Long-Term Deficits in Episodic Memory after Ischemic Stroke: Evaluation and Prediction of Verbal and Visual Memory Performance Based on Lesion Characteristics

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We investigated the relationship between ischemic lesion characteristics (hemispheric side, cortical and subcortical level, volume) and memory performance, 1 year after stroke. Verbal and visual memory of 86 patients with stroke were assessed with Rey Auditory-Verbal Learning Test and the Doors Test, respectively. Lesion characteristics and presence of white matter lesions were assessed on magnetic resonance imaging early after stroke. Multiple regression analyses were used to investigate prediction of verbal and visual memory performance by lesion side (left *v* right hemisphere), lesion level (cortical *v* subcortical), and lesion volume. We controlled for the influence of demographic characteristics, language disability, and visuospatial difficulties on memory. The results demonstrated that poor verbal memory (immediate and delayed recall and recognition) could be predicted by lesion characteristics: patients with left hemispheric, subcortical, and large lesions showed poor memory performance. Poor visual recognition memory could not be predicted by lesion characteristics but only by low educational level. Our results suggest that lesion characteristics play an important role in episodic verbal memory poststroke if demographic and clinical characteristics are taken into account. **Key Words:** Cerebrovascular accident—magnetic resonance imaging—cognition disorders—memory disorders—neuropsychological tests.

Cognitive impairment is a common sequel of stroke.[1] It plays an important role in acute functional recovery[2] and in long-term outcome such as independency and quality of life.[3,4] Memory is one of the cognitive domains frequently affected by stroke.[5,6] Memory function–involving the ability to register, store, save, and retrieve information when needed[7]–is particularly important in the process of rehabilitation after stroke, as it is required for learning new skills and relearning old ones.[8]

There are many case studies on memory impairment after stroke and its relationship with lesion location. However, recently, group studies have been performed that investigated acute and chronic cognitive impairment (including memory impairment) after stroke and its relationship with a wide range of determinants, such as vascular risk factors, pre-existent neuropathology, and lesion characteristics of volume and location.[1,9-12] Yet only few of these studies[9,13] investigated memory impairment in the chronic phase of stroke in large samples, using specific indicators of verbal memory function and considering different stages of memory processing (i.e., encoding, storage, and retrieval). However, it has been

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frequently assumed that different neuroanatomic stroke sites lead to different types of memory impairment in terms of the type of information and stages of processing.[5,6,14]

Verbal memory deficits have been consistently demonstrated to occur primarily after left hemispheric stroke, and nonverbal (visuospatial) memory deficits principally after right hemispheric stroke.[7] However, there is increasing evidence suggesting that this distinction is not absolute: left hemispheric lesions have been reported to produce visual memory impairments, whereas verbal memory deficits are also observed after right hemispheric stroke.[5,6,14] Results of functional imaging studies on the hemispheric lateralization of memory also diverge. Several studies have shown that verbal encoding of words produced left hemispheric activations, whereas nonverbal encoding of unfamiliar faces produced right hemispheric activations.[15,16] However, some recent studies demonstrated either no lateralization of verbal and visual memory function, or only minimal lateralization of verbal memory function to the left hemisphere.[17-19]

Cortical and subcortical lesion levels have been shown to influence memory deficits in patients with brain damage, including patients with stroke. However, only few studies have compared the relative influence of cortical versus subcortical lesions on memory function. These studies showed that patients with stroke with a cortical lesion have more severe memory deficits than patients with a subcortical lesion.[2,20] This finding is not surprising, because several cortical areas play an essential role in episodic memory function. The posterior cortical region of the medial temporal lobe is widely recognized to mediate the associative, contextual, and recollective aspects of episodic encoding and retrieval.[21-23] The hippocampus is the crucial structure in encoding of ongoing information, and the multimodal association areas of the posterior cortex are generally assumed to be the site for long-term storage of episodic memories.[24-27] Furthermore, results from imaging studies have shown that regions of the anterior (prefrontal) cortex also take part in the network mediating episodic memory processing,[28,29] probably facilitating (re)constructive and search processes of encoding and retrieval by its inherent executive functions (i.e., attentional processes, monitoring, and coordination).[7,24] Functional imaging studies have demonstrated a hemispheric asymmetry in the memory processes of the prefrontal cortex, first postulated by Tulving et al[30] in the hemispheric encoding/retrieval asymmetry (HERA) model, which involves an increased activity in left prefrontal regions during intentional encoding, whereas episodic retrieval primarily activated right prefrontal brain regions.[17,28,31]

However, although the essential role of cortical structures in episodic memory is evident, recent studies increasingly show the important role of subcortical structures as well.[12,32-36] Although lesions of the subcortical structure of the thalamus are long associated with memory disorders, results of recent imaging studies have suggested that memory deficits may also result from focal lesions of the anterior and medial cortical portions of the thalamus, particularly if there is involvement of subcortical white matter tracts such as the mammillothalamic tract.[33,37,38] Furthermore, studies[12,32,34,35] have reported an impairment of short-term and long-term memory, particularly of encoding and recall, after stroke in the basal ganglia. Therefore, it seems that more research is needed to evaluate the influence of cortical and subcortical stroke lesions on memory impairment after stroke.

Only a few studies have examined the influence of lesion volume on poststroke memory function.[13,34] However, lesion volume is known to correlate moderately to strongly with long-term functional outcome and quality of life[39] after stroke.

This study investigates the relationship between ischemic lesion characteristics (side, level, volume) and verbal and visual episodic memory performance 1 year after stroke in a relatively large patient sample. Based on the previously discussed findings of episodic memory deficits after stroke, we expected that patients with left rather than right hemispheric lesions would manifest more verbal memory dysfunctions, and that a larger volume would give rise to more severe disturbances.

Methods

Procedure

The study population consisted of patients with a first-ever ischemic stroke admitted to one of 6 participating stroke departments in the Netherlands. Stroke has been defined as a rapidly developing sign of focal or global disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no apparent origin other than vascular.[40] The research protocol was approved by our medical ethics committee. All patients gave their informed consent. Patients included had a single first-ever supratentorial nonlacunar ischemic infarction of the anterior, medial, or posterior cerebral artery; were aged between 18 and 85 years; had a premorbid Barthel Index greater than or equal to 18; and had a stable neurologic condition 1 week after stroke. They did not have any mental comorbidity (e.g., dementia or psychiatric disorder) that might influence neuropsychological outcome. Lacunar infarctions were defined as infarctions of the deep white matter of the brain, caused by an occlusion of small perforating arteries, with a diameter ranging from 3 to 4 mm to a diameter of 15 to 20 mm and located at the site of the basal ganglia, internal capsule, or corona radiata.[41,42] Patients with premorbid cognitive limitations or beginning dementia, assessed by (hetero-)anamnesis with patient and/or family, were excluded. Participants received normal drug treatment and were not treated with thrombolysis or neuroprotective agents, because this was not yet