Injury of the Papez circuit in a patient with traumatic spinal cord injury and concomitant mild traumatic brain injury

Little is known about brain injury in concomitant mild traumatic brain injury (TBI) following traumatic spinal cord injury (TSCI). In this study, we reported on a male patient with memory impairment who showed injury of the Papez circuit following TSCI and concomitant mild TBI. A 59-year-old male underwent posterolateral fusion on T1–L6, due to an L1 burst fracture after falling from a height of 10 meters. The patient had a T1 incomplete lesion (American Spinal Injury Association impairment scale C) and he complained of memory impairment, which was detected after transfer to the rehabilitation department. The patient met the criteria of mild TBI and showed memory impairment at 4 weeks after onset as follows: Wechsler Adult Intelligence Scale: 101 and the Memory Assessment Scale (global memory: 61 (1%ile >), short term memory: 71 (3%ile), verbal memory: 73 (4%ile), and visual memory: 66 (1%ile) (Wechsler, 1981; Williams, 1991). The study protocol was approved by the institutional review board of Yeungnam University Hospital (approval No. YUMC 2015-07-064).

Diffusion tensor imaging (DTI) has enabled diagnosis of brain injuries not detected on conventional brain MRI and has been used in diagnosis of brain injuries which were concomitant with TSCI (Wei et al., 2008). However, little is known about brain injury in concomitant mild TBI, which accounts for 70–90% of all cases of TBI, following TSCI (De Kruijff et al., 2001).

Memory impairment is a major clinical feature following mild TBI (Kurca et al., 2006). The Papez circuit, consisting of the hippocampus, fornix, mammillary body, anterior thalamic nucleus, cingulate gyrus, cingulum, and parahippocampal gyrus, is an important neural structure for memory, particularly episodic memory (Papez, 1995; Markowitsch, 1997). DTI has enabled diagnosis of brain injuries not detected on conventional brain MRI and has been used in diagnosis of brain injuries which were concomitant with TSCI (Wei et al., 2008). However, little is known about brain injury in concomitant mild TBI, which accounts for 70–90% of all cases of TBI, following TSCI (De Kruijff et al., 2001).

In this study, we reported on a patient with memory impairment who showed injury of the Papez circuit was detected on DTI following TSCI and concomitant mild TBI. A 59-year-old male who suffered an L1 burst fracture after falling from a height of 10 meters while driving a car underwent posterolateral fusion on T1–L6, with regional autograft bone and allograft bone at the neurosurgery department of a university hospital. After 2 weeks from onset, he was transferred to the rehabilitation department of the same hospital to undergo rehabilitation. The patient had a T1 incomplete lesion (American Spinal Injury Association impairment scale C) and he complained of memory impairment, which was detected after transfer to the rehabilitation department. The patient met the criteria of mild TBI: loss of consciousness - 2 minutes, post-traumatic amnesia - approximately 4 minutes, Glasgow Coma Scale score - 15, and no specific lesion on conventional brain MRI performed at 4 weeks after onset (Figure 1A) (Alexander, 1995). The patient showed memory impairment at 4 weeks after onset: Wechsler Adult Intelligence Scale: 101 and the Memory Assessment Scale (global memory: 61 (1%ile >), short term memory: 71 (3%ile), verbal memory: 73 (4%ile), and visual memory: 66 (1%ile) (Wechsler, 1981; Williams, 1991). The study protocol was approved by the institutional review board of Yeungnam University Hospital (approval No. YUMC 2015-07-064).

DTI data were acquired at 4 weeks after onset using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips, Ltd., Best, The Netherlands) with single-shot echo-planar imaging. For each of the 32 non-collinear diffusion sensitizing gradients, 70 contiguous slices were acquired parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm2; repetition time = 10,398 ms; echo time = 72 ms; parallel imaging reduction factor = 2; b = 1,000 s/mm2; and a slice thickness of 2.5 mm. The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRI) Software Library was used to analyze DTI data with routine options (0.5 mm step lengths, 5,000 streamline samples, curvature thresholds = 0.2). Prior to the fiber tracking, eddy current correction was applied to correct the head motion effect and image distortion using FMRI Software Library.

Figure 1: Brain MRI imaging and diffusion tensor tractography for a 59-year-old male patient with traumatic spinal cord injury and concomitant mild traumatic brain injury.

(A) T2-weighted brain magnetic resonance images at 4 weeks after onset show no abnormality. (B) Results of diffusion tensor tractography for each neural tract of the Papez circuit: the entire Papez circuit, including thalamocortical tract (green), cingulum (sky-blue), fornix (red), and mammillothalamic tract (blue), was well reconstructed, except for the left thalamocortical tract (red arrow) and the mammillothalamic tract (purple arrow), which were thinner compared to a normal control subject (61-year-old male). (C) Diffusion tensor tractography for the Papez circuit in a normal control subject (61-year-old male). R: Right, A: anterior.
Each neural tract of the Papez circuit was determined by selecting fibers passing through seed and target regions of interest (ROIs) as follows (Concha et al., 2005; Kwon et al., 2010; Jang and Yeo, 2013): thalamocortical tract: seed ROI - the cingulate gyrus, target ROI 1 - anterior limb of the internal capsule, target ROI 2 anterior thalamic nuclei; fornix: seed ROI - mammillary body, target ROI - crus of the fornix; mammillothalamic tract: seed ROI-anterior thalamic nucleus; target ROI 1 - portion of isolated mammillothalamic tract, target ROI 2 - mammillary body; cingulum: seed ROI - middle portion of the cingulum, target ROI - posterior portion of the cingulum.

On 4-week DTT, the entire Papez circuit including the thalamocortical tract, fornix, mammillothalamic tract, and cingulum was reconstructed in both hemispheres except for the left thalamocortical tract between the anterior thalamic nuclei and cingulated gyrus, and the right mammillothalamic tract between the mammillary body and anterior thalamic nuclei, which were thinner compared with the opposite side and a normal control subject (61-year-old male) (Figure 1B).

In this study, DTT findings of the neural tracts of the Papez circuit were investigated in a patient with TSCI who suffered from concomitant mild TBI. Injuries of the left thalamocortical tract were found between the anterior thalamic nuclei and cingulated gyrus and the right mammillothalamic tract between the mammillary body and anterior thalamic nuclei. Because no definite brain lesion was detected on conventional brain MRI, traumatic axonal injury was the most likely pathogenetic mechanism for the injury of the Papez circuit (Alexander, 1995; Povlishock and Christman, 1995). This patient showed severe memory impairment, even though whole cognition in terms of the Wechsler Adult Intelligence Scale was within normal range. As a result, severe memory impairment of this patient appeared to be ascribed, at least in part, to injury of the Papez circuit. Our result suggests the importance of evaluation of the Papez circuit in patients complaining of memory impairment following TSCI, particularly mild TBI which does not show a definite brain lesion on conventional MRI, like in this patient.

Since the introduction of DTT, to the best of our knowledge, only one study reported on concomitant brain injury in patients with TSCI, using DTI (Wei et al., 2008). In 2008, Wei et al. evaluated the white matter using ROI method in seven patients with definite structural brain lesions on conventional MRI and found that fractional anisotropy was reduced in the same portion (genu and splenium) of the corpus callosum. As a result, this is the first study to demonstrate anisotropy was reduced in the same portion (genu and splenium) of white matter using ROI method in seven patients with definite structural brain lesion on conventional MRI, like in this patient.

In conclusion, injury of the Papez circuit was demonstrated in a patient with TSCI who had suffered from concomitant mild TBI, using DTT. In this patient, injury of the Papez circuit appeared to be related to memory impairment. Therefore, evaluation of the Papez circuit using DTT would be helpful in patients with concomitant mild TBI who show memory impairment following TSCI.

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP), No. NRF-2015R1A2A2A01004073.

Sung Ho Jang, Hyeok Gyu Kwon
Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Daemyungdong, Namku, Daegu, Republic of Korea (Jang SH)
Department of Physical Therapy, College of Health Sciences, Catholic University of Pusan, Pusan, Republic of Korea (Kwon HG)

Correspondence: Hyeok Gyu Kwon, Ph.D., MS6715@hanmail.net.

doi: 10.4103/1673-5374.224384

Author contributions: SHJ was responsible for research design and data acquisition. HGK was in charge of conception and design of this study, acquisition and analysis of data, and manuscript authorization. Both of these two authors approved the final version of this paper.

Conflicts of interest: The authors report no disclosures relevant to the manuscript.

Research ethics: All subjects provided informed consent for participation and the study was approved by the institutional review board of Yeungnam University Hospital (approval No. YUMC 2015-07-064). The study followed the Declaration of Helsinki and relevant ethical principles.

Declaration of participant consent: The authors certify that they have obtained the appropriate participant consent forms. In the forms, participants have given their consent for their images and other clinical information to be reported in the journal. Participants understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Data sharing statement: Datasets analyzed during the current study are available from the corresponding author on reasonable request.

Plagiarism check: Checked twice by iThenticate.

Peer review: Externally peer reviewed.

Open access statement: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under identical terms.

References
Alexander MP (1995) Mild traumatic brain injury: pathophysiology, natural history, and clinical management. Neurology 45:1253-1260.
Concha L, Gross DW, Beaulieu C (2005) Diffusion tensor tractography of the limbic system. AJNR Am J Neuroradiol 26:2267-2274.
Davidoff G, Thomas P, Johnson M, Berent S, Dijkers M, Doljanac R (1988) Closed head injury in acute traumatic spinal cord injury: incidence and risk factors. Arch Phys Med Rehabil 69:869-872.
De Kruijf JR, Twinstra A, Leffers P (2001) Diagnostic criteria and differential diagnosis of mild traumatic brain injury. Brain Inj 15:99-106.
Jang SH, Yeo SS (2013) Thalamocortical tract between anterior thalamic nuclei and cingulated gyrus in the human brain: diffusion tensor tractography study. Brain Imaging Behav 7:236-241.
Kurca E, Sivak S, Kucera P (2006) Impaired cognitive functions in mild traumatic brain injury patients with normal and pathologic magnetic resonance imaging. Neuroradiology 48:46-56.
Kwon HG, Hong JH, Jang SH (2010) Mammillothalamic tract in human brain: diffusion tensor tractography study. Neurosci Lett 481:51-53.
Lee HD, Jang SH (2014) Changes of an injured fornix in a patient with mild traumatic brain injury: diffusion tensor tractography follow-up study. Brain Inj 28:1485-1488.
Markovitsch HJ (1997) Varieties of memory: Systems, structures, mechanisms of disturbance. Neurol Psychiatry Brain Res 3:57-56.
Niogi SN, Mukherjee P, Ghaier J, Johnson CE, Kobister R, Lee H, Suh M, Zimmermann RD, Manley GT, Candellius BD (2008) Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury. Brain 131:3209-3221.
Papez JW (1995) A proposed mechanism of emotion. 1937. J Neuropsychiatry Clin Neurosci 7:103-112.
Parker GJ, Alexander DC (2005) Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue. Philos Trans R Soc Lond B Biol Sci 360:893-902.
Povlishock JT, Christman CW (1995) The pathobiology of traumatically induced axonal injury in animals and humans: a review of current thoughts. J Neurotrauma 12:555-564.
Richards JS, Brown L, Hagglund K, Bua G, Reeder K (1988) Spinal cord injury to identify concomitant traumatic brain injury. Results of a longitudinal investigation. Am J Phys Med Rehabil 67:211-216.
Weichert D (1981) Manual for the wechsler adult intelligence scale-revised. New York: Psychological Corporation.
Wei CW, Tharmakulasingam I, Cridelley A, Kideckel DM, Mikulis DJ, Bradbury CL, Green RE (2008) Use of diffusion-tensor imaging in traumatic spinal cord injury to identify concomitant traumatic brain injury. Arch Phys Med Rehabil 89:S85-91.
Williams JM (1991) MAS: Memory Assessment Scales: professional manual. Williams, FL: Psychological Assessment Resources.
Yang DS, Kwon HG, Jang SH (2016) Injury of the thalamocingulate tract in the Papez circuit in patients with mild traumatic brain injury. Am J Phys Med Rehabil 95:34-38.