The association between California Verbal Learning Test performance and fibre impairment in multiple sclerosis: evidence from diffusion tensor imaging

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Abstract
The California Verbal Learning Test (CVLT) is recognized as a standard clinical tool for assessing episodic memory difficulties in multiple sclerosis (MS), but its neural correlates have not yet been examined in detail in this patient population. We combined neuropsychological examination and diffusion tensor imaging (DTI) analysis in a group of MS patients (N = 50) and demographically matched healthy participants (N = 20). We investigated the degree of impairment of the uncinate fascicle (UF), the superior longitudinal fascicle (SLF), the fornix (FX) and the cingulum (CG). The patients were impaired on all CVLT parameters and the DTI parameters correlated moderately with disease-related variables. Regression analyses in the complete study sample showed that CVLT learning scores correlated with impairment of the right UF. This association reached marginal significance in the patient sample. In contrast to other studies claiming retrieval deficits, our results suggest that encoding and consolidation deficits may play a major role in verbal memory impairments in MS. The findings also provide evidence for an association between degree of myelination of prefrontal fibre pathways and encoding efficiency. Finally, DTI-derived measurements appear to reflect disease progression in MS. The results are discussed in light of functional MRI studies investigating compensatory brain activity during cognitive processing in MS.

Keywords
California Verbal Learning Test, diffusion tensor imaging, limbic, multiple sclerosis, perpendicular diffusivity, prefrontal

Introduction
Memory disturbances appear to be a prevalent symptom in multiple sclerosis (MS),1 having a detrimental effect on daily living2,3 and vocational outcome.4 Recall after a 20–25 min delay is commonly affected in MS.5–8 Nevertheless, the occurrence of an isolated impairment in a particular stage of the memory process is highly unlikely, since inflammation usually occurs simultaneously in various brain regions. Accordingly, it has been suggested that memory impairments in MS also depend on insufficient encoding5,10 and consolidation of the material.11

A widely used instrument to investigate verbal mnemonic processes in neurological and psychiatric patients is the California Verbal Learning Test (CVLT).12,13 A number of variables can be derived from the CVLT, presumably reflecting different memory processes.14 For instance, the mean number of words, which can be recalled immediately after each of the five learning trials, can be regarded as an index for the ability to encode information (see also Hildebrandt et al.5, Benedict et al.15, Grober and Kawas16, and Fernández et al.17 for an experimental adaptation). This parameter proved to be more reliable than the score on an individual trial or the learning curve, and in a factor analysis it appeared to load more on a general memory factor than other parameters.14

Gathering information about consolidation with the CVLT appears to be somewhat complicated, since a...