Case Report

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Complex striate-frontal projection and specific frontal gyrus dysfunctions concern with the delusional misidentification syndrome: A case report and literature review

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Abstract

Delusional misidentification, a rare syndrome in which a patient displays persistent delusional misidentification of individuals or objects, occurs in several types of dementia. However, the pathology of delusional misidentification is still unclear, and there was no data pertaining to striate-frontal projection. Here, we report a case of delusional misidentification following frontotemporal dementia in which complex striate-frontal and some specific frontal gyrus dysfunction were observed. In our presented case, delusional misidentification progressed following frontal atrophy. Believing that her actual daughter had been replaced by her niece, her symptoms of delusional misidentification and frontal atrophy progressed in the short term, and social arrangement was necessary three months after the onset. There were no abnormal neurological findings including parkinsonism and general cognitive function test scores were preserved. Validated by dopamine transporter single-photon emission computed tomography, right unilateral striatal uptake decreased significantly without parkinsonism or Parkinson's disease. In addition, of specific concern, functional magnetic resonance images showed left opercular inferior frontal gyrus and

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right superior frontal gyrus dysfunctions. Our case study highlights complex striate-frontal projection and specific frontal gyrus dysfunctions associated with the pathology of delusional misidentification syndrome.

Keywords
Delusional misidentification, fMRI, DAT, opercular inferior frontal gyrus, superior frontal gyrus, striate-frontal

Introduction

Delusional misidentification is a class of syndrome in which a patient displays persistent delusional misidentification of individuals or objects.[1] Delusional misidentification occurs not only in psychosis, especially in schizophrenia, but also in particular cases of dementia, such as Alzheimer's disease, dementia with Lewy bodies (DLB) and frontotemporal dementia (FTD).[2] Several types of dementia can induce delusional misidentification, albeit at a very rare occurrence, suggesting that specific functional abnormalities, rather than specific pathological abnormalities, are associated with this syndrome. Recent studies using functional magnetic resonance imaging (fMRI) support this pathological hypothesis,[1,3] although there is a lack of data to support the pathology of delusional misidentification. Here, we report a case of delusional misidentification following FTD in which complex striate-frontal, and some specific frontal gyrus dysfunction, were observed.

Case report

A right-handed Japanese woman in her late 70s progressively showed forgetfulness, leading to the misidentification of individuals. She believed that her actual daughter had been replaced by her niece. During the examination period, her husband died suddenly due to acute myocardial infarction. However, she was unable to recognize her husband's death. There was no personal or familial neurological or psychiatric history. She worked as a cleaning staff before the appearance of symptoms but was unable to keep working 3 months after the onset of symptoms, which progressively worsened. In April 2023, she was admitted to the Division of Neurology, Department of Medicine, Jichi Medical University, Shimotsuke, in Japan, one year after the onset.

There were no abnormal neurological findings, including parkinsonism. General cognitive function test scores were preserved, her Mini-Mental State Examination[4] score was 26/30, the Revised Hasegawa Dementia Scale[4] was 22/30 and the Frontal Assessment Battery[5] was 12/18. However, the full-scale intelligence quotient of the Wechsler Adult Intelligence Scale-IV[6] was 73 (composite score). The facial recognition part of the Visual Perception Test for Agnosia was 15/16 in famous people and 6/6 in familial people, which indicates that almost all of her answers were incorrect.[7] The Behavioral Inattention Test[8] was 94/146 in the usual examination part (normal cutoff ≤ 131) and 59/81 in the behavioral examination part (normal cutoff ≤ 68).

There were no remarkable findings in the hematological, biochemical and cerebrospinal flood analyses were unremarkable. Cranial MRI identified severe frontal lobe

atrophy, which was more evident in the right lobe (Figure 1A and B). Single-photon emission computed tomography with ^{123}I-N-isopropyl-p-iodoamphetamine single-photon emission computed tomography (^{123}I-IMP SPECT) showed a decrease in cerebral blood flow (CBF) in the vast majority of the right frontal area, in certain lesions of the right temporal lobe and in the left opercular inferior frontal gyrus (Figure 1C). Dopamine transporter (DAT) SPECT imaging using ^{123}I-ioflupane showed a significantly reduced value of the right specific binding ratio (SBR) (Figure 1D). In contrast, iodine-131-labeled metaiodobenzylguanidine scintigraphy showed a completely normal range of values (Figure 1E). The patient was diagnosed as having a clinical and imaging-supported behavioral variant FTD with delusional misidentification.[9]

In addition, fMRI was performed using a previously established method[10] to analyze her delusional misidentification pathology, and two types of analyses were conducted after preprocessing. Regions of interest identified from contrasts were used to compute psychophysiological interactions.[11] Details of the fMRI method are described in the Supplement. During the fMRI session, the patient was presented with two photographs in a randomized sequence. These depicted the same individual (her daughter or niece), or two different individuals. She was then required to determine whether the images represented the same person (Figure 2A). We analyzed the fMRI contrast among three conditions: 'false identification', 'correct identification' and 'correct differentiation'. We defined the fMRI contrast between 'false identification' versus 'correct identification' as contrast no. 1. This contrast focused on the difference in stimulus when presented with different pairs of individuals and reflects the input system of human identification. We defined the fMRI contrast between 'false identification' versus 'correct differentiation' as contrast no. 2. This contrast focused on the difference in response when viewing a different pair of individuals, reflecting the output system of human identification. The number of each response is shown in Figure 2B. The fMRI analysis of contrast no. 1 revealed higher changes in activity in the left middle temporal gyrus and bilateral angular gyrus during false identification compared to correct identification. Additionally, these areas were functionally connected to the left opercular inferior frontal gyrus (Figure 2C), where CBF decreased in ^{123}I-IMP SPECT. The fMRI analysis of contrast no. 2 showed increased bilateral precuneus activity during false identification compared to correct differentiation. These areas were functionally connected to the areas associated with visual perception and the right superior frontal gyrus (Figure 2D), where CBF decreased in ^{123}I-IMP SPECT.

After diagnosis, she has been living in the nurse home maintaining her daily activity while receiving a major tranquilizer (quetiapine fumarate; 50 mg per day) for over a year. Detailed of her clinical information is written in the Supplemental Manuscript. The reporting of this study conforms to CARE guidelines.[12] The patient data have been de-identified, and written informed consents both to publish and related to treatment were obtained from the patient and her family.

Discussion

Our case of FTD with delusional misidentification, validated by DAT SPECT and fMRI, revealed two important results: (1) right unilateral striatal DAT uptake decreased

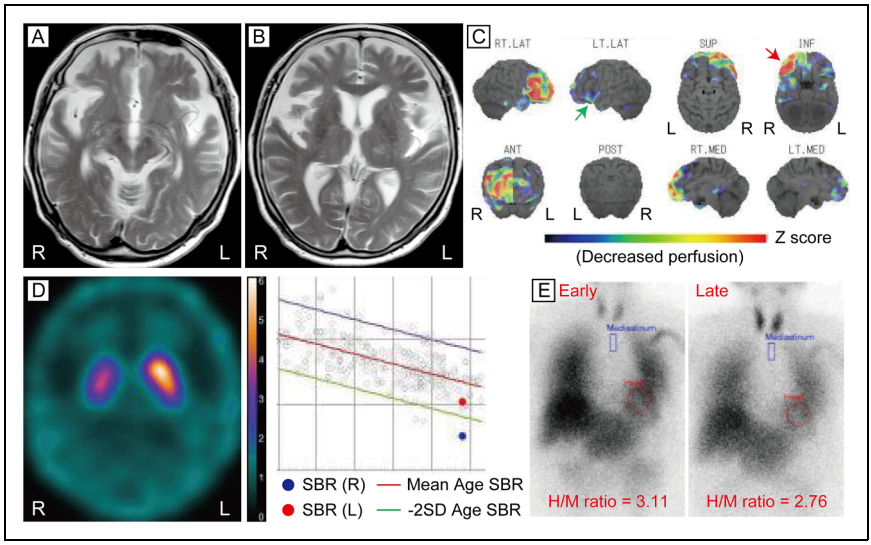

Figure 1. (A and B) Magnetic resonance imaging (MRI) T2 weighted images of the frontal lobe showing severe frontal lobe atrophy, which was more evident in the right lobe. (C) ^{123}I-IMP SPECT and three dimensional-stereotactic surface projection (3DSSP) analysis showing a decrease in cerebral blood flow (CBF) in the vast majority of the right frontal area, including the superior frontal gyrus (red arrow), in certain lesions of right temporal lobe, and in the left opercular inferior frontal gyrus (green arrow). (D) Dopamine transporter (DAT) SPECT imaging using ^{123}I-ioflupane showing a significantly lower right specific binding ratio (SBR), but (E) normal iodine-131-labeled metaiodobenzylguanidine (^{131}I-MIBG) scintigraphy results.

significantly; (2) dysfunction of the left opercular inferior frontal gyrus and the right superior frontal gyrus was involved. Figure 3 depicts these pathological relationships.

Delusional misidentification is commonly observed in psychotic disorders such as schizophrenia.[13] However, there are unknown factors, such as long-term side effects of drug use, and the prevalence of psychosis itself remains uncertain.[13,14] Therefore, in this study, the pathology of delusional misidentification focused on dementia. Two previous studies attempted to clarify the reasons for delusional misidentification, both of them suggesting concerns with the right frontal gyrus[3,15] which corresponds to our result of precuneus to right superior frontal gyrus connectivity involving when human misidentification occurs (Figure 2D). Frontal lesions were associated with about 34.5% of cases of human misidentification, and FTD is a major neurodegenerative disease.[2] In contrast, most FTD patients do not misidentify humans throughout their lives, suggesting that frontal dysfunction is not the exclusive cause of human misidentification. Although right frontal lobe atrophy and dysfunction were evident in our case (Figure 1A-C), we emphasize that CBF of the left opercular inferior frontal gyrus decreased (Figure 1C, green arrow), corresponding to fMRI contrast no. 1 (Figure 2C).

Based on the relationship between the striatum dopamine system and delusional misidentification, there are only a few studies[16] that contradict our expectation, noting that

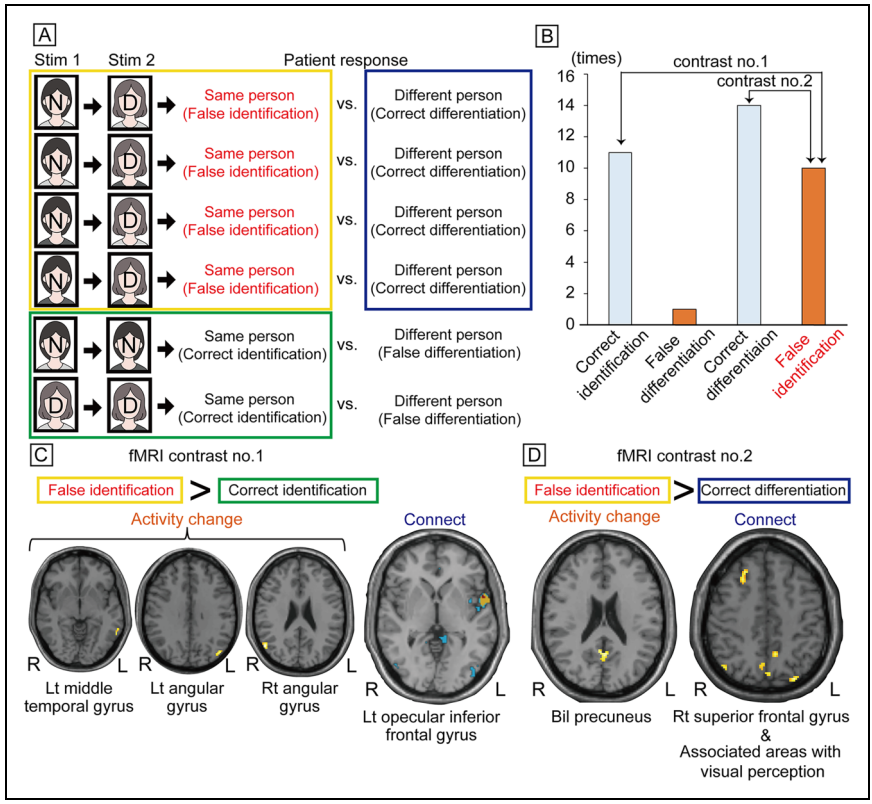

Figure 2. (A) Functional magnetic resonance imaging (fMRI) test design and (B) task results. 'False identification' occurred when the patient viewed a pair of different individuals and incorrectly identified them as the same person, 'correct identification' is when the patient viewed a pair of images of the same individual and correctly identified them as the same person, and 'correct differentiation' is when the patient viewed a pair of different individuals and correctly identified them as different persons. Results of fMRI (C) contrast no. 1 and (D) contrast no. 2. According to contrast no. 2, in addition to the right superior frontal gyrus, the bilateral middle occipital gyrus and right lingual gyrus were also involved. However, bilateral precuneus, bilateral middle occipital gyrus and right lingual gyrus were also associated with visual perception, while only the right superior frontal gyrus was not involved in visual perception.

DLB is the most causative dementia-related disease causing delusional misidentification.[17] We emphasize that right unilateral striatal DAT uptake decreased considerably, although there was no evident α-synucleinopathy (Figure 1E). We speculate that concern with striatum-cortex rather than with the substantia nigra-striatum is associated with the pathology of delusional misidentification.[18,19] It is possible that striatum-cortex disturbances influence DAT expression in the striatum without any clinical signs of Parkinsonism or α-synucleinopathy, resulting in a remarkable decrease in right SBR uptake.[20] Additional cases of delusional misidentification need to be studied using DAT SPECT.

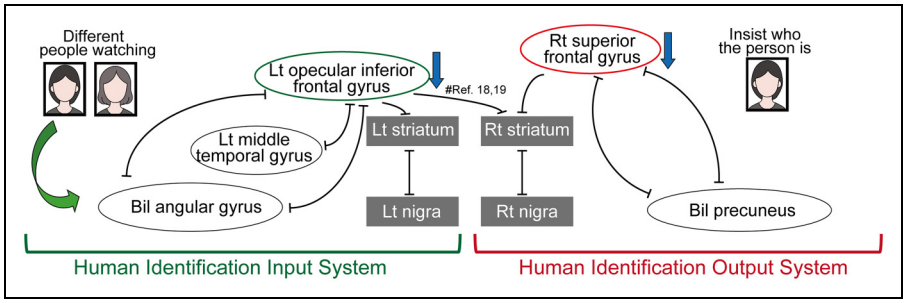

Figure 3. Pathological diagram. The left side of this figure illustrates the human identification input system, while the right side depicts the output system. In the input system, activity in the left middle temporal gyrus and bilateral angular gyrus changes. These areas are connected to the left opercular inferior frontal gyrus. In the output system, there is a change in the activity of the bilateral precuneus, which is connected to the right superior frontal gyrus. Notably, cerebral blood flow (CBF) decreased in both the left opercular inferior frontal gyrus and the right superior frontal gyrus. According to the striatum-cortex connections, the left opercular inferior frontal gyrus connects bilaterally to the striatum, whereas the right superior frontal gyrus connects unilaterally to the right striatum.[18,19] Right specific binding ratio (SBR) decreased dramatically in this case.

Conclusion

In summary, our case study shows complex striate-frontal projection and specific frontal gyrus dysfunctions associated with the pathology of delusional misidentification syndrome.

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Authors' contributions

Kosuke Matsuzono, Kyoko Otsuka and Honoka Hiki were the case's attending doctors. Yoshiyuki Onuki performed and analyzed fMRI. Kosuke Matsuzono drafted the manuscript. Yuhei Anan, Takafumi Mashiko, Reiji Koide, Naoto Kunii, and Kensuke Kawai helped to draft the manuscript. Shigeru Fujimoto conceived the study and participated in its coordination. All authors read and approved the final manuscript.

Availability of data and materials

All data generated or analyzed during this presented case are included within this article. Any other identifying information related to the authors and/or their institutions, funders, approval committees, etc., that might compromise anonymity: Not applicable.

Consent to participate

Written informed consent was obtained from the patient and her daughter for this study.

Consent for publication

For this study, photos and writing of our manuscript, the patient and her daughter have given their written informed consent.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

All procedures were performed in accordance with The Ethical Committees of Jichi Medical University and were exempt from approval from the institutional review board based on our guidelines (approval #Rin-Dai 22-009), and with the principles of the 1964 Declaration of Helsinki.

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Supplemental material

Supplemental material for this article is available online.

References

1. Devinsky O. Delusional misidentifications and duplications: right brain lesions, left brain delusions. *Neurology* 2009; 72: 80–87.
2. Cipriani G, Vedovello M, Ulivi M, et al. Delusional misidentification syndromes and dementia: a border zone between neurology and psychiatry. *Am J Alzheimers Dis Other Demen* 2013; 28: 671–678.
3. Darby RR, Laganiere S, Pascual-Leone A, et al. Finding the imposter: brain connectivity of lesions causing delusional misidentifications. *Brain* 2017; 140: 497–507.
4. Kim KW, Lee DY, Jhoo JH, et al. Diagnostic accuracy of mini-mental status examination and revised Hasegawa Dementia Scale for Alzheimer's disease. *Dement Geriatr Cogn Disord* 2005; 19: 324–330.
5. Dubois B, Slachevsky A, Litvan I, et al. The FAB: a frontal assessment battery at bedside. *Neurology* 2000; 55: 1621–1626.
6. Benson N, Hulac DM and Kranzler JH. Independent examination of the Wechsler Adult Intelligence Scale-Fourth edition (WAIS-IV): what does the WAIS-IV measure? *Neurology* 2000; 55: 1621–1626.
7. Wada Y and Yamamoto T. Selective impairment of facial recognition due to a haematoma restricted to the right fusiform and lateral occipital region. *J Neurol Neurosurg Psychiatry* 2001; 71: 254–257.
8. Hartman-Maeir A and Katz N. Validity of the behavioral inattention test (BIT): relationships with functional tasks. *Neurology* 2000; 55: 1621–1626.

9. Rascovsky K, Hodges JR, Knopman D, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011; 134: 2456–2477.
10. Van Essen DC, Smith SM, Barch DM, et al. The WU-Minn human connectome project: an overview. *Neuroimage* 2013; 80: 62–79.
11. Friston KJ, Buechel C, Fink GR, et al. Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage* 1997; 6: 218–229.
12. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.
13. Karakasi MV, Markopoulou M, Alexandri M, et al. In fear of the most loved ones. A comprehensive review on Capgras misidentification phenomenon and case report involving attempted murder under Capgras syndrome in a relapse of a schizophrenia spectrum disorder. *J Forensic Leg Med* 2019; 66: 8–24.
14. Odom-White A, de Leon J, Stanilla J, et al. Misidentification syndromes in schizophrenia: case reviews with implications for classification and prevalence. *Aust N Z J Psychiatry* 1995; 29: 63–68.
15. Thiel CM, Studte S, Hildebrandt H, et al. When a loved one feels unfamiliar: a case study on the neural basis of Capgras delusion. *Cortex* 2014; 52: 75–85.
16. Varvat J, Thomas-Anterion C, Decousus M, et al. Atypical Lewy body disease revealed by burning mouth syndrome and a pseudo-psychiatric syndrome. *Rev Neurol (Paris)* 2010; 166: 547–549.
17. Josephs KA. Capgras syndrome and its relationship to neurodegenerative disease. *Arch Neurol* 2007; 64: 1762–1766.
18. Nambu A, Tokuno H and Takada M. Functional significance of the cortico-subthalamo-pallidal 'hyperdirect' pathway. *Neurosci Res* 2002; 43: 111–117.
19. Haber SN, Kim KS, Mailly P, et al. Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical connections, providing a substrate for incentive-based learning. *J Neurosci* 2006; 26: 8368–8376.
20. Palermo G, Giannoni S, Bellini G, et al. Dopamine transporter imaging, current Status of a potential biomarker: a comprehensive review. *Int J Mol Sci* 2021; 22: 11234.