Selective verbal memory impairment due to left fornical crus injury in a patient with intraventricular hemorrhage

The fornix, a part of the Papez circuit, transfers information of episodic memory between the medial temporal lobe and the medial diencephalon (Aggleton and Brown, 1999). The right medial temporal lobe is known to be specialized for visual memory and the left medial temporal lobe for verbal memory (Tucker et al., 1988; Aggleton and Brown, 1999).

Many studies have reported on fornix injury, however, most of them focused on bilateral injury (Tucker et al., 1988; Aggleton et al., 2000; Nakayama et al., 2006; Sugiyama et al., 2007; Tsivilis et al., 2008; Wang et al., 2008; Jung et al., 2009; Chang et al., 2010; Hong and Jang, 2010; Yeo et al., 2011). To the best of our knowledge, three studies have reported on injury of the unilateral fornical crus (Tucker et al., 1988; Hong and Jang, 2010; Yeo et al., 2011). Among these studies, Tucker et al. (1988) reported on a patient who showed severe verbal memory impairment after unilateral transaction of the left fornical crus during surgery for removal of astrocytoma. Hong and Jang (2010) reported on a patient who showed selective verbal memory impairment due to left fornical crus injury, which was ascribed to diffuse axonal injury following head trauma. Subsequently, Yeo et al. (2011), who investigated the effect of intraventricular hemorrhage on white matter in 10 patients with intraventricular hemorrhage, reported on one patient with left fornical crus injury and nine patients with fornical body injury without clinical data on memory impairment, except for the Mini-Mental State Examination (MMSE). To the best of our knowledge, this is the first study which demonstrates selective verbal memory impairment due to left fornical crus injury following spontaneous intraventricular hemorrhage.

It is difficult to precisely assess the fornix due to its long, thin appearance and its location within the brain. In addition, discrimination of the whole fornix from adjacent neural structure using conventional brain CT or MRI is impossible. By contrast, diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), has enabled three-dimensional visualization of the fornix, and many studies have reported on fornix injury using DTT (Nakayama et al., 2006; Sugiyama et al., 2007; Wang et al., 2008; Jung et al., 2009; Chang et al., 2010; Hong and Jang, 2010; Yeo et al., 2011).

In the current study, using DTT, we report on a patient who showed selective verbal memory impairment due to left fornical crus injury following intraventricular hemorrhage. A 33-year-old, right-handed male underwent conservative management for spontaneous intraventricular hemorrhage in the left lateral ventricle at the department of neurosurgery in a university hospital. Brain CT at onset showed that the hematoma was mainly located on the lateral side of the left fornix (Figure 1A). One month after onset, he was transferred to the rehabilitation department of a university hospital in order to undergo rehabilitation. Cognitive function was evaluated twice (1 month and 4 months after onset) using two scales: the MMSE and the MAS (Folstein et al., 1975; Wechsler D, 1991). The MMSE (full score 30, cut-off score < 25) showed a full score of 30 at both evaluations: 1 month and 4 months after onset. At 1 month after onset, verbal memory had greater impairment than visual memory as evaluated via the MAS (global memory: 58; 1%ile, visual memory: 77; 6%ile, and verbal memory: 53; 1%ile >); in contrast, at 4 months after onset, the patient showed marked improvement of visual memory with selective impairment of verbal memory (global memory: 70; 2%ile, visual memory: 108; 70%ile, and verbal memory: 56; 1%ile >).

DTTs were acquired twice (1 month and 4 months after onset) using a 1.5-T Philips Gyroscan Intera system (Philips, Ltd, Best, the Netherlands) equipped with a Synergy-I Sensitivity Encoding (SENSE) head coil using a single-shot, spin-echo planar imaging pulse sequence. For each of the 32 non-collinear diffusion sensitizing gradients, we acquired 60 contiguous slices parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix = 96 × 96, reconstructed to matrix = 192 × 192 matrix, field of view = 240 mm × 240 mm, repetition time = 10,398 ms, echo time = 72 ms, parallel imaging reduction factor (SENSE factor) = 2, echoplanar imaging factor = 59 and b = 1,000 s/mm², number of excitations = 1, slice gap = 0 mm and thickness = 2.5 mm. Eddy current-induced image distortions were removed using affine multi-scale two-dimensional registration at the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac.uk/fsl). DTI-Studio software (CMRR, Johns Hopkins Medical Institute, Baltimore, MD, USA) was used for evaluation of the fornix. For analysis of the fornix, the seed region of interest (ROI) was drawn at the junction between the body and column of each fornix on a coronal image with the color map. Target ROIs were placed on the crus of the right and left fornix on a coronal image with the color map. Fiber tracking was started at any seed voxel with a fractional anisotropy (FA) > 0.2 and ended at a voxel with a fiber assignment of < 0.2 and a tract turning angle of < 70 degrees.

One-month DTT for the fornix showed a discontinuation of the left fornical crus, which was not observed in four male age- and sex-matched right handed normal control subjects (mean age 33.25 years (range 29–39 years)) and the discontinued left fornical crus was degenerated toward the fornical body as shown on 4-month DTT (Figure 1B). By contrast, the left fornical column was extended to the left medial temporal lobe on both 1- and 4-month DTTs.

In the current study, we reported on a patient who showed selective verbal memory impairment due to left fornical crus injury on DTT. The patient showed left fornical crus injury on both 1- and 4-month DTTs. We evaluated the patient’s cognitive function using two neuropsychological tests: the MMSE and the MAS. The MMSE is a screening test for general cognitive function by evaluating the subject’s orientation, memory, attention, calculation, visuospatial, and language abilities (Folstein et al., 1975). The MAS is a comprehensive standardized memory assessment test that yields scores for four factors: total memory, short-term memory, verbal memory, and visual memory (Williams, 1991). The patient’s general cognitive function was within normal range with a full MMSE score of 30 at both 1 and 4.
Figure 1 Brain CT and diffusion tensor tractography (DTT) images of a 33-year-old male patient with injury of the left fornical crus following intraventricular hemorrhage.

(A) Brain CT at onset showed that the hematoma was mainly located on the lateral side of the left fornix. (B) One-month DTT for the fornix of the patient showed a discontinuation (arrows) of the left fornical crus, and the discontinued left fornical crus was degenerated toward the fornical body on 4-month DTT. (C) DTT for the fornix of four male age- and sex-matched normal control subjects. R: Right; A: anterior.

months after onset. However, the patient showed impairment in both visual and verbal memory at 1 month after onset (more severe impairment in verbal memory); in contrast, at 4 months after onset, the patient showed selective verbal memory impairment with marked improvement of visual memory. Because the left medial temporal lobe is known to be specialized for verbal memory, so the patient's selective verbal memory impairment was ascribed to the left fornical crus injury (Tucker et al., 1988; Aggleton et al., 1999). The extension of the left fornical column to the left medial temporal lobe appears to be attributed to neural reorganization following injury of the left fornical crus (Yeo and Jang, 2013).

The hematoma in the present case was mainly located on the lateral side of the left fornix. Several studies have reported that periventricular neural tissue could be injured by intraventricular hemorrhage through mechanical or chemical mechanisms: (1) mechanical: following intraventricular hemorrhage, the increased intracranial pressure or direct mass effect can reduce cerebral perfusion pressure and cause secondary ischemic injury to periventricular white matter. (2) Chemical: a blood clot itself can cause extensive damage to the ependymal layer, subependymal layer, or periventricular tissues by release of potentially damaging substances, such as free iron, which may generate free radicals or inflammatory cytokines (Wasserman and Schlichter, 2008; Chua et al., 2009; Dai et al., 2009; Yeo et al., 2011). Therefore, we presumed that the left fornix crus was injured by the hematoma, although we could not determine whether the injury could be ascribed to a mechanical or chemical pathophysiological mechanism.

In conclusion, we report on a patient who showed selective
verbal memory impairment due to injury of the left fornical crus following intraventricular hemorrhage. This study is limited to a single case report. Further studies involving a larger number of patients are required.

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