



Injury of the prefronto-caudate tract in a patient with apathy following intracerebral hemorrhage in the caudate nucleus

Sung Ho Jang¹ · Seong Ho Kim² · Hyeok Gyu Kwon³

Received: 5 December 2018 / Accepted: 7 January 2019
© Belgian Neurological Society 2019

Introduction

The caudate nucleus (CN), as a part of the basal ganglia, interconnects with the prefrontal cortex (PFC), temporal cortex, frontal eye field, and cerebellum. These connections are involved in motor and cognitive functions [1]. Specifically, the prefronto-caudate tract is involved in apathy, anxiety, depression, and disinhibition [2]. Apathy is classically defined as a lack of feeling, emotion, interest and concern, and clinically presents as the absence of motivation, voluntary movement or speech [3]. Injury of the CN, PFC, or the prefronto-caudate tract in particular, connected to the medial PFC, and orbito-frontal cortex (OFC) is related to apathy [4, 5].

Diffusion tensor tractography (DTT), a three-dimensional imaging tool, is based on diffusion tensor imaging (DTI). This technique measures characteristics of water diffusion in brain tissue, allowing assessment of the state of neural connectivity [6]. Probabilistic DTT, that reflects the distribution of underlying fiber structure, is widely used for researching the neural connectivity of neural structures in the human brain. Several studies have investigated the prefronto-basal ganglia circuit including the prefronto-caudate tract in patients with schizophrenia, attention-deficit/hyperactivity

disorder, and major depressive disorder [7–10]. However, little is known on this topic in patients with intracerebral hemorrhage (ICH).

In this study, we report on a patient with apathy in whom injury of the prefronto-caudate tract was detected on DTT following ICH in the caudate nucleus.

Case report

A 55-year-old male underwent extraventricular drainage (both prefrontal approaches) for intraventricular hemorrhage at the neurology department of a university hospital (Fig. 1a). A brain CT at that time also showed ICH in the right CN (Fig. 1a). At 8 months after the drainage procedure, he was admitted to the rehabilitation department of the same university hospital because he was not significantly recovering cognition and gait despite rehabilitation at a local rehabilitation hospital beginning 3 weeks after the drainage. The patient showed severe apathy (Apathy Scale score: 21 [full score: 42]). Brain MR images taken at 8 months after the ICH showed leukomalactic lesions in the right CN (Fig. 1b). The patient's daughter provided signed, informed consent, and our institutional review board approved the study protocol.

DTI data were acquired at 9 months after the ICH using a six-channel head coil on a 1.5 T (Philips, Ltd., Best, the Netherlands) with 32 gradients. 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, $b = 1000$ s/mm², and a slice thickness of 2.5 mm. Head motion effect and image distortion due to eddy current were corrected by affine multi-scale two-dimensional registration. Fiber tracking was performed with the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Diffusion Software with the default tractography option. For analysis of the CN, the seed region of interest was given at the CN that was isolated using adjacent structures (medial boundary: the lateral ventricle;

✉ Hyeok Gyu Kwon
khg0715@hanmail.net

Sung Ho Jang
strokerehab@hanmail.net

Seong Ho Kim
shkim@medical.yeungnam.ac.kr

¹ Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Gyeongsan, Republic of Korea

² Department of Neurosurgery, College of Medicine, Yeungnam University, Gyeongsan, Republic of Korea

³ Department of Physical Therapy, College of Health Sciences, Catholic University of Pusan, 57 Oryundae-ro, Geumjeong-gu, Pusan 46252, Republic of Korea

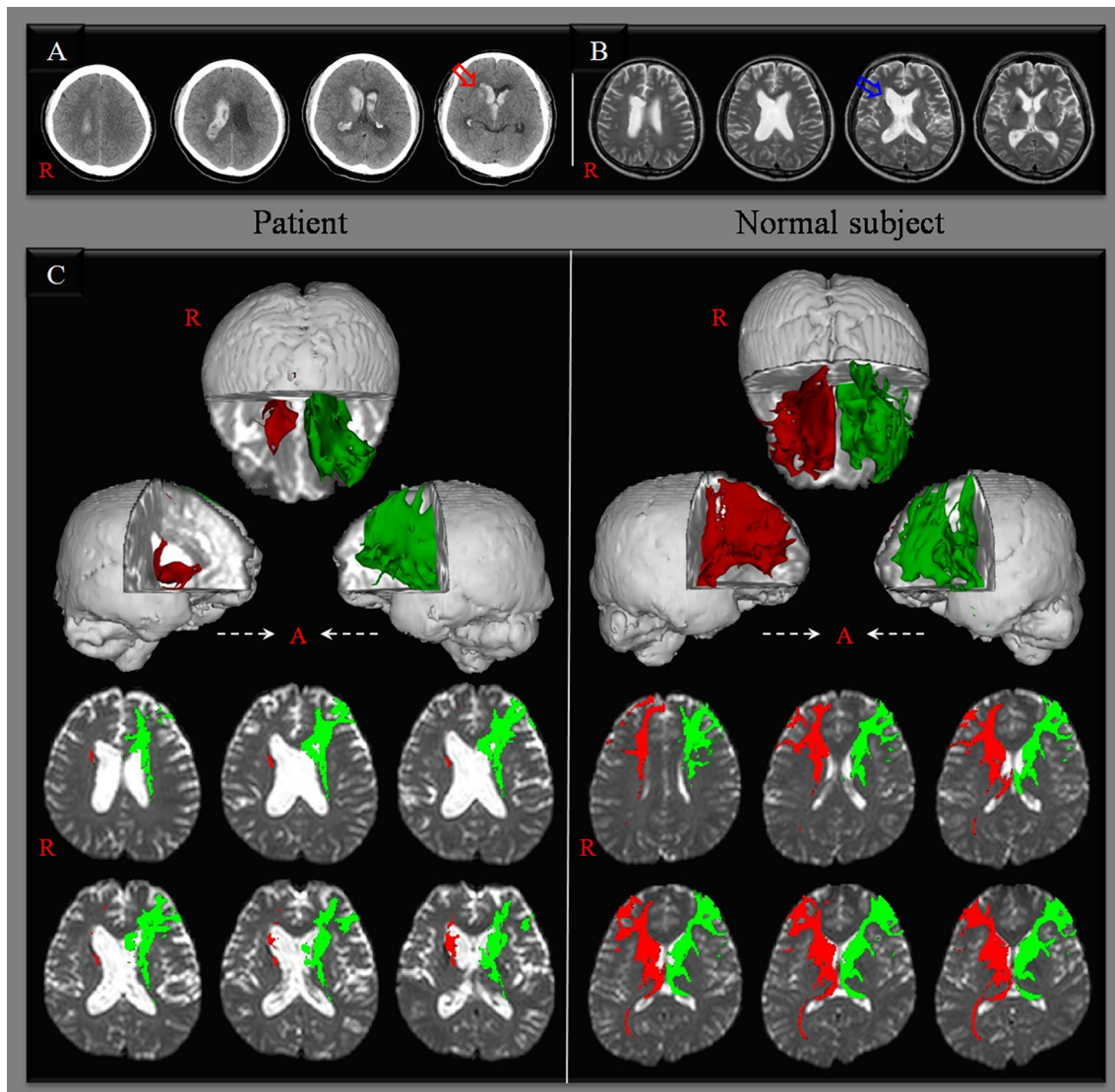


Fig. 1 **a** Brain CT at onset shows intracerebral hemorrhage in the right caudate nucleus (CN) (red arrow). **b** Brain MRI shows leukomalacic lesion in the right CN (blue arrow) at 8 months after onset. **c**

The neural connectivity of the CN to the prefrontal cortex including the medial prefrontal cortex and orbitofrontal cortex is decreased in the right hemisphere. (Color figure online)

lateral boundary: the anterior limb of the internal capsule). The threshold of 10 streamlines was applied for the results of fiber tracking.

The neural connectivity of the CN to the PFC including the medial PFC (Brodmann area [BA]: 10 and 12) and OFC (BA: 11 and 13) was decreased in the right hemisphere (Fig. 1c).

Discussion

In the current study, injury of the prefronto-caudate tract in a patient with apathy following ICH in a caudate nucleus was demonstrated by DTT. We found injury of the prefronto-caudate tract. In detail, connectivity of the CN

to the medial PFC and OFC was injured in the right hemisphere (lesion side). We believed that ICH on the CN was attributed to injury of the prefronto-caudate tract (medial PFC) and contributed to the patient's apathy. Many studies report lesions on the CN in patients with apathy using conventional CT or MRI [2, 4, 5, 11–14., 4, 5, 11–14]. Bathia and Marsden reported that 28% of patients with a CN lesion lacked initiative and voluntary behavior [5]. In 1997, Bokura and Robinson found that 6 of 21 patients with a CN lesion showed a lack of motivation [13]. These studies were compatible with our results. Thus, our results suggest the importance of evaluation for the connectivity of the CN to the PFC in patients with apathy following ICH in the CN.

Using DTT, a few studies have reported on injury of the prefronto-caudate tract in patients with schizophrenia, attention-deficit/hyperactivity disorder, and major depressive disorder [7–10]. Only one DTT study has reported on apathy associated with injury of the prefronto-caudate tract in a patient with mild traumatic brain injury [15]. In 2017, Jang and Kwon demonstrated that aggravation of apathy in a patient was associated with worsening injury of the prefronto-caudate tract particularly medial PFC and OFC in both hemispheres following mild traumatic brain injury using follow-up DTTs [15]. To the best of our knowledge, this is the first study to prove injury of the prefronto-caudate tract in patients with ICH. However, the limitations of this study should be considered. First, because it is a case report, this study is limited. Second, we could not examine associations between the severity of apathy and injury of the prefronto-caudate tract. Third, probabilistic DTT can produce both false-positive and -negative results due to multiple fiber orientations in a voxel. Therefore, we suggest further studies involving large numbers of patients and overcoming the limitations of DTT.

In conclusion, injury of the prefronto-caudate tract in a patient who developed severe apathy following ICH was demonstrated by DTT. We believe that analysis of the prefronto-caudate tract using DTT would be useful in understanding the causes of apathy after ICH.

Acknowledgements This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean Government (MSIP) (No. 2018R1A2B6000996).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard The authors declare that they acted in accordance with ethical standards laid down in the 1964 Declaration of Helsinki.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Herrero MT, Barcia C, Navarro JM (2002) Functional anatomy of thalamus and basal ganglia. *Childs Nerv Syst* 18(8):386–404. <https://doi.org/10.1007/s00381-002-0604-1>
- Mendez MF, Adams NL, Lewandowski KS (1989) Neurobehavioral changes associated with caudate lesions. *Neurology* 39(3):349–354
- Marin RS (1996) Apathy: concept, syndrome, neural mechanisms, and treatment. *Semin Clin Neuropsychiatry* 1(4):304–314. <https://doi.org/10.1053/SCNP00100304>
- Caplan LR, Schmammann JD, Kase CS, Feldmann E, Baquis G, Greenberg JP, Gorelick PB, Helgason C, Hier DB (1990) Caudate infarcts. *Arch Neurol* 47(2):133–143
- Bhatia KP, Marsden CD (1994) The behavioural and motor consequences of focal lesions of the basal ganglia in man. *Brain* 117(4):859–876
- Behrens TE, Berg HJ, Jbabdi S, Rushworth MF, Woolrich MW (2007) Probabilistic diffusion tractography with multiple fibre orientations: what can we gain? *Neuroimage* 34(1):144–155. <https://doi.org/10.1016/j.neuroimage.2006.09.018>
- Rose SE, Chalk JB, Janke AL, Strudwick MW, Windus LC, Hannah DE, McGrath JJ, Pantelis C, Wood SJ, Mowry BJ (2006) Evidence of altered prefrontal-thalamic circuitry in schizophrenia: an optimized diffusion MRI study. *Neuroimage* 32(1):16–22. <https://doi.org/10.1016/j.neuroimage.2006.03.003>
- Casey BJ, Epstein JN, Buhle J, Liston C, Davidson MC, Tonev ST, Spicer J, Niogi S, Millner AJ, Reiss A, Garrett A, Hinshaw SP, Greenhill LL, Shafritz KM, Vitolo A, Kotler LA, Jarrett MA, Glover G (2007) Frontostriatal connectivity and its role in cognitive control in parent-child dyads with ADHD. *Am J Psychiatry* 164(11):1729–1736. <https://doi.org/10.1176/appi.ajp.2007.06101754>
- Swahen LJ, Hartman CA, Zwiers MP, Heslenfeld DJ, Franke B, Oosterlaan J, Buitelaar JK, Hoekstra PJ (2016) Stimulant treatment history predicts frontal-striatal structural connectivity in adolescents with attention-deficit/hyperactivity disorder. *Eur Neuropsychopharmacol* 26(4):674–683. <https://doi.org/10.1016/j.euroneuro.2016.02.007>
- Myung W, Han CE, Fava M, Mischoulon D, Papakostas GI, Heo JY, Kim KW, Kim ST, Kim DJ, Kim DK, Seo SW, Seong JK, Jeon HJ (2016) Reduced frontal-subcortical white matter connectivity in association with suicidal ideation in major depressive disorder. *Transl Psychiatry* 6(6):e835. <https://doi.org/10.1038/tp.2016.110>
- Trillet M, Croisile B, Tourniaire D, Schott B (1990) Disorders of voluntary motor activity and lesions of caudate nuclei. *Rev Neurol (Paris)* 146(5):338–344
- Owen AM, Doyon J, Petrides M, Evans AC (1996) Planning and spatial working memory: a positron emission tomography study in humans. *Eur J Neurosci* 8(2):353–364
- Bokura H, Robinson RG (1997) Long-term cognitive impairment associated with caudate stroke. *Stroke* 28(5):970–975
- Fukuoka T, Osawa A, Ohe Y, Deguchi I, Maeshima S, Tanahashi N (2012) Bilateral caudate nucleus infarction associated with a missing A1 segment. *J Stroke Cerebrovasc Dis* 21(8):908 e911–902. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2011.09.022>
- Jang SH, Kwon HG (2017) Apathy due to injury of the prefronto-caudate tract following mild traumatic brain injury. *Am J Phys Med Rehabil* 96(7):130–133. <https://doi.org/10.1097/PHM.0000000000000630>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.