

Diaschisis after thalamic stroke: a comparison of metabolic and structural changes in a patient with amnesic syndrome

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Introduction – We present a patient with a left anteromedial thalamic lesion with an amnesic syndrome. The patient underwent neuropsychological testing, cerebrospinal fluid (CSF) analyses, magnetic resonance imaging (MRI) [T2, flair, and diffusion tensor imaging (DTI)] and [18F]-2-fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) to assess indirect effects of thalamic lesions on cortical function. **Case report** – A 67-year-old right-handed woman was admitted to a university-based memory unit because of memory and concentration problems. Neuropsychological testing revealed dysfunction of episodic memory, semantic memory and working memory. General intellectual function and attention capacity were preserved. MRI revealed an anteromedial thalamic lesion in the left hemisphere. FDG-PET showed decreased uptake in the frontal, parietal and temporal lobes of the left hemisphere. Regions of interest (ROI) in white matter were selected and left and right hemispheres were compared. Fractional anisotropy (FA) in ROI representing thalamo-cortical connections were decreased in the left hemisphere when compared with the right. **Conclusion** – The results show the importance of a network that include the anterior and dorsomedian nuclei, which influence the activity in areas of the cortex responsible for memory processes. The imaging findings suggest that areas of cortical diaschisis after thalamic infarction correspond to areas affected by thalamo-cortical fibre loss as measured with FA.

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Introduction

The amnesic syndrome of thalamic origin is most often referred to as a memory deficit which mainly affects the ability to store new information in episodic memory.

It has been suggested that memory impairment after thalamic lesions may represent disconnection of thalamo-cortical projections (1) and that thalamic lesions may be associated with ipsilateral cortical atrophy (2). Cortical diaschisis and crossed

cerebro-cerebellar diaschisis after thalamic lesions have been described with single-photon emission computed tomography (SPECT) and positron emission tomography (PET) (3, 4).

Using diffusion tensor imaging (DTI) measures of the fractional anisotropy (FA) index gives quantitative measures of white matter tracts (5). Reduced FA may represent axonal loss and correlates with cognition (6, 7). To explore the network and pathophysiology of a thalamic lesion associated with memory problems, we used DTI and

co-registration with PET. This allows for comparison of cortical metabolic changes and altered diffusion anisotropy in white matter.

Case report

A 67-year-old right-handed woman was admitted to our university-based memory unit because of problems with memory and concentration. She could not recall the exact time of onset, but reported that her memory problems developed within a month about 5 months prior to admission. In this period she also reported fatigue, apathy, feelings of sadness, impatience and frustration. She had loss of appetite and spent most of her time at home with minimal activity.

She had known familial hypercholesterolemia and had been treated with cholesterol lowering medication for 18 years. At the time of admission, she was treated with 80 mg of fluvastatin daily as well as with anti-hypertensive medication. Treatment with donepezil had also been initiated by her general practitioner.

Six years before admission she underwent a probable cerebrovascular episode of the right hemisphere with motor weakness and tempo retardation in her left leg; however, no magnetic resonance imaging (MRI) changes were detected at the time of admission. She reported no memory problems after this particular episode. When she was examined at the memory unit, minor motor weakness and retardation were still found in her left leg.

At the first examination, the patient was assessed with the Neurobehavioral Cognitive Status Examination (Cognistat) (8) and Mini Mental State Examination (MMSE). MMSE score was 28/30, as the patient could recall only one out of three words after 3 min of distraction. The results from Cognistat revealed memory problems and mild deficit

on the subtest similarities (verbal abstraction and concept formation), naming and calculation. The results on the subtests orientation, attention, judgement, spontaneous speech, comprehension and repetition were within the normal range.

The patient was assessed in a formal neuropsychological examination 6 months after her first examination. Description of test procedures may be found in a standard text (9). She was fully cooperative and aware of her memory problems. Neuropsychological testing revealed decline in episodic memory (defective learning during repeated trials and delayed recall), semantic memory (reduction in understanding the meaning of words) and working memory (Letter-Number Sequencing, WAIS-III). Memory impairment involved both verbal and visual memory with slightly better performance on visual memory. Both verbal memory for stories and for unrelated words was reduced, but the performance for recognition of words was relatively intact. The scores for attention and concentration tests including Trail Making A/B, Digit Symbol-Coding (WAIS-III) and Stroop (Color-Word Interference Test, D-KEFS) tasks were in the normal range. General intellectual function was preserved, especially for abstract reasoning ('Matrix Reasoning'). The full-scale intelligence quotient (IQ) estimated from two subtests (Vocabulary and Matrix Reasoning) on Wechsler Abbreviated Scale of Intelligence was 84. She had no clear signs of aphasia, but some minor problems with naming, indicative of a mild semantic memory disorder. Procedural memory (memory for previously acquired abilities), such as doing ordinary homework and cooking, was preserved.

The patient's apolipoprotein E (APOE) genotype was 3/3. Blood tests showed elevated cholesterol (7.8 mmol/l, normal range: 3.9–7.8)

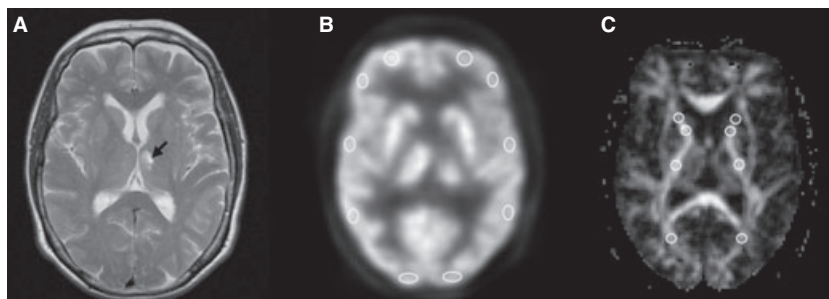


Figure 1. T2-weighted magnetic resonance imaging, [^{18}F]-2-fluoro-deoxy-D-glucose positron emission tomography and diffusion tensor imaging findings. (A) shows the anteromedial thalamic lesion in the left hemisphere (arrow); (B) shows left cortical and anteromedial thalamic hypometabolism; (C) shows the fractional anisotropy (FA) map. Decreased FA was observed particularly in the anterior limb of the internal capsule and the anterior thalamic radiation (Fig. 2B). An illustration of some region of interest positions are shown with white circles in B and C.

and low-density lipoprotein (LDL) cholesterol (6.5 mmol/l, normal range: 2.0–5.3), but other blood tests were within normal range.

Her cerebrospinal fluid (CSF) analyses including 181 phosphorylated tau proteins (P-Tau₁₈₁), tau protein (tTau) and amyloid β 1-42-peptide (A β ₄₂) were normal. The electroencephalogram (EEG) revealed short episodes (1–1.5 s) of polymorphic theta waves in frontotemporal regions mostly pronounced in the left hemisphere. No spikes or sharp waves were observed.

A 1.5-T Siemens Magnetom Sonata MRI scanner (Siemens Medical Solutions AG, Erlangen, Germany) was used for acquisition of MRI and DTI data, and the [18F]-2-fluoro-deoxy-D-glucose (FDG)-PET scan was performed on a Siemens Biograph 16 PET/CT scanner (Siemens Medical Solutions AG).

Spherical regions of interest (ROI) (mean sizes 35/69 mm² for FA maps/FDG-PET images, respectively) were placed according to anatomical landmarks and ROI in the left and right hemispheres were compared. Care was taken to avoid partial CSF volume effects in the chosen ROI. To illustrate the difference in FDG uptake we placed ROI in the frontal, parietal, temporal and occipital lobes, as well as in cerebellum. To compare the FA indices between hemispheres, we placed ROI which included the anterior and posterior limbs of the internal capsules, the anterior and superior thalamic radiations, the forceps major, the superior region of corona radiate and the superior cerebellar peduncles. An illustration of some representative ROI is shown in Fig. 1B and C.

For ROI analyses and processing of MRI and DTI data we used the nICE (nordic Image Control and Evaluation) Basis and Diffusion Module (NordicImagingLab AS, Bergen, Norway).

MRI revealed an anteromedial lesion in the left thalamus (Fig. 1A). No changes were seen in the right hemisphere corresponding to her possible cerebrovascular episode 6 years earlier.

PET with FDG showed decreased activity in the left anterior thalamus region as well as in the left frontal lobe and to a lesser extent in the left parietal and temporal lobes (Figs 1B and 2A). The uptake of FDG in the right cerebellum was slightly lower than that in the left, suggesting a crossed cerebro-cerebellar diaschisis (Fig. 2A).

The FA index values in the selected ROI showed decreased values in white matter of the left hemisphere, in particular in the anterior limb of the internal capsule and in the anterior thalamic radiation. We did not find any differences in the FA indices between the left and the right cerebellar peduncles (Fig. 2B).

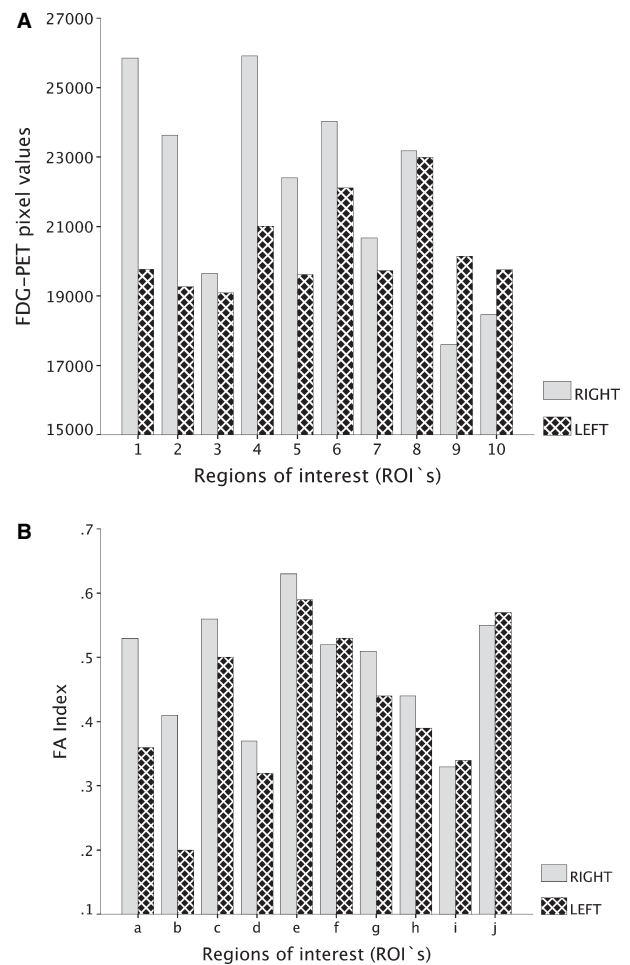


Figure 2. Comparison of region of interest (ROI) values in the left and right hemispheres. (A) shows the [18F]-2-fluoro-deoxy-D-glucose positron emission tomography mean pixel values in the selected ROI. ROI: frontal lobe (1, 2); temporal lobe (3, 4); parietal lobe (5, 6); occipital lobe (7, 8); cerebellum (9, 10). (B) shows the fractional anisotropy (FA) mean index values in the selected ROI. ROI: anterior limb of the internal capsule (a–c); anterior thalamic radiation (a–d); superior thalamic radiation (c,e,f); posterior limb of internal capsule (e,f); forceps major (g); superior region of corona radiata (h,i); superior cerebellar peduncle (j).

Discussion

The patient had a long-lasting amnesic syndrome as a result of an infarction localized to an area largely corresponding to the anteromedian region of the left thalamus.

Her cognitive profile did not show any deficit of cognitive functions other than memory. Memory dysfunction was related to both learning and storing deficits, especially in the verbal domain, and also included aspects of semantic memory and working memory. Dysfunction of visual memory was slightly milder than that of the

verbal memory for stories and the verbal memory for words. The better performance for recognition of words is consistent with earlier findings after stroke in the left thalamus (10).

This classic amnesic syndrome serves to illustrate the basis of both cognitive loss and cortical diaschisis, demonstrating a close correspondence to hypometabolism and structural changes as shown by FDG-PET and MRI-based FA index measures. The patient showed wide spread hypometabolism of the left prefrontal cortex, consistent with the observation that her amnesic problems also include a deficit in working memory. It is not known whether our findings match the initial status after the infarction, or whether compensatory changes in fibre tracts may have occurred in the intervening months. FA index measures and FDG-PET may be useful to visualize such changes, e.g. as a result of cognitive rehabilitation or other types of therapy.

We found a reduced FA index ipsilateral to the thalamic lesion, corresponding to ipsilateral cortical hypometabolism. Further, we observed slightly reduced FDG uptake in the contralateral cerebellum, suggesting a cerebro-cerebellar diaschisis. We found no motor affection and no corresponding alterations of FA indices (cerebellar peduncles). These findings suggest that diaschisis may occur directly because of axonal loss (as shown with altered FA), as well as indirectly, reflecting reduced function.

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