Study proposal:

The role of the anterior and dorsomedial thalamic nuclei in episodic memory encoding and retrieval

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Backgound:

The functional role of the hippocampus in episodic encoding and retrieval has been widely explored using lesion data and neuroimaging techniques. Much less is known about the functional role of the relevant diencephalic structures. Recent anatomical, lesion, and electrophysiological data have led John Aggleton to propose that the anterior and dorsomedial thalamic nuclei play different functional roles in episodic memory (e.g., Aggleton & Brown, 2006). The dorsomedial nucleus receives projections from parahippocampal and perirhinal cortex and has widespread reciprocal interconnections with dorsolateral, medial, and orbital prefrontal cortex. The anterior thalamic nuclei, comprising anterior medial, anterior ventral, and anterior dorsal components, each have complex anatomical connectivity that is different to that of the dorsomedial nucleus, and different to each other (Aggleton et al., 2010). In particular, the anterior ventral nucleus receives inputs from the subiculum (hippocampus), granular retrosplenial cortex, and the more lateral parts of the medial mammillary nucleus. Unlike the dorsomedial thalamic nucleus, it has only very light connections to rostral cortical sites, but has widespread direct connections back to the subliculum, presubiculum and parasubiculum, and extensive projections to retrosplenial cortex, which form an indirect route back to the hippocampus. Lesions to the anterior thalamic nuclei cause secondary cellular changes in the hippocampus and retrosplenial cortex, and disrupt plasticity in retrosplenial cortex.

Functionally, Aggleton (Aggleton & Brown, 2006; Aggleton et al., 2010) has suggested that, in humans, the circuits involving the dorsomedial thalamic nucleus support broad discriminations between familiar and unfamiliar information, and strategic aspects of memory processing, whereas the circuits involving the anterior thalamic nuclei, particularly the anterior ventral thalamic nucleus, support conscious recollection of the details of specific, personally experienced past episodes. These aspects of episodic memory ("knowing" versus "remembering") are behaviourally dissociable in humans (Gardiner & Richardson-Klavehn, 2000). In our study, we will dissociate recollection and familiarity by inducing a level of processing effect and behaviourally by using confidence ratings and Receiver Operating Characteristic (ROC) analysis.

Subjects and experimental design:

Subproject stroke: 30 (minimum20) patients with lesions either in the anterior or dorsomedial thalamic nuclei, and 30 control subjects matched for age, IQ, gender will participate.

During fMRI subjects will perform a memory paradigm consisting of 4 runs of studying and retrieval of visually presented German words. In the study phase, words will be either encoded deeply (semantic processing) or shallowly (phonemic processing). In the test phase subjects are asked to make an old/new together with a confidence judgement. Additionally, we will record a high resolution structural MRI and DTI. Total scanning time will be approx. 1h 20min.

Subjects will be tested neuropsychologically and will also participate in an MEG Experiment using the same paradigm.

Subproject 7T: 40 healthy student participants will perform the same word list study paradigm, but using the double amount of stimuli and performing study and test phase 24-48h apart (to account for better episodic memory performance in the student population compared to the elderly subjects in the stroke subproject). 20 students will perform the study phase in the 7T scanner and the test phase in the 3 T scanner and 20 students vice versa. Scanning time for the study phase will be 23 minutes and for the test phase 52 minutes.

Analysis:
In the stroke subproject we will focus the analysis on activation in hippocampus and frontal regions as well as connectivity between these regions in patients with thalamic lesions compared with healthy subjects, as well as secondary structural (VBM and DTI: FA, fiber tracking) changes due to these lesions.
In the 7T subprojects we aim to differentiate contributions of activation and connectivity of the dorsomedial and anterior thalamic nuclei to memory functions.