Validation and Development of Overnight Learning Paradigms of Memory Consolidation in Slow-Wave Sleep

Background. A growing literature supports a role for sleep after training in long-term memory consolidation and enhancement[1]. Consequently, interrupted sleep results in cognitive and behavioural deficits[2]. Recent animal evidence shows that optimal memory consolidation during sleep requires a certain amount of uninterrupted sleep[3]. Human studies have also demonstrated that there is a clear minimum requirement of sleep continuity to ensure optimal sleep dependent memory processes[4]. The effects of just one "good night's" sleep can improve an adult's performance on a reaction time task learned and practiced the previous day[5].

Rationale. Sleep continuity is disrupted in various medical disorders ranging from schizophrenia[6], attention deficit hyperactivity disorder[7] and epilepsy to obstructive airways disease. The optimisation of sleep is also an emerging target of pharmacological intervention in neurodegenerative disorders in childhood and old age. However, while there are a number of experimental paradigms to measure memory consolidation, there is a need to develop and validate measures that can be routinely applied in clinical translational research settings. Additionally, much of what we know about sleep and learning is derived from adult studies; sleep is a developmental process, and the organisation of sleep stages in early childhood is completely different to that in adults; and sleep disruption is implicated in several developmental disorders. The extrapolation of adult findings to children is thus both hazardous and inappropriate. Furthermore, children are likely to require tasks which are a) more engaging and motivating b) presented in different ways (eg., on an ipad and using cartoon characters) and c) for differing durations[8].

Goal. Our proposal is to adapt a set of valid and reliable learning tasks for children that will allow us to qualify these learning effects in children. We intend to test which specific tasks, and which specific outcomes best allow us to qualify learning effects in typically developing children. This study will generate a widely applicable measurement tool to assess pertinent cognitive outcomes of a wide variety of diseases and interventions.

People and Environment. Deb K Pal is Professor of Paediatric Epilepsy at the Institute of Psychiatry. His special interest is the cause and mechanisms of neurodevelopmental impairments in children with epilepsy. Paul Gringras is Professor of Paediatric Sleep Medicine at Evelina Children's Hospital (ECH). He has published extensively in children's sleep disorders, autism and developmental disabilities; and he directs the Sleep Research Labs at ECH. Anna Smith PhD is Lecturer in Cognitive Neuropsychology at IoP and specialises in fMRI studies of paediatric neurodevelopmental disorders including ADHD and dyslexia. The research will bridge the two campuses of King's Health Partners and will be the first to exploit the brand new children's sleep research facility at the Paediatric Neurosciences Centre, ECH. The centre already has comprehensive sleep and EEG testing equipment, as well as a soon to open EEG-fMRI facility.

Aims.
1. Review existing adult cognitive task paradigms for their suitability for children.
2. Develop more engaging tasks for children using animation and simple gaming technology.
3. Characterise the relationship between sleep and learning task performance in a representative group of healthy children aged 4-12 years, using the condition of mild sleep restriction.

4. Select a combination of 2-3 tasks on the basis of validity and reliability measures as the basis for a routine measure of cognitive outcome in various disease and intervention models in children.

Research Plan. The study design will be a repeated measures crossover design of 30 healthy child volunteers, aged 4 to 12 years, with equal sex distribution. The sample size is based on similar work on sleep fragmentation in adults with obstructive sleep apnoea. Each child will be admitted twice for overnight study to the Evelina Children's Hospital Sleep Research Labs and will have full EEG and sleep monitoring recording. In phase 1, they will be admitted with unrestricted sleep, and in Phase 2 they will experience sleep restriction (popcorn and movie night). Phase 1 and 2 will be separated by a period of at least one week. A subset will be readmitted on two or more occasions for test-retest reliability studies. After completion of baseline medical and neuropsychological examination, children will be asked to learn and practice different sets of tasks in a series of consecutive trials over a period of about 15 minutes. They will then be asked to repeat these tasks at differing intervals, eg the following morning before discharge home.

Baseline measures: Routine health and behaviour questionnaires; Medical exam; Full scale IQ; Socio-economic data; Sleep behaviour questionnaire.

Learning Tasks: We will specifically be considering a number of tasks that broadly tap declarative memory tasks (memories for facts and events), declarative emotional (memories for events, which are associated with an affective response) and procedural (memories for skills and habits that are acquired through repeated practice) in children. We will focus on a number of tasks that have potential utility in children including:
Motor sequence learning tasks, Serial reaction time task, word pair and memory recall tasks[9].

Electrophysiological measures. Technological improvements means that whilst previous research has focussed on 'macroscopic' estimates of Rapid Eye Movement (REM) and non-REM sleep stages, more specific parameters, including REM density, sleep spindles, slow oscillations, and spectral analysis are now regarded as increasingly important for different types of offline memory processing[10, 11]. Sleep will be fully characterised with polysomnographic studies that will capture macroscopic (total sleep time and sleep stage percentages) and microscopic (arousal index, REM density, spindle count) aspects of sleep architecture.

Statistical Analysis: We will perform multivariate analyses of overnight learning (improvement in task performance) against relevant sleep parameters, eg spindle count. We will assess improvement in task performance with practice; and test-retest reliability of learning tasks.

Timetable. Months 1-6: development of new tasks; Months 6-18: recruitment of volunteers and sleep study scoring, entry to database; Months 19-24: data analyses and write-up.

Outputs. We will generate a toolbox of 2-3 learning tasks that are valid for children, engaging enough to show a practice enhancement, and with adequate reliability to use as a single measure of outcome. Our future directions are to use these tools to quantify the impact of various childhood disease conditions (eg epilepsy, autism, stroke) on learning, and to pilot the use of these tools in academic or commercial intervention studies (eg in collaboration with Eli Lilly & Co., Neuroscience Discovery, Wyndlesham, Surrey).