and analyse the effect of sleep state, Day1 and Day2 sessions were merged into one single WR condition. Day3 sessions were merged into one single SD condition.

3.2.3 Experimental tasks and stimuli

Participants completed all tasks in a dark room with their head rested on a chinrest and the position of the screen adjusted such that the screen centre was aligned to their eyes. All tasks were programmed and presented using Psychtoolbox3.0 (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997) running on Matlab R2015b (Mathworks Inc., Natick, MA, USA). Because one of the aim of this study was to evaluate multiple perceptual and cognitive functions within the same individuals, a reduced number of trials were included, in favour of including multiple distinct tasks while keeping the entire task battery tolerable.

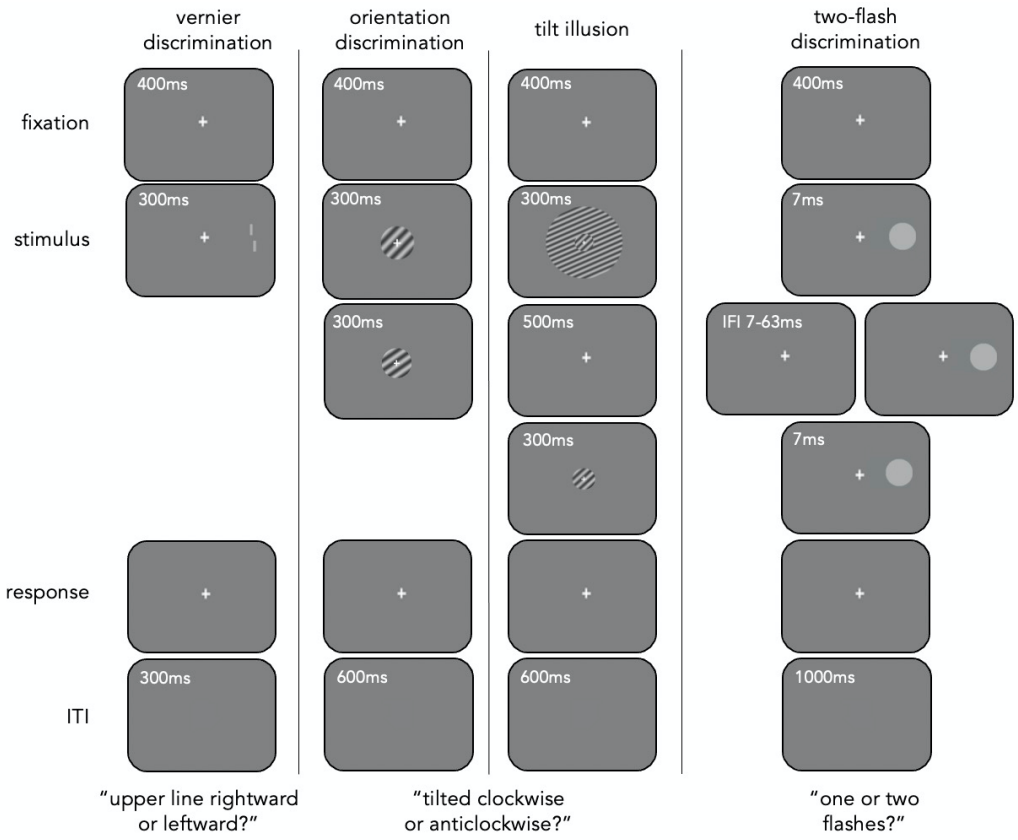

Figure 3.2: psychophysical task stimuli and procedures. Each trial began with a fixation cross, then stimuli were presented, followed by a response window. Participants had no time limits for responding. If participants did not respond within a few seconds, the experimenter prompted them to continue the task. An inter trial interval (ITI) with a blank window (background with no fixation cross) was included after participant response and before the following trial. Each task included 90 trials and lasted for approximately 5 minutes. Times of each trial sequence are indicated in the figure, but these were not visible during the experiment.

Vernier discrimination. This task measured visual hyperacuity, the smallest noticeable difference in spatial location between two distinct objects. Stimuli were two vernier lines presented on an ASUS VG248QE monitor (screen size 54x30cm; screen resolution 1920x1080, refresh rate 144Hz) on grey background [127.5 127.5 127.5] at a distance of 61.5cm. Task is illustrated in Figure 3.2 (first column). A fixation cross appeared in the centre of the screen for 400ms before stimulus presentation and remained on screen until participants' response. Participants were instructed to always fixate the cross. Two vernier lines were briefly presented for 300ms at 5° eccentricity, 0° polar angle (right side of the screen). The lines (0.75° visual angle, grey - rgb [175 175 175]) were vertically aligned at a distance of 0.3° visual angle or 18' arc. The 5° eccentricity was chosen after piloting to compromise with screen resolution. Specifically, since the minimal misalignment possible due to monitor characteristics was 1 pixel (0.0246° visual angle or 1'48'' arc), an eccentricity of 5° was chosen for presentation of the vernier lines since at this eccentricity the vernier threshold is between 1' and 3' arc (Levi et al., 2000; Levi and Waugh, 1994; Shiu and Pashler, 1994; Whitaker et al., 1992). Participants made unspeeded decisions on whether the upper line was located rightward or leftward relative to the lower line. The horizontal offset between the two vernier lines was varied trial by trial using a method of constant stimuli. A range of 9 absolute lines offset (from 1 pixel to 9 pixel offset) was used for all participants. Participants completed 90 trials per session, 10 trial for each absolute stimulus parameter (i.e. absolute horizontal offset between lines).

Orientation discrimination task. Orientation discrimination task assessed sensitivity to line orientations. Stimuli comprised two consecutive gratings (Figure 3.2, second column) presented in the centre (0° eccentricity) of a Dell curved monitor (70x39cm; refresh rate 60Hz) at a distance of 61.5cm. The two gratings were 0.75° of visual angle in radius and were presented consecutively with no delay for 300ms each. One grating was oriented at 45° in every trial, while the other grating could take one out of 9 orientation values greater or smaller than 45°. The order of the fixed and variable grating was pseudo-random. Participants made an unspeeded decision on whether the grating presented in the second interval tilted clockwise or anti-clockwise relative to first. A total of 90 trials were completed in each session, 10

trials for each absolute orientation parameter (i.e. the absolute difference of orientation between the two consecutive gratings). The range of orientation parameters was determined for each participants via a staircase calibration task performed in the first training session (Supplementary Note S3.1; Supplementary Table S3.1). This allowed to account for inter-individual differences in perceptual ability and match perceived task difficulty across individuals.

Tilt illusion. The tilt illusion task assessed contextual modulation on orientation perception. Task is illustrated in Figure 3.2 (third column). Similar to the orientation discrimination task described above, each trial consisted of two consecutive gratings presented in the centre of the screen (a Dell curved monitor 70x39cm; refresh rate 60Hz) located at a distance of 61.5cm. One of the grating was always 45° in orientation and was surrounded by an annular grating of 60° orientation. The other grating took one of 9 possible orientations in each trial. The central and annular gratings had a radius of 0.75° and 3° visual angle, respectively. Individuals were instructed to compare the two consecutive central gratings and report if the second was tilted clockwise or anti-clockwise relative to the first. Each grating was presented for 300ms, with an Inter Stimulus Interval (ISI) of 500ms. The interval in which the annular grating appeared was pseudorandom. To adapt the task difficulty to individuals' perceptual ability, a calibration run was completed on the first preparatory session before the experiment (Supplementary Note S3.2; Supplementary Table S3.2). A total of 90 trials were completed in each session, 10 for each orientation value.

Two-flash discrimination. The two-flash discrimination task assessed temporal resolution of visual perception, namely the minimal temporal interval required to perceive consecutive stimuli as distinct. Stimuli were two disks (hereafter flashes) coloured in dark grey (rgb [175 175 175]) and presented on a lighter grey background (rgb [127.5 127.5 127.5]) of an ASUS VG248QE monitor (screen size 54x30cm; screen resolution 1920x1080, refresh rate 144Hz) positioned at a distance of 61.5cm from participants eyes. The flashes had 0.75° diameter in visual angle and were presented in the right side of the screen (5° eccentricity and 0° polarity) for one single frame (1/144Hz = 7ms). A fixation cross appeared 400ms before the stimulus and remained

on screen until participants' response. In each trial, the Inter-Flash-Interval (IFI) between the first and second flash was varied pseudo-randomly using the method of constant stimuli. The range of IFI included 9 different values, with a minimum IFI of 1 frame (7ms) and a maximum IFI of 9 frames (63ms). In 50% of trials the IFI was blank (two-flash condition), and in the other 50% of trials the grey disk remained on screen during the IFI (single-flash condition). Figure 3.2 (fourth column) illustrates single-flash and two-flash trials. Participants were instructed to maintain their eyes fixated on the central cross and to report if they perceived one or two flashes by pressing one of two buttons with their right hand. A total of 90 trials were completed in each session, 10 for each IFI parameter.

3.2.4 Data analysis

To measure perceptual differences between WR, SD and REC, Day1-3PM, Day2-11AM and Day2-6PM sessions were merged into one single WR condition. Day3-11AM and Day3-3PM sessions were merged to create one single SD condition. REC condition was one single Day4-11AM session. Merging between sessions of the same sleep state also allowed to increase the number of trials and improve fitting of psychometric function to the data and estimation of perceptual threshold. From all conditions, trials with response times longer than 2 seconds and shorter than 200ms were excluded to remove extreme lapses (i.e. responses occurring when participants did not pay attention or had microsleeps) and accidental button presses (i.e. responses occurring before participants could visually process the stimuli).

Psychophysical analysis. Psychophysical analyses were used to characterise perceptual judgements as a function of changes in stimulus parameter and to estimate perceptual thresholds. Psychometric function fitting procedures were performed on Matlab using Palamedes toolbox (Prins and Kingdom, 2018). To illustrate the psychometric curves, the *quickpsy* library on RStudio was used (Linares and Lopez-Moliner, 2016).

For the orientation discrimination, vernier discrimination and two-flash discrimination tasks, proportion of correct responses were fitted with a psychometric function with four parameters α, β, γ and λ (Wichmann and Hill, 2001):

$$\psi(x;\alpha,\beta,\gamma,\lambda) = \gamma + (1 - \gamma - \lambda)\, F(x;\alpha,\beta) \qquad (1)$$

where F is a Quick function (Kingdom and Prins, 2016):

$$F(x;\alpha,\beta) = 1 - 2^{\left(-\left(\frac{x}{\alpha}\right)^{\beta}\right)} \qquad (2)$$

I estimated α and ß, the location and slope of the psychometric function that characterize the sensory mechanism underlying perceptual discrimination. Specifically, α in the Quick function estimates the central location of the psychometric curve, which approximates the 75% accuracy point in the accuracy psychometric function. Here, α corresponds to the perceptual threshold and was the parameter of interest. ß represents the slope of the psychometric function and reflects the change in accuracy in relation to variation in stimulus parameters (Gold and Ding, 2013). A sensory system that discriminates well between stimuli of different intensities has high sensitivity (Ulrich and Vorberg, 2009) as reflected by a steep slope of the psychometric function (large ß). Finally, parameters γ and λ correspond to the guess rate and lapse rate and define the lower and upper bound of the function F respectively. Guess rate was set to 0.5, since observers had a 50% chance of responding correctly in each 2IFC task. Lapse rate was fixed at 0 since empirical estimation of lapse rate resulted in multiple failed psychometric model fits, likely due to overparameterization (Kingdom and Prins, 2016). The value of 0 was chosen after empirically observing that higher values of lapse rate (between 0.02 and 0.05) also resulted in multiple failed psychometric model fits in tasks were participants discriminated high-intensity, easy stimulus parameters with 100% accuracy.

For the tilt illusion task, psychometric function in Eq.1 and Eq.2 were used to fit the proportion of “tilted clockwise” responses rather than proportion correct. To estimate that magnitude of the tilt illusion from the psychometric curve, the PSE was chosen as the parameter of interest. The PSE corresponds to the difference in tilt orientation at which observers perceive the two central gratings as equally tilted, as evidenced by the equal proportion (50%) of clockwise or anti-clockwise

reports. Parameters γ and λ were both fixed at 0, a value that minimized poor or failed fits as described above.

Statistical analysis. To evaluate the effects of sleep deprivation, a series of Friedman tests for each task data were calculated, including sleep state condition as an independent variable (WR, SD, REC) and threshold (or PSE for the tilt illusion), slope, RT and accuracy as dependent variable. The Friedman test is the non-parametric alternative of the repeated-measure ANOVA and was employed since many of the assumptions of parametric tests could not be reliably tested with the current sample size (e.g. normality). Post-hoc Wilcoxon tests were conducted to assess the difference between WR-SD, SD-REC and WR-REC conditions. A Bonferroni correction for 3 planned comparison was applied, and p-values in text are reported after Bonferroni correction (namely original p-value is multiplied by 3 and assessed at α = 0.05). Additionally, non-parametric effect sizes were estimated from post-hoc Wilcoxon test results to calculate the magnitude of pairwise differences between sessions (Fritz et al, 2012). Non-parametric effect size *r* was calculated using the following equation (Fritz et al, 2012):

$$r = \frac{z}{\sqrt{N}}$$

where z is the z-score calculated from the Wilcoxon signed-rank test (as illustrated in Field, 2012, p.670) and N is the sample size.

3.3 Results

Descriptive and inferential statistics of behavioural performance in all four tasks in WR, SD and REC conditions are presented in Table 3.1. Overall, performance across tasks was differently affected by sleep deprivation.

3.3.1 Vernier discrimination

Vernier discrimination task measured visual hyperacuity at 5° eccentricity in the right visual field. Psychometric functions fitted to each participants (thin lines) are shown in Figure 3.3 (top panel) by condition. The thick dots and lines represent the group average proportion of correct response by stimulus parameter and the relative psychometric function (generated for illustration purpose only). Participant

*Table 3.1: summary of performance measures in the psychophysical tasks assessed by sleep condition. Central columns report mean (or median) and standard deviation (or inter-quartile range) of various performance measures. Columns 9 and 10 report inferential statistics. The last three columns report non-parametric effect sizes calculated for the specified comparison. Significant results are in bold. Response Times (RT) are expressed in seconds. Accuracy values reported correspond to the proportion of correct trials. Threshold are expressed in relative stimulus parameter units (arc min for vernier discrimination, orientation degree for orientation discrimination and tilt illusion task, millisecond for two-flash discrimination task). Slope are arbitrary units. *median. Abbreviations: WR: Well-Rested condition; SD: Sleep Deprived condition; REC: post Recovery Sleep condition. RT: Response Time.*

Behavioural performance indices												
		WR		**SD**		**REC**		**Friedman**			***r***	
		mean	**std**	**mean**	**std**	**mean**	**std**	χ^2	***p***	***WR vs SD***	***WR vs REC***	***SD vs REC***
Vernier discrimination	RT	0.51	0.06	0.55	0.08	0.53	0.09	$\chi^2(2) = 1.71$	0.424	0.56	0.05	0.29
	accuracy	.90	0.03	.87	0.04	0.88	0.06	$\chi^2(2) = 2.81$	0.245	0.54	0.34	0.07
	threshold (arc min)	2.66	1.01	2.87	1.14	3.12	1.65	$\chi^2(2) = 1.0$	0.607	0.20	0.34	0.13
	slope	1.20	0.29	1.02	0.34	1.37	0.66	$\chi^2(2) = 6.85$	**0.032**	0.46	0.21	0.48
Orientation discrimination	RT	0.48	0.05	0.51	0.08	0.45	0.06	$\chi^2(2) = 9.0$	**0.011**	0.28	0.59	**0.65**
	accuracy	.85	0.03	.76	0.05	0.82	0.05	$\chi^2(2) = 15.3$	**<0.001**	**0.86**	0.48	**0.74**
	threshold (deg)	0.23	0.12	0.48	0.21	0.30	0.11	$\chi^2(2) = 9.48$	**0.009**	**0.80**	0.46	0.54
	slope*	1.00	0.37	0.90	0.40	1.08	0.77	$\chi^2(2) = 1.420$	0.492	0.02	0.24	0.21
Tilt illusion	RT	0.53	0.07	0.58	0.06	0.52	0.09	$\chi^2(2) = 14.5$	**<0.001**	**0.66**	0.25	**0.65**
	slope	3.62	1.23	2.30	1.07	4.02	2.02	$\chi^2(2) = 15.6$	**<0.001**	**0.88**	0.18	**0.80**
	PSE*	2.29	2.95	3.87	4.35	2.0	2.58	$\chi^2(2) = 6.330$	**0.042**	0.53	0.12	0.38
Two-flash discrimination	RT	0.54	0.08	0.64	0.11	0.54	0.10	$\chi^2(2) = 14.0$	**<0.001**	**0.88**	0.01	**0.79**
	accuracy	.86	0.05	.80	0.06	0.83	0.05	$\chi^2(2) = 4.94$	0.084	0.62	0.60	0.51
	threshold (ms)	13.4	6.20	24.5	16.2	16.6	6.45	$\chi^2(2) = 3.23$	0.199	0.55	0.49	0.42
	slope	0.80	0.27	0.66	0.27	0.80	0.35	$\chi^2(2) = 2.0$	0.368	0.49	0.01	0.51

performance in the vernier discrimination task was not significantly different between WR, SD and REC conditions (Table 3.1). Specifically, results of a non-parametric Friedman test revealed no significant difference in vernier discrimination threshold between WR, SD, and REC conditions (Figure 3.3, bottom panel). Similarly, no significant effect of sleep state on accuracy and RT was observed (Table 3.1). Only the slope of the psychometric curve varied significantly across sessions (Table 3.1), indicating that the change in accuracy as a function of line misalignment differed between sessions. However, post-hoc Wilcoxon signed-rank test revealed no significant pairwise difference between sessions. Overall, perceptual discrimination of vernier lines seemed largely unaffected by one night of sleep deprivation, indicating preserved visual hyperacuity at 5° eccentricity in the right visual field after one night of sleep deprivation.

3.3.2 Orientation discrimination

Orientation discrimination task measured orientation sensitivity, namely the minimal orientation difference that can be accurately discriminated. The psychometric curves in Figure 3.4 (top panel) illustrate individuals' ability to discriminate a range of small orientation differences. Results of Friedman test revealed significant differences in performance between sleep state conditions for RT, accuracy and threshold (Table 3.1). Post-hoc Wilcoxon signed-rank test revealed that, on average, SD had a large effect on perceptual threshold which was significantly increased compared to WR condition [p = 0.004, r = 0.8], indicating reduced sensitivity to different orientations. The effect of SD on accuracy was large, and accuracy was significantly reduced in SD relative WR [p = 0.004, r = 0.86] and REC [p = 0.017, r = 0.74]. Finally, SD had also a large effect of RT relative to REC, as RT was significantly faster after recovery sleep compared to SD [p = 0.04, r = 0.65]. Overall, these results indicate that one night SD had large effects on perceptual discrimination of lines orientation, reducing orientation sensitivity and accuracy, and slowing response times.

3.3.3 Tilt illusion

The influence of sleep deprivation on contextual modulation on visual perception was assessed by measuring the magnitude of the tilt illusion. The tilt illusion

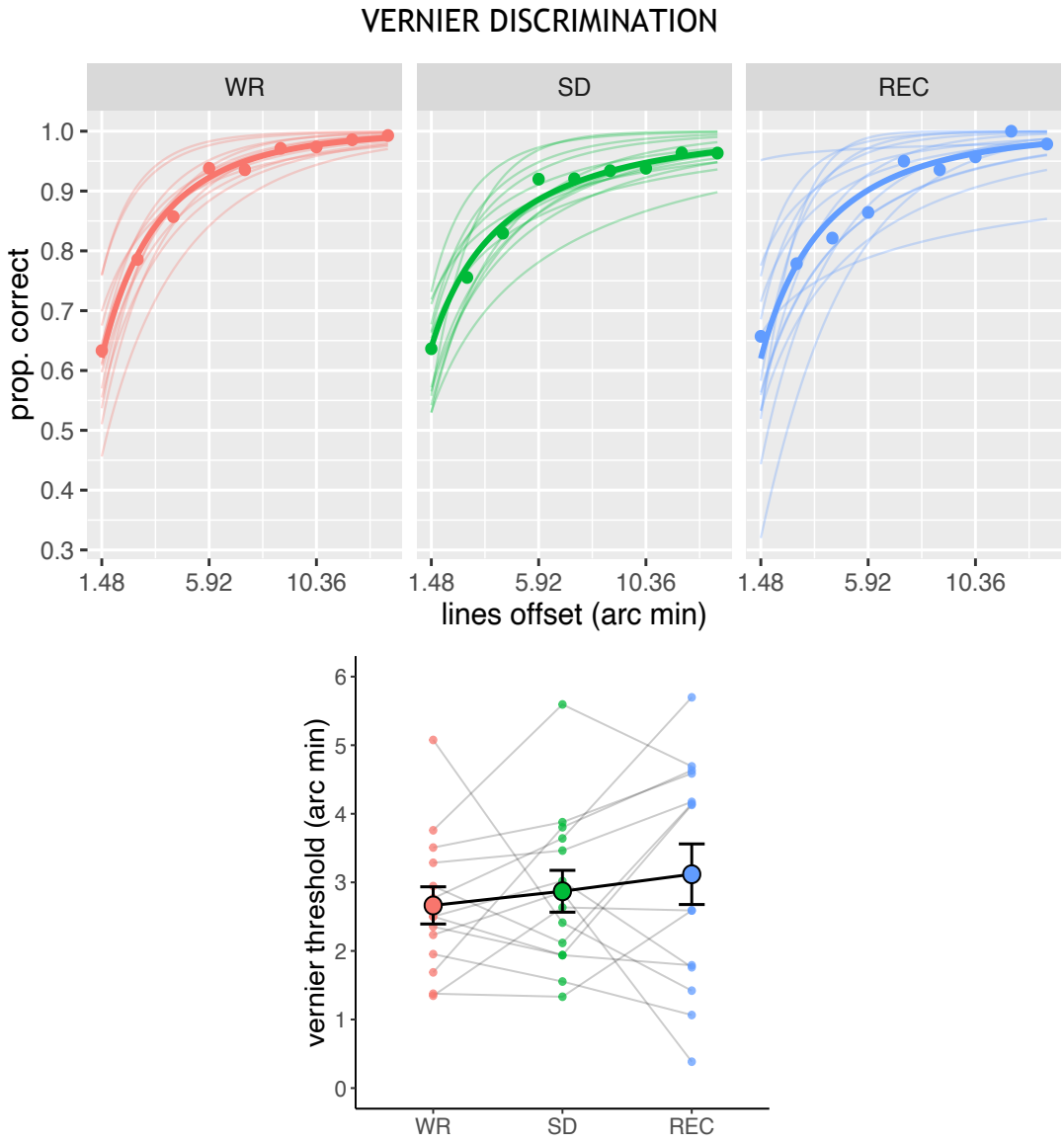

Figure 3.3: vernier discrimination task performance. Top row shows psychometric functions of individual participants (thin lines) as well as the mean proportion of correct responses across individuals by stimulus parameters (dots) and the associated psychometric function (thick line). Discriminating vernier offset was more difficult for smaller misalignment as evidenced by poorer accuracy at lower lines offset (left side of the psychometric function). Bottom row illustrates vernier threshold, namely the lines offset at which accuracy was around 75%, of individual participants by condition (thin dots and thin lines). On average, vernier threshold (thick dots with error bars indicating standard error of the mean) was similar across conditions, indicating that sleep deprivation did not affect the ability to discriminate spatial positional offsets.

magnitude was considered as the PSE from the psychometric function fitted to the proportion of "tilted clockwise" trials. Figure 3.5 shows the psychometric curves of individual subjects and the group average by different conditions. I evaluated the influence of sleep state on tilt illusion PSE using a Friedman non-parametric test to

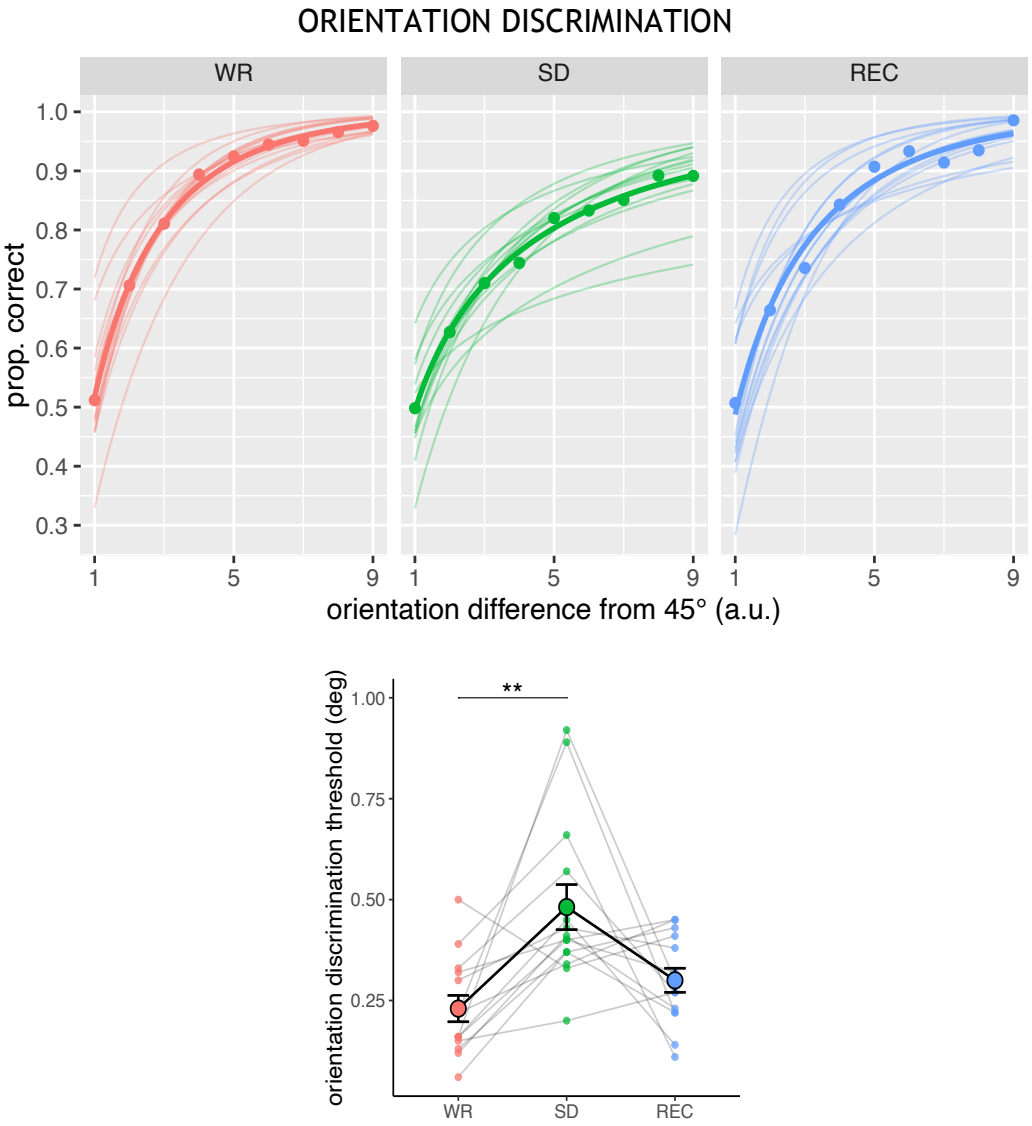

*Figure 3.4: orientation discrimination task performance. Top row: psychophysical performance of individual observers (thin lines) and group average (thick lines and dots). Orientation difference is shown in arbitrary units because they were calibrated for each participant. On average, performance was significantly lower after SD relative to WR as can be observed from the lower proportion of correct trials across almost all stimulus parameters. Bottom row: orientation discrimination threshold estimated from the psychometric function of individual participants (thin dots and thin lines) for each condition, shown in orientation degrees. 13/14 participants showed reduced sensitivity to orientation as evidenced by increased orientation discrimination threshold. Discrimination thresholds (thick dots, with error bars indicating standard error of the mean) significantly increased after sleep deprivation relative to baseline WR condition. **: p=0.005.*

account for severe non-normal distribution of PSE values in REC condition. Results revealed that there was a significant effect of sleep state on PSE (Table 3.1). Figure 3.5, bottom row, shows that, on average, PSE became more negative after SD, indicating an increase in tilt illusion magnitude with sleep loss (large effect, *r* =

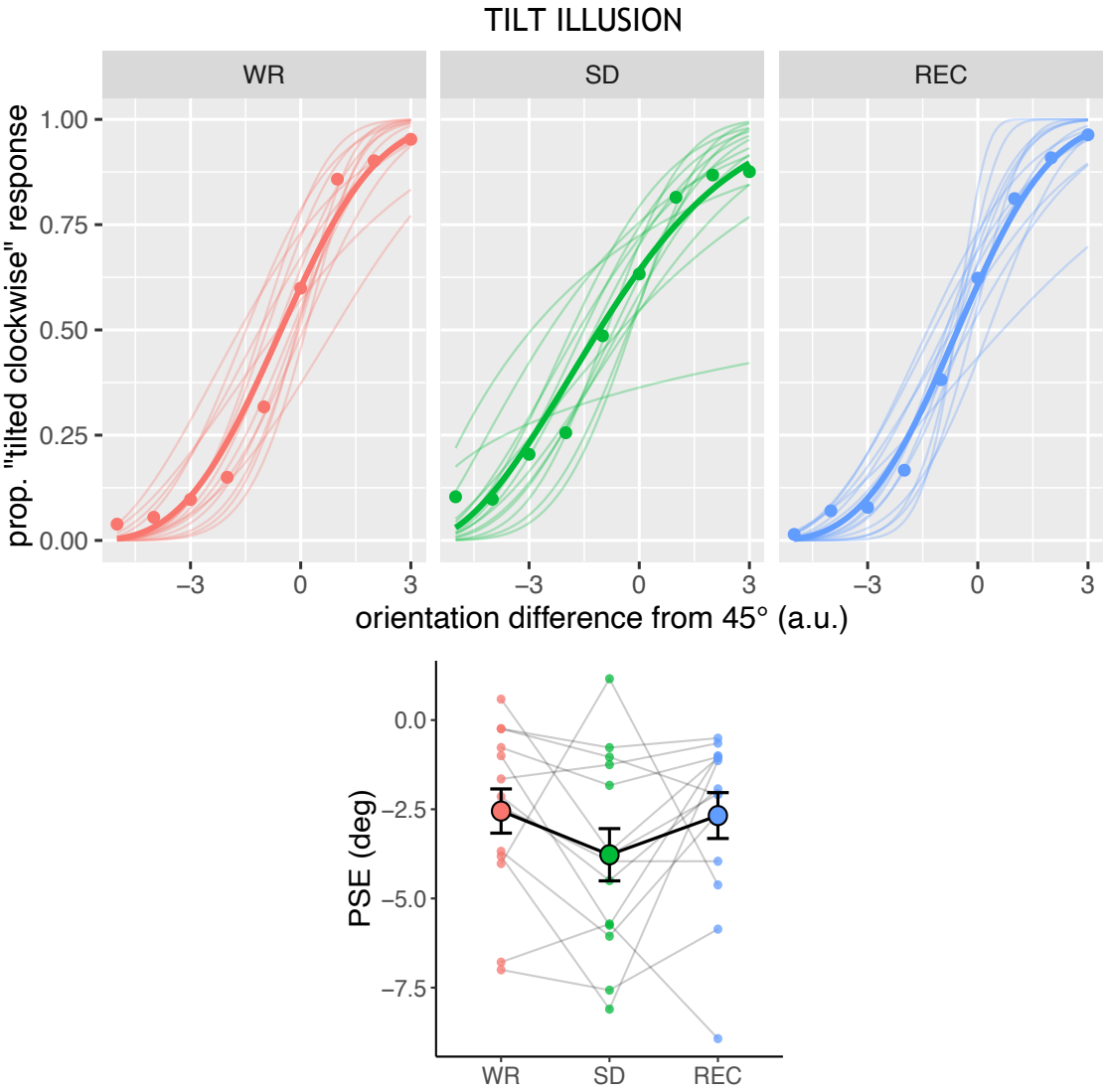

Figure 3.5: tilt illusion task performance. Top row: psychometric curves fitted to the proportion of trials in which observers reported the second grating as tilted clockwise relative to the first. Thin lines are for individual observers, the thick dots and line represent group average. Curves have a shallower slope on average in the SD condition relative to both WR and SD conditions, indicating less sensitivity to orientation differences. The stimulus parameters are shown in arbitrary units since different stimulus parameters were used for each participant to ensure that the range of stimuli tested was of similar subjective difficulty for all observers. Bottom row: mean PSE (with standard error of the mean) by condition. Thin dots represent PSE of individual subjects. PSE varied significantly between conditions, but pairwise differences were not statistically significant.

0.53). However, post-hoc Wilcoxon signed-rank tests assessing pairwise differences between WR, SD and REC were not significant [all $p > 0.05$]. Another parameter of interest in the tilt illusion task was the slope of the psychometric function, which reflects sensitivity of orientation discrimination in the presence of surrounding context. Psychometric function slope in the tilt illusion task was significantly

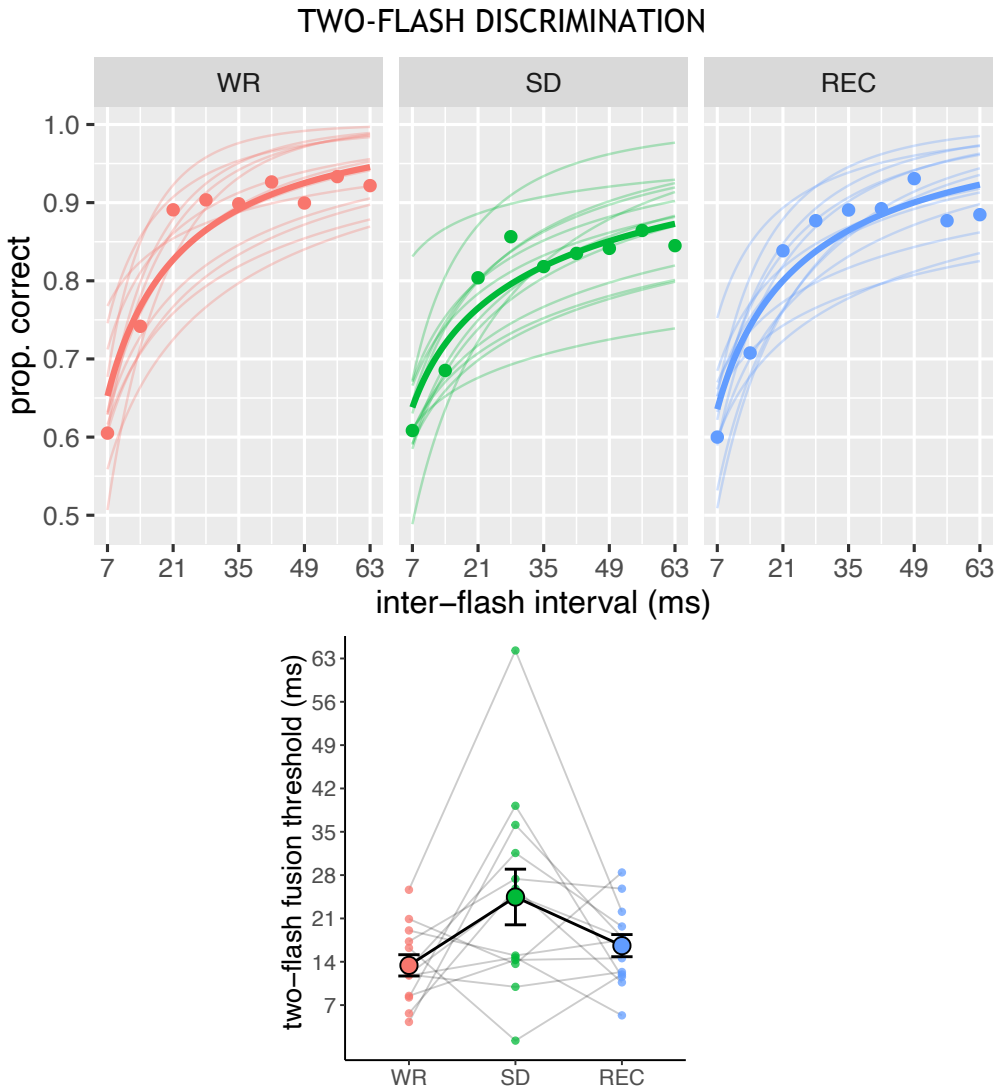

Figure 3.6: two-flash discrimination task performance. Top row: proportion of correct trials by stimulus parameters were fitted with a psychometric function and plotted for each participant (thin lines). Thick lines and dots represent group average accuracy by stimulus parameter and relative psychometric function fitted only for illustration. On average, performance accuracy was significantly lower in SD relative to both WR and REC conditions, as evidence by fewer proportion of correct responses on across all stimulus parameters. Bottom row: two-flash fusion threshold, namely the IFI at which two flashes are perceived as a single steady flash. Two-flash fusion threshold varied significantly between sessions, but post-hoc t-test tests revealed no significant pairwise difference after Bonferroni correction (WR vs SD p = 0.096).

influenced by sleep condition (Table 3.1; Figure 3.5, top row), and post-hoc Wilcoxon signed-rank tests revealed a significantly shallower slope in SD condition relative to both WR [$p < 0.001$, $r = 0.88$] and REC [$p = 0.004$, $r = 0.80$], indicating a large reduction in sensitivity to orientation differences after sleep loss and subsequent restoration of visual discrimination ability with a night of recovery sleep.

Finally, RT varied significantly between sessions as evidenced by Friedman test [Table 3.1]. Post-hoc Wilcoxon signed-rank test revealed that RT was significantly slower in SD compared to both WR [p = 0.032, r = 0.66] and REC [p = 0.04, r = *0.65*], revealing a large reduction in response speed of participants after one night of sleep deprivation and subsequent recovery with a night of sleep.

3.3.4 Two-flash discrimination

Estimation of individual's psychophysical threshold was biased by runs with aberrant performance, so these runs were excluded (Supplementary Note S3.3; Supplementary Table S3.3). Specifically, I removed the Day1AM (WR) run from 1 subjects, Day2PM (WR) run from 2 subjects and the Day3AM (SD) runs from 2 subjects. This allowed to estimate perceptual threshold using psychometric functions in all subjects and all conditions. Additionally, one participant was excluded because performance accuracy in SD condition was >3std worse than the average group performance across all conditions.

On average, participants reported perceiving 1 flash in 54.2% of trials (std 4.9%) in WR, 51.5% (std 6.8%) in SD and 54.3% (std 6.6%) in REC. These results indicate that the IFI values employed allowed two-flash trials to be integrated in about half the trials. Figure 3.6 (top panel) illustrates the psychometric functions fitted to proportion of correct responses by IFI interval for each individual as well as the group average (thick line and dots). A large variability between individuals is observed in all conditions and particularly in SD.

On average, participants' accuracy and sensitivity to resolve consecutive flashes did not vary significantly across sessions as revealed by Friedman tests on accuracy, slope and threshold (Table 3.1). Only performance speed (i.e. RT) was affected across sessions (Table 3.1). Specifically, SD had a large and significant effect on RT as evidenced by slower RT in SD relative WR [p < 0.001, r = 0.88] and REC condition [p = 0.007, r = 0.79].

Despite the exclusion of runs with aberrant performance, some estimates of perceptual threshold from psychometric functions exceeded the range of stimulus

parameters tested (7ms to 63ms IFI). This is clearly evident in Figure 3.6 (bottom panel) in the form of extremely small and extremely large threshold values. Additional analysis excluding subjects with threshold estimate beyond parameters range (N = 6) also showed larger average threshold in SD [mean (std) = 13.9 (4.73)] relative to WR [mean (std) = 22.0 (10.3)] and REC [mean (std) = 18.5 (6.05)], but no significant effect of session [$\chi^2(2) = 3.25$, $p = 0.197$].

3.4 Discussion

This study was set out to investigate the influence of sleep deprivation on low-level visual perceptual functions. Sleep deprivation affected task performance differently between tasks, indicating selective alteration in perception of low-level visual features following a night of sleep deprivation. The main deficit was in orientation sensitivity, as evidenced by a large increase in psychophysical threshold in the orientation discrimination task and shallower psychometric function slope in the tilt-illusion task. In contrast, visual hyperacuity was not significantly affected by sleep loss, as shown by preserved performance accuracy and discrimination threshold in the vernier task after one night of sleep deprivation. Finally, sleep deprivation also affected performance in the two-flash discrimination task, indicating reduced temporal discrimination accuracy.

3.4.1 Effects of sleep deprivation on spatial resolution of visual perception

Sensitivity to orientation is a fundamental property of visual system which underlies the ability to perceive boundaries, edges and contours and recognize objects. Humans are sensitive to very fine orientation differences, smaller than 1° (Andrews et al., 1973; Westheimer et al., 1976). In line with this, well-rested subjects in this study had an average orientation discrimination threshold of 0.23°, meaning that they were capable of resolving orientation differences around 0.23° with approximately 75% accuracy. After one night of sleep deprivation the average orientation discrimination threshold more than doubled across participants, indicating that sleep deprivation reduced sensitivity to orientation. Consistent with this finding, also the slope of the psychometric curve in the tilt-illusion task was

shallower in SD relative to WR condition, a further indication of decline in orientation sensitivity after sleep deprivation.

To the best of my knowledge, this is the first study reporting lower orientation sensitivity in sleep deprived subjects. Previously, Killgore and colleagues (2007) tested matching of line orientations in a LOT after 22 hours of sustained wakefulness but they did not find any impairment relative to a baseline well-rested session. Several differences between the present and Killgore and colleagues' (2007) study however exist. Firstly, the task in Killgore et al. (2007) required to identify the correct orientation of two target lines among several alternatives, and stimuli were presented no time limit. Critically, the range of orientation parameters spanned 180° in steps 18°, which is almost 2 orders of magnitude greater than the orientation sensitivity threshold. The perceptual task was thus rather easy (average accuracy was >90%) and not assessing the full extent of the capacity for orientation discrimination. Conversely, the psychophysical task presented in this chapter was designed to assess the maximum capacity of orientation discrimination for each observer, hence I used a range of stimulus parameters with minimal orientation differences that were calibrated for each individual. This task was thus more sensitive to alterations in orientation discrimination abilities between conditions. Moreover, Killgore and colleagues (2007) only tested performance at baseline and after 22 hours of sleep deprivation, whereas in this study the SD condition included up to 32 hours awake. More recently, Stenson and colleagues (2022) used a computerized LOT requiring to rotate a target line so that is was parallel to a reference line. After 24 hours of sleep deprivation, they also did not observe any difference in performance accuracy in line orientation, in line with the findings of Killgore and colleagues (2007). Yet, the range of orientation tested did not include orientation values around the orientation discrimination threshold, so the task was likely too easy for participants and not adequate to measure the influenced of sleep deprivation on orientation discrimination threshold, similar to Killgore et al. (2007). Overall, these results suggest that sleep deprivation may reduce the ability to detect the smallest spatial details of visual stimuli, and this can be evidenced by tasks that are most sensitive to the limits of visuo-spatial perception.

Sleep deprivation did not affect all spatial tasks uniformly, however. Vernier discrimination threshold was not significantly affected by a night of sleep deprivation. No previous studies had measured the influence of sleep deprivation on visual hyperacuity to the best of my knowledge. The results reported here are thus novel and will benefit from replication in additional studies. Here vernier discrimination was tested at 5° eccentricity, always on the right visual field. The average vernier threshold in WR was 2.66 minutes of arc, in line with previously reported vernier thresholds with similar stimulus parameter (duration, eccentricity, viewing distance) (Levi et al., 2000; Levi and Waugh, 1994; Shiu and Pashler, 1994; Whitaker et al., 1992). Overall, these results may be biased by the small sample size. In fact, since the effect size of the difference between WR and SD and between SD and REC was small, the limited number of participants may have hampered the statistical power of the analysis. Increasing the sample size could enhance the study's power and allow to clarify the impact of sleep deprivation on vernier discrimination.

Moreover, to better exploit the repeated-measure nature of the study with multiple subjects performing different tasks in different conditions, a more suitable approach to analyse this dataset could be to use linear mixed effect models. These models take into account the within subject variability that is shared across different tasks, as well as between-subject variability within each task. As such linear mixed effect models could allow for a more accurate and comprehensive analysis of repeated measure data, and reveal, for example, whether the effects of SD across different tasks may be driven by few subjects particularly sensitive to sustained wakefulness.

3.4.2 Influence of sleep deprivation on temporal resolution

I investigated whether temporal resolution of visual perception was affected by sleep deprivation by measuring the minimum interval at which two distinct flashes are fused and perceived as one. I found no significant changes in the two-flash fusion threshold after sleep deprivation, but I observed reduced accuracy and significantly slower response times.

Overall, previous studies have provided mixed results concerning the influence of sleep deprivation on temporal resolution. On the one hand, Leonard and colleagues (1998) reported no change in CFF threshold after 32 hours work shift in medical doctors, indicating preserved temporal resolution. However, participants in the study by Leonard and colleagues (1998) could take naps during their work shift, so it cannot be ruled out that few hours of sleep contributed to restoring or preserving temporal resolution. On the other hand, laboratory studies of acute total sleep deprivation have indicated a decline in temporal resolution after sleep deprivation (Lee et al., 2002; Kong et al., 2014). Lee and colleagues (2002) found reduced CFF after 37 hours of sleep deprivation and Kong et al. (2014) reported poorer accuracy after 22 awake during a Rapid Serial Visual Presentation (RSVP) requiring temporal processing of visual elements. Results presented in this chapter are thus in partial agreement with previous studies in which temporal resolution was measured before and after total sleep deprivation. The reduced accuracy and slower RT in fact seems to suggest that the ability to discriminate temporal stimuli was impaired after sleep deprivation, consistent with the results of Kong et al. (2014) and Lee et al. (2002). Moreover, it appears that two-flash fusion threshold was little affected by SD in about half participants, while it was largely increased in the other half. This likely reflects inter-individual differences in the vulnerability to the consequences of prolonged time awake which has been well documented before (Chee and Tan, 2010; Van Dongen et al., 2004). Moreover, the significant reduction in overall performance accuracy after SD, together with the significant main effect of sleep state on two-flash fusion threshold, seem to argue against a preservation of temporal resolution after sleep deprivation as indicated by the non-significant pairwise difference in two-flash fusion threshold between WR and SD. Possibly, repeating the task with a larger sample size could help to unveil whether there exist a true reduction in temporal resolution after sleep deprivation.

Nonetheless, the results presented here are potentially biased by the poor estimate of threshold values in 7/13 participants – as evidenced by estimated values beyond the range of the IFI tested of 7-63ms. This warrants caution in interpretation of the effects of sleep deprivation on temporal resolution of visual perception in this study. For example, threshold values below 7ms seems unlikely when average temporal

resolution is estimated around 30-40ms (Allan, 1971; Reeves, 1996). The most likely explanation is that the onset and offset time of the stimuli were not temporally precise, due to LCD monitor characteristics (Elze and Tanner, 2012; Rohr and Wagner, 2020). As a result, flashes might have been presented at slower IFI than designed. Similar issues with temporal LCD monitors have been reported before (Garaizar et al., 2014), and, together with the results of this chapter, stress the importance of calibrating equipment when running millisecond-precise psychophysical investigations.

3.4.3 Selective effects of sleep deprivation on low-level perception

Taken together, results show that one night of sleep deprivation does not uniformly influence low-level perceptual functions, but that the effects depend on different tasks and perceptual function. Sleep deprivation appears to distort the perceived orientation of visual stimuli but not their spatial position. What could underlie the selective effects of sleep deprivation on perceptual functions and what makes low-level perceptual properties more or less susceptible to sleep deprivation however remains unclear. Lim and Dinges (2008) argued that the reduction in vigilant attention could affect the ability to optimally perform a cognitive task and lead to performance impairments. Reduction in vigilance however does not explain why performance in the vernier discrimination task was preserved, since vigilant attention should uniformly impair performance independent of task. Task-specific effects could thus also depend on the characteristics of task-relevant neural circuits and their susceptibility to prolonged time awake. For example, perception of orientation relies on the specialized activity of populations of neurons in primary visual cortex which are broadly tuned to specific angle degrees (Hubel and Wiesel, 1962; Priebe, 2016). One possibility is that sleep deprivation affects the tuning of such orientation selective neurons and makes neurons less sensitive to differences in orientations, for example by broadening the range of orientation to which they respond to (Laventhal et al., 2003). Similar mechanisms have been proposed to underlie lower orientation discrimination threshold in the elderly population (Betts et al., 2007; Casco et al., 2017) and are supported by electrophysiological recording in primary visual cortex of senescent cats and primates (Hua et al., 2006; Laventhal et al., 2003). In sleep deprived individuals, it has been suggested that local sleep

mechanism could induce alterations in local neuronal processing and contribute to the observed cognitive impairments (Krueger et al., 2019; Van Dongen et al., 2011). Whether the tuning curve of orientation sensitive neurons is altered by sleep deprivation and whether this alteration could be related to local sleep mechanisms however remains to be tested.

This chapter aimed to investigate the effects of sleep deprivation on multiple visual tasks that involve intricate processing mechanisms, starting from the retina. Consequently, variations in low-level processing mechanisms may underlie the differential impact of sleep deprivation on these tasks. Specifically, alterations in retinal processing could influence the early stages of visual perception, subsequently affecting task performance to varying degrees. In relation to the reported visuo-spatial perceptual impairments, it is noteworthy that the observed increase in orientation sensitivity threshold occurred for stimuli presented in the fovea, while the relatively stable vernier acuity was assessed at 5° eccentricity and not specifically tested in the fovea. This suggests that the susceptibility to sleep deprivation could be influenced by low-level visual processing, potentially including alterations in retinal processing.

In conclusion, this chapter aimed to evaluate the influence of sleep deprivation on low-level visual perception. Using perceptual tasks requiring discrimination of low-level spatial and temporal features, I found selective effects of sleep deprivation on visual perceptual abilities. Sleep deprivation markedly reduced orientation sensitivity and led to poorer accuracy in a temporal discrimination task while it did not significantly affect visual hyperacuity. These alterations in low-level perception after sleep deprivation could reflect domain-specific effects of sleep deprivation and different susceptibilities of visual circuits to prolonged use and prolonged wakefulness.

3.5. Supplementary material

Supplementary Note S3.1: calibration of stimulus parameters for the orientation discrimination task. The calibration task was a 2-up-1-down staircase orientation discrimination task with 90 trials. Like in the main task, two consecutive gratings were shown and subjects judged if the second tilted leftward or rightward. One of the two gratings was always oriented at 45°. The orientation difference between the two consecutive gratings at the beginning of the staircase was 1° and was increased or decreased (i.e. a staircase reversal) by 0.05° every time participants gave two consecutive correct responses or one incorrect response, respectively. A perceptual threshold was calculated from the mean stimulus parameter of all reversals excluding the first 2. The full range of 9 orientation parameters presented in the main experiment included two values below threshold and 7 values above threshold (max 4.1*threshold), in steps of ½ threshold. The range of orientation differences (deg) shown for each participants is shown in supplementary Table S3.1.

Table S3.1: orientation differences used during the orientation discrimination task.

	Orientation discrimination task: stimulus parameters (deg)								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
P01	0.02	0.13	0.23	0.34	0.45	0.55	0.66	0.77	0.87
P02	0.03	0.17	0.31	0.45	0.59	0.73	0.87	1.01	1.15
P03	0.04	0.23	0.41	0.60	0.79	0.98	1.16	1.35	1.54
P04	0.04	0.24	0.44	0.64	0.84	1.04	1.24	1.44	1.64
P05	0.03	0.17	0.31	0.45	0.59	0.73	0.86	1.00	1.14
P07	0.02	0.13	0.25	0.36	0.47	0.58	0.69	0.80	0.92
P09	0.02	0.14	0.25	0.36	0.48	0.59	0.70	0.81	0.93
P10	0.02	0.13	0.24	0.34	0.45	0.56	0.66	0.77	0.88
P11	0.03	0.18	0.33	0.48	0.63	0.78	0.93	1.08	1.23
P12	0.03	0.17	0.31	0.45	0.60	0.74	0.88	1.02	1.17
P13	0.03	0.16	0.30	0.44	0.57	0.71	0.84	0.98	1.12
P14	0.03	0.18	0.32	0.47	0.61	0.76	0.90	1.05	1.20
P15	0.07	0.45	0.83	1.20	1.58	1.95	2.33	2.70	3.08
P16	0.03	0.18	0.33	0.48	0.63	0.78	0.93	1.08	1.23

Supplementary Note S3.2: calibration of stimulus parameters for the tilt-illusion task. The calibration task consisted of a matching orientation task, where two gratings, a reference and a variable grating (radius 0.75° visual angle), were positioned on either sides of a central fixation cross at 5° eccentricity. The reference grating had 45° orientation and was surrounded by an annular grating of 60° orientation (radius 3° visual angle). The variable grating had a random orientation between 30° and 60°. Subjects were asked to fixate the central cross and rotate the variable grating by pressing left and right arrows on a keyboard until its perceived orientation matched the orientation of the reference grating. They repeated this operation 4 times. The average and standard deviation of the orientation difference between the variable and reference grating (i.e. the PSE) across the 4 calibration trials were then used to determine the range of stimulus parameters for the experimental task. Specifically, the orientation values corresponding to the PSE and 8 orientations values symmetrically distributed around the PSE (in multiples of 10x the standard deviation of the PSE from the 4 calibration trials) were included in the experiment sessions for a total of 9 stimulus parameters. The range of orientation differences calibrated for each participant is shown in the supplementary table (S3.2).

Table S3.2: range of orientation differences used in the tilt illusion task calibrated for each participant.

	Tilt illusion task stimulus parameters (deg)								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
P01	-14.01	-11.87	-9.74	-7.61	-5.48	-3.35	-1.22	0.91	3.05
P02	-15.05	-12.25	-9.45	-6.65	-3.85	-1.05	1.75	4.55	7.35
P03	-18.28	-14.53	-10.78	-7.03	-3.28	0.47	4.22	7.97	11.72
P04	-22.96	-18.97	-14.98	-10.99	-7.00	-3.01	0.98	4.97	8.96
P05	-21.16	-18.37	-15.58	-12.79	-10.00	-7.21	-4.42	-1.63	1.16
P07	-19.00	-16.00	-13.00	-10.00	-7.00	-4.00	-1.00	2.00	5.00
P09	-16.50	-13.50	-10.50	-7.50	-4.50	-1.50	1.50	4.50	7.50
P10	-17.00	-13.50	-10.00	-6.50	-3.00	0.50	4.00	7.50	11.00
P11	-23.40	-18.80	-14.20	-9.60	-5.00	-0.40	4.20	8.80	13.40
P12	-19.80	-16.10	-12.40	-8.70	-5.00	-1.30	2.40	6.10	9.80
P13	-19.80	-16.10	-12.40	-8.70	-5.00	-1.30	2.40	6.10	9.80
P14	-19.80	-16.10	-12.40	-8.70	-5.00	-1.30	2.40	6.10	9.80
P15	-40.00	-32.50	-25.00	-17.50	-10.00	-2.50	5.00	12.50	20.00
P16	-19.80	-16.10	-12.40	-8.70	-5.00	-1.30	2.40	6.10	9.80

Supplementary Note S3.3: original threshold including all data and subjects are shown in the Supplementary Table S3.3 (extreme values highlighted red). Estimated threshold includes many outliers, with values that exceed the range of parameter tested (7-63 ms IFI). To evaluate if estimates of perceptual threshold could be improved, I identified, among individuals with perceptual estimates exceeding the IFI range (i.e. P01,P04,P05,P07,P09,P11,P15), runs during which performance was extreme, defined by performance accuracy for all stimulus parameters below or above 75% (i.e. threshold). For P01, P04, P07 and P09, no extreme runs were identified. For P05, two runs were excluded (WR-Day2-6PM and SD-Day3-11AM). For P11, one run was excluded (SD-Day3-11AM). For P15, one run was excluded (WR-Day2-6PM). After exclusion of selected runs, at least one run per sleep state condition remained for each subject which allowed to calculate the effect of sleep state condition including all participants.

Table S3.3: psychophysical thresholds estimated from the two-flash discrimination task for each individual before exclusion of runs with extreme performance.

2-flash fusion threshold (ms)			
	WR	**SD**	**REC**
P01	25.6	64.3	22.1
P02	8.5	14.3	14.6
P03	20.9	13.6	28.4
P04	5.7	25.8	10.67
P05	6.5	155.0	11.6
P07	10.0	88.3	9.5
P09	11.8	14.7	5.3
P10	12.0	24.8	17.9
P11	16.2	1.1	11.9
P12	17.3	27.4	25.8
P13	11.9	9.9	12.35
P14	19.1	15.0	17.5
P15	0.6	36.1	18.0
P16	13.0	31.6	19.7
Mean(std)	**12.6 (6.7)**	**37.3 (40.9)**	**14.8(8.1)**

Chapter 4.
Influence of sleep deprivation on high-level visual perception

In the previous chapter, I reported selective impairments in low-level perceptual function after sleep deprivation. Here I extend this investigation to high-level perception by measuring how sleep deprivation affects the ability to categorise distinct ambiguous objects.

4.1 Introduction

4.1.1 Category selectivity in human visual cortex

Visual perception is a subjective, rich, integrated, colourful and meaningful representation of the external physical world. One of its function is to recognize objects in a visual scene (Groen et al., 2017). Object recognition is a high-level visual function that builds upon a hierarchy of processing steps. As described in Chapter 3, low-level visual areas (e.g. V1, V2, V4) are sensitive to elementary details of visual inputs, such as orientation (Hubel and Wiesel, 1959), contrast (Buracas and Boynton, 2007) and luminance (Goodyear and Menon, 1998). By contrast, high-level visual areas in the occipito-temporal cortex (e.g. Lateral Occipital Complex, Inferior Temporal Cortex, Fusiform gyrus) are sensitive to abstract, semantic features such as faces (Kanwisher and Yovel, 2006), houses (Epstein et al., 1998) and tools (Amedi et al., 2001). For example, the anterior portion of the fusiform gyrus is preferentially activated by stimuli of faces and is known as the as the Fusiform Face Area (FFA; Kanwisher and Yovel, 2006). Similarly, the parahippocampal area posterior to the entorhinal cortex exhibits selective responses for stimuli of houses and scenes (Epstein et al., 1998) and has been named the Parahippocampal Place Area (PPA). This characteristic of high-level visual system is known as category selectivity (or neural selectivity) and refers to the preferential response of distinct neuronal population to specific stimulus categories (Grill-Spector and Malach, 2004; Grill-Spector and Wiener, 2017).

Activity in high-level visual regions such as FFA appear to correlate with perceptual contents rather than with the external, physical stimulus (Grill-Spector and Wiener, 2017). In studies of bistable perception such as the Rubin face-vase, where physical stimulus is constant, but perception alternates between competing interpretations, activity in FFA is higher when subjects report perceiving a face rather than the non-face competing object (Andrews et al., 2001; Hasson et al., 2001; Tong et al., 1998).

Moreover, FFA activity is also observed when imagining faces with closed eyes (Ishai et al., 2002; Mechelli et al., 2004) and when perceiving faces in pure noise (Liu et al., 2014; Zhang et al., 2008; Zimmerman et al., 2014) or in noise-degraded house stimuli (Summerfield et al., 2006). Finally, electrical brain stimulation to face-selective regions can induce deficits in the perception of faces (Jonas et al., 2016; Parvizi et al. 2012) and brain lesion to the anterior fusiform gyrus is associated with impairments in face recognition, a condition known as prosopagnosia (Barton et al., 2003; Wada and Yamamoto, 2001). Overall, high-level category selective regions seem to play a crucial role in generating a perceptual representation of object categories (Grill-Spector and Malach, 2004; Martin, 2007).

4.1.2 Bottom-up and top-down processes in visual perception

The construction of internal representations of external stimuli from low-level to high-level regions occurs primarily bottom-up (DiCarlo et al., 2012). That is, progressive, feed-forward analysis of sensory inputs from low-level to high-level features is sufficient to differentiate between distinct stimuli and generate differentiated representations of stimulus categories such as houses and faces (DiCarlo et al., 2012; Kay and Yeatman, 2017). Critically however, internally-generated processes, in the form of selective attention, task instructions or expectations, strongly modulate bottom-up sensory processing (Abdelhack and Kamitani; 2018, Harel et al., 2014). This top-down modulation is operated by projections from frontal and parietal regions onto visual cortical regions (Baldauf and Desimone, 2014; Saalman et al., 2007) and can facilitate and speed up the transduction of physical sensory inputs into an accurate internal representation of the external world. For example, attention to or expectation of a face stimulus increases neuronal populations' activity in FFA, enhancing sensitivity to the attended face information (Esterman and Yantis, 2010; Gandolfo and Downing, 2019; Puri et al., 2009; Wojciulik et al., 1998).

The degree of top-down modulation of bottom-up processing adapts to the characteristics of the physical stimulus. When sensory information is rich and clear, bottom-up processing is mostly sufficient to evoke differentiated neural representations of distinct stimuli (DiCarlo et al., 2012). However, when sensory

information is degraded, ambiguous or unclear, stronger top-down activity can compensate for the limited bottom-up evidence by interpreting contextual information to guide object recognition (Abdelhack and Kamitani, 2018; Bar et al., 2001; Fan et al., 2020). Together, bottom-up and top-down processes contribute to generate an accurate and fast perceptual representation of the external world.

4.1.3 Impact of sleep deprivation on high-level perception

The occurrence of perceptual alterations with increasing time awake is well-documented across many studies (Babkoff et al., 1989; Bliss et al., 1959; Luby et al., 1962; Tyler, 1955; Waters et al., 2018; Williams et al., 1961). Such alterations affect predominantly the visual domain (Waters et al., 2018), and can manifest as simple perceptual distortions (i.e. metamorphopsias, where the shape of objects appear distorted; Petrovsky et al., 2014), illusions (a misperception of an existing stimulus; Babkoff et al., 1989) and psychotic-like hallucinations (a percept without a corresponding stimulus; Meyhofer et al., 2017). The severity and frequency of SD-induced perceptual alterations grows with increasing time awake: perceptual distortions occur after 24 hours of sleep deprivation, while illusions and hallucinations are reported after prolonged sustained wakefulness of 36-48 hours (Waters et al., 2018). Crucially, this evidence has mostly come from qualitative reports, and experimental investigation of how sleep deprivation is linked to high-level perceptual alterations and illusions is lacking.

Some evidence of visual processing deficits after sleep deprivation has been provided by fMRI studies (Chee and Asplund, 2013; Chee, 2015). fMRI studies with sleep deprived volunteers have revealed reduced activity in high-level extrastriate visual regions, including PPA and FFA (Chee et al., 2010; Kong et al., 2011; Lim et al., 2010; Poh and Chee, 2017). This was shown to occur before as well as during presentation of visual stimuli (Chee et al., 2010), and was particularly prominent in trials where participants were slow at responding (Chee and Tan, 2010). However, category selectivity in high-level visual regions was found to be unaffected by 24 hours of sleep deprivation in one study (Poh and Chee, 2017).

One hypothesis that has been put forward is that sleep deprivation affects visual processing by attenuating top-down attentional resources (Chee and Asplund, 2013; Chee and Tan, 2010). In line with this, reduction of activity in fronto-parietal regions that mediate attentional and cognitive control operations has been shown in parallel to reduced activation of visual cortical regions after sleep deprivation (Chee et al., 2010; Chee and Tan, 2010). Moreover, when stimulus contrast is manipulated to evaluate how bottom-up/top-down processes are affected, sleep deprivation uniformly reduced behavioural performance and neural activity in extrastriate regions regardless of contrast level. This reveals deficits that are not dependent on the clarity of bottom-up signal but are more consistent with a general reduction of top-down attentional capacities (Chee and Tan, 2010).

Nonetheless, it's not immediately clear how reduced top-down attentional resources could be linked to increased perceptual distortions commonly reported after sleep deprivation (Waters et al, 2018). Moreover, previous fMRI studies were mainly designed to assess attentional capacity in sleep deprived subjects, and very few addressed perceptual processing abilities (e.g. Chee and Tan, 2010). In particular, little is known about how sleep deprivation affects high-level perceptual abilities such as object recognition and categorisation. Similarly, the neural mechanisms that could underlie perceptual alterations are far from understood.

1.3.4 Aims and hypotheses

Overall, this chapter has three main aims. Firstly, this chapter aims to confirm whether high-level visual perception is affected by sleep deprivation. This is expected based on the evidence of degraded neural activity in visual regions (Chee et al., 2010; Kong et al., 2011; Lim et al., 2010; Poh and Chee, 2017) and subjective reports of perceptual alterations (Waters et al., 2018). Secondly, it aims to better understand the nature of perceptual alterations in sleep deprived state, for example if illusory perceptions become more frequent. Finally, another aim is to investigate the neural changes in high-level visual regions that occur after sleep deprivation. Specifically, whether sleep deprivation reduces category selectivity and whether the deficit would be dependent on stimulus clarity (evidencing alteration in bottom-up

visual processing) or independent of stimulus clarity (evidencing generic reduction in top-down attentional resources).

To these aims, a novel visual discrimination task was developed that required volunteers to discriminate images of faces, houses and blank, empty grey squares (3AFC). Stimulus clarity (Signal to Noise Ratio, SNR) was manipulated by dithering images with white noise, which allowed to vary the degree of top-down and bottom-up visual processing. Behaviourally, I measured perceptual discrimination accuracy at three levels of stimulus perceptual clarity: low, mid and high SNR. I also measured the frequency of face responses in non-face trials and house responses in non-house trials as a means to detect occurrence of illusory perceptions. At the neural level, I measured category selectivity in face and place selective regions to assess if differentiation of object representations was altered by sleep deprivation. Category selective regions were identified as brain voxels that preferentially responded to faces or houses relative to other categories during a functional localizer completed during preparatory sessions before the experiment.

4.2 Methods

Details of the sample and experimental procedures were described in Chapter 2. Here I present the details relevant to the perceptual discrimination task that was employed to assess the influence of sleep deprivation on high-level perception.

4.2.1 Participants

14 healthy volunteers (19-32 years old, 3 males) completed this study and were financially compensated for their participation. All participants had normal or corrected-to-normal vision by means of MR-compatible goggles. In the final sample of analysis 1 participant was excluded due to misunderstanding of instructions. This study received ethical approval by the Ethics committee of Cardiff University.

4.2.2 Experimental procedure

Figure 4.1 illustrates the protocol underwent by each participant. The experiment was completed over 4 consecutive days. Three Well-Rested (WR) sessions were scheduled for the evening of Day1 starting at 6:30PM, the morning of Day2 starting

at 9:30AM and the evening of Day2 from 8:30PM. Between Day1 and Day2 volunteers slept at their own house to minimize the discomfort of sleeping in an unfamiliar environment. On the night between Day2 and Day3 participants remained awake in the laboratory under constant supervision and were allowed to use their smartphone or computer and chat with the experimenter. Two sleep deprived (SD) sessions were completed on Day3, respectively in the morning starting at 8:30AM and in the evening starting at 5:30PM. Participants then went home to sleep and returned to the laboratory the next day for a final post-Recovery sleep session (REC). On the morning of Day4, the REC session in the MR scanner with the perceptual discrimination task was scheduled around 10:30AM. In each session, participants completed 2 runs of the perceptual discrimination task (each approximately 8

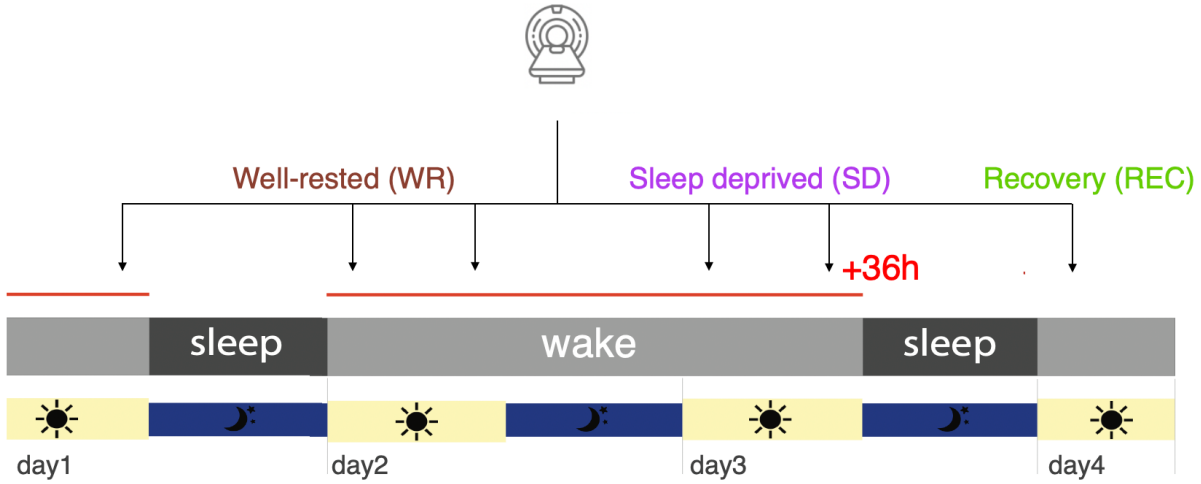

Figure 4.1: experimental protocol adopted to investigate how sleep deprivation influenced high-level visual perceptual discrimination. Each participant completed of 3 WR sessions, 2 SD sessions and 1 REC sessions over four consecutive days.

minutes long) inside the MRI scanner. Moreover, between 3 and 4 preparatory sessions took place between two and five days before Day1. These served as training sessions to ensure learning effects were controlled for and to allow participants to familiarize with the task and procedure (Supplementary Figure S2.1). Also, in one of the preparatory sessions, two functional localizer runs of approximately 8 minutes each were completed to identify face and place selective regions in the brain.

4.2.3 Perceptual discrimination task

Participants completed a perceptual discrimination task that required discrimination of greyscale faces, houses and blank stimuli. The task was designed to evaluate

illusory perceptions in healthy observers. This was inspired by tasks where noisy blank stimuli are presented unknown to observers who are instructed to report trials when they perceive faces (e.g. Liu et al., 2014; Righart et al., 2010; Zhang et al.,2008; Zimmerman et al., 2019). The task was also designed to measure perceptual categorisation ability by varying stimulus clarity (i.e. SNR). Stimulus SNR was manipulated by dithering the greyscale stimuli with white noise. Specifically, 11 different intensities of white noise were used (from 0 to 220 out of 255 rgb values, in steps of 22, using a custom-made Matlab code for dithering). Stimulus signal was greyscale value determined for each observer via a calibration task during the preparatory session (Supplementary Note S4.1; Supplementary Table S4.1). Examples of stimulus categories and SNR levels are shown in Figure 4.2. Stimuli were selected from the web among face portrait stimuli (also including neck and shoulders) and images of one or two-storey houses with frontal door and windows. Each trial began with a fixation cross appearing in the centre of the screen (200ms), followed by the stimulus (300ms) and a response window (1500ms). Each trial lasted a total of 2 seconds. Volunteers laid on a MR bed and were instructed to fixate the central cross and to report if they perceived a face, a house or a blank grey square by pressing one of three buttons on a response pad with their right hand. Including blank trials and blank response options allowed to avoid the use of face/house responses when participants did not perceive a face or house. The aim was to maximise trials where face and house responses actually reflected face and house perceptions. Stimuli were squared images (10° visual angle per side) projected with a ProPixx Full (VPX PRO -51001C) in the centre of a MR-compatible screen of size 39x21.6cm with black background. Stimuli of faces, houses and blank grey squares could appear with equal probability in each trial and the same face/house stimulus was not repeated within each run. Viewing distance was 88cm. Two runs of 220 trials each were completed in each session, each including 20 trials per stimulus SNR intensity. During the perceptual discrimination task inside the MR scanner, a researcher monitored participants' button presses to make sure that they remained awake. If a participant did not respond for more than two consecutive trials, the experimenter prompted them to continue performing the task from the MR intercom system.

4.2.4 Functional localizer task

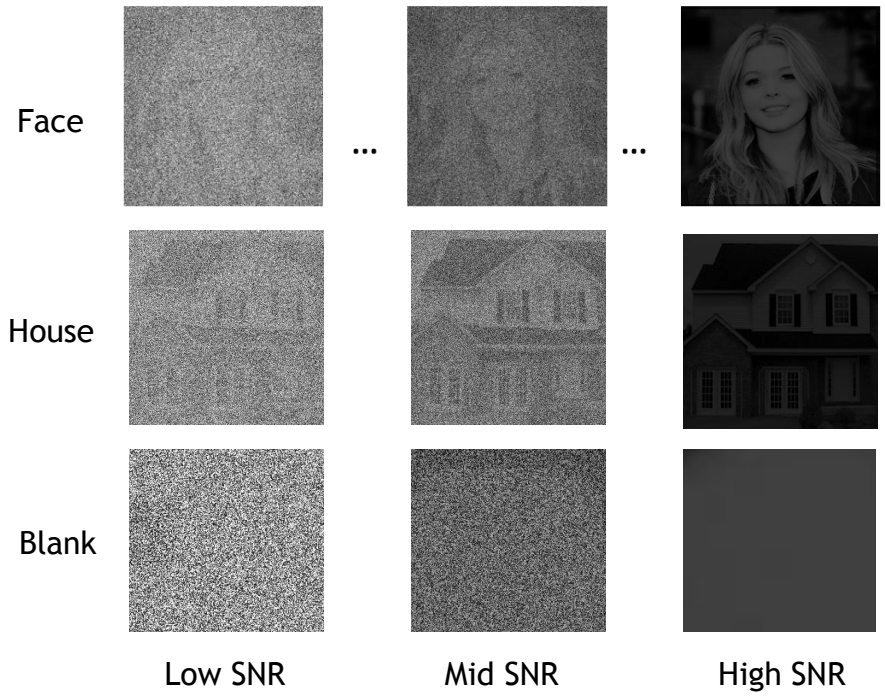

Figure 4.2: example stimuli used in the perceptual categorisation task. Greyscale images of faces, houses or blank squares were dithered using white noise to vary perceptual difficulty of the task. 11 different noise intensities were used, which were grouped into 3 levels (low, mid and high) for analysis. Greyscale signal intensity was calibrated for each individual to match perceived task difficulty between subjects.

A functional localizer task was run to identify brain regions in each subject that showed preferential activation for houses and for faces relative to other stimuli. The functional localizer task was adapted from the publicly available functional localizer experiment developed at the University of Stanford (http://vpnl.stanford.edu/fLoc/, Stigliani et al., 2015). An MR-compatible screen of size 39x21.6cm at a distance of 88cm was used for stimulus presentation. Stimuli were greyscale images of faces, house, bodies, objects and characters presented on a greyscale scrambled background. In addition, trials with pure grey blank images were also presented and served as baseline. In each 4-second trial, 8 different images belonging to the same category were flashed consecutively for 500ms. Participants were instructed to fixate the images and press a button whenever an oddball image (a background presented in isolation without any foreground stimulus) was presented. A total of 36 trials per stimulus category were presented in pseudorandom order for a total of 216 trials.

4.2.5 MR image acquisition

Functional images during the perceptual discrimination task runs and the functional localizer runs were acquired with a 3 Tesla Siemens Prisma scanner using a T2*-weighted Echo Planar Imaging (EPI) multiband BOLD sequence (TR = 2 seconds; TE = 30ms; flip angle = 70°; voxel size = 2x2x2mm; Field of View (FoV) = 192x192mm; slice number = 64). A T1-weighted sequence (MPRAGE) was also acquired in each session to obtain high-resolution structural images (TR = 2.10 seconds; TE = 3.24 ms; flip angle = 8°; FoV = 256 x 256; voxel size = 1x1x1 mm). The first 10 volumes acquired at the beginning of each sequence were discarded to account for T1-equilibrium effects.

4.2.6 Data analysis

Behavioural: perceptual discrimination accuracy. Behavioural data from the perceptual discrimination task was preprocessed as follows. All trials without a valid response (no button press within the 1.5s response window) were excluded from analysis. Concatenation of morning and evening runs of Day1 and Day2 (creating a single WR session), morning and evening runs of Day3 (creating a single SD session) and morning runs of Day4 (creating a single REC session) was applied in order to analyse difference between sleep states independent of circadian effects and maximise the amount of trials for each condition (WR, SD, REC). Finally, different stimulus SNR intensities were grouped into three levels: “low SNR” level (1-4 SNR, characterized by high amount of white noise and high perceptual difficulty), “mid SNR” level (5-8 SNR, characterized by medium amount of white noise), “high SNR” level (9-11 SNR, characterized by low or null amount of white noise and low perceptual difficulty). Mean accuracy in each sleep state condition was calculated by averaging the proportion of correct responses for each SNR level (low, mid, high) across trials from face, house and blank categories. A two-way ANOVA was then calculated to assess the impact of sleep state and SNR level on accuracy. To further characterize the change in discrimination performance after SD, average relative (only including valid responses) frequencies of face, house and blank responses were calculated by different SNR levels and compared between sleep state conditions by means of a two-way ANOVA. Finally, the frequency of wrong house, face and blank responses was calculated and compared between conditions to evaluate whether

illusory perception (namely more frequent wrong face and house responses) increased after SD.

fMRI preprocessing. Acquired BOLD data from functional localizer as well as perceptual discrimination task runs were preprocessed using a pipeline created with SPM12 and custom-made Matlab scripts. Images were first corrected for magnetic field distortion along the phase encoding direction using a B0 fieldmap acquired during each scan. After distortion correction, functional images were realigned and resliced to correct for rigid head movement during scanning and to estimate motion parameters that were later used as regressors of no interest to account for nuisance variability in BOLD timeseries. Then, a two-step co-registration procedure was applied subject-wise to ensure that the functional images of each subject shared the same coordinates across different brain scans and could be compared. Firstly, functional images of each scan were co-registered to the T1 structural image acquired during the same session. Secondly, session-specific T1 and associated functional images obtained in step 1 were co-registered to the T1 structural scan of the preparatory session during which the functional localiser was run and which served as reference. Finally, functional images were smoothed using a 4mm smoothing kernel.

Identification of face-selective and place-selective Region of Interest (ROI). To identify subject-specific voxels selectively activated by face and place stimuli during the functional localiser, a general linear model (GLM) was created including five regressors of interest (one for each stimulus category of faces, places, bodies, objects and words). The 6 rigid body motion parameters were also included as regressors of no interest to account for residual motion variability. Two contrasts ("Face – Others" and "Place – Others") were computed and the resulting t-maps were binarized with a threshold of T>3 in order to identify voxels that showed significantly greater response to faces compared to other stimuli (i.e. face selective voxels) and to houses compared to other stimuli (i.e. place selective voxels).
Moreover, three additional contrasts ("Bodies – Others", "Objects – Others" and "Words – Others") were calculated to identify regions preferentially responding to bodies, objects and words respectively. T-maps of the contrasts were binarized with

a threshold of T>3. These regions were used for control analyses to confirm specificity of effects of sleep deprivation on face/house selectivity.

fMRI analysis of category selectivity. All analyses were performed in subject space to respect differences in brain structure between individuals. The aim of these analyses was to address how category selectivity in face-selective and house-selective regions was influenced by sleep deprivation. BOLD data processing steps (summarized in Figure 4.3) included: global signal normalization (for each volume, each voxel BOLD magnitude was divided by the whole brain average BOLD magnitude of the same volume), 0.01Hz high-pass filter (removing slow signal drift associated with scanner magnetization) and regression of 6 rigid-body motion parameters run by run. Then, BOLD timeseries from face and place selective voxels were averaged to obtain a single ROI-level BOLD timeseries for face-selective-ROI and place-selective-ROI respectively. Next, I extracted and concatenated the BOLD amplitude 4 seconds after each trial of interest, to account for delay in neurovascular coupling (time-to-peak of hemodynamic response function: 4-6 seconds or 2-3TR; Huettel et al., 2014). Control analysis were conducted with different extraction lags (from 0 to 5 TR lags, representing 0 to 10 seconds from stimulus onset; Supplementary Note S4.2). Results of category selectivity calculated with different TR lags are reported in Supplementary Figure S4.1 and Figure S4.2. This process was repeated for each run and scanning session and resulting BOLD values were concatenated and averaged within all WR scanning sessions, all SD scanning sessions, and all REC scanning sessions, respectively. Finally, a category selectivity index previously used in other fMRI studies measuring functional selectivity (Grill-Spector et al., 2007) was calculated for each condition as follows:

$$\frac{(m_p + m_{np})}{\sqrt{\frac{{\sigma_p}^2 - {\sigma_{np}}^2}{2}}} \qquad (4.1)$$

where m_p is the mean BOLD response evoked by preferred stimulus category (i.e. faces for face-selective regions), m_{np} is the mean BOLD response to non-preferred

categories (e.g. houses and blanks for face-selective ROI), σ is the standard deviation of the BOLD response.

Analysis of Wrong Face and House Responses (WFHR). One question in this study was whether illusory perceptions increased after SD. Illusory perception here were operationalized by measuring WFHR, trials with face responses in house or blank trials and house responses in face or blank trials. In other words, in these trials participants reported perceiving a face (or a house) when the stimulus was actually not a face (or a house). Critically, to determine whether WFHR evoked differentiated neural responses in face-selective and house-selective brain regions, I first calculated category selectivity in Wrong Face Response (WFR) trials and Wrong House Response (WHR) trials, respectively, and then run a one-sample t-test to test if category selectivity was significantly different from zero. Category selectivity was calculated using Equation 4.1, where m_p is the mean BOLD activity evoked by wrong

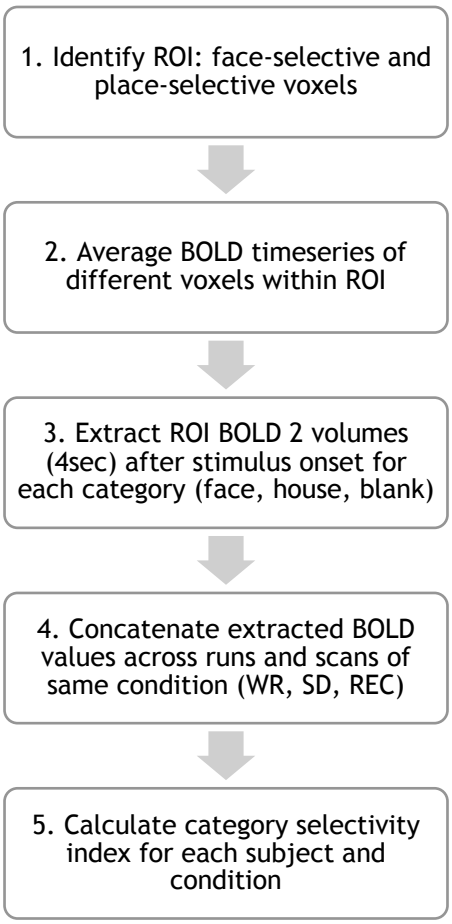

Figure 4.3: analysis pipeline used to derive BOLD responses evoked by stimulus categories that were used in calculation of neural selectivity index. All analysis were performed on each subject's brain.

responses of ROI-preferred category and m_{np} is the mean BOLD activity evoked by all responses of the ROI-non-preferred category. Table 4.1 describes how category selectivity contrasts for WFHR were calculated. A significant non-zero category selectivity would indicate that preferred-category responses elicited larger activation relative to non-preferred-category responses, even in the absence of the preferred-category stimulus. Finally, I addressed the questions of whether neural differentiation for WFHR changed after SD by calculating a one-way ANOVA between category selectivity indices from WR, SD and REC sessions, separately for face-selective and house-selective ROI.

Brain-behaviour correlation. I further explored the relationship between perceptual discrimination and category selectivity by means of correlation. Firstly, I estimated the psychophysical discrimination threshold separately for houses and faces as a measure of performance specific for face discrimination and house discrimination. The psychophysical threshold was estimated by fitting a psychometric function to the proportion of correct face trials and house trials separately (Supplementary Note S4.3). Secondly, I calculated, for each individual, WR-SD differences in psychophysical thresholds and in category selectivity. Finally, I estimated the Pearson's correlation between the z-normalised difference in threshold and the z-normalised difference in category selectivity, for houses and faces separately.

Table 4.1: schematic illustrating trials conditions that made up the analysis of category selectivity for wrong face and house responses. Equation 4.1 was used for calculation of category selectivity index.

Category selectivity in WFHR trials				
	stimulus			**operation**
response	*face*	*house*	*blank*	*Face-response selectivity:*
face	A1	A2	A3	**[A2+A3] – [B2+B3+C2+C3]**
house	B1	B2	B3	*House-response selectivity:*
blank	C1	C2	C3	**[B1+B3] – [A1+A3+C1+C3]**

4.3 Results

The frequency of invalid trials (i.e. trials without a response within the 2 seconds response window) was significantly different between sleep conditions [$F(2,24) = 11.39$, $p < 0.001$]. In SD state participants on average did not respond on 13.1%

(std=11.9) of trials, significantly more frequently than the 1.1% (std = 1.6) of invalid trials in WR condition [t(12) = 3.18, p = 0.008] and the 2.1% (std=4.2) in REC condition [t(12) = 3.68, p = 0.003]. This result indicate that sleep deprived subjects had more frequent attentional lapses and microsleep in SD condition, revealing greater difficulty remaining focused on completing the task after the night of sleep deprivation. Results reported below include only valid trials unless otherwise specified.

4.3.1 Reduced perceptual discrimination accuracy after sleep deprivation

To assess how sleep deprivation affected perceptual discrimination of stimulus categories, a two-way ANOVA was calculated evaluating the effects of sleep condition (WR, SD, REC) and SNR level (low, mid, high) on performance accuracy. Figure 4.4 illustrates perceptual discrimination accuracy by sleep state and SNR level. A significant difference in accuracy was observed between different SNR levels [F(2,24)= 331.4, p < 0.001]. Participants had more difficulty discriminating stimuli with low SNR compared to mid [t(38) = -18.3, p < 0.001] and high SNR stimuli [t(38)

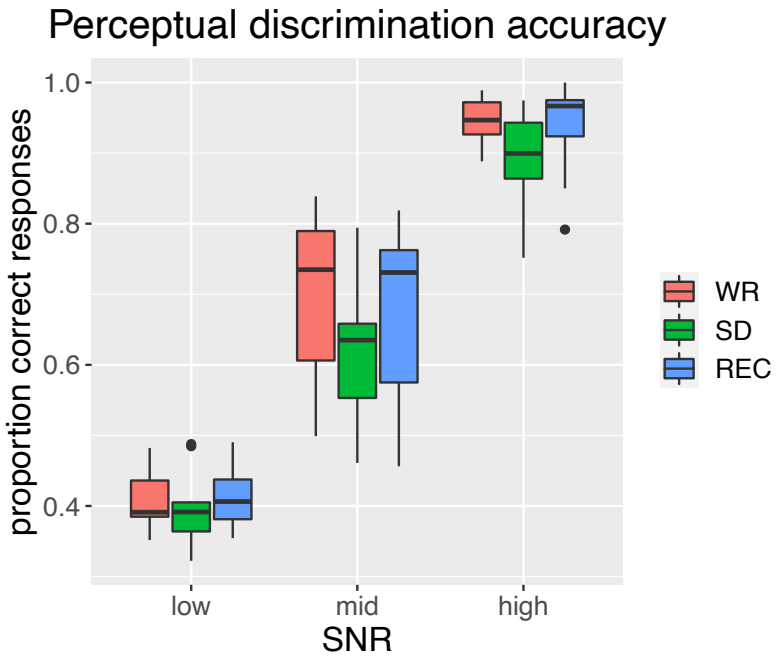

Figure 4.4: perceptual discrimination accuracy by sleep state and SNR level. Boxplots illustrate median (thick black line) and inter-quartile range (coloured box). Participants' performance was poorer at lower SNR levels, confirming effective manipulation of perceptual difficulty via modulation of stimulus SNR. Moreover, one night of sleep deprivation affected perceptual discrimination equally at all SNR levels. WR: Well-Rested; SD: Sleep deprived; REC: post-recovery-

= -50.2, $p < 0.001$], and that high SNR stimuli were easier to discriminate than mid SNR [t(38) = 17.8, $p < 0.001$]. Accuracy was also significantly different between sleep conditions [F(2,24)= 10.09, $p < 0.001$]. On average, accuracy was significantly lower after SD relative to WR [t(38) = -5.54, $p < 0.001$] and REC condition [t(38) = -3.58, $p < 0.001$]. Moreover, from visual inspection it appears that the accuracy reduction from WR to SD was different between SNR levels. However the sleep condition by SNR interaction was just above the alpha threshold [F(4,48) = 2.533, $p = 0.052$]. As such, these results confirm that sleep deprivation had uniform effects across levels of perceptual difficulty, in line with a top-down impairment hypothesis.

To further investigate what pattern of behaviour underlie the reduction in accuracy after SD, I calculated the frequency of response for each category by sleep condition. Table 4.2 shows mean percentage (and standard error) of face, house and blank responses in WR, SD and REC states. On average, the frequency with which observers reported face, house and blank responses across sessions was significantly different [F(2,24) = 62.42, $p < 0.001$]. Specifically, participants reported "blank" more frequently than "face" [t(38) = 14.3, $p < 0.001$] and "house" [t(38) = 12.2, $p < 0.001$] across sessions (Table 4.2), revealing a bias to respond "blank". Furthermore, this frequency of response by category varied significantly between sessions [F(4,48) = 4.786, $p = 0.002$]. Table 4.2 shows that the frequency of blank responses increased from WR to SD, while the frequency of face and house responses decreased. Post-hoc t-test however revealed that these changes were not statistically significant after Bonferroni correction for multiple comparison.

Table 4.2: response frequency by category. Mean percentage (with standard deviation) of face, house, blank responses across all stimulus SNR levels. Only valid trials are included.

	Response frequency (%)		
	Face	**House**	**Blank**
WR	22 (4.5)	23 (8.4)	55 (11.9)
SD	21 (4.9)	20 (7.7)	59 (12.0)
REC	21.3 (5.0)	18.3 (6.8)	60.3 (11.2)
Mean	21.43	20.43	58.10

Finally, to evaluate if perceptual illusions varied across sleep state conditions, I calculated the effects of sleep condition and response category (face and house) on wrong response frequency with a two-way ANOVA. Table 4.3 illustrates mean WFR and WHR by sleep states. A main effect of response category on wrong response frequencies was observed [$F(2,24) = 5.081$, $p = 0.044$], with WHR being more frequent than WFR. There was also a main effect of session [$F(2,24) = 4.646$, $p = 0.012$], where the frequency of WFHR on average decreased after REC relative to SD [$t(25) = 4.21$, $p < 0.001$]. Overall, these results do not support the hypothesis of increased illusory perception after SD.

Table 4.3: percentage of illusory perception trials as measured by WFR trials and WHR trials. Values represent group average (standard deviation).

Frequency of illusory perceptions (% of valid trials)			
	Face (WFR)	**House (WHR)**	**Mean**
WR	2.8 (2.1)	5.6 (5.0)	4.2 (4.0)
SD	3.6 (2.5)	5.3 (5.6)	4.5 (4.3)
REC	2.6 (2.7)	3.1 (3.6)	2.8 (3.1)
Mean	**3.0**	**4.7**	**/**

4.3.2 Face and place-selective regions in occipito-temporal cortex

An example of the resulting face-selective and house-selective ROI is shown in Figure 4.5. Overall, across subjects face selective regions (yellow) clustered around two distinct areas, the bilateral or right anterior fusiform gyrus (corresponding to FFA), more anterior in Figure 4.5, and the inferior lateral occipital cortex (corresponding to Occipital Face Area, OFA), more posterior in the picture. Similarly, place selective voxels (light blue) were found anteriorly around the entorhinal gyrus near the parahippocampal gyrus (corresponding to PPA) and posteriorly around the superior lateral occipital cortex (corresponding to Occipital Place Area, OPA).

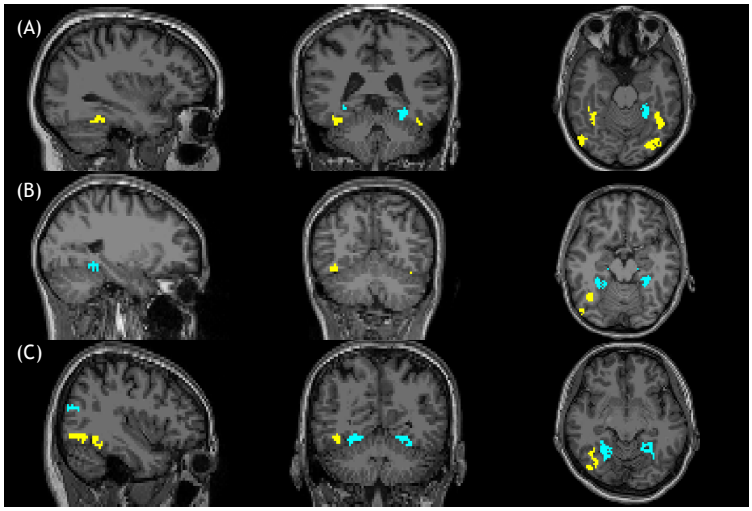

Figure 4.5: category selective regions of three volunteers (A,B,C) obtained from the functional localizer task. These regions showed a significantly stronger BOLD response to faces (yellow) or houses (light blue) compared to other object categories. Face selective regions include FFA and OFA (Gobbini and Haxby, 2007; Haxby et al., 2000; Kanwisher et al., 1997); house selective regions include PPA and OPA (Dilks et al., 2013; Epstein and Kanwisher, 1998).

4.3.3 Reduced category selectivity after sleep deprivation

Selectivity for stimulus categories. Category selectivity in face and place selective regions is illustrated by different SNR levels and sleep state conditions in Figure 4.6. A two-way ANOVA assessed the influence of SNR and session on category selectivity separately for face and house selective regions. In face-selective regions, I observed a main effect of SNR level [$F(2,24) = 60.23$, $p < 0.001$] and a main effect of session [$F(2,24) = 8.529$, $p = 0.002$], but no significant interaction [$F(4,48) = 1.343$, $p = 0.268$]. High SNR elicited greater category selectivity than both mid [$t(38) = 12.4$, $p < 0.001$] and low SNR [$t(38) = 9.85$, $p < 0.001$]. Mid SNR elicited greater category selectivity than low SNR [$t(38) = 7.73$, $p < 0.001$]. Finally, category selectivity was significantly lower in SD relative to WR [$t(38) = -4.70$, $p < 0.001$] and REC [$t(38) = -4.53$, $p < 0.001$].

In house-selective regions, there was a main effect of SNR [$F(2,24) = 29.20$, $p < 0.001$], a main effect of session [$F(2,24) = 12.32$, $p < 0.001$], and a significant SNR by session interaction [$F(4,48) = 4.240$, $p = 0.005$]. Post-hoc t-test revealed that house selectivity was reduced from WR to SD for mid SNR [$t(12) = 3.63$, $p = 0.027$]

and high SNR stimuli [t(12) = 4.35, p = 0.008], and was increased after REC relative to SD at high SNR [t(12) = -3.88, p = 0.018].

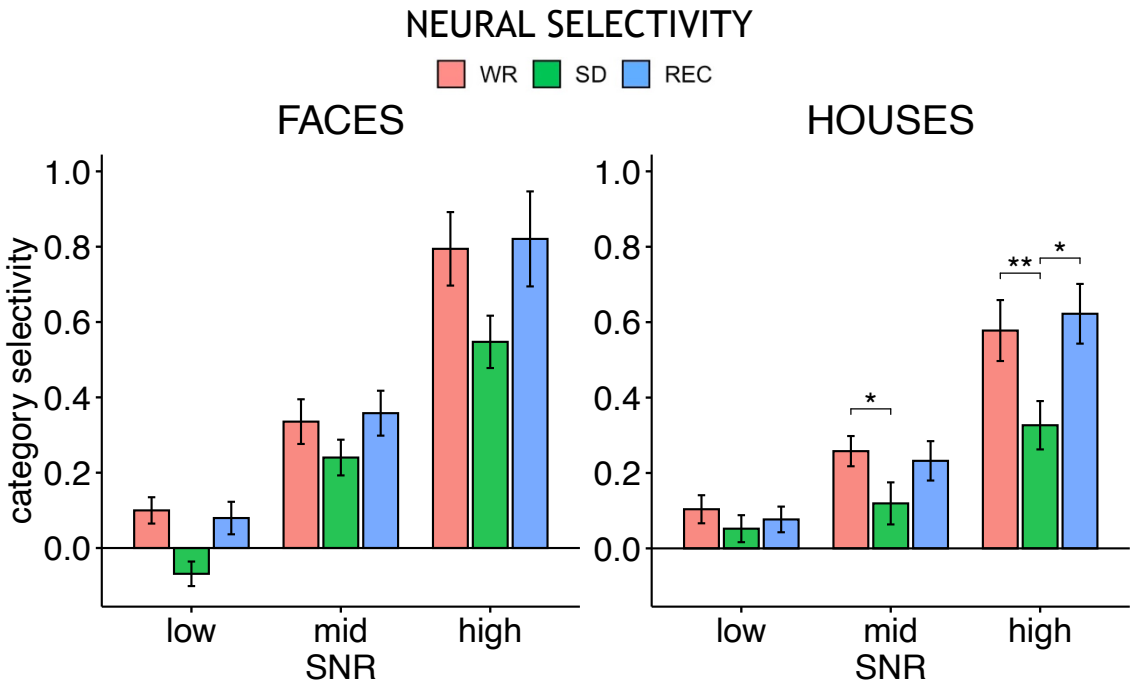

*Figure 4.6: group-average category selectivity in face-selective (left panel) and house-selective (right panel) regions are shown grouped by stimulus SNR and by sleep state condition. On average, category selectivity was larger at higher SNR levels and decreased after sleep deprivation. Error bars indicate standard error of the mean. *p<.005; **p<.001.*

In house-selective regions, the magnitude of reduction in category selectivity after sleep deprivation depended on the SNR level. Figure 4.7 illustrates that sleep deprivation reduced category selectivity more at higher SNR levels. Overall, the larger difference at higher SNR levels reveals greater curtailment of neural differentiation for clearer pictures. These results are opposite those expected based on the hypothesis of sleep deprivation influence on bottom-up sensory processing, namely of greater degradation of processing at lower SNR levels relative to higher SNR levels.

Finally, to exclude that the reduction in category selectivity was driven by trials in which participants responded but did not adequately attend to stimuli, additional analyses including only correct trials were performed (Supplementary Note S4.4). These analyses confirmed the main results reported above with the exception of the

interaction between SNR and session in house-selective regions which was not significant.

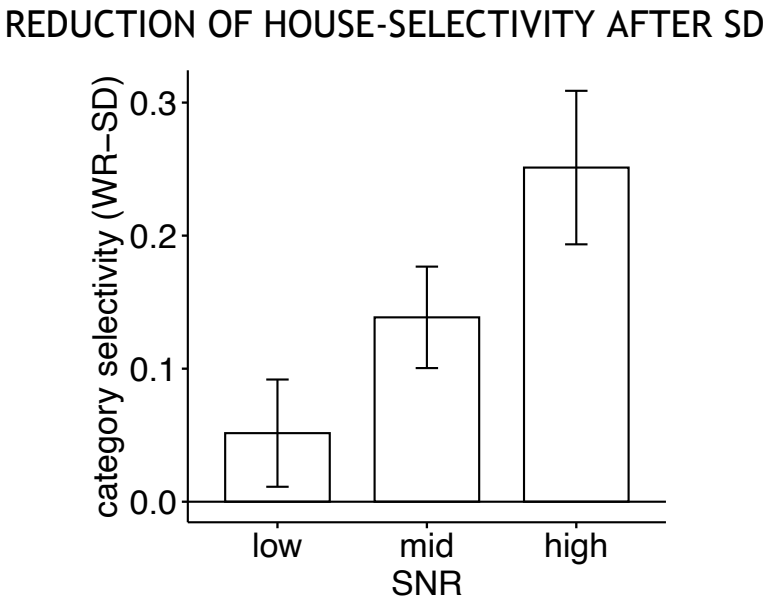

Figure 4.7: difference in house selectivity between WR and SD sessions was larger for clearer pictures.

To further evaluate the specificity of SD effects on face and house selective regions, preferential responses to face stimuli and to house stimuli was extracted from control regions previously identified via the functional localizer, namely body-selective, object-selective and word-selective regions. Control analyses are described in Supplementary Note S4.5 and illustrated in Supplementary Table 4.2 and Supplementary Figure S4.3. Control analyses largely confirmed that the category selectivity reduction after sleep deprivation was specific to face and house-selective regions.

Overall, category selectivity was reduced after sleep deprivation and restored by recovery sleep. This provides support for the hypothesis that sleep deprivation would impair high-level visual processing. Moreover, category selectivity was modulated by SNR level, with higher SNR levels eliciting greater category selectivity across sessions. This confirms that manipulation of stimulus clarity by noise degradation effectively evoked larger differentiation of perceptual representation in high-level visual regions, as designed. Finally, the uniform reduction in category selectivity after sleep deprivation in face-selective regions and the larger reduction for higher

SNR stimuli in house-selective regions suggest that generic top-down reduction in attentional resources, rather than bottom-up processing disruption, characterised neural deficits after sleep deprivation.

Category selectivity during Wrong Face/House Responses. I assessed category selectivity in WFHR trials to determine if illusory perceptions were underlain by differentiation of neural responses in high-level visual cortex, and whether this was altered by sleep deprivation. Figure 4.8 illustrates category selectivity in WFR (left panel) and WHR (right panel) for different sessions. During WR state, activity in face-selective regions was increased for face-responses in non-face trials relative to blank and house responses in non-face trials, as evidenced by a one-sample t-test against zero [t(12) = 4.018, p = 0.002, *uncorrected*]. Similarly, significant non-zero category selectivity was found for wrong house responses in house-selective regions [t(12) = 2.848, p = 0.015, *uncorrected*]. This indicates differentiation of neural responses of ventral visual cortex based on observers' perceptual reports rather than physical stimulus, possibly highlighting part of a neural mechanism of illusory perceptions. After SD, selectivity to face responses was also significantly different from zero [t(12) = 2.848, p = 0.015, *uncorrected*], while selectivity to house responses was not

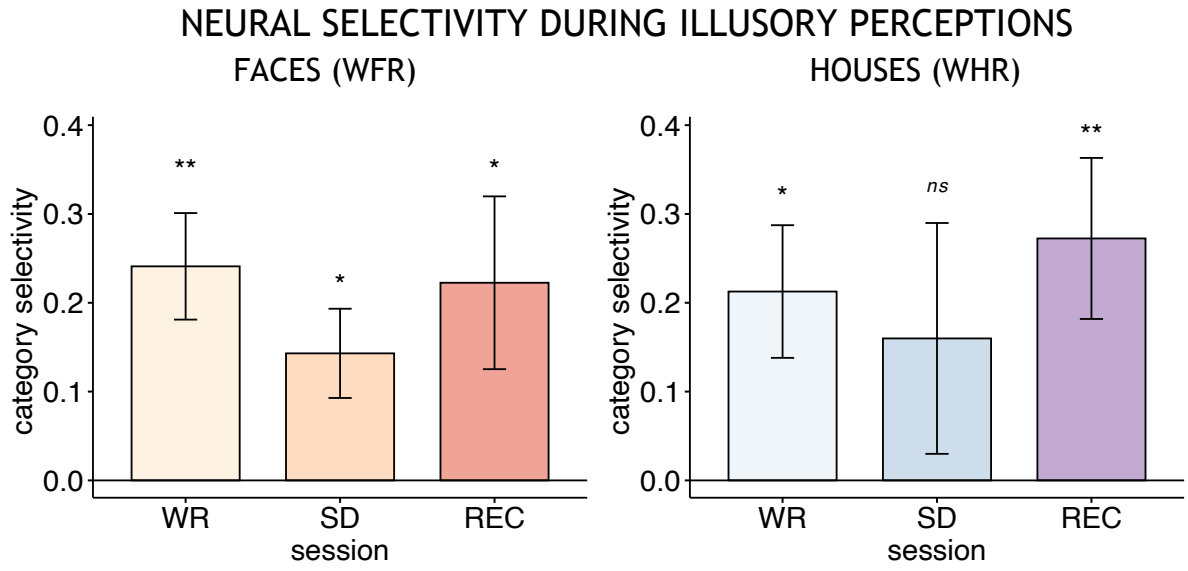

*Figure 4.8: category selectivity during illusory perceptions. Category selectivity for face illusory perceptions in face-selective regions (left panel) was non-zero. Similarly, category selectivity for illusory perceptions of houses in house-selective regions (right panel) was non-zero in WR and REC sessions. Category selectivity did not vary significantly between sessions. * denotes statistically significant difference from zero, as measured by a one-sample t-test. *: p < 0.05; **: p < 0.005.*

statistically significant [t(12) = 1.23, p = 0.242]. After REC, selectivity for preferred response category was significant in house-selective-ROI [t(12) = 3.004, p = 0.001, *uncorrected*], and in face-selective-ROI [t(11) = 2.287, p = 0.047, *uncorrected*] (N=12 since one participants never reported face in house/blank trials in REC). A one-way ANOVA showed no significant main effect of sleep state condition on either face-response-selectivity [F(2,22) = 0.867, p = 0.434] or house-response-selectivity [F(2,24) = 0.334, p = 0.72].

4.3.4 Correlation between category selectivity and perceptual discrimination threshold

Having observed a reduction in both perceptual discrimination accuracy and category selectivity after SD, I further carried out correlation analysis to explore whether the reduction in perceptual abilities after SD was related to the changes observed in category selectivity. As a measure of performance specific for face discrimination and house discrimination, psychometric functions were fitted to the proportion of accurate face trials and accurate house trials respectively, for each observer (Supplementary Figure S4.4 and Figure S4.5). Figure 4.9 illustrates the correlation between the WR-SD difference in category selectivity and category

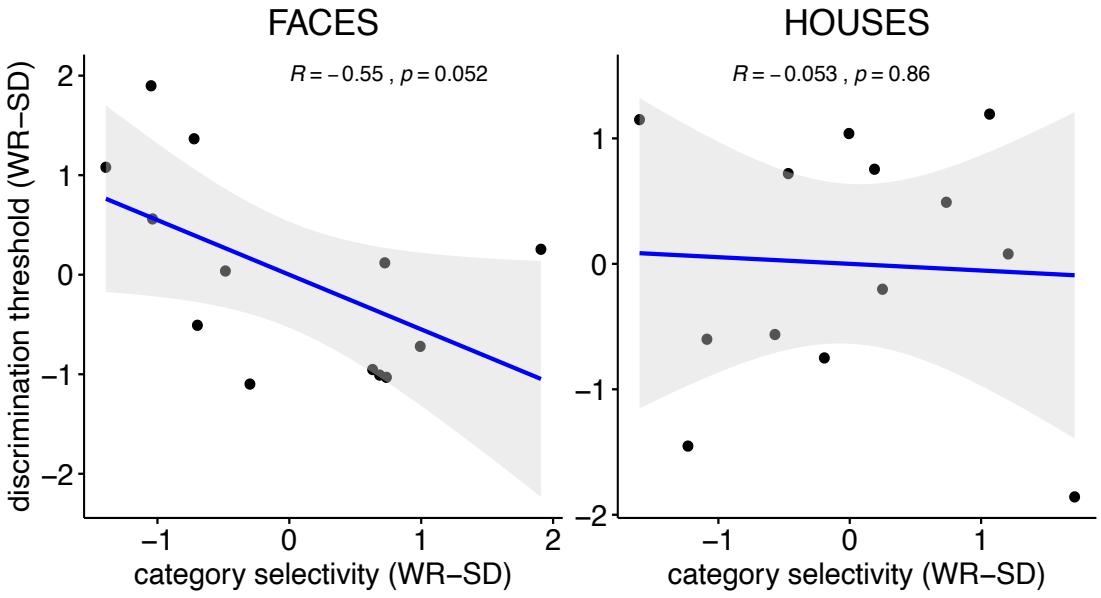

Figure 4.9: correlation between indices of discrimination performance and neural specialisation. WR-SD differences in category selectivity and discrimination threshold are shown for each individual (values are z-normalised). Only a trend for a correlation between the reduction in face-discrimination threshold and the reduction in face-selectivity was observed (p = 0.052).

discrimination threshold, for face (left panel) and house (right panel) stimuli. Pearson's correlation between discrimination threshold difference and category selectivity difference were not significant for either faces [r(11) = -0.55, p = 0.052] nor houses [r(11) = -0.05, p = 0.863].

4.4 Discussion

In this chapter, I investigated how sleep deprivation affected the high-level perceptual ability to discriminate object categories. The ability of volunteers to discriminate noise-degraded faces, houses and blank stimuli was impaired after one night of sleep deprivation and restored after one subsequent night of recovery sleep. At the behavioural level, the impairment in performance was characterized by reduced categorisation accuracy, but there was no evidence of increased perceptual illusions from WR to SD. At the neural level, this was paralleled by reduced category selectivity in face and place selective regions in occipito-temporal cortex, indicating dedifferentiation of perceptual representations. Overall, results suggest that sleep deprivation is detrimental for visual categorisation of objects and for functional specialisation in high-level visual regions.

4.4.1 Impaired high-level perceptual discrimination after sleep deprivation

Sleep deprivation significantly reduced the ability of observers to categorise faces, houses and blank stimuli. Previous studies reported that with increasing time awake the frequency and severity of visual illusions grew (Babkoff et al., 1989; Petrovsky et al., 2014; Waters et al., 2018). Based on such evidence, here I investigated whether perceptual discrimination impairment after one night without sleep would be driven by more frequent illusory perceptions, namely trials where participants reported seeing a face or a house when it was not presented. However, here I found that the frequency of WFHR did not significantly change from WR to SD, indicating that perceptual illusions did not increase after SD. Compared to previous studies that used questionnaires or interviews to evaluate perceptual illusions, here I used an objective perceptual discrimination task with noise-degraded stimuli in an attempt to directly induce and measure perceptual illusions. However, the perceptual task was limited with respect to the range of possible illusions it could

detect, which were restricted to the response options available (i.e. face and house, since blank is an absence of perceptual content by definition). It cannot thus be excluded that participants experienced misperceptions or visual alterations of contents different from the available response options that they could not report. Moreover, here no evidence of changes in neural selectivity during illusory responses was observed across sessions. Yet, t-tests revealed that face and house selective regions responded selectively during WFR and WHR respectively in WR session. One limitation of these analyses was the much lower number of WFR trials (see Table 4.3) relative to correct non-face responses in non-face trials, which were used to calculate neural selectivity for WFHR responses. Future work could thus analyse trials of all subjects and add weights to account for differences in the number of trials of the conditions, in order to estimate a more robust distribution of brain responses to WFHR across WR, SD and REC sessions.

4.4.2 Reduced category selectivity in occipito-temporal cortex in sleep-deprived healthy volunteers

In parallel to impaired categorisation of objects, category selectivity in face-selective and place-selective regions was reduced after sleep deprivation. Importantly, the reduced category selectivity was found also when incorrect trials were excluded from analysis, confirming that results were not driven exclusively by a subset of trials in which participants did not pay attention and responded randomly. Furthermore, analyses of category selectivity in control regions (word, bodies and object-selective) revealed that the selectivity reduction after sleep deprivation was not a generic effect on all areas in the occipito-temporal region, but was specific to the brain areas specialised in processing the stimulus-features of the task. Specifically, face and house-selective regions showed reduction in selectivity to face and house stimuli respectively after sleep deprivation, whereas words and objects-selective regions were not affected by sleep deprivation. Interestingly, the body-selective region showed reduction in selectivity to faces (but not houses) after sleep deprivation. Crucially, this is explained by the characteristics of face stimuli, which were portrait photos of faces with neck and shoulders.

These results thus show that SD led to a dedifferentiation of faces and houses representations in occipito-temporal cortex. This is the first evidence of perceptual dedifferentiation after sleep deprivation to the best of my knowledge, and suggests that SD degrades object representations in category-selective visual cortical regions.

Previous studies have provided evidence of reduced visual processing capacity after SD in the form of attenuated BOLD response in FFA and PPA (Chee et al., 2010; Lim et al., 2010) as well as reduced repetition suppression in PPA in response to distracting house stimuli (Kong et al., 2011). Yet, one study that measured category selectivity in PPA and FFA found no difference before vs after a night of SD (Poh and Chee, 2017). This finding however could be partly due to the short duration of the sleep deprivation employed, which was less than 24 hours, and to the specific task design of the experiment, which focused on selective attention rather than perceptual discrimination. The findings presented in this chapter thus extend previous results by showing that sleep deprivation is not only associated with generalized attenuation of BOLD response amplitude in task-relevant regions as previously shown (Chee et al., 2010; Lim et al., 2010), but that it also degrades the quality of perceptual representations.

4.4.3 Role of bottom-up and top-down mechanisms in high-level perceptual deficits

Results presented in this chapter show local perceptual processing deficits in visual regions critical for object recognition, including ventral temporal (FFA, PPA) and lateral occipital (OFA, OPA) regions. These neural deficits occurred in parallel to impairments in category discrimination at the behavioural level, although they were not correlated. What could have underlain these deficits in high-level visual processes observed after one night of sleep deprivation?

Firstly, one possibility is that a failure of bottom-up sensory processing in early visual regions caused degradation of perceptual representations. However, if reduced bottom up sensory processing underlay deficits in perceptual discrimination, results would have shown a larger decline of performance and neural selectivity at lower-SNR stimuli compared to higher-SNR stimuli (Chee and Tan, 2010). This is because

lower-SNR stimuli carry weaker signal information that could easily get lost if sensory processing resources are disrupted, whereas stimuli with higher SNR carry stronger information that could be picked up even when bottom-up sensory processing is impaired. Against this hypothesis, here I observed that performance decline and neural selectivity for faces was not significantly different between levels of stimulus SNR. Moreover, the attenuation of neural selectivity for houses was larger at higher relative to lower SNR level (although this was not confirmed after exclusion of incorrect trials from analysis), a trend opposite that predicted by the bottom-up sensory failure hypothesis. These results are in line with previous studies that showed uniform reduction of performance after sleep deprivation across different magnitudes of stimulus contrast in a selective attention task (Chee and Tan, 2010) and across levels of memory load in a working memory task (Chee and Chuah, 2007). Together, these results provide no evidence for a degradation of bottom-up sensory processing in sleep-deprived individuals.

Secondly, another explanation for perceptual impairments could involve deficits in top-down modulation such as reduced attentional resources. In line with this view, previous studies have shown attenuated activity in prefrontal and parietal regions in parallel to reduced extrastriate neural responses during task execution, indicating reduced top-down modulation of sensory processing (Chee et al., 2011; Chee et al., 2010; Lim et al., 2010). In this chapter, the uniform reduction in perceptual discrimination and neural selectivity could reflect a generic attenuation of attentional capacity including reduction in vigilant attention that equally affected stimulus processing independent of its perceptual clarity (Chee and Tan, 2010).

Finally, the degradation in perceptual representations could occur independent of other processes, originating from compromised neural processing in high-level, category selective visual regions. One possible mechanism that could explain this would be local sleep (Krueger et al., 2008; Van Dongen et al, 2011), whereby prolonged wakefulness and repeated use of a neural circuit increase the propensity of that circuit to enter the biphasic On-Off mode of activity typical of NREM sleep, causing it to disengage from coordinated processing of task-relevant stimuli and thus compromise stimulus evaluation processes. It has been suggested that attenuated

BOLD signal observed after sleep deprivation in task-relevant regions could be underlain by reduced processing capacity when local neural populations fall asleep (Chee et al., 2010). Yet, more experimental evidence with high temporal resolution and high spatial specificity is required to link local sleep episodes to alterations in brain function and behavioural performance.

Overall, it is not clear what underlies perceptual impairments and reduced category selectivity in high-level visual regions. One limitation of this study was that the role of brain regions involved in bottom-up and top-down processes such as early visual cortex and fronto-parietal regions was not directly assessed. Moreover, here also the role of distinct regions belonging to the same category-selective network (e.g. FFA vs OFA) was not assessed, despite evidence that they may have distinct functional roles (Fox et al., 2009; Tsantani et al., 2021) Further research is needed to better understand how sleep deprivation degrades high-level visual perception. In particular, further analyses need to directly assess the response of low-level visual regions such as V1 to different stimulus categories after sleep deprivation. This would allow to confirm whether the SD impairment of neural selectivity is specific to high-level visual regions or whether it arises from altered processing in low-level visual areas. In particular, evidence that V1 response to stimulus (house/face) vs blank is reduced after sleep deprivation would suggest that the degraded functional selectivity reported in this chapter could arise from altered processing of low-level visual characteristics early in the visual processing hierarchy.

4.4.4 Limitations and conclusions

One limitation in this study is that the interpretation of statistical analyses relied solely on p-values and employed parametric tests (e.g., ANOVA), despite the small sample size being inadequate for robustly testing assumptions of normality. As a result, this approach tends to offer a binary perspective on the results, where a significant or non-significant outcome is seen as evidence either against or for the null hypothesis. Importantly, this approach does not provide information about the magnitude of the observed difference. To determine the size of the observed effect and ascertain whether the lack of statistically significant effect truly indicates an absence of effect, future research can incorporate additional measures, such as

effect size calculations and Bayes factor analysis. Effect size measures give insights into the practical significance of the observed differences, revealing the magnitude of the effects beyond statistical significance. Additionally, employing Bayes factor analysis can help further assess the strength of evidence supporting the experimental hypothesis that sleep deprivation leads to a reduction in high-level perception. By incorporating these approaches, future work can obtain a more comprehensive understanding of the effects of sleep deprivation on high-level visual perception, their practical implications, and the degree of support for their hypotheses.

In conclusion, this chapter has shown that one night of sleep deprivation is associated with deficits in object discrimination and that the neural representation of different objects in high-level visual cortex is less differentiated. This perceptual dedifferentiation reveals task-specific and localized impairments in visual processing after sleep deprivation, but the underlying mechanisms remain unclear. Future studies should further investigate how sleep deprivation leads to deficits in high-level, visual perceptual function. One possible avenue is to compare WR and SD functional connectivity at rest between early visual regions (e.g. V1,V2,V3) and higher-level visual areas (e.g. FFA, PPA) as well as between fronto-parietal region (e.g. Intraparietal Sulcus, Kay and Yeatman, 2017) and FFA/PPA, to evaluate whether alterations in bottom-up and/or top-down processing streams could be involved.

4.5 Supplementary material

Supplementary Note S4.1: calibration of signal intensity for each observer. In order to match perceived difficulty of the categorisation task across volunteers and control for inter-individual differences in perceptual sensitivity, the greyscale intensity (i.e. signal intensity) of face, house and blank stimuli was determined for each individual during a preparatory session in the fMRI scanner. The calibration task required volunteers to discriminate face, house and blank stimuli with superimposed with noise fixed at [130 130 130] (rgb values) and variable signal intensity. The stimulus signal intensity was varied trial by trial by means of a 2-up-1-down staircase procedure. Signal intensity at the beginning of the block was [20 20 20] (rgb values) and varied in steps of [1 1 1] (rgb values). After 220 trials the calibration task stopped and the signal intensity threshold was estimated as the average of all staircase reversals (excluding the first two). The signal intensity threshold obtained for each observer (Table S4.1) was then used in the main experiment.

Table S4.1: greyscale values for face, house and blank stimuli used in the main experiment and calibrated for each observer to control for inter-individual perceptual sensitivity.

	Signal intensity: (rgb value)
P01	[13 13 13]
P02	[15 15 15]
P03	[20 20 20]
P04	[17 17 17]
P05	[17 17 17]
P07	[14 14 14]
P09	[16 16 16]
P10	[17 17 17]
P11	[10 10 10]
P12	[14 14 14]
P13	[13 13 13]
P14	[17 17 17]
P15	[15 15 15]
P16	[15 15 15]

Supplementary Note S4.2: Control analysis of category selectivity in house-selective (Figure S4.1) and face-selective brain regions (Figure S4.2). Category selectivity was measured 0, 2, 4 (main text), 6, 8 and 10 seconds after stimulus onset. Results show

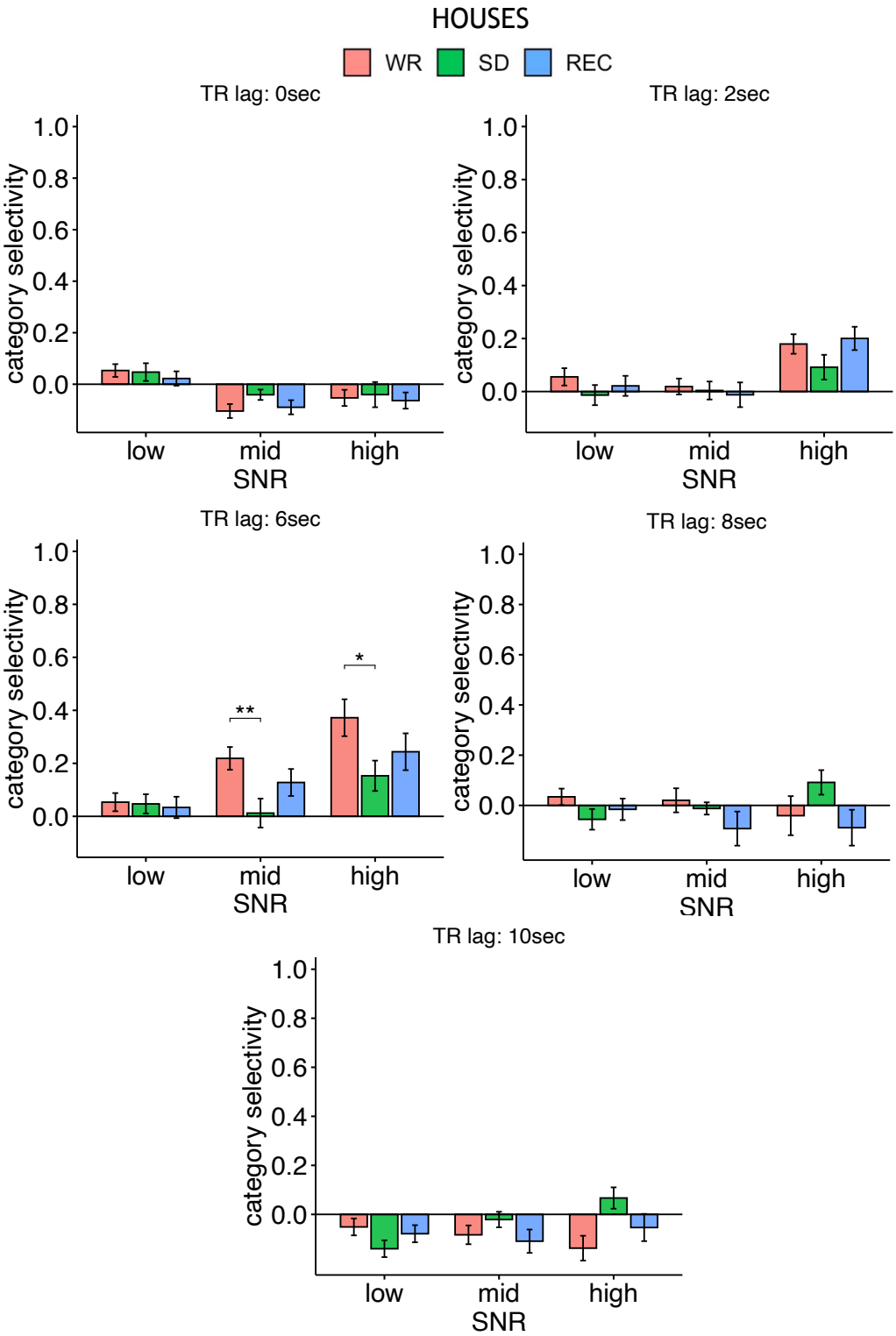

Figure S4.1: neural selectivity for house stimuli in house-selective regions extracted from BOLD response 0-10 seconds after stimulus onset.

highest category selectivity at 4 and 6 seconds after stimulus onset, consistent with the peak of hemodynamic response function which occurs between 4 and 6 seconds after stimulus onset (Dale and Buckner, 1997; Huettel et al., 2014).

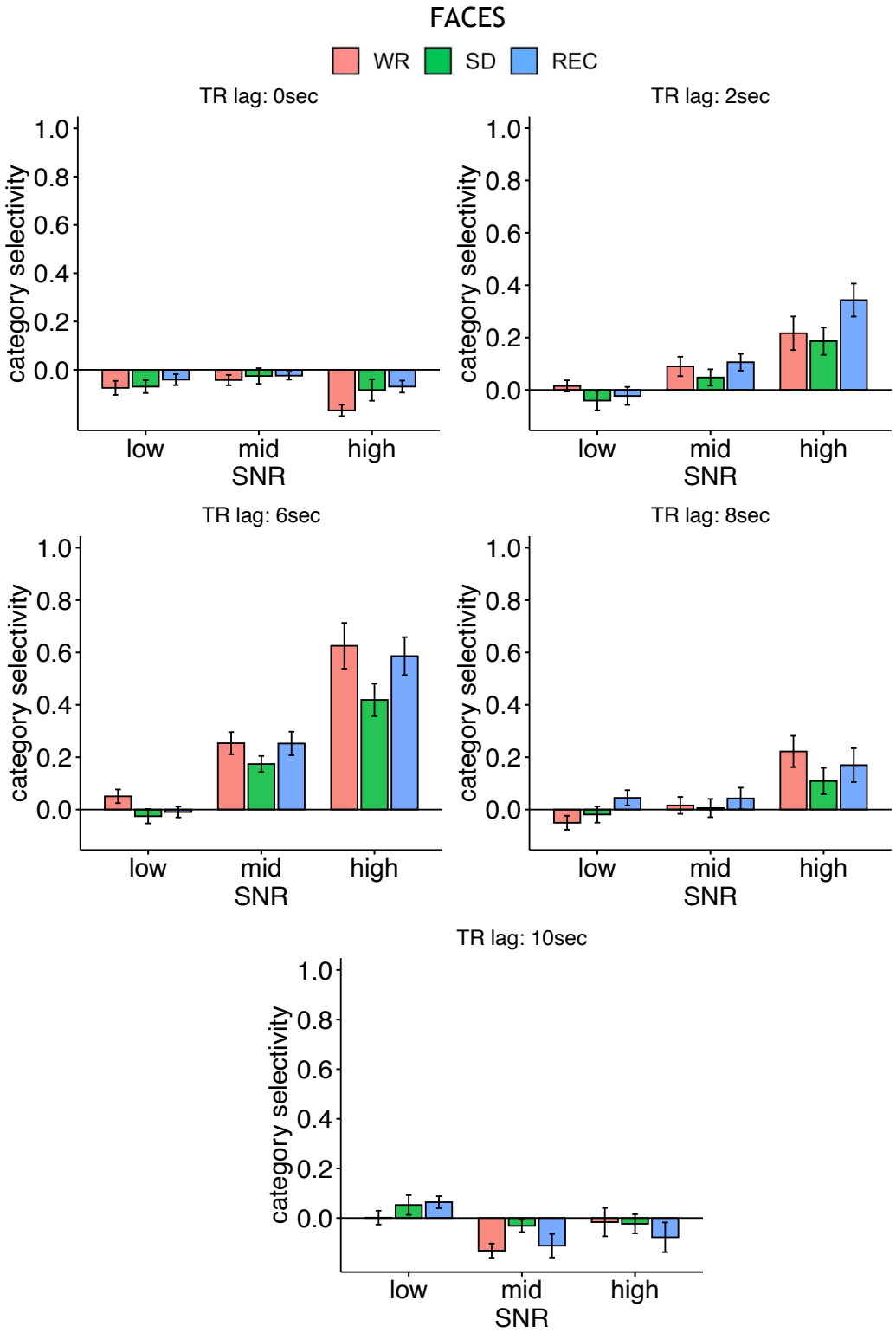

Figure S4.2: neural selectivity for face stimuli in face-selective regions extracted from BOLD response 0-10 seconds after stimulus onset.

Supplementary Note S4.3: Estimation of perceptual threshold for discrimination of faces and houses. I fitted the proportion of correct face trials and proportion of correct house trials with a psychometric function with four parameters α, ß, γ and λ (Wichmann and Hill, 2001):

$$\psi(x;\alpha,\beta,\gamma,\lambda) = \gamma + (1 - \gamma - \lambda)\, F(x;\alpha,\beta) \qquad (1)$$

Where F is a Weibull function (Kingdom and Prins, 2016):

$$F(x;\alpha,\beta) = 1 - exp\left(-\left(\frac{x}{\alpha}\right)^{\beta}\right) \qquad (2)$$

The main parameter of interest was the parameter α, corresponding to the threshold of the psychometric function. Here threshold was the middle point of the psychometric function between parameters γ and λ. Parameters γ and λ define the lower and upper bound of the function F respectively. γ was a free parameter. λ corresponds to the lapse rate and was fixed at 0 because estimating it empirically resulted in failed psychometric model fits, likely due to overparameterization (Kingdom and Prins, 2016). Estimated psychometric functions are illustrated in Figure S4.4 and Figure S4.5.

Supplementary Note S4.4: analysis of category selectivity of correct responses. To confirm that the reduction in category selectivity was not an artifact derived from inclusion of a subset of poor-performance trials but reflected a true degradation of neural specialisation for object categories in high-level visual cortex, additional analysis were performed including only correct trials. However, since two subjects did not respond correctly in any low SNR trial in REC condition, the influence of session and SNR on category selectivity for accurate responses was evaluated with (1) a model excluding REC condition and (2) a model excluding the two participants. Firstly, the two-way ANOVA excluding REC condition revealed a significant main effect of sleep state [$F_{house}(1,12) = 16.15$, $p = 0.002$; $F_{face}(1,12) = 10.72$, $p = 0.007$] and SNR level on category selectivity [$F_{house}(2,24) = 5.678$, $p = 0.009$; $F_{face}(2,24) = 20.47$, $p < 0.001$] but no significant interaction [$F_{house}(2,24) = 0.061$, $p = 0.941$; $F_{face}(2,24) = 0.268$, $p = 0.768$]. Secondly, the two-way ANOVA excluding the two observers who did not respond correctly in any low SNR trial in REC condition revealed significant main effects of sleep state [$F_{house}(2,20) = 9.393$, $p = 0.001$; $F_{face}(2,20) = 7.385$, $p = 0.004$] and SNR level [$F_{house}(2,20) = 7.535$, $p = 0.004$; $F_{face}(2,20) = 16.68$, $p < 0.001$] on category selectivity, but no significant interaction [$F_{house}(4,40) = 1.219$, $p = 0.318$; $F_{face}(4,40) = 0.469$, $p = 0.758$]. Overall, these results confirm those presented in the main text obtained including correct and incorrect trials.

Supplementary Note S4.5: analysis of category selectivity in control regions. To evaluate specificity of the effects of sleep deprivation on face and house selective regions, the preferential response to face vs other stimuli and house vs other stimuli was calculated in control areas within the occipital-temporal region, including regions preferentially responding to words, bodies and objects as identified from the functional localiser (see main text). Results of a two-way anova are shown in Table S4.2 and the magnitude of category selectivity by session and by SNR is illustrated in figure S4.3.

Table S4.2: results of category selectivity analyses in control regions.

		ANOVA results			
Contrast	ROI	factor	F	df	*p*
Face vs other	bodies	SNR	24.13	2,24	**<0.001**
		Session	4.931	2,24	**0.016**
		Session*SNR	0.31	4,48	0.87
	objects	SNR	1.363	2,24	0.275
		Session	0.631	2,24	0.541
		Session*SNR	0.996	4,48	0.419
	words	SNR	28.89	2,24	**<0.001**
		Session	2.359	2,24	0.116
		Session*SNR	0.699	4,48	0.596
House vs other	bodies	SNR	10.44	2,24	**<0.001**
		Session	0.215	2,24	0.808
		Session*SNR	2.117	4,48	0.093
	objects	SNR	4.974	2,24	**0.015**
		Session	0.574	2,24	0.571
		Session*SNR	1.656	4,48	0.176
	words	SNR	6.443	2,24	**0.006**
		Session	0.608	2,24	0.553
		Session*SNR	5.35	4,48	**0.001**

Firstly, the presence of non-zero face/house selectivity in control regions and particularly in high SNR stimuli (Figure S4.3) is explained by the fact that high-level visual areas in the occipito-temporal regions are not exclusively activated by a single category but they tend to respond more to the preferred stimulus category relative to others (e.g. Grill-Spector et al, 2007). Consistent with this, the magnitude of face selectivity in FFA/OFA regions and house-selectivity in PPA/OPA regions observed here was larger than in control regions.

Moreover, the main effect of SNR observed in control regions for both face and house stimuli (Table S4.2) indicates that control areas showed category selectivity mainly when stimuli were clearly visible.

Control analyses also revealed a main effect of session in body-selective regions for face vs other stimuli. As argued in the main text, this is likely explained the characteristics of face stimuli, which were portrait images with neck and shoulder.

Finally, there was also an interaction in word-selective regions for the house vs others contrast, indicating that the change in house-selectivity by SNR depended on the session. However, post-hoc t-tests revealed no significant pairwise differences after correcting for multiple comparison.

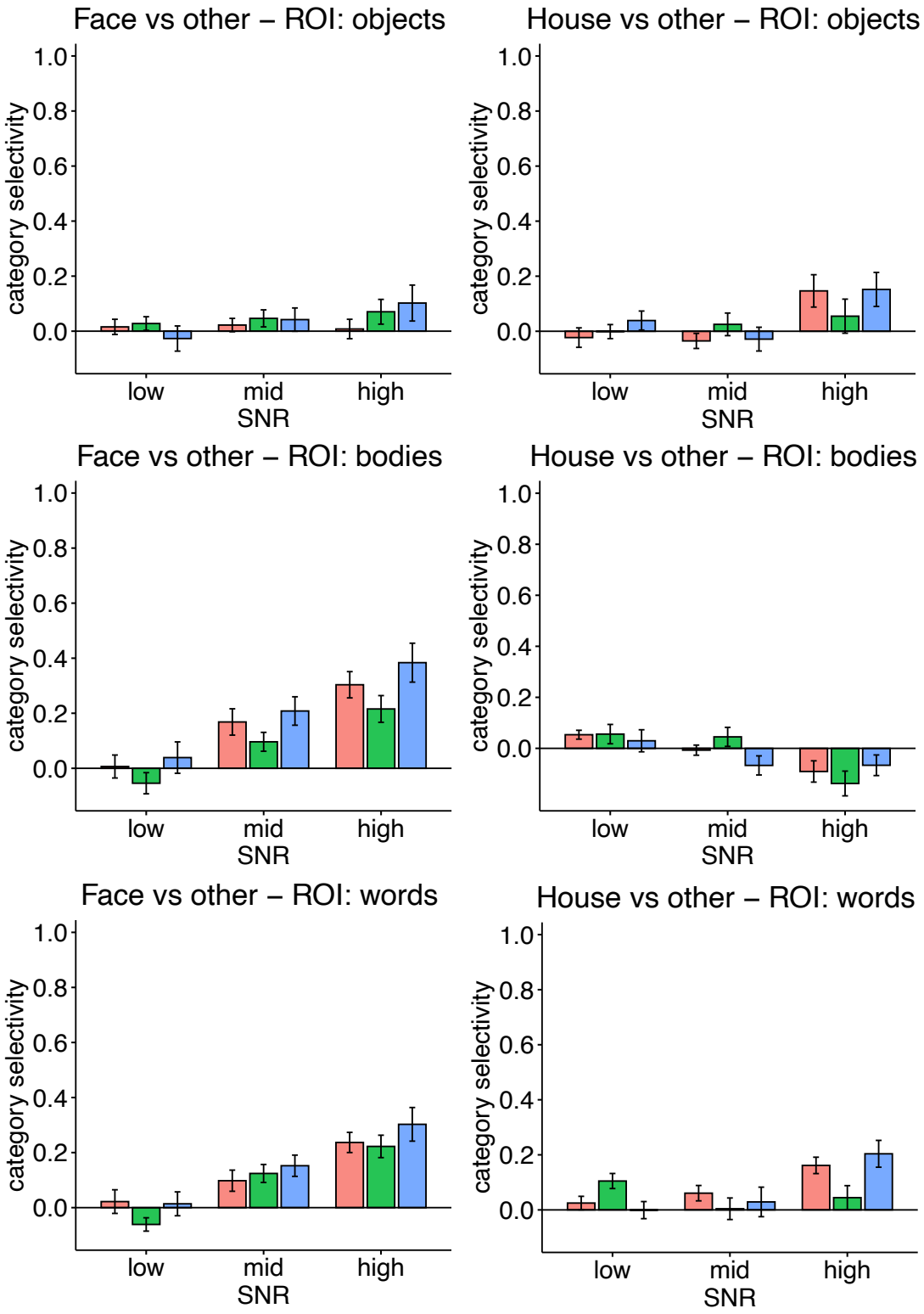

Figure S4.3: neural selectivity for face (left column) and house stimuli (right column) in control regions. Control regions including areas which preferentially responded to objects, to bodies and to words respectively were identified from a functional localizer conducted before the experiment

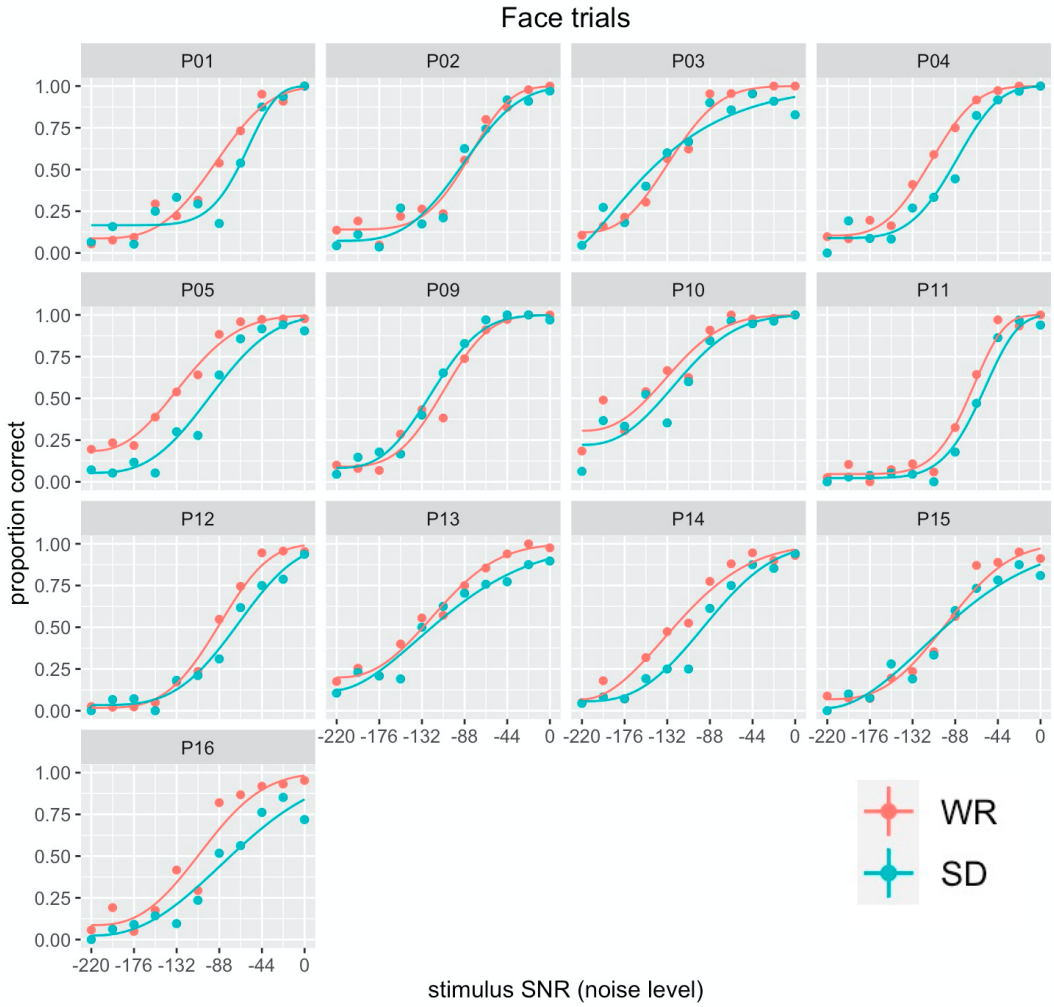

Figure S4.4: psychometric functions used to estimate face discrimination threshold in WR and SD. Lines are the psychometric curves fitted to the proportion of correct responses (dots) for each stimulus SNR level. Threshold was estimated as the stimulus SNR value corresponding to the midpoint on the psychometric function. WR: Well-Rested; SD: Sleep deprived. SNR level ranges from -220 to 0 and represent rgb values of white noise used to degrade stimuli perceptual clarity and modulate trial difficulty.

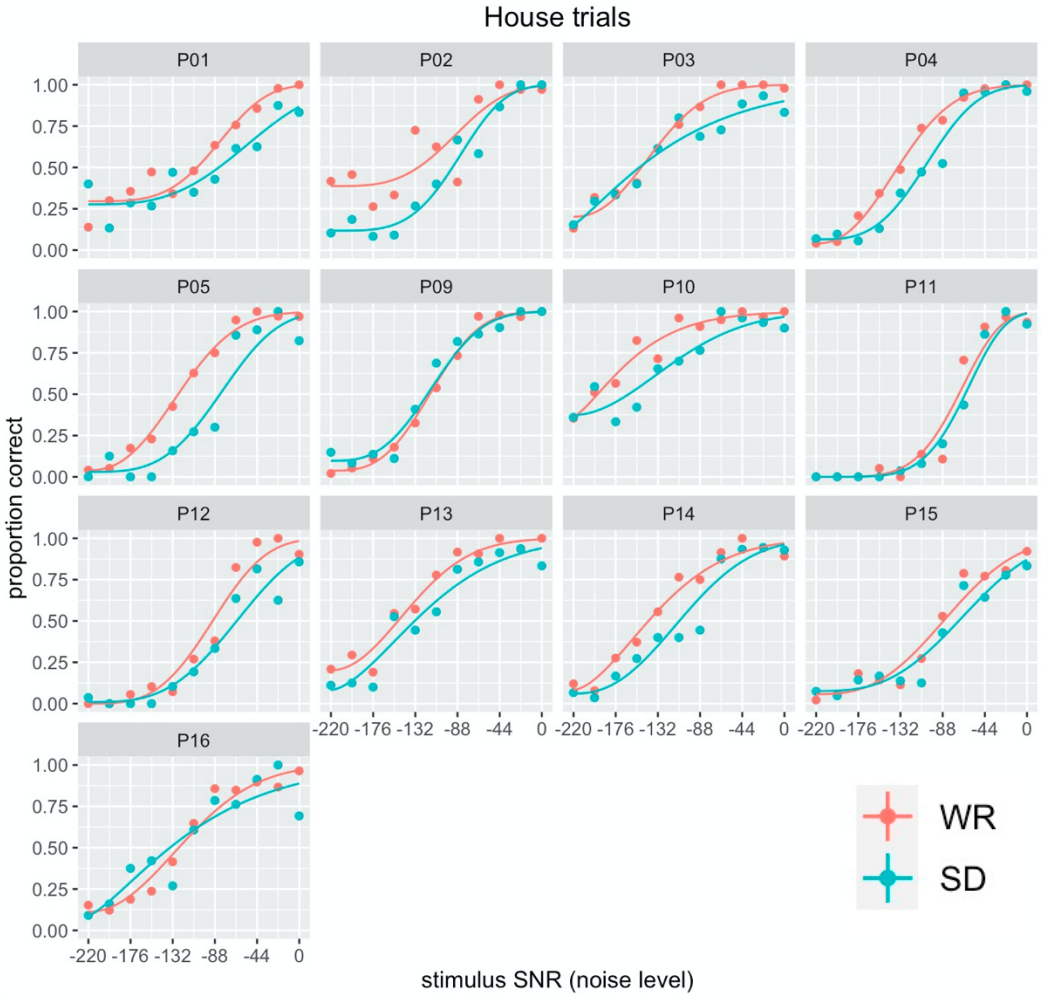

Figure S4.5: psychometric functions used to estimate house discrimination threshold in WR and SD. Lines are the psychometric curves fitted to the proportion of correct responses (dots) for each stimulus SNR level. WR: Well-Rested; SD: Sleep-deprived.

Chapter 5.
Effects of sleep deprivation on metacognitive abilities

In previous chapters, I have shown that sleep deprivation is associated with impairments in low and high-level visual perceptual functions. Here I aim to further expand the understanding of cognitive impairments after sleep deprivation focusing on perceptual metacognition.

5.1 Introduction

When we make decisions, we evaluate our certainty on the decision evidence and adjust our behaviour accordingly. For example, when driving in darkness at night we might be uncertain about the distance towards an upcoming, and thus decide to slow down more. Such self-monitoring or introspection process, known as metacognition, is key to optimal decision making, since it allows us to take the best course of action upon evaluation of our knowledge or state of being.

Different measures of metacognition have been assessed in studies of sleep deprivation. Firstly, metacognitive bias – the overall level of confidence - has been evaluated by averaging confidence ratings in response accuracy. Studies of working memory (Baranski et al., 1994), perceptual comparison (Baranski et al., 2007) and complex medical decisions (Aidman et al., 2019) have found reduced metacognitive bias after prolonged wakefulness in parallel to poorer performance. However, other studies reported increased confidence ratings in parallel to impaired performance after sleep deprivation in a task of recognition memory (Harrison and Horne, 2000a) or after restricted sleep (Mathew et al., 2019). The influence of sleep deprivation on metacognitive bias thus appears unclear.

Another measure, metacognitive sensitivity – the extent to which confidence ratings discriminate between correct and incorrect trials - has been assessed by calculating the correlation between objective performance accuracy and subjective confidence. The influence of SD on metacognitive sensitivity however has also received contrasting evidence. In some studies, the correlation between accuracy and confidence was preserved after a night of sleep deprivation (Baranski, 2007; Baranski et al., 1994), indicating preserved self-awareness of performance. Yet, others have found poorer correlation between subjective and objective measures of

performance after sleep loss (Aidman et al., 2019; Blagrove and Akehurst, 2000), suggesting, that sleep deprived observers have impaired metacognitive sensitivity.

The inconsistencies between results summarised above make it difficult to draw a unitary conclusion regarding the influence of SD on metacognitive abilities. Interestingly, a recent systematic review of 10 studies failed to find a consistent effect of SD on metacognitive bias and sensitivity (Jackson et al., 2018). The authors thus concluded that metacognition is relatively spared by SD (Jackson et al., 2018). Another recent review and meta-analysis also concluded that the conservative estimates of performance after SD observed in most studies indicate preserved metacognition (Boardman et al., 2021). However, they also stress that caution should be taken when interpreting and generalizing these results due to the large methodological differences between study designs, and inadequate measurement of metacognitive indices (Boardman et al., 2021).

In fact, one strong limitation of previous metacognition studies in sleep deprived individuals is the inadequate measurement of metacognitive sensitivity (Boardman et al., 2021). Specifically, when metacognitive sensitivity is inferred from the correlation between accuracy and confidence, it is strongly influenced by metacognitive bias (Fleming and Lau, 2014; Maniscalco and Lau, 2012). In such cases, reductions in average confidence ratings could drive reductions in metacognitive sensitivity, independent of the true capacity of discriminating one's own performance accuracy. For example, expectation of performance impairment after SD may bias observers to report lower confidence ratings on average. As a consequence, this would alter the ratio of low confidence to high confidence responses and confound the relationship between high-confidence-correct-responses and low-confidence-incorrect-responses, leading to biased estimates of metacognitive sensitivity. Critically, all SD studies that have investigated metacognitive sensitivity used correlation measures (Aidman et al., 2019; Blagrove and Akehurst, 2000; Baranski, 2007; Baranski et al., 1994), so no adequate investigation of metacognitive sensitivity has been carried out to date, and the findings of SD effects on metacognitive sensitivity may just reflect bias in confidence rather than actual deficits in performance awareness.

Another limitation of previous studies is that they have not controlled the level of performance accuracy in WR and SD sessions (Boardman et al., 2021). Fixing performance accuracy between WR and SD sessions is important to make sure that any change in metacognition is attributable to metacognitive processes rather than to changes in task difficulty (Maniscalco and Lau, 2012). In fact, observers are better able at distinguishing correct from incorrect responses when they perceive the task as easy rather than difficult. In the context of perceptual metacognition, perceptual changes due to sleep deprivation such as those shown in Chapter 3 of this thesis could impair observers' ability to make perceptual judgements. Consequently, observers may be less confident in responses simply because they perceive the task as more difficult. The level of perceptual difficulty should thus be matched between WR and SD sessions for an accurate measurement of metacognition, and should be neither too easy nor too difficult.

To this goal, adaptive staircase methods allow to precisely adapt task difficulty to an individual's capacity by adjusting the stimulus intensity based on the history of observer performance, increasing difficulty if the observer answers correctly and reducing difficulty if the observer answers incorrectly. Psychophysical staircase methods are thus ideal to estimate metacognitive measures when perceptual performance may vary between conditions, such as before and after sleep deprivation.

In this chapter, I thus aimed to accurately investigate whether sleep deprivation affects metacognition by correcting for the methodological limitations present in previous assessments of metacognition in sleep deprived state. I measured objective performance and confidence ratings during three perceptual discrimination tasks where stimuli were presented with an adaptive staircase procedure to keep perceptual difficulty fixed between sessions. Then, I calculated metacognitive sensitivity employing a method derived from SDT that is independent of metacognitive bias (Fleming and Lau, 2014 ; Maniscalco and Lau, 2012; Fleming et al., 2010). I thus dissociated measure of metacognitive sensitivity from measure of metacognitive bias, which both characterize metacognitive capacity.

If sleep deprivation affects metacognitive abilities, I expected to observe changes in metacognitive sensitivity and/or changes in metacognitive bias (over or under-confidence in response accuracy) at the same level of performance accuracy.

5.2 Methods

5.2.1 Participants

Full details of the sample are described in Chapter 2. In the final sample of analysis presented in this chapter, 14 participants (19-32 years old, 3 males) were included.

5.2.2 Experimental procedure

Complete details of the experimental procedure are described in Chapter 2. Here, I report the details of the protocol of relevance for this chapter. Participants were

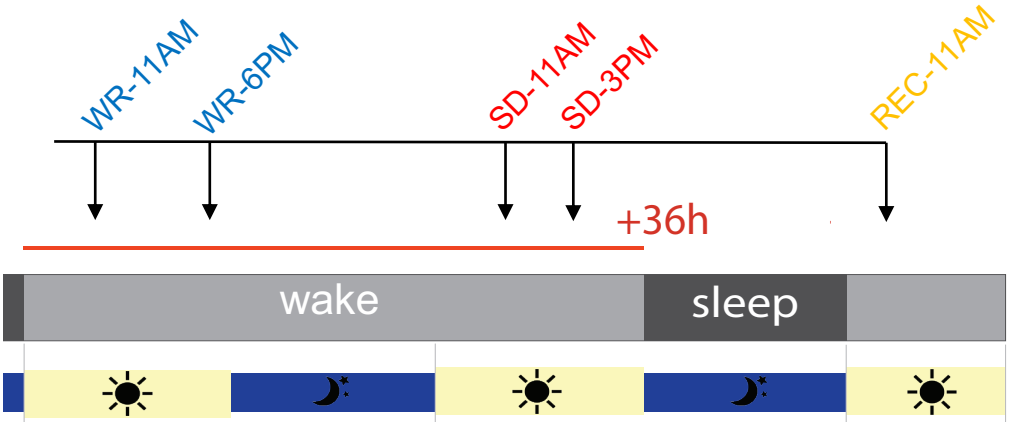

Figure 5.1: Behavioural sessions included in the analysis of metacognitive abilities across prolonged wakefulness included in this chapter. For each participant, 2 WR sessions, 2 SD sessions and 1 REC sessions completed over three consecutive days are included. Sustained wakefulness lasted a total of 36 hours. Abbreviations: WR: Well-Rested sessions; SD: Sleep-Deprived sessions; REC: Recovery sessions.

asked to maintain a regular sleep-wake cycle in the week prior to the sleep deprivation experiment and to refrain from consuming caffeine, alcohol or other psychoactive substances. Figure 5.1 illustrates the protocol underwent by each participant. Volunteers completed 5 different sessions: two after a night of normal sleep starting at 11AM and 6PM (WR-11AM and WR-6PM), two on the consecutive day after a night of sleep deprivation starting at 11AM and 3PM (SD-11AM and SD-3PM), respectively after 28 and 32 hours awake, and one the following day at 11AM after

a night of recovery sleep (REC-11AM). During the night of sleep deprivation, participants remained awake all night in the research centre under constant supervision and completed a battery of tasks. Participants were allowed to use their phones and computers. Volunteers went home in the evening after completion of the SD-PM session and slept in their own bed. Importantly, between 3 and 4 preparatory sessions took place in the week preceding the experimental sessions. These served as training sessions to ensure learning effects were controlled for and to allow participants to familiarize with the task and procedure.

5.2.3 Perceptual metacognition tasks

Participants completed three visual perception tasks – orientation discrimination, vernier discrimination, two-flash discrimination (Figure 5.2A). Tasks were the same as those described in Chapter 3, but stimuli were presented with the adaptive staircase method rather than with the method of constant stimuli. Moreover, in each trial, on top of reporting first-order perceptual judgements, participants provided a confidence rating of response accuracy on a scale from 1 (not confident of having responded correctly) to 5 (very confident of having responded correctly). Each confidence rating expressed subjective certainty of first-order judgement accuracy, i.e., how certain participants were that their perceptual judgement was accurate. Participants had unlimited time to provide both the perceptual judgement and the confidence ratings, and they were instructed to respond as accurately as possible. Participants reported first-order perceptual judgement on the keyboard with their right hand (by pressing left/right arrow buttons) and confidence ratings on the same keyboard using their left hand (by pressing “Q”, “W”, “E”, “R” and “SPACE” for 1 to 5 respectively). Tasks were programmed in Matlab R2015b (Mathworks Inc., Natick, MA, USA) using Psychtoolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997).

Stimulus parameters in each task varied trial-by-trial by means of a 2-up-1-down staircase procedure (Levitt, 1971; also see Chapter 2 for a detailed explanation). If participants were correct on two consecutive trials, stimulus parameter was lowered by one step in the following trial (making the trial more difficult relative to the

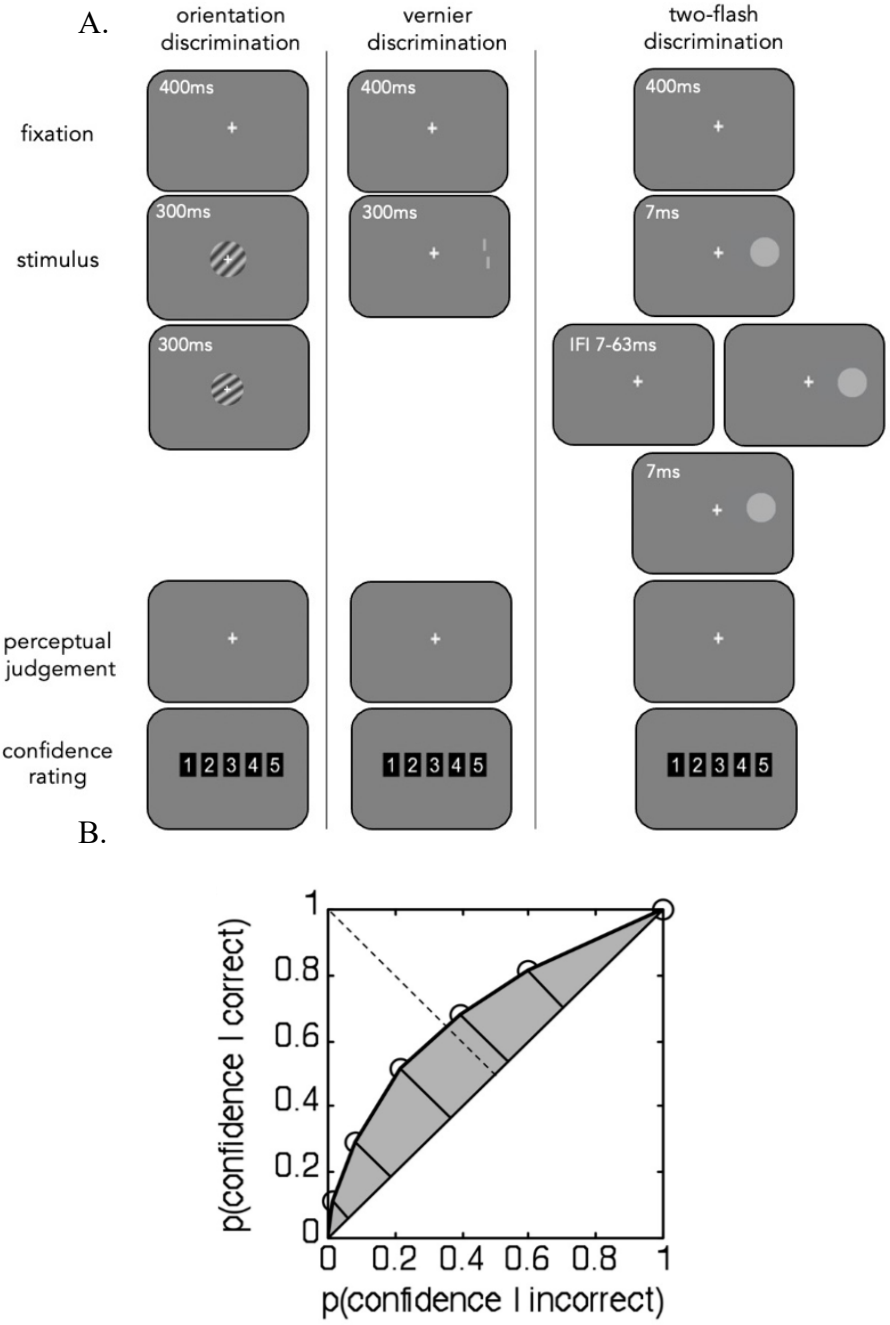

Figure 5.2: (A) Perceptual tasks and stimuli. All tasks involved a 2-alternative-forced-choice perceptual discrimination followed by a confidence rating of response accuracy on a 5-point scale. Volunteers had no time-limits to provide perceptual and confidence response, but were prompted by the experimenter if they took longer than few seconds to respond to make sure they remained awake. (B) example of Type 2 ROC curve obtained used to calculate metacognitive sensitivity (adapted from Fleming and Lau, 2014). The area under the type 2 ROC curve (dark-gray area) quantifies metacognitive sensitivity.

previous trial). If participants gave one incorrect response, stimulus parameter was increased by one step in the following trial (making the trial easier relative to the

previous trial). This staircase procedure was a key element in this study. Specifically, the 2-up-1-down staircase adapts stimulus parameters around subjective perceptual threshold, leading to a constant performance accuracy (around 71%; Song et al., 2011; Fleming et al., 2010). This was adopted to match task performance between sessions, regardless of differences in perceptual discrimination abilities between subjects and sessions. Importantly, since stimuli were presented around perceptual threshold, participants could rarely be absolutely certain about their perceptual judgements, so they were instructed to report relative confidence using all confidence values of the scale.

Orientation discrimination. Stimuli were displayed on grey background (rgb [127.5 127.5 127.5]) of a curved monitor (70x39cm; refresh rate 60Hz) positioned at a distance of 61.5cm. A fixation cross appeared in the centre of the screen for 400ms before the stimulus. Two gratings - 0.75° visual angle in size and lasting 300ms each, were then presented consecutively in the centre of the screen. One grating was at 45° and the other could be tilted clockwise or anticlockwise. Participants were instructed to fixate the centre of the screen and to report how the second grating was oriented relative to the first (clockwise or anticlockwise). The orientation differences between the two consecutive gratings varied trial by trial following a 2-up-1-down staircase procedure. The starting orientation difference between the two gratings and how much this changed from trial to trial was determined for each volunteer by a calibration task completed during the preparatory session (see Supplementary Note S3.1). Starting orientation parameter corresponded to orientation discrimination threshold estimated from the calibration task, and the step size of orientation difference was 1/3 of the threshold value. Supplementary Table S5.1 reports the starting orientation parameter and step size that were used for each volunteer. A total of 90 trials were completed in each session.

Vernier acuity. Stimuli were presented on an ASUS VG248QE monitor (50x30cm; refresh rate 144Hz) on grey background [127.5 127.5 127.5] at a distance of 61.5cm. A fixation cross appeared in the centre of the screen for 400ms before stimulus presentation. Participants were instructed to always fixate the central cross. Two vernier lines were then presented for 300ms at 5° eccentricity, 0° polar angle (right

side of the screen). The lines (0.75° visual angle in length or 45' arc (minutes of arc), grey - rgb [175 175 175]) were vertically aligned with a gap of 0.30° visual angle (18' arc). Participants were instructed to report if the upper line was located rightward or leftward relative to the lower line. The lines horizontal offset was varied trial-by-trial following a 2-up-1-down staircase procedure in steps of 1 pixel (0.0246° visual angle or 1'48'' arc). Participants completed 90 trials per session.

Two-flash discrimination. Stimuli were one or two consecutive of grayscale colour (rgb [175 175 175]) presented on an ASUS VG248QE monitor (50x30cm; refresh rate 144Hz) with lighter grey background (rgb [127.5 127.5 127.5]) positioned at a distance of 61.5cm. The flashes had 0.75° diameter in visual angle size and were presented on the right side of the screen (5° eccentricity and 0° polarity). A fixation cross appeared 400ms before the stimulus and remained on screen for the entire duration of the trial. In each trial, either one single flash or two consecutive flashes were presented. Participants were instructed to maintain their eyes fixated on the central cross and to report if they perceived one or two flashes pressing the left and right arrow button respectively with their right hand. A single flash was presented in 50% of trials and two flashes were presented in the remaining trials. In two-flash trials, each flash was presented for the duration of one frame (1/144Hz = 7ms) and the Inter Flash Interval (IFI) was in multiple of 7 ms. In single-flash trials, the flash onset and offset time was matched in duration to two-flash trials, so that participants could not discriminate one vs two flash trials based on flash duration. IFIs was experimentally manipulated trial-by-trial by means of a 2-up-1-down staircase procedure. A total of 90 trials were completed in each session.

5.2.4 Data analysis

Session analysis and planned comparisons. In this chapter, analyses were performed between individual sessions, differently from previous chapters where individual WR and SD sessions were merged. This was done to account for potential between-session differences in how each observer mapped subjective level of confidence to each confidence ratings. In other words, the mapping between the subjective level of confidence of each observer and the confidence ratings was session-specific and

could not be "averaged" between sessions. For this reason, only sessions in Day2 (WR), Day3 (SD) and Day4 (REC) were analysed (see Figure 2.1).

Statistical analysis were carried out by means of ANOVA and planned t-test. The critical contrasts were between WR (WR-11AM and WR-6PM) and SD (SD-11AM and SD-3PM) sessions, and between SD (SD-11AM and SD-3PM) and REC (REC-11AM) sessions. Due to the multiple comparisons (n=6) planned to evaluate between-session differences, the Family Wise Error Rate (FWER) - chance of wrongly rejecting at least one true null hypothesis (Type I error), was increased. I corrected for FWER using Bonferroni method, and reported adjusted p-values.

Data preprocessing. To exclude trials contaminated by motor errors or moments of microsleep, trials with perceptual decision response times (RT) <0.2 seconds or >2 seconds, as well as trials with confidence rating RT >2 seconds, were excluded from analysis. Moreover, to prevent statistical differences between sessions being driven by few subjects with extreme performance, I excluded from analyses subjects whose accuracy was lower or higher than 3 standard deviation of the grand mean of all subjects and sessions, for each task.

Objective task performance. Task performance was evaluated by calculating the proportion of correct responses in each session and task. By design of the adaptive staircase, I expected performance accuracy to be around 71%, however, due to technical error in stimulus presentation with staircase method, accuracy in various sessions of all three tasks was higher than 71% (Supplementary Table S5.2, Table S5.3 and Table S5.4). Specifically, this occurred when stimulus parameters reached the maximum screen resolution (lines offset of 1 pixel in the vernier discrimination; IFI of 1 frame in the two-flash discrimination task; 0° for the orientation discrimination) and could not further decrease following consecutive correct responses. Hence, to try and match performance between sessions and allow to estimate unbiased metacognitive sensitivity, trials that were blocked at the maximum resolution were remove (i.e., consecutive correct trials between the first correct trial at the max resolution and the first incorrect trial at the max resolution). This allowed to match between-session performance only in the two-flash

discrimination task, whereas in the orientation discrimination and vernier discrimination tasks it remained different between sessions (full details in the results section). As a measure of objective task difficulty, I also calculated the average stimulus parameter presented during each session.

Metacognitive bias. Metacognitive bias was calculated by averaging confidence ratings in each session for each subject. Furthermore, I also analysed average confidence ratings separately for correct and incorrect trials.

Metacognitive sensitivity. Finally, I calculated metacognitive sensitivity from the interrelationship between confidence rating and performance accuracy in each trial using the type 2 Receiver Operating Characteristic (ROC) curve (Fleming and Lau, 2014; Fleming et al., 2010; Song et al., 2011). Type 2 ROC is a non-parametric measure that characterizes the probability of being correct for each level of confidence. To construct the type 2 ROC curve index (Figure 5.2B), I considered each of the 5 confidence levels as a criterion that splits confidence ratings into "low confidence" and "high confidence". Then, for each criterion point, the rate of *confidence|correct* and *confidence|incorrect* was calculated and plotted, yielding the type 2 ROC curve. The Area Under the type 2 ROC curve (AUROC2) was then calculated as an index of metacognitive sensitivity. Metacognitive sensitivity was calculated for each subject in each session. One important advantage of this approach is that the AUROC2 is robust to changes in metacognitive biases (Fleming and Lau, 2014). It thus provides an index of metacognitive sensitivity that is independent of differences in overall confidence levels (e.g. more liberal or conservative), and is thus more appropriate in scenario when individuals may change their tendency to give higher or lower confidence between repeated measures.

5.3 Results

In the orientation discrimination task, 1 subject was excluded from analyses since their performance in one session was >3 standard deviation below the mean. Similarly, 1 subject was excluded from analyses of the vernier discrimination task, and 1 subject was excluded from analyses of the two-flash discrimination task. This

outlier removal ensured that performance differences between sessions were not driven by any single individual with extreme performance.

5.3.1 Objective task performance

Performance accuracy in the orientation discrimination task (Figure 5.3, left panel) was significantly different between sessions [$F(4,48) = 4.159$, $p = 0.008$]. Group average accuracy in SD sessions was significantly lower compared to WR and REC sessions. Specifically, accuracy was lower in the SD-11AM session relative to WR-11AM session [$t(13) = -3.27$, $p = 0.041$] and REC-11AM session [$t(11) = -3.71$, $p = 0.018$].

Performance accuracy was also significantly different between sessions in the vernier discrimination task [$F(4,48) = 3.124$, $p = 0.023$]. As illustrated in Figure 5.3 (central panel), mean group accuracy appears lower in the SD-11AM sessions compared to other sessions, but the planned comparisons were not significant after Bonferroni correction.

Finally, in the two-flash discrimination task (Figure 5.3, right panel), I observed no main effect of session [$F(4,48) = 2.337$, $p = 0.068$], indicating that performance accuracy did not vary significantly between sessions.

Overall, these results indicate that only in the two-flash discrimination task performance was matched between sessions, which allowed to compare metacognitive sensitivity estimates unbiased by task performance.

5.3.2 Objective task difficulty

The adaptive staircase procedure allowed to adjust stimulus parameters trial by trial to adapt task difficulty to individuals' perceptual discrimination ability. The average stimulus parameter during each task (Table 5.1) indicates how objectively difficult the task was for participants in different sessions.

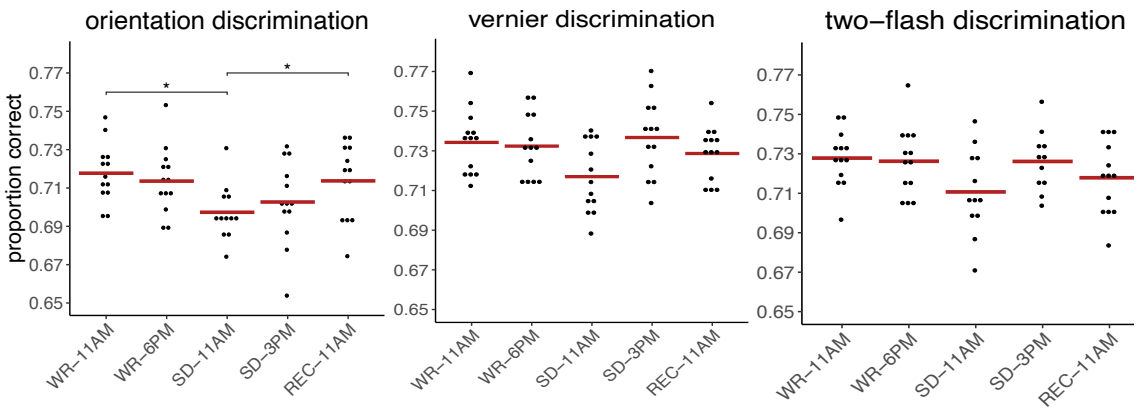

*Figure 5.3: proportion of correct responses for each task and session. Dots represent individual subjects. Red lines represent subject averages for each session. Accuracy varied significantly between sessions in the orientation discrimination and vernier discrimination task, Significant pairwise differences after Bonferroni correction are illustrated by * ($p<0.05$). In the two-flash discrimination task, task performance did not vary significantly between sessions.*

In the orientation discrimination task, there was a main effect of session on orientation parameter [$F(4,48) = 11.83$, $p < 0.001$]. After Bonferroni correction, the orientation difference in SD-11AM session was significantly larger relative to the WR-11AM [$t(12) = 4.22$, $p = 0.007$], WR-6PM [$t(12) = 3.80$, $p = 0.015$] and REC-11AM session [$t(12) = 3.92$, $p = 0.012$]. Similarly, orientation difference in the SD-3PM session was also significantly larger relative to the WR-11AM [$t(12) = 4.70$, $p = 0.003$], WR-6PM [$t(12) = 3.75$, $p = 0.017$], and REC-11AM session [$t(12) = 4.10$, $p = 0.009$]. These differences indicated that during SD sessions the staircase task presented objectively easier stimuli to adapt to individuals' reduced orientation sensitivity.

In the vernier discrimination task, average vernier lines offset varied between sessions [$F(4,48) = 4.898$, $p = 0.002$]. Table 5.1 shows that lines offset was larger in both SD sessions relative to the WR and REC sessions, and planned t-tests revealed significant differences between SD-3PM and both WR-11AM [$t(12) = 3.40$, $p = 0.032$] and WR-6PM [$t(12) = 3.39$, $p = 0.032$].

Finally, there was also a main effect of session on IFI in the two-flash discrimination task [$F(4,48) = 5.154$, $p = 0.001$], with longer IFI on average after SD sessions, but the differences between sessions were not significant after Bonferroni correction.

Table 5.1: average stimulus parameter (standard deviation) across all trials for different tasks and sessions.

	Average stimulus parameter during staircase				
	WR-11AM	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**
orientation discrimination orientation difference (deg)	5.35 (1.08)	5.83 (1.25)	9.80 (3.43)	8.73 (2.94)	6.14 (1.32)
vernier discrimination lines offset (arc min)	2.83 (0.27)	2.75 (0.24)	3.53 (1.10)	3.23 (0.57)	2.97 (0.40)
two-flash discrimination IFI (ms)	14.1 (2.19)	14.5 (3.12)	21.0 (11.1)	22.1 (10.1)	14.7 (2.55)

5.3.3 Subjective estimates of performance: confidence ratings and metacognitive bias

Average metacognitive bias for all sessions and tasks are shown in Figure 5.4. In the orientation discrimination task, there was a main effect of session on metacognitive bias [$F(4,48) = 3.59$, $p = 0.012$].

Further investigating CR for correct and incorrect perceptual responses by means of a two-way ANOVA (accuracy X session) revealed a significant main effect of session [$F(4,48) = 6.208$, $p < 0.001$], a significant main effect of accuracy [$F(1,12) = 80.09$, $p < 0.001$], and a significant interaction between session and accuracy [$F(4,48) = 3.347$, $p = 0.017$]. Figure 5.5 (left panel) shows that on average observers rated correct responses with higher confidence compared to incorrect responses. Family-wise planned t-tests were conducted to assess how CR varied across WR vs SD and SD vs REC sessions separately for correct and incorrect trials. For correct trials, there were no differences between sessions. For incorrect trials, confidence ratings increased after SD. Specifically observers gave higher confidence ratings in the SD-11AM session relative to the both the WR-11AM session [$t(12) = 4.42$, $p = 0.005$] and the WR-6PM session [$t(12) = 3.47$, $p = 0.028$]. Observers also were more confidence of incorrect responses in the SD-3PM session relative to both the WR-11AM session [$t(12) = 3.83$, $p = 0.014$] and the WR-6PM session [$t(12) = 4.26$, $p = 0.007$]. Finally, confidence in incorrect responses was significantly higher in SD-3PM relative to REC-

11AM session [t(12) = 3.25, p = 0.042]. Overall, these results show a selective increase in confidence for incorrect trials with increasing time awake.

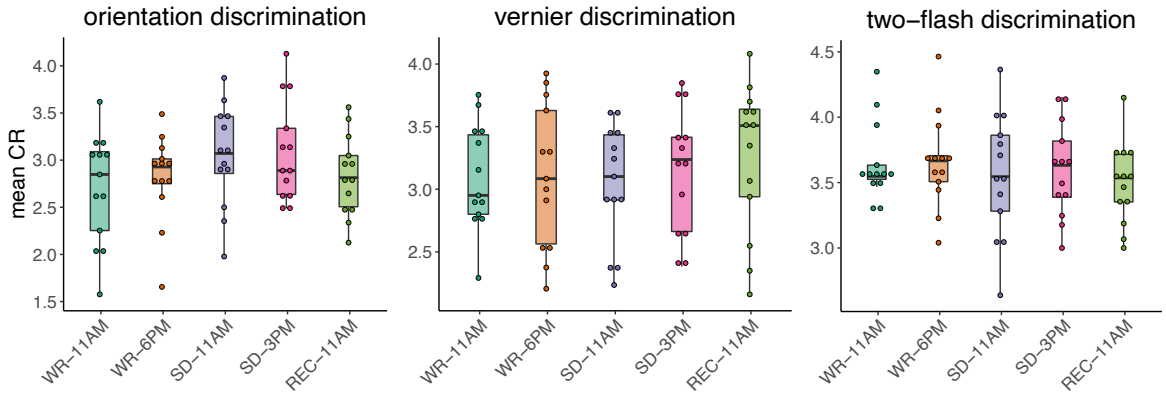

Figure 5.4: Metacognitive bias. Individual dots illustrate the average level of confidence (scale 1-5) in different sessions and in different tasks for individual participants. Average confidence did not vary on average between sessions.

In the vernier discrimination task, metacognitive bias did not vary between sessions [F(4,48) = 0.902, p = 0.47]. Investigating the combined effect of accuracy and session on CR using a two-way ANOVA revealed a main effect of accuracy [F(1,12) = 108.7, p < 0.001] and an interaction between accuracy and session [F(4,48) = 5.959, p < 0.001]. On average, confidence ratings were higher for correct relative to incorrect responses (Figure 5.5, central panel). However, no significant pairwise differences between sessions were found for either correct nor incorrect trials after correction for multiple planned comparison.

In the two-flash discrimination task, I found no main effect of session on metacognitive bias [F(4,48) = 1.715, p = 0.162], indicating that overall confidence ratings was similar between WR, SD and REC sessions. Investigating the combined effect of accuracy and session on CR using a two-way ANOVA revealed a main effect of session [F(4,48) = 3.61, p = 0.012], a main effect of accuracy [F(1,12) = 45.65, p < 0.001] and an interaction between accuracy and session [F(4,48) = 12.15, p < 0.001]. Planned t-test addressing pairwise differences between sessions separately for correct and incorrect trials revealed that CR in incorrect trials were significantly higher in the SD-3PM session relative to WR-11AM session [t(12) = 3.92, p = 0.012] and REC-11AM session [t(12) = 7.18, p < 0.001], and were also higher in SD-11AM session relative to REC-11AM session [t(12) = 3.79, p = 0.012] (Figure 5.5, right

panel). The increase in confidence ratings in from WR to SD session and the reduction after REC show that on average participants were overconfident in incorrect responses after SD, and this pattern was renormalised after recovery sleep.

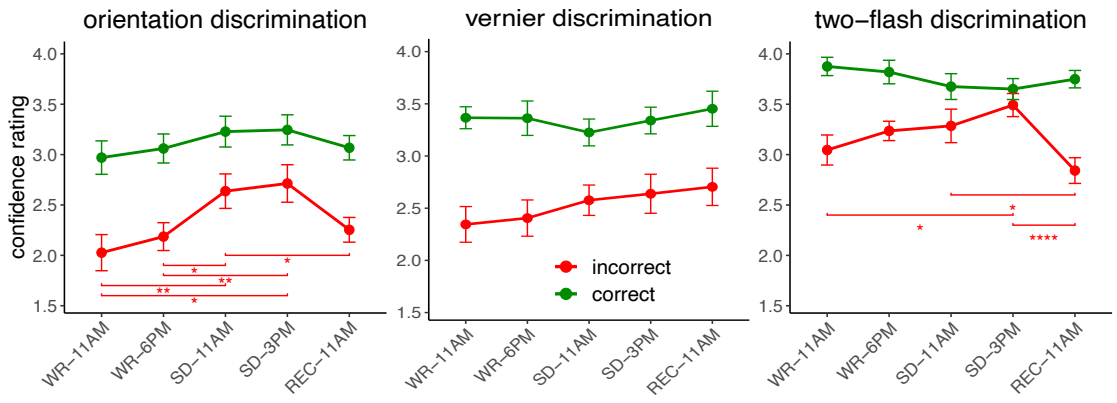

*Figure 5.5: mean confidence rating for correct (green) and incorrect (red) perceptual judgements across sessions for the three perceptual tasks. Points represent averages across subjects, error bars represent standard error of the mean. * denotes significant pairwise differences after Bonferroni correction. *: p<0.05;**: p<0.01; ****: p<0.001.*

5.3.4 Metacognitive sensitivity

Figure 5.6 shows AUROC2 in different tasks, which illustrates how mean group metacognitive sensitivity varied from WR to SD to REC sessions.

In the orientation discrimination task (Figure 5.6, left panel), results of a one-way ANOVA showed a main effect of session on AUROC2 [$F(4,48) = 3.858$, $p = 0.008$], indicating that metacognitive sensitivity varied between sessions. Visual inspection of results suggested that AUROC2 was on average lower in SD relative to WR and REC sessions. Planned comparison however were not significant after Bonferroni correction for multiple comparison.

In the vernier discrimination task (Figure 5.6, central panel), there was a main effect of session on AUROC2 [$F(4,48) = 4.205$, $p = 0.005$], but planned t-tests revealed no significant pairwise differences after Bonferroni correction.

In the two-flash discrimination task, I also observed a main effect of session on AUROC2 [$F(4,48) = 10.33$, $p < 0.001$]. The reduction in metacognitive sensitivity after

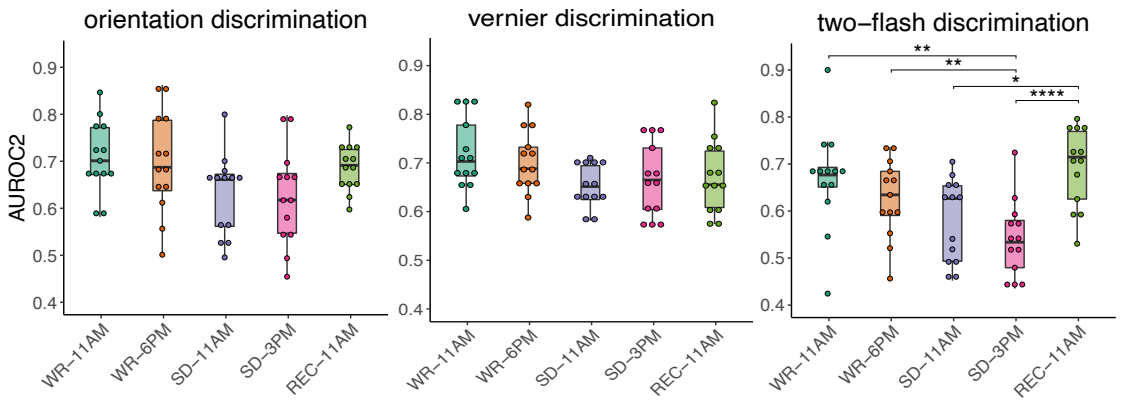

*Figure 5.6: metacognitive sensitivity, quantified by area under type 2 ROC curve (AUROC2), is shown for the three different tasks and each session. Each dot represents the AUROC2 of one single participant. In the two-flash discrimination task (right panel), metacognitive sensitivity was significantly reduced in SD sessions and was restored by recovery sleep. * denotes significant pairwise differences after Bonferroni correction. *: p<0.05; **: p<0.01; ****:p<0.001.*

SD is illustrated in Figure 5.6 (right panel). AUROC2 was significantly lower in the SD-3PM session relative to the WR-11AM [t(12) = -5.08, p = 0.002], and WR-6PM [t(12) = -5.05 p = 0.002] sessions. Furthermore, AUROC2 was higher in the REC-11AM session relative to the SD-3PM session [t(12) = 6.90, p < 0.001] and relative to the SD-11AM session [t(12) = 3.90, p = 0.013]. These results indicate that metacognitive sensitivity for temporal discrimination was significantly reduced after approximately 32 hours of sustained wakefulness, but this effect was reversed by one night of recovery sleep.

5.4 Discussion

This study evaluated the impact of sleep deprivation on perceptual metacognition. I measured metacognitive bias and metacognitive sensitivity in three different perceptual tasks, and found different effects of sleep deprivation on metacognitive indices between tasks. Results revealed, for the first time, selective reduction in metacognitive sensitivity that was observed in a temporal judgement task, indicating impairments in self-awareness of performance after 32 hours awake.

5.4.1 Reduced metacognition of temporal perceptual judgements after sleep deprivation

The key finding of this chapter was the reduction in metacognitive sensitivity in a temporal discrimination task observed after 32 hours of wakefulness including one

night of sleep deprivation. Critically, this effect was observed in sessions that were matched in task accuracy. Moreover, the metacognitive sensitivity index that was compared was not influenced by metacognitive bias. Overall, results reveal selective deficits in the ability to discern accurate from inaccurate perceptions after sleep deprivation.

Previous studies have provided contrasting evidence regarding the effects of SD on metacognition (Boardman et al., 2021; Jackson et al., 2018). The results of this thesis provide a significant contribution to this line of research in a few important ways. Firstly, these results are the first to reveal metacognitive sensitivity impairments after SD independent of metacognitive bias. This is a key aspect that previous studies ignored, and which largely motivated this investigation. Specifically, previous studies assessed metacognitive sensitivity by using correlational measures between confidence and accuracy (Blagrove and Akehurst, 2000; Baranski, 2007; Baranski et al., 1994). This approach however is confounded by overall confidence ratings reported by an observer (Fleming et al., 2014; Maniscalco and Lau, 2012). In fact, the tendency to give lower confidence ratings given after SD as shown in previous studies (Blagrove and Akehurst, 2000; Baranski, 2007; Baranski et al., 1994) could alter the correlation between confidence and accuracy, thereby biasing correlation-based estimates of metacognitive sensitivity. By using SDT derived type 2ROC measure to calculate metacognitive sensitivity (Fleming and Lau, 2014; Fleming et al., 2010), I controlled for the confounding effect of metacognitive bias, and showed that metacognitive sensitivity was significantly reduced independent of the overall level of confidence reported. This indicates that SD is detrimental for the ability to recognise correct and incorrect perceptual judgements.

Another key contribution of this chapter is that metacognitive sensitivity reduction after prolonged wakefulness was shown between sessions with the same level of task performance. This is an important point, as changes in task performance may underlie differences in metacognitive sensitivity since observers are better able to recognize their performance accuracy when the task is easy compared to when it is difficult. In the two-flash discrimination task where I observed metacognitive

sensitivity reduction, task performance remained around 72% (range 71-73%) on average across sessions and was not significantly different.

This allows to conclude that performing the task was equally difficult for observers in WR and SD sessions, so their poorer ability to self-monitor performance does not depend on how easy or difficult they found the task. To achieve constant task performance between sessions I employed a staircase method, which by design adapts task difficulty to individual perceptual capacity and hence accounts for between sessions changes in cognitive abilities. The staircase method employed in the tasks presented here however did not work out as expected, and it required to be adjusted by excluding a subset of trials (discussed in limitation section below).

5.4.2 Being confidently wrong after sleep deprivation

The results presented here also contribute to the debate concerning the impact of SD on metacognitive bias, the tendency to give high or low confidence ratings. Many studies reported that individuals tend to be less confident after sleep deprivation (Aidman et al., 2019; Baranski, 2007; Baranski et al., 1994). These studies however did not control task performance, so it is possible that the lower confidence relates to an impression of greater task difficulty when the cognitive resources available are impaired. In this chapter, I did not observe a significant change in overall confidence ratings from WR to SD sessions. However, I found that the influence of SD on confidence ratings depended on response accuracy. In orientation discrimination task I observed that confidence ratings for incorrect responses were on average higher after SD compared to WR sessions. This suggests that sleep deprivation increased participants' belief that their incorrect responses could be correct. These results are consistent with the overconfidence in incorrect responses after SD reported by previous studies of temporal memory (Harrison and Horne, 2000) and working memory (Mathew et al., 2019). Here, I extended these findings by showing that the tendency to overestimate performance in incorrect trials disappears after one night of recovery sleep (evidenced in both the orientation discrimination and two-flash discrimination task), a finding that stresses the direct effect of SD on metacognitive abilities and the restorative properties of sleep.

5.4.3 Mechanisms of metacognitive impairments

Overall, what underlies the deficit in metacognitive abilities after SD is not well-understood. There is consensus overall in indicating that a prominent consequence of sleep deprivation is reduction of vigilance level, which could underlie the marked performance impairments in monotonous tasks (Lim and Dinges, 2008). Whether reduced vigilance could also underlie the reduction in metacognitive sensitivity however is unclear. In principle, it would seem unlikely that observers reported higher confidence if they failed to adequately attend a stimulus (e.g. an attentional lapse). However, studies investigating how attention influences perceptual confidence have provided contrasting results, with some showing that when a perceptual decision is made under low attention observers are overconfident (Rahnev et al., 2012) and others indicating that lower attention is associated with reduced confidence (Zizlsperger al, 2012). The relationship between vigilant attention, confidence ratings and metacognitive sensitivity thus remains to be clarified.

Importantly it is well-established that metacognitive judgements rely on neural mechanisms operating in prefrontal and medial lateral frontal cortex (Baird et al., 2013; Fleming and Dolan, 2012). Sleep deprivation has been shown to alter activity in frontal regions during a variety of tasks (Chee et al., 2010; Chee and Choo 2004; Drummond et al., 1999). Whether prefrontal alterations are related to general attentional mechanisms or to specific high-level cognitive components (e.g. working memory) however is still unclear (Lim and Dinges, 2010). Future studies could assess brain activity during metacognitive tasks to further understand the mechanisms that underlie metacognitive impairments. This could also provide a better understanding of the debated impact of sleep deprivation on prefrontal cortex.

Finally, it has also been debated whether different metacognitive tasks rely on same or different neural substrates (Rouault et al., 2018). Here, observers' ability to discriminate accurate from inaccurate responses after sleep deprivation was only impaired in the two-flash discrimination task. This perceptual task requires observers to discriminate one from two flashes presented in rapid succession (minimum 7ms) and tests the limits of temporal resolution of visual perception. No

clear deficit in metacognitive sensitivity between WR and SD sessions was found in the other two tasks, orientation discrimination and vernier discrimination, which rely on different visuo-spatial perceptual functions. The present results show selective, task-specific deficits in metacognitive sensitivity and may indicate that metacognitive mechanisms related to visuo-temporal perception are more susceptible to one night of sleep deprivation. Future research should employ neuroimaging methods such as fMRI during multiple metacognitive tasks in order to better elucidate the impact of SD on neural mechanisms of metacognition.

5.4.4 Limitations and conclusions

One limitation of this study was that the staircase task did not work as planned by design. In fact, the minimum stimulus parameter allowed by the monitor resolution in each task was close to the observers' perceptual threshold, so participants could accurately discriminate multiple consecutive stimuli at the maximum screen resolution without stimulus parameter further decreasing, as supposed by task design. As a result, performance was originally higher in WR relative to SD sessions and I opted to exclude correct trials stuck in the staircase to mimic a valid one. With this correction, task performance was matched in one of the three assessed tasks.

Another limitation was that many statistical ANOVA tests calculated in this chapter revealed a main effect of session, but there were no significant differences between WR and SD sessions after correcting for the number of planned comparison. One example are the planned t-tests between metacognitive sensitivity estimates in orientation discrimination and vernier discrimination tasks. One possibility is that this study was underpowered to detect the pairwise planned differences in some of the tasks (e.g. vernier discrimination). In fact, the original sample size was 14 which is not uncommon in sleep deprivation studies (Aidman et al., 2017; Mathew et al., 2019), but after exclusion of outliers it was further decreased (N=13 in the orientation discrimination task and N=13 in the vernier discrimination task). Nonetheless, it is important to note that the key findings in this chapter were observed in the two-flash discrimination task with N=13, which could further imply a larger magnitude of effect relative to other tasks that is detectable with smaller sample size.

In conclusion, here I dissociated the effects of sleep deprivation on metacognitive sensitivity from task performance and metacognitive bias. Sleep deprivation impaired metacognitive sensitivity in a task of visuo-temporal resolution, and for the first time I showed that this impairment was independent of task performance and of metacognitive bias. I also found that sleep deprived observers tended to be overconfident of their wrong perceptual judgements, and that recovery sleep reversed all changes provoked by SD. Overall, these findings have implications for real-world situation such as driving, nightshifts and military and medical operations, when self-evaluation of performance over prolonged awake periods is critical for one's own and others' safety.

5.5 Supplementary material

Table S5.1: orientation discrimination parameters calibrated for individual participants and used in the staircase task.

Participant	Starting orientation difference (deg)	Step size (deg)
P01	0.21	**0.071**
P02	0.28	**0.093**
P03	0.38	**0.125**
P04	0.40	**0.133**
P05	0.28	**0.093**
P07	0.22	**0.075**
P09	0.23	**0.075**
P10	0.21	**0.071**
P11	0.30	**0.100**
P12	0.28	**0.095**
P13	0.27	**0.091**
P14	0.29	**0.097**
P15	0.75	**0.250**
P16	0.30	**0.100**

Table S5.2: original accuracy of orientation discrimination task before exclusion of staircase-stuck trials.

Orientation discrimination task										
	Original accuracy					Proportion of valid trials				
	WR-11AM	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**	**WR-11AM**	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**
P01	71.1	72.2	55.0	72.0	68.9	1.00	0.98	0.58	0.82	0.96
P02	74.4	68.9	55.2	68.5	68.9	0.88	0.97	0.91	0.99	1.00
P03	72.2	72.2	69.4	72.2	75.6	0.98	0.99	0.94	0.93	0.91
P04	72.2	74.2	68.6	70.6	73.3	0.96	0.92	0.96	0.92	0.96
P05	70.8	68.9	69.5	70.1	69.7	0.94	1.00	0.91	0.92	0.98
P07	75.6	74.4	73.1	71.3	73.3	0.88	0.87	0.87	0.93	0.93
P09	74.4	72.2	68.5	73.6	73.3	0.93	0.92	0.99	0.93	0.97
P10	77.0	72.2	67.4	70.1	70.0	0.88	0.97	0.99	0.86	0.98
P11	74.4	73.9	73.9	70.0	72.2	0.93	0.87	0.88	0.99	0.97
P12	70.0	77.6	71.8	65.4	70.0	0.99	0.86	0.90	0.87	0.98
P13	72.2	70.0	70.8	67.8	73.3	0.97	0.97	0.94	1.00	0.94
P14	76.7	72.2	70.0	75.0	73.3	0.84	0.96	0.98	0.91	0.99
P15	77.3	76.7	69.5	77.5	74.4	0.86	0.87	0.91	0.82	0.97
P16	72.2	75.6	71.4	71.1	77.8	0.94	0.89	0.91	1.00	0.84
Mean	**73.6**	**72.9**	**68.1**	**71.1**	**72.4**	**0.93**	**0.93**	**0.90**	**0.92**	**0.95**
(std)	**(2.4)**	**(2.7)**	**(5.8)**	**(3.0)**	**(2.6)**	**(0.05)**	**(0.05)**	**(0.10)**	**(0.06)**	**(0.04)**

Table S5.3: original accuracy of vernier discrimination task before exclusion of staircase-stuck trials.

Vernier discrimination task										
	Original accuracy					Proportion of valid trials				
	WR-11AM	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**	**WR-11AM**	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**
P01	77.3	76.7	70.4	77.9	75.3	0.80	0.87	0.86	0.82	0.92
P02	81.1	78.9	80.0	77.8	74.4	0.67	0.79	0.76	0.78	0.90
P03	83.3	80.0	77.8	77.8	76.7	0.68	0.79	0.86	0.83	0.89
P04	81.1	83.3	76.7	77.5	82.2	0.71	0.69	0.78	0.81	0.68
P05	78.9	76.7	72.8	76.7	79.8	0.83	0.81	0.82	0.86	0.74
P07	80.0	78.7	70.8	77.3	76.7	0.77	0.74	0.96	0.80	0.81
P09	77.5	79.3	78.7	80.7	78.9	0.79	0.74	0.78	0.73	0.78
P10	80.0	74.4	76.4	70.7	80.0	0.76	0.89	0.80	0.90	0.69
P11	86.4	82.2	75.0	77.6	83.1	0.58	0.71	0.83	0.81	0.64
P12	79.8	87.8	76.7	81.1	82.2	0.77	0.50	0.78	0.66	0.67
P13	74.4	75.6	80.0	80.0	83.3	0.91	0.89	0.77	0.80	0.68
P14	80.9	84.1	78.7	75.6	76.7	0.72	0.59	0.76	0.86	0.80
P15	76.4	79.8	76.9	76.1	79.8	0.81	0.70	0.77	0.87	0.73
P16	91.1	87.8	80.5	82.5	77.5	0.36	0.46	0.84	0.66	0.80
Mean	**80.6**	**80.4**	**76.5**	**77.8**	**79.0**	**0.72**	**0.73**	**0.81**	**0.80**	**0.77**
(std)	**(4.2)**	**(4.2)**	**(3.3)**	**(2.8)**	**(2.9)**	**(0.13)**	**(0.13)**	**(0.06)**	**(0.07)**	**(0.09)**

Table S5.4: original accuracy of two-flash discrimination task before exclusion of staircase-stuck trials.

	Two-flash discrimination task									
	Original accuracy					Proportion of valid trials				
	WR-11AM	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**	**WR-11AM**	**WR-6PM**	**SD-11AM**	**SD-3PM**	**REC-11AM**
P01	76.5	76.4	71.4	69.9	70.8	0.88	0.82	0.81	0.74	0.88
P02	78.7	76.7	78.7	75.0	78.9	0.81	0.79	0.80	0.94	0.70
P03	74.4	77.8	71.1	74.4	74.2	0.93	0.86	0.99	0.92	0.91
P04	79.3	80.2	74.4	73.2	77.8	0.70	0.72	0.81	0.86	0.79
P05	96.6	84.4	68.1	80.5	82.6	0.17	0.63	0.52	0.67	0.69
P07	78.9	74.2	61.4	70.5	78.9	0.74	0.87	0.89	0.80	0.72
P09	78.7	76.7	75.6	78.2	81.1	0.79	0.87	0.90	0.87	0.73
P10	82.2	78.9	70.1	71.8	75.6	0.71	0.81	0.92	0.90	0.82
P11	77.8	77.8	73.3	73.8	82.2	0.83	0.76	0.87	0.80	0.67
P12	70.0	72.7	71.6	76.8	73.0	0.99	0.93	0.94	0.79	0.97
P13	78.7	81.1	78.3	74.4	80.0	0.78	0.70	0.79	0.94	0.71
P14	75.6	73.0	76.4	80.0	72.2	0.89	0.97	0.86	0.76	0.93
P15	81.6	86.4	69.4	62.8	83.3	0.63	0.57	0.88	0.92	0.64
P16	81.8	79.3	73.1	74.1	78.9	0.67	0.73	0.82	0.86	0.81
Mean (std)	**79.3 (5.9)**	**78.3 (3.9)**	**72.3 (4.5)**	**73.9 (4.5)**	**77.8 (4.1)**	**0.75 (0.20)**	**0.79 (0.11)**	**0.84 (0.11)**	**0.84 (0.08)**	**0.78 (0.11)**

Chapter 6.
General discussion

In this final chapter, after reviewing the main aims and results of this thesis, I integrate the findings of different chapters and highlight some points that emerge from the consideration of results in the light of existing theories and recent research. I also offer recommendations on how future studies can address these points.

6.1 Summary of results

The results presented in this thesis were part of a larger explorative research project aimed at extending our current understanding of how sleep deprivation affects cognition, brain function and brain structure. To this aim, a multimodal experiment involving multiple behavioural tasks and neuroimaging brain scans over 4 consecutive days, including 36 hours of continuous wakefulness and one night of recovery sleep was designed. 14 young and healthy volunteers completed all measurements. This thesis addressed in details the effects of sleep deprivation on visual perception and perceptual metacognition and contributed to extending our understanding of the cognitive and brain functions affected by sleep deprivation.

Chapter 3 and 4 focused on low and high-levels of the visual processing hierarchy respectively. Chapter 3 investigated how sleep deprivation influenced elementary visual functions of spatial and temporal resolution. Results revealed novel and selective impairments of visuo-spatial perceptual functions after sleep deprivation, with preserved visual hyperacuity but reduced orientation sensitivity and poorer temporal discrimination of items.

Moving up the perceptual processing hierarchy, Chapter 4 addressed high-level object categorisation and some of the underlying neural mechanisms. I found that sleep deprived volunteers were less accurate at categorising noise-degraded images of faces and houses from blank ones, but this was not paralleled by more frequent illusory perceptions as hypothesized. Furthermore, the perceptual discrimination impairments occurred in parallel to a reduction of category selectivity index in face-selective regions (including FFA and OFA) as well as in place-selective regions (including PPA and OPA), revealing, for the first time, degradation of perceptual representations in high-level visual cortex after sleep deprivation.

Both low-level and high-level perceptual impairments observed after one night of sleep deprivation were restored by one night of recovery sleep, confirming that the effects were specific to sleep-deprived state and that sleep is necessary to maintain optimal cognitive functioning and behavioural performance.

Chapter 5 focused on perceptual metacognition, the ability to evaluate one's own perception and discriminate accurate from inaccurate judgements. Using psychophysical tasks requiring to discriminate threshold stimuli and report confidence in response accuracy, Chapter 5 revealed changes in metacognitive sensitivity independent of perceptual accuracy and confidence bias in sleep deprived observers. Specifically, after one night without sleep volunteers were less able to discriminate accurate from inaccurate temporal perceptual judgements and tended to overestimate their performance when responding incorrectly.

Overall, this thesis shows that 36 hours of prolonged wakefulness are associated with alterations in visual functions and metacognitive abilities that affect how individuals perceive the external world and how they make decisions. These results have implications for situations where accurate perception and evaluation of situations is required even after prolonged wakefulness, such as long work shifts in medical and military operations and long-distance driving. In such circumstances, visual distortions and reduced metacognitive abilities may increase the risk of accidents and inappropriate decisions.

6.2 Effects of sleep deprivation on low and high-level visual perception

Sleep deprivation appears to lead to deficits in both low-level and high-level visual perception. Specifically, here I found impairment in low-level discrimination of orientation as well as in high-level categorization of objects. These perceptual functions rely respectively on primary visual cortical regions and on high-level ventral-visual cortical regions (Carandini et al., 2005; Grill-Spector and Malach, 2004). Since perceptual processing occurs hierarchically and early sensory input influence high-level perceptual representations, it may thus be possible that the low-level visual deficits be linked to high-level perceptual impairments. Yet,

Chapter 4 results seemed to provide no evidence that bottom-up visual processing was degraded. However, this conclusion was based on the finding of equal impairment in performance and neural selectivity across perceptual clarity, while no direct measurement of brain activity in low-level visual regions was carried out. As argued in Chapter 3, it's possible that one night of SD leads to minimal low-level perceptual distortions that do not immediately compromise higher-order cognitive functions and that are only evident in well-calibrated tasks. A link between low-level and high-level perceptual alterations may emerge with increasing time awake beyond 36 hours, as for the case of most severe visual distortions like hallucinations (Waters et al., 2018). Future studies are needed to more specifically disentangle the impact of sleep deprivation on bottom-up sensory processing in early visual regions from top-down modulation of attention and high-level cognitive function.

6.3 Domain-specific and domain-general deficits of sleep deprivation

Sleep deprived volunteers showed performance impairments in several different tasks assessed here. In particular, the performance impairments in perceptual and metacognitive tasks point to detrimental effects of sleep deprivation at multiple cognitive levels and distinct neural circuits, including perceptual functions relying on visual cortical regions as well as high-level metacognitive functions relying on prefrontal cortex. These results are well in line with the general understanding that sleep deprivation negatively affects a wide range of cognitive functions (Killgore, 2010). However, they further stress the question concerning the degree to which these cognitive impairments reflect local, domain-specific deficits and global, domain-general impairments (Lim and Dinges, 2008).

It is possible, in fact, that a reduction in domain-general vigilant attention mediated performance decline across the cognitive tasks tested here by compromising generic abilities to sustain attention and detect stimuli (Lim and Dinges, 2010; Lim et al., 2008). According to the state instability hypothesis described in Chapter 1, this would be instantiated by subcortical, arousal-mediating structures pushing the brain towards a global sleep state, in parallel with failure of fronto-parietal regions to exert top-down control on task-relevant regions and sustain wakefulness and task execution (Chee et al., 2013; Krause et al., 2017; Ma et al., 2015).

Yet, sleep deprivation could have also degraded neural processing in local, task-relevant neural circuits, independent or on top of top-down modulations from subcortical and fronto-parietal regions. This view is consistent with the local sleep theory, according to which repeated use of the same neuronal circuits increases the tendency of such circuits to fall asleep and disengage from coordinated processing of task-relevant information, leading to performance errors (Chee et al., 2011; Hudson et al., 2020; Krueger et al., 2008; Van Dongen et al., 2011).

With respect to these theoretical accounts, results presented in this thesis are limited as they do not offer conclusive support. On the one hand, the uniform performance decline across levels of stimulus difficulty observed in Chapter 3 (i.e. downward shift in psychometric function) and Chapter 4, as well as the slowing of response times in perceptual tasks in Chapter 3 may suggest that performance decline with prolonged wakefulness was mediated by attenuation of domain-general attentional resources. On the other hand, the selectivity of effects reported in perceptual tasks in Chapter 3 appears inconsistent with an exclusive account of reduced vigilance or attention, and could reflect different capacity of task-specific neural networks to sustain sufficient task-relevant processing when local circuits fall asleep due to intense neuronal use. Moreover, the decline in metacognitive sensitivity reported in Chapter 5 likely points to specific neural impairments in prefrontal cortex circuits, which however remain to be empirically assessed in future studies. Finally, the local degradation of perceptual representations in high-level face and place selective visual regions reported in Chapter 4 could reflect both attenuated top-down attentional modulation and intrinsic neural processing failure due to local sleep.

To further understand the domain-general and domain-specific mechanisms that characterize performance impairments after sleep deprivation, future studies can evaluate performance on a series of cognitive tasks that alternate without breaks (e.g. task A - task B - task A). Tasks should rely on distinct neural circuits (e.g. a visual and a tactile task, or a visual task involving stimulus presentation in two different visual field locations). Continuous performance would engage attentional capacity without break, while distinct cognitive functions and associated neural

circuits would be employed in alteration. On the one hand, if domain-general resources become depleted with SD, performance will progressively decline across tasks. On the other hand, if sleep deprivation influences specific cognitive functions, performance will fluctuate between tasks, decreasing at the end of a task block but improving when switching task. Moreover, if the domain-specific hypothesis is confirmed, performance in the second round of task A would be better than performance in a stream of continuous task A of equivalent duration (control task). In parallel, imaging of whole brain activity with high spatial and temporal resolution (e.g. high-density EEG or MEG, or concurrent EEG-fMRI) would allow to track the spectral signatures of performance variability with spatial precision and evaluate spatial localization of local sleep indices (e.g. local increases in low-frequency EEG; Andrillon et al., 2019; Bernardi et al., 2015; D'Ambrosio et al., 2019; Hung et al., 2013; Quercia et al., 2018).

6.4 Metacognitive deficits and altered conscious experience in the sleep deprived state

The deficits in metacognition reported in Chapter 5 might be also useful to explain the occurrence of perceptual alterations such as illusions and hallucinations that are regularly reported by sleep deprived individuals (Waters et al., 2018). Specifically, an interesting view may link metacognition, perceptual alterations and attentional lapses. This view posits that during momentary lapses of attention, when attention disengages from external inputs, subjective perceptual experience becomes influenced by spontaneous ongoing mentation (Andrillon et al., 2019). However, while a healthy, well-rested observer can recognize spontaneous thoughts as internally generated, a sleep deprived observer may fail to do so. Crucially, the failure to recognize this boundary between internally generated and externally generated perceptual content may be related to poorer metacognitive sensitivity. In other words, sleep loss may make an individual less capable of distinguishing accurate (i.e. real, external) from inaccurate (imaginary, internal) perceptions. Previously, auditory hallucinations in psychiatric patients have been associated with metacognitive beliefs (Morrison et al., 1995). Moreover, recent evidence supporting a degradation of the boundary between internally and externally generated perceptual content has come from neuroimaging studies of functional brain networks

in the sleep deprived state (Chee and Zhou, 2019; Krause et al., 2017). For example, Default Mode Network (DMN) and Fronto-Parietal attention Network (FPN), which are respectively expressed during internally orientated and externally oriented cognition and normally inhibit one another (Fox and Raichle, 2007; Fox et al., 2005), become less segregated after sleep deprivation and elements of one intrude into elements of the other (De Havas et al., 2012; Krause et al., 2017; Yeo et al., 2015), revealing critical alterations to brain functional organization.

To further explore the relationship between metacognition and perceptual alterations in the sleep deprived state, future neuroimaging studies may employ qualitative interviews and questionnaires to collect altered subjective experiences during prolonged wakefulness and analyse these (e.g. frequency of reported illusions and hallucinations) in relation to each individual's metacognitive sensitivity and functional brain network organization.

6.5 Considerations on experimental schedule

As described in Chapter 2, the experiment spanned over three consecutive days, incorporating training and preparation sessions (e.g., caffeine avoidance and sleep scheduling) that lasted for a week leading up to the laboratory experience. Given the multitude of cognitive and brain measurements planned for this study, significant effort was invested in designing and optimizing the experimental schedule, recruiting participants, and conducting tests. Multiple experimenters took turns conducting different sessions and ensuring participants adhered to the schedule while staying motivated.

For future studies aiming to assess various cognitive, behavioral, and brain measures within a sustained wakefulness period, careful planning is crucial. This includes pre-determining planned comparisons, designing the task order (e.g., using counterbalancing methods) accordingly, considering effect sizes from this and similar studies to determine an adequate sample size, and achieving sufficient statistical power to robustly evaluate hypotheses. This level of planning is

particularly valuable in demanding sleep deprivation experiments, which require substantial effort and resources from both participants and experimenters.
Moreover, since sleep deprivation studies inherently impose challenges on participants, especially when combined with multiple laboratory testing sessions, experimenters must carefully weigh the trade-off between including additional data (e.g., longer tasks, more testing sessions, or extensive parameter measurements) and potentially increasing participant stress.

6.6 Conclusions

The importance of sleep for brain function can hardly be overstated. Every day, millions of people do not get adequate sleep quality and quantity, and sleep deprivation has tremendous consequences on our ability to be responsive, attentive and accurate when performing tasks. This thesis has contributed to expanding our understanding of the cognitive and brain deficits that arise from sleep deprivation, revealing impairments in low and high-level visual perception and metacognition and alterations in neural function of high-level visual regions. However, more research is needed to understand the mechanisms that underlie these neuro-cognitive deficits. Future studies addressing the neural basis of cognitive impairments after prolonged wakefulness may reveal the role of local sleep in performance errors, and lead to a redefinition of what sleep and wakefulness are for the brain and for our subjective experience.

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