Project Details	
Project Code	MRCNMH26Br Purple
Title	Quietly healing trauma: enhancing emotional processing during sleep with targeted memory reactivation
Research Theme	NMH
Project Type	Wet lab
Summary	Why do some people recover from trauma while others develop post-traumatic stress disorder (PTSD)? Sleep is known to play an essential role for processing our daily experiences and emotions yet its influence on processing trauma remains unclear. This project will explore the therapeutic potential of sleep using targeted memory reactivation (TMR) – a cutting-edge technique that subtly cues the brain during sleep to reshape memories. By investigating how TMR impacts memory processing after a trauma-like experience in healthy adults, this project aims to provide a stepping stone for developing innovative sleep-based interventions to reduce PTSD risk.
Description	Over 80% of people experience a traumatic event during their lifetime; of these, up to ~10% develop post-traumatic stress disorder (PTSD). PTSD is characterised by distressing flashbacks, avoidance, hyperarousal and nightmares, and often reflects emotional dysregulation with an inability to effectively process traumatic memories. Crucially, current therapies fail to deliver long-term control of symptoms in ~50% of sufferers. Defining determinants of vulnerability to PTSD and designing novel, biologically informed prevention and treatment strategies is essential. Sleep is known to play an important role in the processing of daily experiences, since neuronal circuits associated with salient memories are reactivated during sleep to tune their integration into long term storage. Reactivation of hippocampal place cell sequences during non-rapid eye movement sleep (NREM) has been shown to support the consolidation of spatial memories. In contrast, there is significant evidence that REM sleep is instrumental in processing emotional memories and reducing emotional tone. While evidence is limited, longitudinal studies on post-trauma sleep have shown the development of PTSD is associated with more fragmented REM sleep and increased sleep complaints. Manipulating post-trauma sleep and emotional memory processing therefore presents a powerful opportunity to improve PTSD prognosis and prevention. Targeted memory reactivation (TMR) is a technique in which an individual is re-exposed to a cue during sleep (e.g. an auditory tone) which was previously conditioned to a waking experience such as a memory task. Previous research has shown that TMR is able to bias the reactivation of circuits within the brain during sleep that are associated with these memories, thereby influencing subsequent behaviour or improving next-day performance on the tasks. The ability of TMR to manipulate memory processing is leading to a growing interest in its therapeutic potential which may be particularly effective for helping to process trauma. Primary objective: Your project will involve investigations into the role of sleep for processing trauma and identifying whether TMR can be used as a novel intervention to improve this processing. Experimental trauma

	paradigms, such as using videos depicting distressing scenes, have been developed to study peritraumatic processing in an ethical way. These paradigms have been shown to effectively model trauma, inducing sub-clinical PTSD-like symptoms such as intrusive thoughts in healthy individuals. The primary objective will be to design a paradigm combining an experimental trauma with targeted memory reactivation. In collaboration with Anke Karl at the University of Exeter, we will design a trauma film paradigm such as a virtual reality car crash, implementing conditioned auditory stimuli which will then be replayed during specific phases of sleep. In development with Masanori Sakaguchi and Masashi Yanagisawa (University of Tsukuba, Japan), a portable EEG headset will be used for at-home sleep recording in combination with online detection of sleep stages and automated re-presentation of the conditioned auditory stimulus. Once set up, this will then be tested in healthy individuals to identify its therapeutic potential. Response to the experimental trauma will be assessed across the following week using visual analogue scales, emotional response tasks, an intrusion diary, and questionnaires. Secondary objectives: This work fits into a wider research aim to understand the role of sleep for processing trauma. There will therefore be ample opportunity for you to take ownership and drive the direction of your research throughout the PhD including additional experiments based on your interests. This could involve in-vivo electrophysiology experiments in rodents to investigate the underlying impact of TMR on brain circuitry or involve studies with patient populations to further understand peri-traumatic sleep. Location: Your project will involve an interdisciplinary team and collaboration between Bristol, Exeter, and Tsukuba in Japan. You will be based at the University of Bristol with research visits to both the University of Exeter and University of Tsukuba in Japan for training in the use of the EEG headsets and automated sleep scoring and auditory stimulus presentation. Regular meetings with other co-supervisors and collaborators will also occur online throughout the project. Overall, it is expected that this project will pave the way for future investigations into the clinical application of TMR interventions in at-risk populations exposed to real life traumas.
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