Perils of sleep deprivation

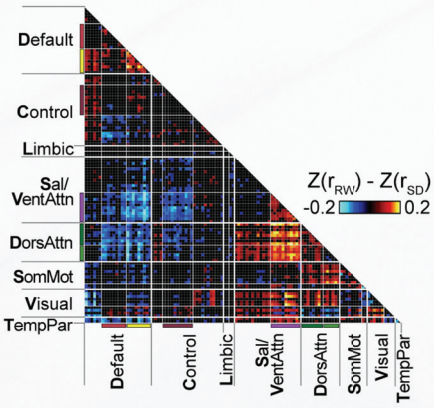
Cognitive neuroscientist **Dr Michael Chee** is investigating the mechanisms underlying the degradation of cognitive performance in the sleep deprived. In this impassioned discussion, he describes cultural influences on sleep and explains how sleep deprivation can affect the brain and behaviour

Why have you chosen to dedicate your research to uncovering the mechanisms underlying the degradation of cognitive function in the context of sleep deprivation?

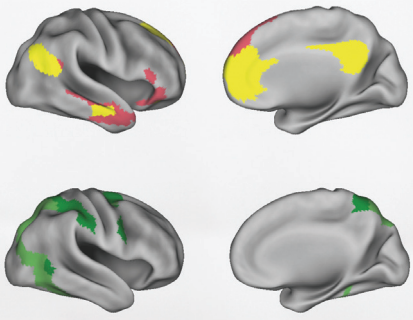
I've always wanted to push the limits of human performance, and cognitive performance is the area in which I've had the greatest opportunity to make a difference. In medical school, I had a neighbour who believed in staying up all night cramming for a big exam the next day. Such a strategy never worked for me, but it's one the East Asian culture tightly embraces. I see more and more people give up sleep in order to chase their ambitions, and they drive their children to do the same. I'd like to provide sound reasons for this to change with the work I've done and continue to do.

Could you outline some of the adverse effects of a night of total sleep deprivation?

Perhaps the most robust effect of sleep deprivation on cognition is its impact on sustained attention. This is relevant for jobs requiring timely and accurate threat detection involving infrequent and unpredictable targets.



Reduced anti-correlation between default A&B and dorsal attention A networks (blue areas in matrix) occurs in the sleep deprived state.



Many aspects of visual processing falter when we undergo sleep deprivation. We become less able to inhibit distractors and have lower capacity to handle information, especially when it is not directly related to the task at hand. We are less able to pick out targets from a rapid stream of pictures and our preparation to respond to visual stimuli is compromised. These changes result from a loss of 'top-down' control of attention that can be visualised using functional magnetic resonance imaging. Changes in functional connectivity of brain circuits also occur because of sleep deprivation and some of these patterns are predictive of who is more vulnerable to its effects.

What are the key aims of your ongoing and future research?

The 'discovery science' portion of the work involves comparing the mental state transitions that sleepy and non-sleepy persons undergo. These are likely to modulate sensory information processing and correspond to episodes of involuntary 'mind-wandering' that in turn might be related to fluctuations in brain connectivity. My hypothesis is that individuals differ in their propensity to have state transitions when sleep deprived, and this might explain how well a person can concentrate mental effort when fatigued. In the 'epidemiology' section of what I do, we will investigate how sleep architecture (such as duration in particular stages, continuity and quality) affects brain ageing in terms of changes to structure, connectivity and behaviour.

Can you discuss the correlation between sleep deprivation and cognitive ageing?

This is an area of growing interest, led by huge epidemiological studies. Groups like ours studying smaller cohorts but in greater detail, have recently shown deleterious effects of short sleep on brain structure in elderly persons. The effects are modest because everyone needs to sleep; even if sleep deprivation exerts a small negative effect on the brain and cognition, multiplied over millions of life years, it is going to have a very large impact on human health. Sleep is an important modifiable lifestyle factor whose effect on health is something we simply must know more about.

How are you involved in mentoring the next generation of cognitive neuroscientists in Singapore?

We are a relatively compact research group, but Singapore has always been known to punch above its weight, and I fully intend to build on that! We collaborate across labs and share resources. I work with Drs Joshua Gooley and Julian Lim on matters relating to sleep deprivation and fatigue. Dr Helen Juan Zhou lends her expertise in functional brain connectivity and imaging methods, and I infuse cognitive neuroscience content. We have a good ecosystem of postdocs, graduate students and research assistants that come from all over the world. Furthermore, our alumni have gone on to secure advanced training positions at some of the world's leading institutions ranging from Yale, Duke and Stanford in the US, to the University of Cambridge in the UK and the Max Planck Institutes in Germany. We have many productive international collaborations with senior principal investigators.

The importance of a good night's sleep

Members of the Centre for Cognitive Neuroscience at **Duke-NUS Graduate Medical School**, Singapore, are investigating changes to the sleep-deprived brain. In doing so, they hope to reduce the impact of the growing trend for sleepless nights in urban society

GETTING ENOUGH SLEEP is vital to the maintenance of human health and wellbeing. Yet, as cultures have shifted towards long hours of work across the world, sleep is being increasingly sacrificed. As most individuals have experienced, lack of sleep has significant effects on human behaviour, causing fatigue, mental fog, difficulty concentrating and emotional sensitivity.

While the importance of sleep has long been known from observation, exactly why humans need sleep has puzzled scientists for centuries. Helping to shed new light on this matter is Dr Michael Chee, Director of the Centre for Cognitive Neuroscience at Duke-NUS Graduate Medical School in Singapore.

Inspired by his own experiences following transmeridian flights across multiple time zones, Chee first began studying the cognitive effects of short-term sleep deprivation in 2003. Since then, he has been hard at work investigating the precise areas of the brain that contribute to loss of function in the sleep deprived. In discovering the mechanisms underlying cognitive decline, Chee hopes to understand exactly why and how lack of sleep affects behaviour.

ATTENTION DEFICITS

Over the past 13 years, Chee has made important headway in understanding sleep deprivation. His very earliest experiments focused on working memory – a form of short-term memory. His analyses revealed that sleep deprivation was associated with lower task-related activation of the frontal and parietal lobes, association areas involved in multiple goal-directed functions, including working memory.

Indeed, the sleep-deprived brain looks very different to the well-rested brain. Lack of sleep affects multiple facets of cognition: attention, memory, executive function and processing speed. In order to investigate this further, Chee began looking at a faculty that is consistently affected by lack of sleep – attention. Although higher order functions like memory and reasoning are also compromised by lack of sleep, they are likely to be secondary to deficits in the fundamental ability to stay awake and perceive the world.

SLEEP DEPRIVATION, INFORMATION PROCESSING CAPACITY AND COGNITIVE PERFORMANCE

OBJECTIVES

- To elucidate the changes in brain functional activation and connectivity underlying loss of visual information processing capacity in sleep-deprived persons
- To establish markers for vulnerability to sleep deprivation
- To study the impact of short sleep at different ages on brain structure, function, connectivity and cognitive performance

KEY COLLABORATORS

Dr Joshua Gooley; **Dr Julian Lim**; **Dr Helen Juan Zhou**, Duke-NUS Graduate Medical School, Singapore

Dr Thomas Yeo, National University of Singapore, Singapore

Dr Scott Huettel, Duke University, USA

Dr David Dinges, University of Pennsylvania, USA

Dr Denise Park, University of Texas at Dallas, USA

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CONTACT

Dr Michael Chee
Director, Centre for Cognitive Neuroscience

Duke-NUS Graduate Medical School
8 College Road, Room 06-18
169857, Singapore

T +65 6516 4916
E michael.chee@duke-nus.edu.sg

www.cogneuro-lab.org

www.facebook.com/cogneuro

DR MICHAEL CHEE graduated from the National University of Singapore and trained in internal medicine and neurology before embarking on subspecialty training at The Cleveland Clinic, USA. After he completed clinical training, he decided to venture into functional magnetic resonance imaging, spending time at the Massachusetts General Hospital NMR Centre in Boston, USA. After returning to Singapore, Chee worked on characterising the bilingual brain, but a lifelong fascination with improving cognitive performance led him to study the neurobehavioural effects of sleep deprivation, as well as brain ageing in healthy adults. He is currently Professor at Duke-NUS Graduate Medical School in Singapore.

DUKE NUS GRADUATE MEDICAL SCHOOL SINGAPORE

CENTRE for COGNITIVE NEUROSCIENCE

Chee's team began investigating attention by assessing visual processing in the sleep deprived. The researchers evaluated peripheral perceptual processing capacity, the ability to process stimuli that are irrelevant to the task at hand but still important, such as noticing a child playing on the side of the road despite the focus of attention being the road ahead. Testing these abilities in young, healthy but sleep-deprived adults, Chee found their ability to process these peripheral events to be significantly impaired.

In some situations, however, peripheral stimuli can be irrelevant and distracting. In this context, it becomes important to suppress the unimportant elements in order to focus attention on the target. In the same sleep-deprived test subjects, Chee found participants became less able to block out these distractions. Interestingly, this reduced ability to inhibit distractors is similar to changes observed in cognitive ageing.

INDIVIDUAL VARIABILITY

Not everybody, however, is affected by a lack of sleep in the same way; it is a common observation that some people need more sleep than others. This variability fascinates Chee, who is endeavouring to unearth the reasons for which some people are able to maintain higher levels of cognitive performance than others.

Through a series of imaging experiments, Chee found that those who are better able to maintain top-down control of attention, measured by activation of frontoparietal brain regions, are also able to perform better under conditions of sleep deprivation. These persons also show differences in functional connectivity – information that might serve as biological markers to identify individuals probably unsuited to demanding all-night or multiple-night occupations. His latest endeavour involves examining if the frequency and type of 'brain state transitions' can also indicate vulnerability.

SIMILARITIES TO COGNITIVE AGEING

The short-term changes to cognitive function in the brains of sleep-deprived individuals resemble the persistent cognitive decline seen in ageing and neurodegenerative diseases, which are becoming a mounting burden as life expectancy increases. There is therefore great interest in identifying the risk factors that cause the structural changes to the brain preceding cognitive decline, such that it can be prevented.

In his studies, Chee suggests sleep could be one such risk factor. Indeed, there is emerging evidence that sleep has an important role in cognitive ageing. Astoundingly, some studies suggest that the quality and duration of sleep in midlife can influence cognitive function 20 years later.

Based on this rapidly accumulating evidence, Chee set out to investigate exactly how sleep contributes to age-related changes in brain structure. The participants, all aged 55 or above, were followed for four years, and underwent a magnetic resonance imaging scan and neuropsychological assessment every two years. Alongside this, the team measured the duration and quality of their sleep. They found that for every hour of lost sleep, the annual decline in cognitive performance increased by over 0.5 per cent. This study shows that short sleep does not just affect performance the next day; it can even cause age-related brain shrinkage and cognitive decline.

CHANGING BEHAVIOUR

Through his years of investigation, Chee has described the effect of sleep deprivation on multiple aspects of cognition. "We've shown how selective attention fails, residual peripheral processing capacity is reduced, ability to suppress distracting visual information degrades, preparatory attention is weakened, visual short-term memory is compromised and the extent to which rapid image processing is hampered," he elaborates. What unites these behavioural changes is the area of the brain affected: the frontoparietal area, which controls attention.

> For every hour of lost sleep, annual decline in cognitive performance increased by over 0.5 per cent

As well as making a significant contribution to neuroscience, this work, and the mechanisms uncovered, could provide a means of reducing the impact of sleep deprivation by identifying those most susceptible to its effects.

By imaging the brains of those who are especially tolerant to sleep deprivation, Chee hopes to identify useful markers and correlating connectivity and activation patterns with physiological and behavioural measures, which may inform individuals of their suitability for occupations requiring regular sleep deprivation.

Chee's ultimate goal, however, is to create a paradigm shift in thinking about sleep and encourage healthier sleeping habits. He is a major proponent for sleep as a key ingredient for good health and is busy gathering evidence to inspire decision makers to change social policy. "I'm here to effect real change. Finding the right levers to pull in order to meaningfully change the habits of masses of people is my long-term aspiration," he concludes.