Supplementary Discussion

Relationship to primacy effect

The discussion so far focused on the differential processing mechanisms of subsequently remembered and forgotten items; however, we also found that the proportion of successfully encoded items depended on list position: Both groups of subjects (epilepsy patients and healthy subjects) showed a significantly higher rate of subsequently remembered words at the beginning of the list (primacy effect); epilepsy patients also recalled items at the end of the list better (recency effect), which was not observed in normal subjects (Fig. 2A, B). The distraction task was monitored online, and was thoroughly conducted by both groups of subjects. Thus, we do not have an explanation for this difference, because patients performed the distracter task as properly as the fMRI subjects (which was monitored online), so that WM for both groups should be similarly erased. However, all analyses presented here focus on the differential processing of items presented at the very beginning of the list as compared to items in the middle of the list. Therefore, it is very unlikely that a possible differential processing of items at the final two positions of the list, where a recency effect was observed for epilepsy patients but was absent for fMRI subjects, significantly affects our findings related to processing at the beginning of the list. Among the previous neuroimaging studies investigating the primacy effect, two are particularly noteworthy in our context. Sederberg and colleagues (2006) recently conducted a word-list learning task similar to our paradigm and calculated subsequent memory effects on oscillatory activity in scalp EEG. They found that an increased posterior gamma power predicted successful free recall at early list positions, whereas wide-spread power decreases were associated with memory formation for items presented later in the list. The increased gamma band activity at early list positions was interpreted as reflecting focused attention, which is known to facilitate LTM encoding. This is consistent with their general finding of decreasing gamma power as a function of serial position. At later list positions, attention becomes less focused because is has to be divided between previously seen and new items. This explanation is in principal consistent with our proposal that successful encoding at the beginning of the list is impeded if items are not processed in a hippocampal-dependent form of WM. Previous studies indicate that directed attention deteriorates if a WM task is conducted simultaneously, in particular when multiple items are being maintained (De Fockert et al., 2001), suggesting that multi-item WM and directed attention rely on very similar processes.

A second study by Strange et al. (2002) employed the same paradigm as in the current study in functional MRI. Again, they found that subsequent memory effects at early and later list positions differed: Encoding of early words was associated with activation of the anterior hippocampus, which was interpreted as reflecting increased novelty/distinctiveness and, again, the allocation of greater attentional resources to these items. As described above, directed attention and WM rely on similar processes and thus interfere with each other, so that their hypothesis that attention facilitates LTM encoding at early list positions is consistent with our data. On the other hand, we did not find serial position effects for subsequently remembered items. Thus, the iEEG and fMRI measures investigated in our study – the slope of DC potentials and BOLD responses in the hippocampus – cannot explain the enhanced encoding probability of items at early list positions, but rather suggest possible mechanisms why items are *not* encoded into LTM.

Anterior cingulate activation and WM/LTM interaction

We found that the anterior cingulate cortex was stronger activated during processing of the third as compared to the first word, regardless of the success of memory formation. Activation of this region is commonly observed during tasks such as the Stroop paradigm, in which mutually interfering processes are executed simultaneously (Carter and van Veen, 2007). In our task, it may index the increasing interference upon presentation of consecutive items. It should be pointed out, however, that this interpretation is currently rather speculative and needs to be corroborated further. The increased activation in the bilateral parahippocampal gyrus is likely to reflect a similar process as the increased activation in the anatomically selected ROI in the left hippocampus.

Supplementary References

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