Case Report

Frégoli Syndrome Accompanied with Prosopagnosia in a Woman with a 40-year History of Schizophrenia.

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Abstract: A 68-year-old woman with schizophrenia after a cerebrovascular accident resulting in right medial temporal and occipital damage developed Frégoli syndrome. Neuropsychological testing revealed that she had impairment in facial recognition compatible with prosopagnosia. The Frégoli syndrome disappeared in three month when, remarkably, her prosopagnosia also disappeared. Our findings are consistent with the hypothesis that combination of hyperactivations of temporo-limbic connection and frontal dysfunction may account for the development of Frégoli syndrome. (Keio J Med 56 (4) : 130–134, December 2007)

Key words: Frégoli syndrome, prosopagnosia, schizophrenia, delusional misidentification syndrome, fusiform gyrus

Introduction

Delusional Misidentification Syndrome (DMS) is traditionally regarded as having three major variants: Capgras syndrome, Frégoli syndrome, and the syndrome of intermetamorphosis. In Capgras syndrome, the patient believes that certain familiar people have been replaced by a group of impostors resembling the original individuals. Frégoli syndrome, less common than Capgras syndrome, is the delusional misidentification of familiar people disguised as others. In the intermetamorphosis syndrome, the least common of the three, the patient experiences changes both in the identity and the appearances of the misidentified persons.[1–5]

Much interest and controversy has prevailed over explanation of the etiology and pathogenesis of DMS and various psychodynamic and organic impairments have been proposed. Recent elucidation of mechanisms of facial identity and facial expression has made it possible to understand the DMS in the context of cognitive neuropsychology, and debate has centered around the relationship between Capgras syndrome and prosopagnosia.

Prosopagnosia is the neuropathological inability to recognize familiar people by their faces, that leaves intact recognition of personal identity from other identifying cues, such as voices and names. Prosopanosia has been observed after bilateral and, less frequently, unilateral lesions of the inferior occipitotemporal cortex.[6,7] Attempts have been made to identify the mental operations that are hampered in prosopagnosia by referring to models of face processing. Among them, probably the most intriguing findings in regard to DMS are those of covert vs. overt face recognition. When given a mixture of photographs of unfamiliar (novel) and familiar faces and asked to sort them into two piles, prosopagnosics are unable to do so; yet remarkably they register a stronger skin conductance response to familiar faces (as do normal subjects), implying that the face-processing machinery is still connected to the limbic system.[8] This observation supports the view that there are two components to the visual recognition of a familiar face, one of which is responsible for conscious recognition of the face and the recall of associated semantic information (the ventral route), whereas the other is responsible for the limbic-mediated emotional arousal which includes the feeling of familiarity that accompanies the implicit recognition of a

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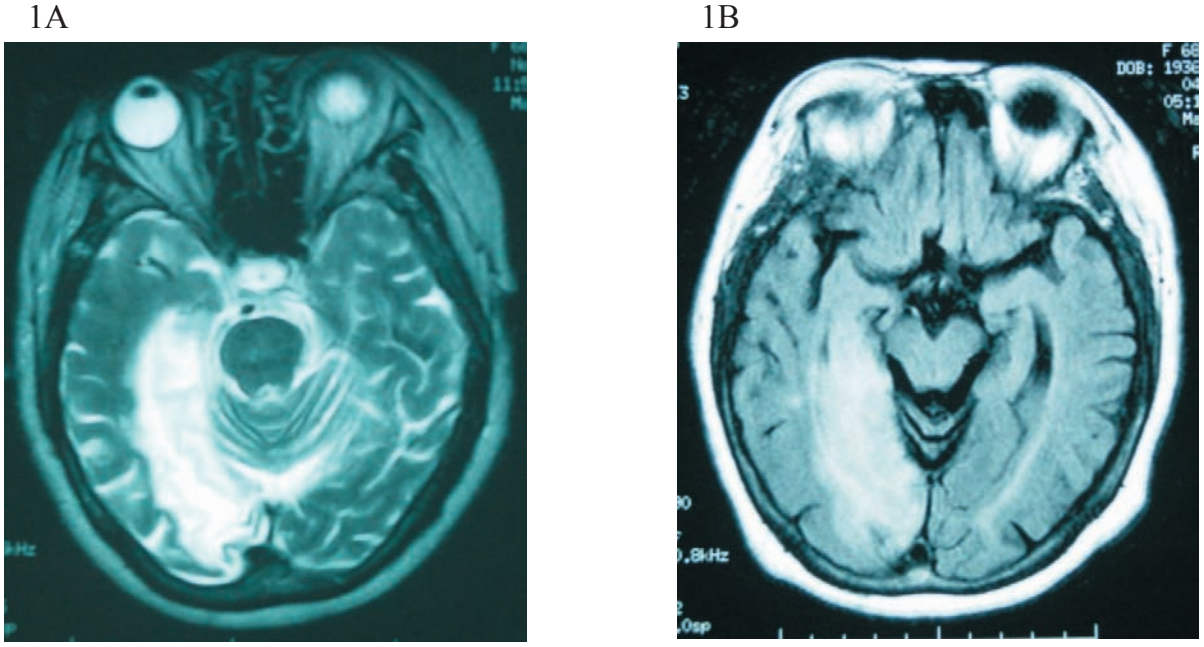

Fig. 1 MRI of the patient's brain. Axial T2-weighted (Figure 1A) and FLAIR (Figure 1B) image show abnormal hyperintensity in the right parahippocampal, hippocampal, lingual, and fusiform gyri.

familiar face (the dorsal route), originally presented by Bruce and Young.[9,10]

In regard to the relationships between the two face processing routes and prosopagnosia or Capgras syndrome, Ellis *et al*.[11,12] have suggested that Capgras syndrome represents a 'mirror image' of prosopagnosia. In this hypothesis, the ventral route is responsible for overt face recognition while the dorsal visual route is responsible for the emotional responses to faces. If brain damage affects the first route, then familiar faces will evoke normal heightened affective responses (indexed by autonomic measures) but there will be no overt recognition: this is prosopagnosia. If brain damage affects the second route, then intact overt recognition will be coupled with a loss of affective responsiveness. This latter case will generate cognitive dissonance, particularly when the person looks exactly like a loved one but fails to evoke the expected emotional response. One resolution of that dissonance is to conclude that the person is an impostor.[11,12]

Regarding this hypothesis, Hirstein and Ramachandran[13] questioned that this hypothesis cannot illustrate why the mere absence of this emotional arousal leads to such an extraordinarily far-fetched delusion, or why the patient does not just think, 'I know that is my father but I no longer feel the warmth?'. With regard to these points, they argued that some additional lesion, perhaps in the right frontal cortex, might be required to generate such extreme delusions. They have also presented the 'inferior temporal-limbic disconnection hypothesis'; 1) the principal cause of Capgras syndrome is a failure of communication between areas of ventral stream processing in the temporal lobe; 2) and a disorder of the right frontal lobe, which ordinarily serves as a global consistency-checking mechanism, may cause such an extraordinarily far-fetched delusion.[13]

As for Frégoli syndrome, Ramachandran applied the same model and suggested that this may occur when the temporal-limbic connection becomes hyperactive, rather than disconnected.[13,14] However, to our knowledge, no clinical cases have yet been reported that from such a neuropsychological view. We herein present and discuss the neuropsychological implications of an interesting case in which a patient with schizophrenia developed Fré goli syndrome accompanied with prosopagnosia during the subacute stage of cerebral infarction.

Case Report

The patient was a 68-year-old right-handed housewife with a 40-year history of delusional schizophrenia. In August 2004, she developed a cerebrovascular accident, following which she developed confusion and gait disturbance. She was admitted to the Komagino Hospital where MRI revealed a regional infarction in an area extending to the right parahippocampal, hippocampal, lingual and fusiform gyri. The right amygdala was unaffected (Fig 1). After two-months' conservative treatment, when she had recovered from the aforementioned neuro-

Table 1 Summary of other neuropsychological test results

			Raw score	Normal score or cut-off point
WAIS-R verbal IQ			83	
performance IQ			unable to perform	
Memory				
RAVLT	immediate		4-6-7-8-9/15*	- - - 13-15/15[20]
	delayed		8/15*	11.62/15[20]
RCFT	copy		unable to perform	
Executive functioning				
Word Fluency	Initial	(sum of three tasks)	22	25.4±1.8[21]
	Category	(sum of three tasks)	19*	42.6±1.4[21]
Wisconsin Card Sorting Test (Keio Version):				
		Categories (trial 1, 2)	1-0*	5.3±1.1 - 5.8±0.5[22]
		Preservative errors (trial 1, 2)	8-6*	3.1±3.9 - 0.3±0.5[22]
Stroop test	part I		55 sec*	16.2±0.8[21]
	part III		78 sec*	29.3±1.5[21]
	part III - I		23 sec*	13.1±1.3[21]
BADS			4/24 point*	>11/24 points[23]

*: impaired

WAIS-R: Wechsler Adult Intelligence Scale -Revised
RAVLT: Rey Auditory verbal learning test
RCFT: Rey Osterrieth complex figure test
BADS: The behavioral assessment of the dysexecutive syndrome

logical symptoms, Frégoli syndrome developed. She began misidentifying a specific male patient as her husband. Although there was no physical similarity between the male patient and her husband, and moreover, her husband had died four years previously, she was adamant in her conviction that the male patient was her husband in disguise. The emergence of this rare DMS and the MRI findings prompted us to investigate her visual recognition performance. It was found that she was unable to identify her doctor or her daughter on photographs or muted video. To evaluate her visual function thoroughly, a comprehensive neuropsychological test battery, VPTA, was administered twice.

The first evaluation was performed in October 2004, when she presented with Frégoli syndrome. On this occasion, the VPTA revealed prosopagnosia and unilateral neglect. her performance in other subtests of VPTA was relatively preserved. On the *Face Recognition Task* in VPTA, her performance was impaired in 7 out of 8 subtests, i.e., *famous face naming, famous face identification, famous face pointing, discrimination of two unfamiliar faces, matching two unfamiliar faces, recognition of facial expression and emotion, and age judgement*.

Immediately after the first evaluation, oral administration of risperidone (2 mg per day) was initiated, and Fré goli syndrome disappeared in the third month after the infarction, when facial recognition had also improved as revealed by VPTA (Fig. 2; Second evaluation, December 2004). The patient's other neuropsychological tests results are presented in Table 1; memory and executive functions were impaired. Notably, the poor performance on BADS indicated dysexecutive syndrome.

Discussion

We described a patient with chronic schizophrenia who presented with Frégoli syndrome and prosopagnosia after infarction of the right cerebral hemisphere. There is little doubt that the cerebral damage, which included the fusiform gyrus, the critical region for face recognition, was responsible for her prosopagnosia.

Prosopagnosics are unable to recognize familiar people by their faces, but they usually do not misidentify people; their typical complaint is "all faces look alike". The remarkable feature of the present case is, therefore, coexistence of prosopagnosia and Frégoli syndrome. For this exceptional phenomenon to occur in this case, the condition of schizophrenia should be considered a key contributing factor. In fact, the most common diagnostic setting in which DMS including Frégoli syndrome is observed is that of schizophrenia. For example, Mojtabai[2] reviewed 34 cases of Frégoli syndrome and found schizophrenia to be the predominant diagnostic category. However, because DMS developed only after the patient had suffered a cerebral insult in the present case, it would appear that neither cerebral infarction nor a preexisting psychopathology of schizophrenia alone are sufficient to account for DMS, but that both are necessary to produce these symptoms. A very plausible possibility is that some organic impairment leads to the hyperactivation of the emotional system, as Ramachandran and Blakeslee[14] has suggested. In this case, one could reasonably speculate

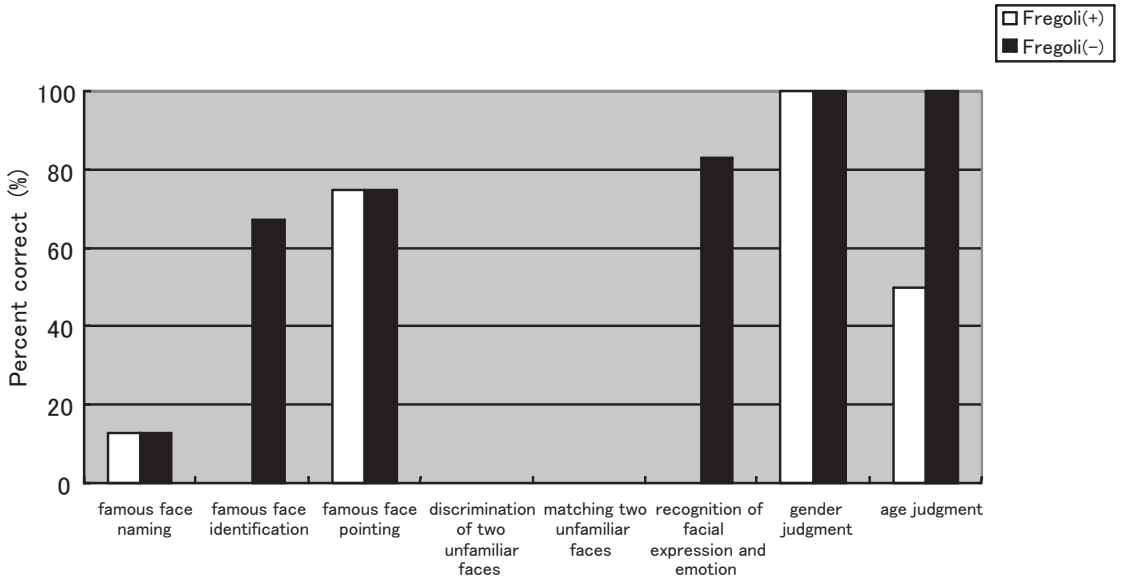

Fig. 2 Face Recognition on *VPTA
Data are the patient's performance on the Face Recognition Task of VPTA. In October 2004, performance was impaired with the exception of gender judgment. Remarkably, at the second evaluation on December 2004, when Frégoli syndrome had disappeared, facial recognition performance had also improved

*VPTA: Visual Perception Test for Agnosia (see text)

that the cerebral infarction acted as the crucial organic factor. Specifically, some reversible effect (e.g. edema) of the infarction appears to have impaired the critical site of face recognition, while activating the input to the intact amygdala, thereby heightening the emotional significance of facial expression. Further research will be needed to confirm this hypothesis. The fact that the prosopagnosia and Frégoli syndrome proceeded and disappeared simultaneously supports this view. The relatively rare combination of these two features was presumed to be created by this exceptional mechanism.

Additionally, because frontal dysfunction is most frequently reported cognitive impairment in schizophrenia, one can speculate that DMS would also be related to some frontal dysfunction. In this context, in her, dysexecutive syndrome, as revealed by poor performance of BADS, which suggested frontal dysfunction, may have completed the picture of DMS. That Feinberg *et al*[4] speculated that combination of executive and memory deficits may account for cases of Frégoli syndrome on traumatic brain injury is in line with this.

Another speculative but intriguing possibility concerns the cognitive style of people with schizophrenia, which is known as the jumping-to-conclusions bias.[17,18] The significance of this reasoning style derives from the assumption that people with such a bias will form unwarranted conclusions on the basis of scant evidence. Because the patient could get little information from faces while suffering from prosopagnosia, it is possible to speculate that the long history of delusional schizophrenia had contributed to her belief that a specific male patient was her husband, according to the jumping-to-conclusions reasoning bias and the emotional dysregulation for the face. This seems to be a reasonable mechanism from the point of view of the cognitive dysfunction in schizophrenia, but accumulation of empirical findings such as the present case reports is needed.

Like other Frégoli cases in the literature, her misidentification only involved one specific person, i.e., her husband, which points to the psychological process as an indispensable factor. Collacot and Napier[19] pointed out that this particular misidentification may have functioned as wish fulfillment. One can speculate that both psychodynamic and organic factors described above contributed to the emergence of Frégoli syndrome in this case.

This statement is one consideration based on the patient's neuropsychological performances and on cognitive neuropsychiatric studies on schizophrenia. Therefore, the propositions made herein await further confirmation from future research. Moreover, our testing was limited due to clinical considerations. However, given the rarity of the disorder and the significance of face rec-

ognition theory, we believe that the present case is worth reporting. Further research into related phenomena, specifically, prosopagnosia with or without Frégoli syndrome in the context of schizophrenia, may shed light on the etiology and pathogenesis of DMS.

References

1. Christodoulou GN : The Delusional misidentification syndromes. Br J Psychiatry 1991; 159(suppl 14): 65–69
2. Mojtabai R: Fregoli syndrome. Aust NZ J Psychiatry 1994; 28: 458–462
3. Feinberg TE, Roane DM: Anosognosia, completion and confabulation: The neutral-personal dichotomy. Neurocase 1997; 3: 73–85
4. Feinberg TE, Eaton LA, Roane DM, Giacino JT: Multiple Fregoli delusions after traumatic brain injury. Cortex 1999; 35: 373–387
5. Lykouras L, Typaldou M, Gournellis R, Vaslamatzis G, Christodoulou GN : Coexistence of Capgras and Fregoli syndromes in a single patient. Clinical, neuroimaging and neuropsychological findings. Eur Psychiatry 2002; 17: 234–235
6. Takahashi N, Kawamura M, Hirayama K, Shiota J, Isono O: Prosopagnosia: a clinical and anatomical study of four patients. Cortex 1995; 31: 317–329
7. De Renzi E, Perani D, Carlesimo GA, Silveri MC, Fazio F: Prosopagnosia can be associated with damage confined to the right hemisphere- an MRI and PET study and a review of the literature. Neuropsychologia 1994; 32: 893–902
8. Stone A, Valentine T: Perspectives on prosopagnosia and models of face recognition. Cortex 2003; 39: 31–40
9. Bruce V, Young A: Understanding face recognition. Br J Psychol 1986; 77: 305–327
10. Morris JS, Öhman A, Dolan RJ: A subcortical pathway to the right amygdala mediating "unseen" fear. Proc Natl Acad Sci USA 1999; 96: 1680–1685
11. Ellis HD, Young AW, Quayle AH, De Pauw KW: Reduced autonomic responses to faces in Capgras delusion. Proc R Soc Lond B Biol Sci 1997; 264: 1085–1092
12. Ellis HD, Lewis MB: Capgras delusion: a window on face recognition. Trends Cogn Sci 2001; 5: 149–156
13. Hirstein W, Ramachandran VS: Capgras syndrome: a novel probe for understanding the neural representation of the identity and familiarity of persons. Proc R Soc Lond B Biol Sci 1997; 264: 437–444
14. Ramachandran VS, Blakeslee S: Phantoms in the brain: Probing the mysteries of the human mind. William Morrow, New York, 1998
15. Japan Society for higher brain dysfunction: Visual Perception Test for Agnosia: VPTA. Shinko-Igaku-syuppansya, Tokyo, 1997 (in Japanese)
16. Goldberg TE, Weinberger DR, Berman KF, Pliskin NH, Podd MH: Further evidence for dementia of the prefrontal type in schizophrenia? A controlled study of teaching the Wisconsin Card Sorting Test. Arch Gen Psychiatry 1987; 44: 1008–1014
17. Moritz S, Woodward TS, Hausmann D: Incautious Reasoning as a pathogenetic factor for the development of psychotic symptoms in schizophrenia. Schizophr Bull 2006; 32: 327–331
18. Mckay R, Langdon R, Coltheart M: Need for closure, jumping to conclusions, and decisiveness in delusion-prone individuals. J Nerv Ment Dis 2006; 194: 422–426
19. Collacott RA, Napier EM: Erotomania and Fregoli-like state in Down's syndrome: dynamic and developmental aspects. J Ment Defic Res 1991; 35: 481–486
20. Lezak MD: Neuropsychological Assessment. Third edition. Oxford university press, New York, 1995.
21. Saito H, Kato M, Kashima H, Asai M, Hosaki H: Frontal dysfunction and word fluency. Higher Brain Function Research. 1992; 12: 223–231 (in Japanese)
22. Kato M: A study on the concept formation and shift of the patients with frontal lesions-a neuropsychological investigation by the New Modified Wisconsin Card Sorting Test. Keio Igaku 1988; 65: 861–885 (in Japanese)
23. Wilson BA, Alderman N, Burgess PW, Emslie H, Evans JJ: Behavioural Assessment of the Dysexecutive Syndrome. Bury St Edmunds, England, 1996