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Transient global amnesia: Only in already disrupted neuronal integrity of memory network?

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ABSTRACT

Transient global amnesia is a well-described clinical syndrome; however, the pathophysiology is perplexing. Structural imaging indicates that punctuate hippocampal lesions are the representative pathophysiology, although functional neuroimaging studies have reported that the various regions comprising the episodic memory network are involved. We hypothesized that the neuronal integrity of the memory network might correlate with amnesia symptoms when there is any insult that can affect the hippocampus. Diffusion tensor images of 5 patients with variable diffusion-weighted imaging findings with or without transient global amnesia symptoms were analyzed. Diffusion tensor image analyses were performed using DTI studio software. A patient with a typical restricted diffusion involving the right hippocampus, but without memory symptoms, had more abundant cingulum fibers. However, the serial cingulum fibers of patients having experienced multiple attacks did not show a decremental tendency. The volume of fibers in the affected side was lower than that of the opposite side. This report suggests that memory-related symptoms of transient global amnesia are related to the disrupted neuronal integrity of cingulum fibers.

1. Introduction

Transient global amnesia (TGA) is a well-described clinical syndrome, which is defined by an anterograde and retrograde amnesia of sudden onset that lasts up to 24 h. Despite clear clinical criteria, the pathophysiology is perplexing [1]. Numerous neuroimaging studies based on diffusion weighted imaging (DWI) have indicated that that punctuate hippocampal lesions which mainly include the CA1 field are the representative imaging findings [2], and the detection rate is increasing to up to 88% by using the modified DWI protocol. However, previous functional neuroimaging studies using positron emission tomography (PET), single photon emission computed tomography (SPECT) and resting-state functional magnetic resonance imaging (RSfMRI) have reported that various regions, especially the bilateral hippocampi and connected parts comprising the episodic memory network, are involved in TGA patients [1,3]. These findings might suggest that transient weakness of the memory network is manifested as TGA.

Based on this evidence, it is suggested that the neuronal integrity of the memory network might correlate with TGA symptoms when there is any lesion affecting the hippocampus and related structures. Our hypothesis was the magnitude of neuronal integrity is related with TGA "symptom", which is the degree of neuronal integrity would be different in patients with "TGA symptom" and patients without "TGA symptom", in situation with both of them have focal hippocampal DWI lesions. We further evaluated the inverse theory via a case who had 4 episodes of TGA attack.

2. Patients and methods

2.1. Clinical vignettes

2.1.1. Patient 1 (PA1): typical DWI lesions involving the right hippocampus without memory symptoms

A 58-year-old woman visited the hospital due to abrupt dizziness associated with nausea and vomiting. The dizziness lasted 2–3 min and was made worse by a change in position, especially when right side down. Neurological examination did not show spontaneous nystagmus in the primary position; however, Dix-Hallpike test showed torsional and upbeat nystagmus at right side down position. There was no other cranial nerve sign, motor or sensory deficit, or dysmetria on finger to-nose and heel-to-shin test. Her Mini-Mental State Examination (MMSE) score was 29 which in the normal range. Benign paroxysmal positional vertigo was suspected; however, DWI showed a tiny dot-like hyperintensity in the right hippocampal tail (Fig. 1-A). FLAIR imaging revealed a few non-specific hyperintensities and axial source MRA images did not show abnormal findings.

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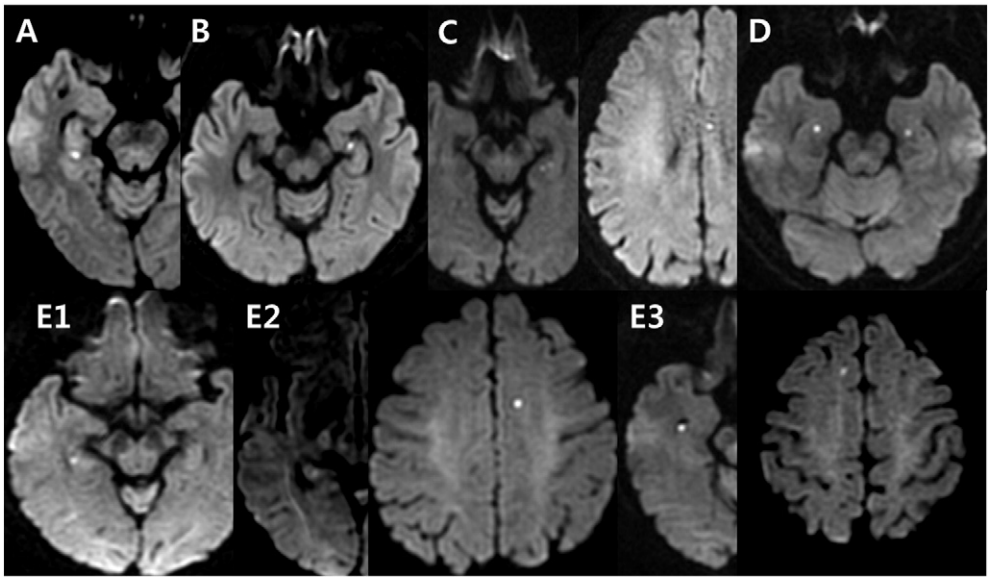

Fig. 1. Diffusion-weighted imaging of patients. Focal hyperintensities in the right hippocampal tail (A, PA1), left hippocampal (B, PA2), left hippocampus and cingulum (C, PA3), head of bilateral hippocampi (D, PA4), right hippocampus (E1, PA5, second attack), right hippocampus and left cingulum (E2, PA5, third attack), right hippocampal head and cingulum (E3, PA5, fourth attack).

2.1.2. Patient 2 (PA2): typical DWI lesions involving the left hippocampus without memory symptoms

A 67-year-old man who has 6 years of education visited our dementia center for progressively declining cognition. He had no history of developmental or general medical disease except hypertension which had been continuously treated with oral aspirin 100 mg and calcium channel blocker. He occasionally forgot even important appointments hence his wife had to help him with managing daily schedule. He was always accompanied by wife when going out. He became dependent on his wife in every routine house affairs including financial one. However, he and his wife did not report any sudden memory impairment during recent 1–2 weeks. His MMSE score was 20 which is below the normal range by his age and education years. Our impression was dementia due to degenerative disease like Alzheimer's disease, but against our expectations, his DWI revealed a focal high signal in the left hippocampal body (Fig. 1-B). FLAIR and MRA images revealed moderate entorhinal cortical atrophy.

2.1.3. Patient 3 (PA3): typical DWI lesions involving left hippocampus and cingulum with typical TGA

A 62-year-old woman was referred to our memory clinic due to 4 h of anterograde amnesia which had developed 3 days previously. Her daughter reported that she had started to ask the same repeated questions after vomiting with emotional upset. The symptoms spontaneously disappeared, but she could not remember the episode. Her neurologic examination revealed no abnormal findings. However, bright dot-like lesions in the left hippocampus and cingulum were revealed in DWI (Fig. 1-C). FLAIR and MRA images were normal.

2.1.4. Patient 4 (PA4): typical DWI lesions involving bilateral hippocampi with typical TGA

A 59-year-old woman presented with an episode of witnessed, sudden-onset memory loss after shopping. Her friends' description of the event suggested that there was retrograde and anterograde amnesia with her repetitive questioning. The episode spontaneously resolved after 3 h. She was fully conscious and alert and neurological examination was normal. A clinical diagnosis of TGA was made, and DWI after 48 h showed focal restrictions in the head of the bilateral hippocampi (Fig. 1-D). The other sequences were normal.

2.1.5. Patient 5 (PA5): multiple DWI lesions including in the hippocampus and cingulum in patients with four episodes of TGA

On 05.21.2007, a 57-year-old woman with hypercholesterolemia and a moderately fatty liver visited our memory clinic with complaints of 5 h of severe anterograde amnesia occurring 9 days previously. DWI and FLAIR imaging taken at the time of visit showed no abnormal findings. On 08.27.2009, she developed a second episode of anterograde amnesia with mild retrograde amnesia for 7 h. Her husband reported that she had asked the same question repeatedly from the morning of the day. She had fully recovered, had a normal neurological examination and did not recall the event. There was no epileptiform discharge at EEG, but the DWI showed a focal restricted diffusion in the right hippocampus (Fig. 1-E1). The third attack occurred at 05.29.2012. She and her mother had argued over a trivial problem around 8:30 a.m., and she did her routine daily activities without any problem. At 8 p.m., she began to repeatedly ask the same question. The symptoms continued for about 3 h including a period when she was in the emergency department. DWI performed 48 h later showed punctuate high signals at the left cingulum and right hippocampus (Fig. 1-E2). The most recent attack occurred in the morning at 05.26.2013 after she experienced sobbing. She did not remember the reason for the crying and persisted in repeating the same questions for 7 h. DWI performed after 48 h showed dot-like high signals in the right hippocampal head and body and in the right cingulum, and revealed a decreased ADC value (Fig. 1-E3). MRA images revealed no abnormal findings.

2.2. MRI acquisition

MRI was performed at the Konkuk University Medical Center using a Magnetom Skyra 3.0 Tesla unit (GE, Erlangen, Germany) with an 8-channel high-resolution head coil. The axial DTI sequences were TR/TE, 8600/67 ms; section thickness, 3.5 mm; matrix 128 × 128; diffusion directions, 6; b-value, 1000.

2.3. DTI analysis

Raw image data were transferred in DICOM format. The DTI analyses for the patients were performed by an experienced neurologist using DTI studio software (www.mristudio.org, Johns Hopkins Medical Institute, Baltimore). For reconstructing the cingulum tract, the oval-shape