The experimental deception task

The experimental task consisted of an incidental study phase and a recognition memory test phase during which the participants were asked to tell the truth or a lie. First, we prepared colour photographs of 51 common living things and 51 common inanimate objects. Three of each type of these photographs were used as study buffers (three at the beginning and three at the end of a study list) to exclude primacy and recency effects on memory performance. The remaining 96 photographs were divided into two sets of equal numbers of animate and inanimate stimuli. One set was used as study items in the study phase and as target items to be recognized later in the test phase, and the other set was used as distracters in the test phase. These two sets of photographs were matched for visual complexity, familiarity and arousal (all $P > 0.1$), as rated by a separate group of 20 normal adults (10 women, 10 men; mean age 32.9 years), who did not participate in the present experimental deception task. Each set of 48 stimuli was further divided into four lists of 12 stimuli each. Then, four lists of photographs were compiled by combining 12 stimuli from one set and 12 stimuli from another. These four lists consisting of 24 stimuli were again matched for visual complexity, familiarity and arousal (all $P > 0.1$).

For the recognition memory phase, four actors (two men and two women) were videotaped over 96 trials. In each scene (lasting 6 s with a 1-s interval between scenes), one of the actors randomly showed a colour photograph of stimuli, while asking, in Japanese, 'Did you see this photograph?' Each actor showed 24 stimuli, one by one in randomized order, except that the same actor did not appear sequentially.

During the study phase, the participants viewed 48 study stimuli and six buffer stimuli, presented one at a time for 5 s on a computer screen. All the stimuli were presented visually in white squares on a black background. The interstimulus interval was 1 s, during which cross-fixation was presented. To ensure that the participants paid attention to the stimuli, they were instructed to indicate verbally whether each photograph represented an animate or an inanimate object.

During the test phase (the main part of the present study), the participants viewed a video consisting of 96 scenes. In total, 48 studied and 48 unstudied stimuli were presented by the four actors. The participants were asked to say whether each photograph was familiar (i.e. 'I saw') or not (i.e. 'I didn't see') after the actor had asked the question, 'Did you see this photograph?' In addition, participants were also requested to tell the truth in response to three actors (Truth condition) and to tell a lie in response to the remaining actor (Lie condition). We used unequal stimulus classes (25% lie and 75% truth) on the assumption that truthful responses are frequent and ordinary, whereas deceptive responses should be infrequent and extraordinary. In fact, previous studies of executive function, such as the Stroop effect, have suggested that a lower proportion of incongruent trials (homologous with deceptive responses in the present study) increases the cognitive conflict associated with responding to the stimuli (Carter *et al.*, 2000; Swick and Jovanovic, 2002; Fellows and Farah, 2005). The actor to whom a lie was to be told was counterbalanced across the participants.

The experiment yielded four types of responses: true responses for the studied items, true responses for the unstudied items, deceptive responses for the studied items, and deceptive responses for the unstudied items. In this study, collapsing across item type (i.e. studied or unstudied items), the data were analysed for honest and deceptive responses in the Parkinson's disease patients and normal controls. Mathematically, the effect of cognitive demand on deception was expressed by a deception task index (i.e. the percent of correct responses in the Truth condition minus that in the Lie condition). The deception task index reflected the difficulty making deceptive responses regardless of the participant's basic recognition memory performance, and was therefore used for correlation analyses.

To investigate the possibility that the Parkinson's disease patients' apparent impaired ability to lie was due to forgetting to which actor they had to give deceptive responses, after the task was completed, both the patients and the controls were asked whether or not they had forgotten the target person they had to deceive throughout the task. They were also presented with face photographs of the four actors, and were asked to indicate the actor to whom they had been instructed to tell a lie. Throughout the entire task session, all the verbal responses made by the patients and the normal controls were recorded on a digital sound-recording machine. These data were subsequently used for the evaluation of performance accuracy and error pattern.

PET data acquisition and voxel-based analysis

After a fasting period of at least 5 h, PET images were obtained using 185–218 MBq FDG. Dynamic PET scans were performed in three-dimensional mode using a Siemens Biograph DUO PET scanner (Siemens Medical System, Inc., USA). Subjects were scanned under resting conditions with their eyes closed and ears unplugged. To minimize the effects of external stimuli during the FDG-uptake period of 1 h, the subjects stayed in a quiet room wearing eye masks. In-plane and axial resolutions of the scanner were 3.38 mm and 3.38 mm, respectively. An attenuation correction was performed with a CT scan. The data obtained were reconstructed using ordered subset expectation maximization (OSEM) algorithms (16 subsets × 6 iterations) with Gaussian filter with FWHM = 2.0 mm in 256 × 256 matrix, pixel size of 1.33 × 1.33 mm and a slice thickness of 2.0 mm. PET images and the values of arterial input function measurements were converted to cerebral metabolic rate of glucose images according to a model based on the autoradiographic technique (Phelps *et al.*, 1979). The interval between the neuropsychological tests and PET scanning was <4 weeks.

The PET data were analysed with SPM5 (Wellcome Department of Imaging Neuroscience, London, UK). All the PET images were normalized to the FDG-template based on the MNI reference brain (re-sampled voxel size $2 \times 2 \times 2\ mm^3$). Then, all the images were smoothed using an isotropic Gaussian kernel of 10 mm to increase the signal-to-noise ratio and to compensate for differences in gyral anatomy between individuals. To reduce between-subject variation in global metabolic rates, the count of each voxel was normalized to the total count of the brain using proportional scaling.

The deception task indices were entered as covariates of interest in the analysis of the Parkinson's disease patients, with the aim of identifying regions showing decreased metabolism associated with low performance. The threshold of significance was set at $P < 0.001$ at the voxel level (uncorrected), with a significance of $P < 0.05$ at the cluster level (corrected). To confine our analysis to regions showing hypometabolism in the patients relative to the normal participants, the PET data obtained from our sample of 32 patients were contrasted with those obtained from a group of 14 healthy participants (who did not participate in the present experimental deception task), and a resulting map with a liberal statistical threshold ($P < 0.05$, uncorrected) was used for masking in the correlation analysis. In addition, possible confounding effects of age and sex (i.e. biological factors) were controlled by entering these variables into the model. Then, in separate analyses, the duration of Parkinson's disease, the effect of medication

(i.e. levodopa equivalent dose), the scores of UPDRS part III (motor part), and the scores of MMSE—all of which are possible confounding factors for regional metabolism—were controlled by entering these variables into the model.

Results

Standard neuropsychological tests

Table 1 lists the results of the standard neuropsychological tests and statistical comparison between the Parkinson's disease patients and normal controls, as well as the demographic data. The *t*-test was used to assess the statistical significance for all the variables between the two groups except for sex ratio, for which the chi-squared test was used. The patients performed significantly worse than the controls on the digit span test (backward), the verbal fluency task related to syllables and category, and the trail-making test, indicating that Parkinson's disease patients had executive dysfunction. The patients also performed marginally worse than controls on the ADAS word recall test. No significant difference was found between the two groups in the Stroop task and the Go/No-go task, possibly due to ceiling effects resulting from the level of difficulty of these tests, which were specifically designed for the present study. Also, no difference was found between the patients and controls in the digit span test (forward) and the spatial span tests (forward and backward).

The experimental deception task

During the encoding phase, animate–inanimate judgment was virtually 100% correct for all the Parkinson's disease patients and normal controls, indicating that the participants paid sufficient attention to the stimuli.

For the retrieval session, collapsing across item type (i.e. studied and unstudied items), the data related to mean accuracy were analysed. For the patients, mean accuracies were 80.4% (SD = 9.5) for the Truth condition and 71.5% (SD = 17.1) for the Lie condition. For the normal controls, mean accuracies were 84.8% (SD = 5.1) for the Truth condition and 83.8% (SD = 11.9) for the Lie condition. A 2 (Group: Parkinson's disease patients, normal controls) × 2 (Task: Truth, Lie) analysis of variance (ANOVA) revealed a significant main effect of Group [$F(1,50) = 7.25$, $P = 0.010$], a significant main effect of Task [$F(1,50) = 9.22$, $P = 0.004$] and a significant Group × Task interaction [$F(1,50) = 5.77$, $P = 0.020$]. *Post hoc* tests revealed the reason for this interaction: the Parkinson's disease patients showed a decreased number of correct responses in the Lie condition relative to the Truth condition [$t(31) = 4.06$, $P = 0.0003$], whereas the controls showed no difference in scores between these two conditions [$t(19) = 0.47$, $P = 0.641$]. The results are shown in Fig. 1.

Although one patient stated in the middle of the task that she was not sure of the target person to deceive, the remaining patients stated with confidence after the experiment that they could easily and immediately recognize the target person to deceive throughout the task. However, in the forced-choice recognition test, all the patients, including the patient who had expressed uncertainty, correctly chose the target person

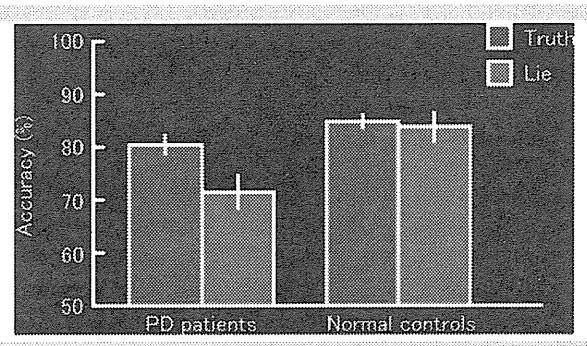

Figure 1 Proportion of correct honest (Truth condition) and deceptive (Lie condition) responses during the deception task in the Parkinson's disease patients and normal controls. Error bars represent standard error. PD = Parkinson's disease.

to deceive. This indicates that the patients' impaired ability to lie cannot be attributable to forgetting who to deceive. In addition, analysis of error pattern during the Lie condition in Parkinson's disease patients revealed that they often made errors by telling the truth (91.8% of all the error responses, but note that this rate includes errors for basic recognition memory performance). More importantly, there were few errors of no response (0.9%) and dual response (7.3%). The extremely low rate for these types of errors indicates that the patients understood sufficiently and performed the task without any difficulty resulting from motor dysfunction. Together, these findings support the view that the patients' deteriorated performance was definitely derived from a failure to inhibit true responses and make deceptive responses.

To clarify the effect of set shifting on the deception task in Parkinson's disease patients, we also compared the accuracy of Truth trials that were preceded by Lie trials with that of the remaining Truth trials that were not preceded by Lie trials in Parkinson's disease patients. If the set-shifting deficits affected the deception task performance, the patients should show worse performance for the Truth trials preceded by Lie trials than for those not preceded by Lie trials. Mean accuracies were 79.1% (SD = 10.3) for the Truth trials preceded by Lie trials and 81.1% (SD = 10.3) for the Truth trials not preceded by Lie trials. We found that there was no significant difference between the two types of trials [$t(31) = 1.32$, $P = 0.198$], suggesting that there was no effect of set-shifting deficits on the deception task.

We further conducted correlation analyses to investigate the relationship between performance of the deception task and cognitive dysfunctions detected by the standard neuropsychological tests in Parkinson's disease patients (i.e. the backward digit span task, the verbal fluency for category and syllables, and the trail-making test). The deception task index was significantly correlated with the performance of verbal fluency for syllables ($r = -0.429$, $P = 0.013$) and with the performance (i.e. time required) of the trail-making test ($n = 30$, because of missing data for two patients, $r = 0.372$, $P = 0.042$). We also found a trend between the deception task index and the performance of verbal fluency for category ($r = -0.303$, $P = 0.092$). However, there was no significant correlation between the deception task index and performance of the digit span (backward) task ($r = -0.245$, $P = 0.179$).

Table 2 Brain regions showing a significant correlation between deception task performance and regional metabolism

Regions (Brodmann's Area)	Coordinates			Z-value	Cluster size
	x	y	z		
Controlling for age and sex (shown in Figure 2)					
Right anterior prefrontal cortex (10)	10	66	−6	4.03	426
Left dorsolateral prefrontal cortex (10/46)	−32	58	10	3.99	261
Controlling for age, sex and disease duration					
Right anterior prefrontal cortex (10)	8	68	−6	4.00	396
Left dorsolateral prefrontal cortex (10/46)	−32	58	10	3.84	198
Controlling for age, sex and levodopa equivalent dose					
Right anterior prefrontal cortex (10)	8	68	−6	4.14	455
Left dorsolateral prefrontal cortex (10/46)	−18	58	12	3.91	225
Controlling for age, sex and UPDRS motor scores					
Right anterior prefrontal cortex (10)	10	68	−6	4.06	588
Left dorsolateral prefrontal cortex (10/46)	−32	60	10	3.91	214
Controlling for age, sex and MMSE scores					
Right anterior prefrontal cortex (10)	8	66	−4	3.56	102
Left dorsolateral prefrontal cortex (10/46)	−32	58	10	3.40	23

The results were masked with the contrast of normal controls versus Parkinson's disease patients.

Cognitive-metabolic correlations

The results are shown in Table 2 and Fig. 2. Significant negative correlations were found between the deception task index and the metabolic rates of the right anterior prefrontal cortex (BA10) and the left dorsolateral prefrontal cortex (BA10/46). Note that the results were masked with the contrast of normal controls versus Parkinson's disease patients, indicating that these two regions were found within the regions showing hypometabolism in the patients relative to the normal participants. Furthermore, the confounding effects of age and sex were also controlled. If the effect of disease duration was further controlled, the results remained virtually unchanged, suggesting that they are not affected by duration of the disease. Similarly, if the effect of medication (i.e. levodopa equivalent dose) was further controlled, the results again remained virtually unchanged, suggesting that they are not affected by Parkinson's disease medication. If the UPDRS scores part III (motor part) were further controlled ($n=31$, because of missing data for one patient), the results again remained virtually unchanged, suggesting that they are not affected by severity of motor symptoms. If the MMSE scores were further controlled, the results for these two regions remained significant ($P<0.001$ at the voxel level, uncorrected, but with smaller cluster size; 102 voxels for the right anterior prefrontal cortex and 23 voxels for the left dorsolateral prefrontal cortex), suggesting that the main findings of this study cannot simply be explained in terms of the severity of general cognitive deficits.

Discussion

In the present study, we tested our hypothesis that patients with Parkinson's disease have difficulty making deceptive responses due to dysfunction of the prefrontal cortex. As predicted, the patients could not successfully make deceptive responses compared with the healthy controls. Furthermore, consistent with previous neuroimaging studies with healthy individuals that have indicated an association between deception and the prefrontal cortex, FDG-PET imaging revealed that the patients' failure in the deception task was significantly correlated with hypometabolism in the prefrontal cortex, regardless of age, sex and other possible confounding factors. To our knowledge, this is the first neuropsychological evidence that dysfunction of the prefrontal cortex is involved in the inability to inhibit true responses and produce deceptive responses in Parkinson's disease patients.

The results of the present study raise two important points. First, certain personality traits of Parkinson's disease patients (Menza, 2000; Ishihara and Brayne, 2006) might be at least partly explained by neuropsychological deficits. In other words, the cognitive deficits may have an influence on ostensible personality traits in Parkinson's disease patients. More specifically, the present results indicate that honesty in Parkinson's disease patients might result from impairment of the executive functions necessary for the processes involved in telling lies. Indeed, the patients showed worse performance in the verbal fluency task and the trail-making test (generally used as measures of executive function) compared with the normal controls. Although these tests are different from the deception task in terms of how the subjects respond (e.g. open-ended responses in verbal fluency and forced-choice responses in the deception task), and therefore are not likely to have direct impact on deception task performance, there is still a possibility that these tests partially share the cognitive and neural mechanisms of deception in terms of higher-order cognitive processes including executive function. In line with this idea, these task performances were significantly correlated with deception task performance. Future studies using an approach similar to that of the present study might further clarify the relationships between cognitive dysfunction and characteristic personality and behavioural traits in Parkinson's disease patients.

Second, the results reveal a direct association between a cognitive control system subserving deception and function of the prefrontal cortex. It is known that brain imaging of healthy people

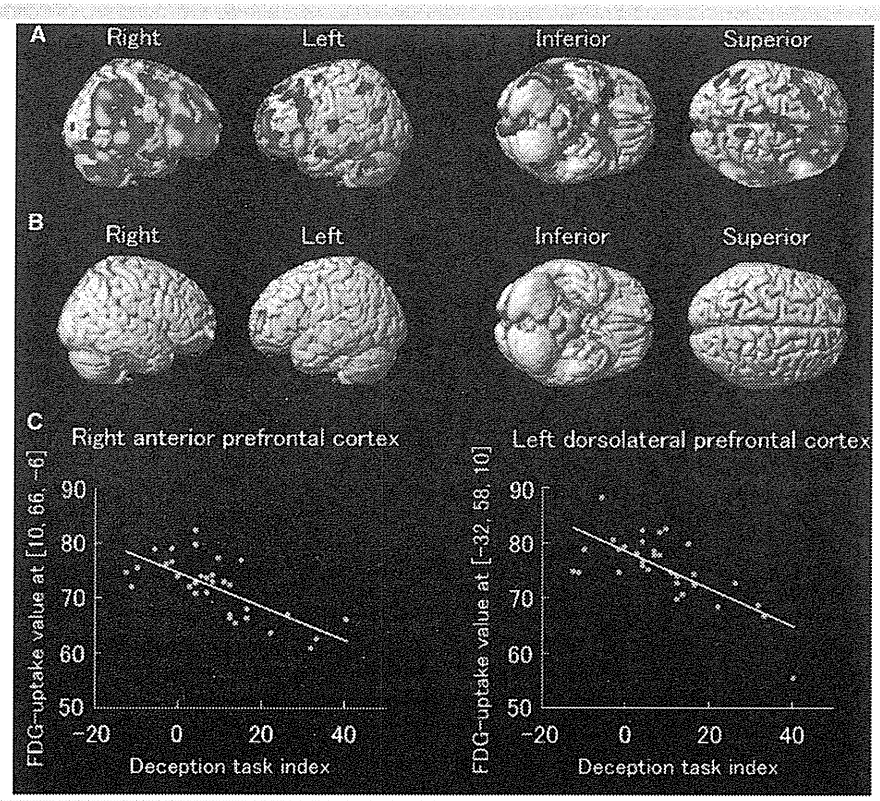

Figure 2 **(A)** Brain regions showing hypometabolism in the Parkinson's disease patients compared with the normal controls. Note that the statistical threshold was relatively liberal in this group comparison ($P<0.05$, uncorrected), since this analysis was done only for generating a mask image included in the cognitive-metabolic correlation analysis within the group of Parkinson's disease patients. The regions are displayed on a surface-rendered standard brain. **(B)** Brain regions showing a significant correlation between performance in the deception task and regional cerebral glucose metabolism in the Parkinson's disease patients ($P<0.001$, uncorrected). Note that the results were masked with the above contrast of the normal controls versus the Parkinson's disease patients to confine our analysis to the regions showing hypometabolism in the Parkinson's disease patients. The possible confounding effects of age and sex were also controlled. **(C)** Scatter plots of the correlations between the deception task indices and the FDG-uptake values in the right anterior prefrontal cortex ($r=-0.719$, $P<0.001$) and the left dorsolateral prefrontal cortex ($r=-0.709$, $P<0.001$). FDG = fluorodeoxyglucose; PD = Parkinson's disease.

cannot provide direct evidence that a certain brain region is necessary for the performance of a specific cognitive task (Frackowiak *et al.*, 1997). That is, some activation in functional brain imaging studies may reflect brain activity that is not essential for the function of interest. Therefore, direct evidence is derived from loss-of-function studies. In the present study, we revealed that the right anterior prefrontal cortex and left dorsolateral prefrontal cortex, which have been activated during deception in a number of carefully designed imaging studies (for reviews, see Spence *et al.*, 2004; Sip *et al.*, 2008; Christ *et al.*, in press), are associated with making deceptive responses. In line with our results, a recent study using transcranial direct current stimulation provided evidence that manipulation of functions in the dorsolateral prefrontal cortex altered the speed and efficiency of deceptive responses (Priori *et al.*, 2008). Furthermore, the association between deception and the left dorsolateral prefrontal cortex in the present study is highly consistent with the findings of a series of neuroimaging studies that we have conducted with healthy individuals (Abe *et al.*, 2006, 2007, 2008).

Based on the previous findings and the present results, we propose that the left dorsolateral prefrontal cortex, the region implicated in a wide range of higher-level cognitive operations such as working memory (D'Esposito *et al.*, 1995; Salmon *et al.*, 1996) and resolution of response conflict (MacDonald *et al.*, 2000; Badre and Wagner, 2004), plays a pivotal role in telling lies. The right anterior prefrontal cortex is also likely to play a critical role in integrating the multiple cognitive processes (Ramnani and Owen, 2004) in deception. One might think that set-shifting deficits, one of the well-known cognitive deficits in Parkinson's disease (Ravizza and Ciranni, 2002; Monchi *et al.*, 2004; Moustafa *et al.*, 2008; Nagano-Saito *et al.*, 2008), affect the results. However, our analysis of set-shifting effect on the response accuracy in Truth trials did not support this interpretation. We believe that our task does not simply measure set shifting, and that dysfunction of the left dorsolateral and right anterior prefrontal cortices specifically prevents Parkinson's disease patients from inhibiting true responses and producing deceptive responses.

It is important to determine how frontal executive dysfunction, possibly disrupting deceptive behaviour, is derived from the neuropathological changes observed in Parkinson's disease patients. One possibility is that prefrontal hypometabolism in Parkinson's disease patients results from degeneration of the substantia nigra pars compacta with subsequent depletion of dopamine in the striatum. A recent study suggests that the dorsolateral prefrontal circuit consisting of the dorsolateral prefrontal cortex, caudate nucleus, globus pallidus, substantia nigra, and thalamus (Cummings, 1993; McPherson and Cummings, 2002) is specifically associated with executive dysfunction in Parkinson's disease patients (Zgaljardic *et al.*, 2006). Alternatively, the executive dysfunction may reflect a functional disturbance of the frontal cortex itself caused by locally impaired mesocortical dopaminergic transmission (Mattay *et al.*, 2002). Although these two models are not mutually exclusive, there is controversy in the recent literature in that some researchers have argued that both the nigrostriatal and mesocortical pathways are disrupted in Parkinson's disease (Monchi *et al.*, 2007), whereas others have shown impaired nigrostriatal dopaminergic function with preserved mesocortical dopaminergic transmission in early Parkinson's disease (Sawamoto *et al.*, 2008). As for dopaminergic transmission, a study in which the 'on' and 'off' medication states are directly compared would also be useful. We can predict that dopaminergic medication would have a beneficial effect on the regions affected by depletion of dopamine, such as the caudate nucleus and thereby its connections to the dorsolateral prefrontal cortex, and that the ability to make deceptive responses would improve in Parkinson's disease patients. In fact, some previous studies have reported the beneficial effects of levodopa on cognitive performance, although it should be noted that the effects depend on the nature of the task (Gotham *et al.*, 1988; Cools *et al.*, 2001; Lewis *et al.*, 2005).

In conclusion, our results provide new evidence that damage to the prefrontal cortex disrupts the processes involved in making deceptive responses in Parkinson's disease patients. It appears that the 'honesty' of patients is caused by an impaired ability to deceive others that results from brain dysfunction caused by the disease. However, there are some limitations of the present study that should be borne in mind for future studies. First, the present study examined only the processes associated with executive control during deception. The participants were instructed to tell a lie, which cannot be viewed as being the same as deception in real life. The neural bases of genuine deception or immoral lying should be investigated further in both healthy individuals and brain-damaged patients. Second, it remains a possibility that the association between difficulty deceiving others and prefrontal dysfunction may not be specific to Parkinson's disease patients, and further studies are needed to examine whether patients with other neurological disorders affecting the prefrontal cortex show similar deficits (see Spence and Kaylor-Hughes, 2008). Third, the present study investigated only patients with mild Parkinson's disease of short duration. Whether our claim is true of patients in general is an important issue to be pursued. Finally, it is also important to determine how (and when) the brain pathology derived from Parkinson's disease causes specific personality traits together with explicit cognitive deficits. A longitudinal assessment with detailed neuropsychological assessment and multimodal neuroimaging in Parkinson's disease patients is required.

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False item recognition in patients with Alzheimer's disease

Nobuhito Abe*, Toshikatsu Fujii, Yoshiyuki Nishio, Osamu Iizuka, Shigenori Kanno, Hirokazu Kikuchi, Masahito Takagi, Kotaro Hiraoka, Hiroshi Yamasaki, Hyunjoo Choi, Kazumi Hirayama, Mayumi Shinohara, Etsuro Mori

Department of Behavioral Neurology and Cognitive Neuroscience, Tohoku University Graduate School of Medicine, Sendai, Japan

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ABSTRACT

Recent evidence suggests that patients with Alzheimer's disease (AD), as compared with normal individuals, exhibit increased false recognition by stimulus repetition in the Deese–Roediger–McDermott (DRM) task or associative recognition memory tasks, probably due to impaired recollection-based monitoring. However, because of possible alternative explanations for the findings of these previous studies, the evidence for impaired recollection-based monitoring in AD patients remains inconclusive. In this study, we employed stimulus repetition in old/new recognition judgments of single-item picture memory without a factor of association between the stimuli and examined whether AD patients showed increased false item recognition as compared with healthy controls. AD patients and healthy controls studied single-item pictures presented either once or three times. They were later asked to make an old/new recognition judgment in response to (a) Same pictures, pictures identical to those seen at encoding, (b) Similar lures, novel pictures similar to but not identical to those seen at encoding, and (c) Dissimilar lures, novel pictures not similar to those seen at encoding. For Same pictures, repeated presentation of stimuli increased the proportion of "old" responses in both groups. For Similar lures, repeated presentation of stimuli increased the rate of "old" responses in AD patients but not in control subjects. The results of the present study clearly demonstrated elevated false recognition by stimulus repetition in single-item recognition in AD patients. The present findings strongly support the view that AD patients are impaired in their ability to use item-specific recollection in order to avoid false recognition.

1. Introduction

One of the more prominent cognitive problems observed in Alzheimer's disease (AD) is the decline in episodic memory (Salmon and Bondi, 2009), the type of memory that allows one to remember past occurrences in one's life (Tulving, 2001). The episodic memory impairments observed in AD patients are mainly characterized by the failure to retrieve desired information, but at times, AD patients also suffer from memory distortion. The memory distortion in AD patients can sometimes be extreme, as in syndromes of delusional misidentification (e.g., Abe et al., 2007; for review, see Forstl et al., 1994). Therefore, an understanding of memory distortion in AD patients is clinically important; however, the underlying mechanisms remain to be fully elucidated.

One approach to evaluating memory distortion is assessment of false recognition in cognitive memory tasks. False recognition is a process whereby people incorrectly claim that they have recently seen or heard a stimulus that they have not actually encountered (Underwood, 1965). One of the most common tasks for assessment of false recognition is the Deese–Roediger–McDermott (DRM) task (Deese, 1959; Roediger and McDermott, 1995; for review, see Gallo, 2010) in which false recognition of non-studied lures is elicited by having subjects study lists of associates. For example, using a modified version of the DRM paradigm in which study and test trials were repeated five times, Budson, Daffner, Desikan, & Schacter (2000) reported that false recognition increased in AD patients, decreased in young adults, and fluctuated in older adults.

The findings of Budson et al. (2000) can be interpreted as indicating that impaired retrieval monitoring processes in AD patients would cause memory distortion (Schacter, Norman, & Koutstaal, 1998a). More specifically, recall-to-reject processes, where recall (or recollection) opposes familiarity in recognition memory tasks (see Yonelinas, 2002), might be impaired in AD patients. Here, "recall" refers to the ability to retrieve previously experienced information in response to some retrieval cue, and recollection is defined as the mental reinstatement of experienced events during which unique details of memory are recalled. Familiarity is a mental awareness that an event has been experienced previously without the unique details or mental reinstatement of the event (Gardiner,

* Corresponding author. Present address: Department of Psychology, Harvard University, 33 Kirkland Street, Cambridge, MA 02138, USA.
E-mail address: abe@wjh.harvard.edu (N. Abe).

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1988; Jacoby, 1991; Mandler, 1980; Skinner and Fernandes, 2007). In the study of Budson et al. (2000), owing to the multiple study/test sessions, control subjects may have increased their recollection of the studied items, determined that the related lures were not presented, and hence rejected these lures as non-studied items. AD patients might be unable to use such a recollection-based monitoring process to reduce false recognition. In line with this idea, some previous studies have reported that AD patients have impaired recall or recollection relative to familiarity. For instance, Bartok et al. (1997) reported that AD patients tend to be impaired more in recall than in recognition tests. Dalla Barba (1997) showed that recollection-based recognition is more affected than familiarity-based recognition in AD patients. These findings suggest that AD patients perform poorly on tasks in which recall or recollection is necessary to oppose familiarity-based false recognition.

However, as Gallo, Sullivan, Daffner, Schacter, & Budson (2004) have pointed out, there are other possible explanations, such as impairment of source memory (e.g., Dalla Barba, Nedjam, & DuBois, 1999; Multhaup and Balota, 1997; Smith and Knight, 2002). In the repeated study/test sessions, the subject needs to monitor several sources of information, including whether the related lure was in the study list, in the test list, or whether it was only imagined (Budson et al., 2002; Kensinger and Schacter, 1999; Schacter, Verfaellie, Anes, & Racine, 1998b). Another possible explanation would be the impairment in remembering the associations between items and list-contexts. If the subjects can successfully remember the list-context in which they studied the item, they may reject the unstudied related lures more effectively.

To test the impaired recall-to-reject hypothesis for false recognition in AD patients without contamination of deficits in source memory, Gallo et al. (2004) used an associative recognition memory task in which subjects studied pairs of unrelated words and were later asked to distinguish between these same studied pairs (intact) and new pairs that contained either rearranged studied words (rearranged) or non-studied words (non-studied). During the study period, the pairs were presented either once or three times. The results showed that repetition increased the hits to intact pairs in both AD and control groups, but repetition increased false alarms to rearranged pairs only in the AD group. Gallo et al. (2004) suggested that repetition increases the familiarity of the words in both rearranged and intact pairs; however, only the control subjects were able to counter this familiarity by recalling the originally studied pairs, which is consistent with the recall-to-reject hypothesis.

As Gallo et al. (2004) noted, however, their findings may also be explained by an impaired memory for associations, although they did not ascribe their findings to deficits in source memory. Repetition of word pairs during a study task may enhance familiarity for test words in both intact and rearranged pairs, such that the discrimination between intact and rearranged pairs depends on the memory for the specific association formed during the task. More specifically, in the task used by Gallo et al. (2004), subjects need to recollect associations between two words in order to make an accurate recognition memory judgment. Here, it should be noted that both of the tasks used in Budson et al. (2000) and Gallo et al. (2004) required the subjects to recollect some kind of associations, namely, item-to-list-context association in Budson et al. (2000) and item-to-item associations in Gallo et al. (2004). Thus, from the previous studies on false recognition in AD patients, the evidence for impaired recollection-based monitoring in AD patients remains inconclusive due to possible alternative explanations, especially associative memory account.

To provide strong evidence supporting the impaired recall-to-reject hypothesis, we investigated false recognition in AD patients using a different kind of item-recognition task from those used in previous studies. Prior studies have used semantically related word lists (Budson et al., 2000), phonologically related word lists (Budson, Sullivan, Daffner, & Schacter, 2003b), or categorized color photographs (Budson et al., 2003a). In the present study, we used previously presented pictures (Same pictures), novel pictures similar to previously presented pictures (Similar lures), and novel pictures not similar to previously presented pictures (Dissimilar lures) as experimental stimuli for the recognition memory task. The experimental paradigm using these stimuli, which have often been reported in previous studies (e.g., Garoff, Slotnick, & Schacter, 2005; Kensinger, Garoff-Eaton, & Schacter, 2007a, 2007b; Kensinger and Schacter, 2007), was suitable for our investigation because it allowed us to measure changes in the ability to discriminate Same pictures from Similar lures (i.e., item-specific recollection) by stimulus repetition without the element of source memory or associative memory. The aim of the present study was to determine whether AD patients would show increased false recognition in response to Similar lures by stimulus repetition and to provide strong evidence supporting the impaired recall-to-reject hypothesis in AD patients.

Table 1
Demographic data (mean ± SD) for the AD patients and the healthy controls.

	AD patients ($n = 18$)	Controls ($n = 18$)	p-Value
Age	74.5 (4.6)	74.8 (4.2)	$p > 0.1$
Sex (female/male)	14/4	11/7	$p > 0.1$
Education	10.7 (2.1)	10.9 (1.8)	$p > 0.1$
MMSE	24.4 (2.1)	28.0 (1.7)	$p < 0.001$

The chi-squared test was used for the gender ratio, and the t-test was used for the remaining variables. Standard deviations are in parentheses. MMSE, Mini-Mental State Examination.

2. Materials and methods

2.1. Participants

Eighteen patients with a clinical diagnosis of probable AD (National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association criteria; McKhann et al., 1984) and 18 healthy elderly adults participated in the experiment. AD patients were recruited from the clinical population at Tohoku University Hospital. Each of these patients was assessed by one or more board-certified neurologists with expertise in diagnosing dementia. Elderly adults who had no history of neurological or psychiatric diseases were recruited from the local community via an advertisement. The exclusion criteria for both groups were a medical history of neurological disease (e.g., stroke, head injury, and epilepsy) or psychiatric illness (e.g., schizophrenia and manic depression) and a documented or suspected history of alcohol or drug abuse. In addition, because we intended to study patients with mild AD, patients who scored less than 20 on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) were excluded. Healthy participants who scored less than 24 (a cutoff level for a diagnosis of dementia) on the MMSE were also excluded. All participants had normal or corrected-to-normal vision. At the time of the study, none of the patients was being or had been treated with specific medication, such as anti-acetylcholinesterase agents. The elderly adults were matched to the patients for gender (4 male and 14 female patients vs. 7 male and 11 female elderly adults), age (patient mean = 74.5 years, range = 67–87 years; elderly adult mean = 74.8 years, range = 67–82 years), and education (patient mean = 10.7 years, range = 8–14 years; elderly adult mean = 10.9 years, range = 8–14 years). The study was approved by the Ethical Committee of Tohoku University and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their caregivers when appropriate. The demographic data of each group are summarized in Table 1.

2.2. Stimuli

We prepared color photographs of 120 common living things and 120 common inanimate objects, which were used in our previous study (Hashimoto et al., in press). These photographs consisted of 60 pairs of different photographs of the same living things and 60 pairs of different photographs of the same inanimate objects. These pairs were divided into three sets (i.e., 40 pairs each) of an equal number of animate and inanimate stimuli. The first members of two sets (80 stimuli) were used as study items in the study phase, and the first members of the other set (40 stimuli) were used as distracters in the test phase. The assignment of these three stimuli sets to either study or to the test phase was counterbalanced across subjects. Of the two sets used in the study phase, the first members of one set (40 stimuli)

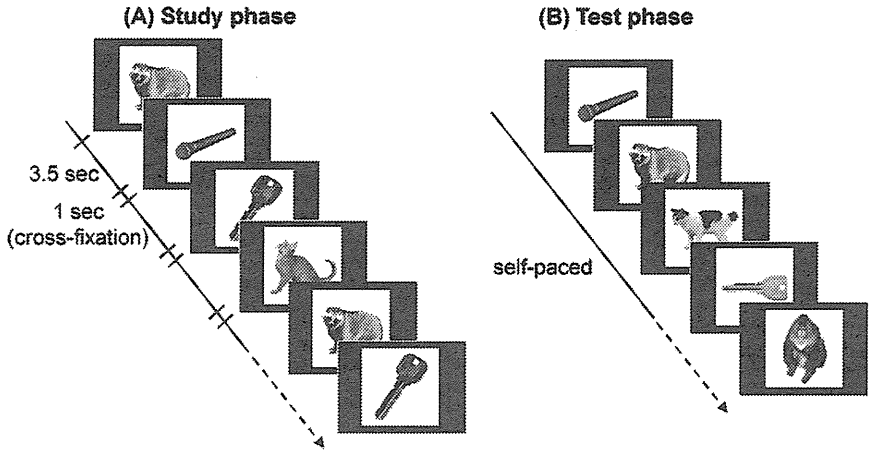

Fig. 1. The experimental design, which involved (A) a study phase and (B) a test phase. (A) During the study phase, participants were asked to judge whether each photograph represented a living or a non-living thing and to memorize each photograph. Half of the stimuli were presented once, and the remaining stimuli were presented three times. (B) During the test phase, participants were asked to judge whether each stimulus was new or old. They were requested to indicate "old" if the stimulus was presented as it was during the study phase and "new" if the stimulus was a non-studied object or was presented with different perceptual details from the studied object.

were used as target items to be recognized later in the test phase (for the "Same" condition, see below for details), whereas the second members of the other set (40 stimuli) were used as target items to induce false recognition in the test phase (for the "Similar" condition, see below for details). The assignment of the first and second members of the stimulus sets to either the "Same" or the "Similar" condition was also counterbalanced across subjects.

2.3. Procedure

The experiment consisted of an intentional study phase followed by the recognition memory test phase that required the participants to indicate whether the presented stimulus had been studied. Before the experiment, the participants were given a thorough explanation of the task procedure and were familiarized with the task by completing a short practice session. To ensure that the participants comprehended the task procedure, they were required to explain the instructions to an experimenter in their own words.

During the study phase (Fig. 1A), the subjects were presented with a total of 80 stimuli. Each stimulus was presented for 3.5 s with an interstimulus interval of one second during which a fixation point (a cross) was constantly presented. Half of these 80 stimuli were presented once, and the other half were presented three times. Therefore, the total number of trials was 160. The stimuli were presented one by one in a randomized order. The subjects were then asked to indicate whether the stimulus represented an animate or inanimate object by pressing buttons and were asked to memorize each stimulus for the later recognition memory test.

During the test phase, the subjects performed an old/new recognition task in a self-paced manner (Fig. 1B). Five different kinds of stimulus type were presented: (a) 20 stimuli that had been presented once during the study phase (Same-1× stimuli), (b) 20 novel stimuli similar to the 20 that had been presented once during the study phase (Similar-1× stimuli), (c) 20 stimuli that had been presented three times during the study phase (Same-3× stimuli), (d) 20 novel stimuli similar to the 20 that had been presented three times during the study phase (Similar-3× stimuli), and (e) 40 novel stimuli not similar to the 80 that had been presented during the study phase (Dissimilar stimuli). These stimuli were presented one by one in a randomized order. The subjects were asked to indicate whether they had studied each stimulus by pressing buttons. After each trial, the experimenter initiated the next trial by pressing a button.

3. Results

3.1. Demographic data

Comparisons of demographic data between the two groups were performed using the χ^2 test for gender ratio and the t-test for other components (Table 1). There were no significant differences in age ($t(34) = 0.227$, $p > 0.1$), gender ($\chi^2 = 1.178$, $p > 0.1$) or education ($t(34) = 0.260$, $p > 0.1$). On the MMSE scores, the AD patients scored significantly lower than the healthy controls ($t(34) = 5.621$, $p < 0.001$).

3.2. Recognition memory test

The mean proportion of "old" responses for all types of stimuli in the two groups is summarized in Table 2. First, we performed a 2 (stimuli: Same and Similar) × 2 (repetition: 1× and 3×) analysis of variance (ANOVA) for the AD patient data. We found significant main effects of stimuli ($F(1,17) = 145.040$, $p < 0.001$) and repetition ($F(1,17) = 55.148$, $p < 0.001$) with no interaction between the two factors ($F(1,17) = 0.491$, $p > 0.1$). This indicates that the repeated presentation of stimuli increased the rate of "old" responses to both Same pictures (true recognition) and Similar lures (false recognition) in AD patients.

We then performed a 2 (stimuli: Same and Similar) × 2 (repetition: 1× and 3×) ANOVA for the healthy control data. We found significant main effects of stimuli ($F(1,17) = 141.760$, $p < 0.001$) and repetition ($F(1,17) = 25.159$, $p < 0.001$) with a significant interaction between the two factors ($F(1,17) = 38.597$, $p < 0.001$). Post-hoc tests revealed a significant difference in the proportion of "old" responses for Same pictures between the single and repeated presentations ($t(17) = 9.301$, $p < 0.001$), whereas there was no significant difference for Similar lures between the single and repeated presentations ($t(17) = 0.452$, $p > 0.1$). This indicates that the repeated presentation of stimuli increased the rate of "old" responses to Same pictures (true recognition) but not to Similar lures (false recognition) in control subjects.

To further compare performance across the groups, two types of memory indices were calculated: memory for items and memory for perceptual details. The memory index for items (MI) was calculated as the difference between hits to Same pictures and false alarms to Dissimilar lures. This difference reflects the participants' ability to correctly discriminate Same pictures from Dissimilar lures. The memory index for perceptual details (MD) was calculated

Table 2
Mean proportions of "old" responses for each stimulus type.

Stimulus type	AD patients ($n = 18$)	Controls ($n = 18$)
Same-1×	70.0 (19.7)	75.3 (11.6)
Same-3×	87.5 (13.0)	95.8 (5.5)
Similar-1×	50.3 (19.8)	43.1 (13.5)
Similar-3×	65.0 (18.9)	44.4 (14.7)
Dissimilar	30.3 (20.3)	10.8 (7.2)

Standard deviations are in parentheses.

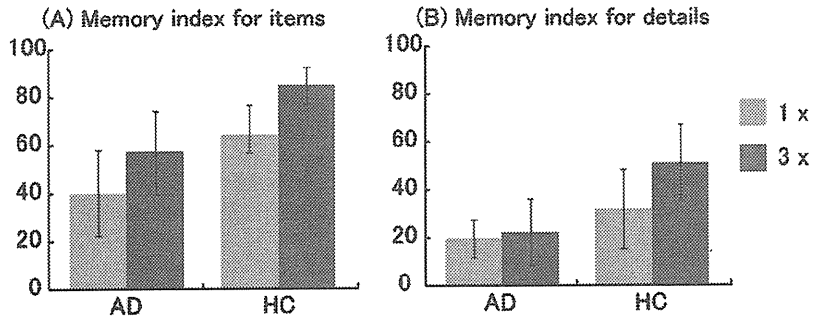

Fig. 2. Two memory indices for recognition memory in the two groups. (A) The memory index for items was calculated as the difference between the proportion of hits to Same pictures and the proportion of false alarms to Dissimilar lures. (B) The memory index for details was calculated as the difference between the proportion of hits to Same pictures and the proportion of false alarms to Similar lures. Error bars represent standard deviations. AD, patients with AD; HC, healthy controls.

as the difference between hits to Same pictures and false alarms to Similar lures. This difference reflects the participant's ability to correctly discriminate Same pictures from Similar lures. These measures were used over other measures of discrimination (d' or A') because they tend to be more sensitive (Snodgrass and Corwin, 1988) and because they may be more appropriate for recognition memory tests that investigate recall-to-reject processes (e.g., Gallo et al., 2004). These measures are also useful in that they reflect a subject's memory regardless of whether he or she has a liberal or conservative response bias (i.e., extremely high rate of "old" or "new" responses) derived from individual differences.

Fig. 2 shows the MI and MD for each group. A 2 (group: AD patients and healthy controls) × 2 (repetition: 1× and 3×) ANOVA was conducted separately for each type of memory index. For the MI, there were significant main effects of group ($F(1,34) = 34.994$, $p < 0.001$) and repetition ($F(1,34) = 94.150$, $p < 0.001$) without an interaction between the two factors ($F(1,34) = 0.607$, $p > 0.1$). The lack of interaction indicates that the ability of the AD patients and the healthy controls to discriminate Same pictures from Dissimilar lures was affected by stimulus repetition in a similar manner.

A different pattern emerged in the analysis of the MD. There were significant main effects of group ($F(1,34) = 27.806$, $p < 0.001$) and repetition ($F(1,34) = 19.079$, $p < 0.001$) with a significant interaction between the two factors ($F(1,34) = 10.641$, $p < 0.005$). Post-hoc tests revealed that AD patients did not show a difference between the single and repeated presentations ($t(17) = 0.701$, $p > 0.1$), whereas the healthy controls showed a higher index in the repeated presentation than in the single presentation ($t(17) = 6.213$, $p < 0.001$). This indicates that the ability of the AD patients and the healthy controls to discriminate Same pictures from Similar lures was differentially affected by stimulus repetition.

Finally, we examined whether AD patients were less susceptible to similarity-based false recognition than were healthy controls, especially in the Similar-1× condition. This analysis was inspired by previous findings that AD patients were less susceptible to false recognition in response to lure stimuli after a single list exposure in the DRM paradigm than were healthy controls (Balota et al., 1999; Budson et al., 2000). To control for response bias, we calculated the corrected false recognition rates that were obtained by subtracting the proportion of "old" responses to Dissimilar lures from the proportion of "old" responses to Similar lures. The corrected false recognition rates for Similar-1× and Similar-3× were 20.0 (SD = 16.2) and 34.7 (SD = 16.3) for AD patients and 32.2 (SD = 13.0) and 33.6 (SD = 13.0) for healthy controls, respectively. We found a significant difference in the corrected false recognition rate for Similar-1× between AD patients and healthy controls ($t(34) = 2.494$, $p < 0.05$). There was, however, no significant difference in the corrected false recognition rate for Similar-3× between AD patients and healthy controls ($t(34) = 0.227$, $p > 0.1$). This indicates that AD patients were originally less susceptible to similarity-based false recognition than were healthy controls, but stimulus repetition canceled out this effect.

4. Discussion

In the present study, we used an item-recognition memory paradigm to investigate false recognition in AD patients and healthy controls. Specifically, we focused on whether the repeated presentation of stimuli differentially affected the ability to discriminate the targets and the lures perceptually similar to the targets between these two populations. The results showed that the repeated presentation of stimuli increased the proportion of "old" responses to Same pictures in both groups and to Similar lures in the AD patients but not in control subjects. Further analysis revealed that repeated presentation of the stimuli raised a memory index for items in both groups, whereas unlike the healthy controls, repeated presentation of the stimuli did not show an improvement in the memory index for perceptual details in AD patients. The present study provides clear evidence to support the impaired recall-to-reject hypothesis in AD patients in a single-item recognition task, which excludes the factor of associative memory.

The present findings showing that false recognition was increased in an item-recognition paradigm by stimulus repetition in AD patients have provided strong support for the impaired recall-to-reject hypothesis in AD patients. As mentioned in the Introduction, Budson et al. (2000) used a modified version of the DRM task to argue that impaired item-specific recollection increases familiarity-based false recognition in AD patients. Similarly, Gallo et al. (2004) used an associative recognition task to argue that impaired recall-to-reject processes lead to an elevated level of familiarity-based false recognition in AD patients. However, the evidence for impaired recollection-based monitoring in AD patients from these studies was inconclusive because of the possible alternative explanations that could not be ruled out in these previous studies, namely, certain kinds of associative memory deficits. To avoid these possible confounding factors, we used stimuli consisting of photographs that were semantically concordant but perceptually distinct as Similar lures. We found an increased false item recognition in response to Similar lures by stimulus repetition in AD patients, but not in healthy controls. The pattern of these results is in line with the previous studies (Budson et al., 2000; Gallo et al., 2004) and is highly consistent with the impaired recall-to-reject hypothesis in AD patients.

One might think that, if the repeated presentation of the stimulus increases recollection of studied items and this increased recollection is used to more effectively reject Similar lures, then the healthy controls should show decreased "old" responses to Similar lures in the repeated condition relative to the single presentation

condition. However, our results were against this idea. The proportion of "old" responses to Similar lures remained unchanged between the single and repeated presentation conditions in the healthy controls. One possible reason is that the control subjects were also susceptible to similarity-based false recognition induced by stimulus repetition. Repetition increased the concept-based familiarity of Similar lures, which should have increased false recognition, but it also increased the ability to recall the original stimuli and thus to reduce false recognition by a recall-to-reject strategy (Kelley and Wixted, 2001). These two opposing processes canceled out on average, which indicates a lack of effect of repetition. In fact, Kelley and Wixted (2001) used a manipulation similar to Gallo et al. (2004)'s study and reported no effects of repetition in younger adults. Gallo et al. (2004) also reported no effects of repetition in their control subjects matched in age with AD patients. Budson et al. (2000) also reported a fluctuating pattern in their elderly subjects. The present findings indicate that control subjects were relatively more likely than were AD patients to use a recall-to-reject process to overcome similarity-based false recognition.

Our results also revealed a lower rate of corrected false recognition in the Similar-1× condition for AD patients relative to healthy controls. This suggests that AD patients were originally less susceptible to similarity-based false recognition than were healthy controls in the task using single-item picture memory, possibly as a result of decreased sensitivity to the semantic gist for the visually presented stimuli. Stimulus repetition, however, canceled out this effect. This pattern indicates that the repeated presentation of pictures created an increasingly robust representation of the semantic gist for presented pictures; AD patients showed elevated false recognition due to the lack of item-specific recollection, but healthy controls used recollection to counteract the gist representation. These results are highly consistent with previous works using the DRM paradigm in AD patients (Balota et al., 1999; Budson et al., 2000) and with data from amnesic patients (Schacter, Verfaellie, & Anes, 1997; Schacter et al., 1998b; Schacter, Verfaellie, & Pradere, 1996). Expanding on these previous studies, the present study has provided strong evidence that AD patients are initially less susceptible (but not after stimulus repetition) to similarity-based false recognition, regardless of the experimental paradigms used.

The precise neural dysfunctions accounting for why AD patients are impaired in the ability to use item-specific recollection to reduce false recognition are unknown. We speculate that this impairment in AD patients is associated with dysfunctions in two major areas: (1) in the hippocampus, causing recollection deficits, and/or (2) in the prefrontal cortex, causing disrupted post-retrieval processes. It is widely known that AD patients show both structural and functional abnormalities in the medial temporal lobe (Dickerson and Sperling, 2008; Frisoni, Fox, Jack, Scheltens, & Thompson, 2010). Among the subregions within the medial temporal lobe, the hippocampus has been reported to be closely linked to recollection processes (e.g., Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Mugikura et al., 2010; Vilberg & Rugg, 2007). It is also known that, even in the early stage of the disease, AD pathology might involve the prefrontal cortex, as neuropsychological and neuroimaging studies have demonstrated frontal lobe dysfunction in AD patients (Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991; Dalla Barba et al., 1999). In addition, there is considerable evidence that frontal lobe lesions may produce disruptions in the processes that check for memory errors (Janowsky, Shimamura, & Squire, 1989; Johnson, O'Connor, & Cantor, 1997). Further studies are needed to obtain data that directly elucidate the relationship between neural disruption and false recognition.

In conclusion, the results of the present study strongly support the view that AD patients are impaired in their ability to use item-specific recollection in order to avoid false recognition. One of the questions to be pursued is whether the memory deficits in AD patients observed in previous studies are caused by deficits during the retrieval phase or during the encoding phase. It remains possible that the degraded encoding of stimuli causes the subsequent deficits in the recollection of perceptual details. It is worth investigating whether experimental manipulation during encoding can alter the pattern of task performance in AD patients; on the basis of such findings we may be able to infer whether the encoding deficits are relevant to subsequent false recognition. Alternatively, a study using functional magnetic resonance imaging, which assesses neural responses during the actual performance of a task, may enable us to better assess how the brain dysfunction associated with AD gives rise to these memory impairments.

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Research paper

Neuroanatomy of a neurobehavioral disturbance in the left anterior thalamic infarction

Yoshiyuki Nishio,[1] Mamoru Hashimoto,[2] Kazunari Ishii,[3] Etsuro Mori[1]

[1]Department of Behavioral Neurology and Cognitive Neuroscience, Tohoku University, Sendai, Japan
[2]Department of Psychiatry and Neuropathobiology, Kumamoto University, Kumamoto, Japan
[3]Department of Radiology, Kinki University, Sayama, Japan

Correspondence to
Dr Yoshiyuki Nishio, Department of Behavioral Neurology and Cognitive Neuroscience, Tohoku University Graduate School of Medicine; 2-1, Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan;
nishiou@med.tohoku.ac.jp

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ABSTRACT

Background and purpose Cognitive and behavioural symptoms represent primary clinical manifestations of anterior thalamic infarcts (ATIs) in the tuberothalamic artery territory. The aim of the study is to understand the pathomechanism of cognitive and behavioural disturbances in left ATI (LATI).

Methods 6 patients with isolated LATIs were investigated using neuropsychological assessments, MRI stereotactic lesion localisation and positron emission tomography.

Results The patients were characterised clinically by verbal memory impairment, language disturbances dominated by anomia and word-finding difficulty and apathy. The ventral anterior nucleus (VA) proper, magnocellular VA (VAmc), ventral lateral anterior nucleus (VLa), ventral lateral posterior nucleus (VLp) and mammillothalamic tract were involved in all patients. Compared with healthy controls, the regional cerebral blood flow was lower in the thalamus, the dorsolateral, medial and orbital frontal lobes, the anterior temporal lobe, the inferior parietal lobule and the occipital lobe of the left hemisphere.

Conclusions The authors propose that the Papez circuit disruption at the mammillothalamic tract and possibly thalamomedial temporal disconnection at the VA region is responsible for memory impairment and that the thalamo-anterior temporal disconnection is associated with language disturbance in LATI, respectively.

INTRODUCTION

Clinical observations have documented that the thalamus participates in a great variety of cognitive functions and mental activities, including memory, language, perception and emotion.[1–3] However, the precise functional attributes of the individual thalamic nuclei and fibre systems remain to be elucidated. Clinicoanatomical investigations of thalamic infarctions, in which only subsets of thalamic structures are involved, have been one of the best ways to study the functional anatomy of the human thalamus.[3] The inference of the function of individual thalamic structures on the basis of their anatomical connectivity with other brain regions has also played an important role. Here we highlight the left anterior thalamic infarction (LATI) resulting from occlusion of the left tuberothalamic artery, in which cognitive and behavioural symptoms represent primary clinical manifestations.[3] Using neuropsychological evaluations, MRI stereotactic lesion localisation[4 5] and positron emission tomography (PET), we attempted to delineate neurobehavioral and neuroanatomical profiles of LATI.

METHODS

Subjects

We recruited six right-handed patients (mean age, 76±7.4 years; two women; mean years of education, 9.2±2.9) with a subacute phase of isolated LATI. They were consecutive patients admitted to the Hyogo Institute for Aging Brain and Cognitive Disorders (HI-ABCD), a research-oriented dementia clinic, from 1993 to 2001. All of them presented to the institute with sudden onset of cognitive or behavioural problems, such as forgetfulness, loss of spontaneity and dysnomia. Duration between onset of symptoms and start of examination ranged from 1 to 4 weeks (mean, 3±1.3 weeks). Their past medical history included hypertension, diabetes mellitus and rheumatoid arthritis. The inclusion criteria were as follows: (1) sudden onset of symptoms; (2) presence of circumscribed infarction in the anterior portion of the thalamus with a lack of lesions elsewhere on MRI; (3) no severe stenosis or occlusion of the major cerebral arteries on MR angiography; (4) no history of other neurological and psychiatric diseases and (5) no history of premorbid cognitive impairment or behavioural abnormalities. The clinical diagnosis was made based on an examination by behavioural neurologists and psychiatrists and compared with MRI findings. All procedures used in this study were approved by the ethics committee of the HI-ABCD. Written informed consents were obtained from both patients and their relatives or from the control subjects.

Neuropsychology and behaviour

Neuropsychological assessments were performed within 2 weeks before and after neuroimaging investigations. The batteries and tests used in the study comprised the Mini Mental State Examination,[6] the Wechsler Adult Intelligence Scale-Revised (WAIS-R),[7] the Wechsler Memory Scale-Revised (WMS-R),[8] the Western Aphasia Battery,[9] 100-word object naming,[10] verbal fluency (animals/initial letter),[11] Raven's Coloured Progressive Matrices,[12] the Weigl's Colour-Form Sorting Test[13] and Luria's executive/motor performance tests (fist-edge-palm test, 2-1 tapping test and alternative pattern drawing).[14] These tests represent the domains of general intelligence, anterograde episodic memory, language/semantic knowledge, perceptual organisation/construction and executive function (concept formation, psychomotor speed and executive/motor control). Retrograde episodic memory and the presence and types of behavioural abnormalities were assessed based on interviews of patients and their close family members and a bedside examination. The correspondence between the cognitive

domains and the neuropsychological measures are indicated in table 1.

Stereotactic lesion localisation on MRI

Coronal three-dimensional T1-weighted SPGR images (TR, 14 ms; TE, 3 ms; flip angle, 20°; resolution, 1.5×0.86×0.86 mm) were obtained using a 1.5-T GE Signa Horizon system. The images were reconstructed into 1.0 mm isotropic transverse sections and then normalised to the Montreal Neurological Institute (MNI) T1 template using the affine transformation algorithm implemented in the SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/) software application. The lesions of each patient were traced on normalised images. The detailed localisation of the thalamic and adjacent structures involved was determined on transverse sections using an electronic version of the Schaltenbrand–Wahren (S–W) atlas.[15] The correspondence of the transverse sections between the MNI-T1 template and the S–W atlas was determined by scaling the z-axis with reference to the distance between the top of the thalamus and the AC–PC plane. In-plane two-dimensional linear coregistration was performed with reference to the intercommissural distance, interputaminal distance and contour of the thalamus.

Positron emission tomography

PET images were obtained from the six patients and six healthy subjects (75.2±9.0 years; six females) under resting conditions with their eyes closed using a Shimadzu Headtome-IV scanner. The regional cerebral blood flow (rCBF) was determined using a steady-state technique. The subjects continuously inhaled O_2 at 500 MBq/200 ml/min during a 10-minute scanning session.[16] Arterial blood samples were collected to measure the blood radioactivity concentrations. Data were collected in 128×128 matrices, and the slice interval was 6.5 mm when the z-motion mode was used.[17] The scan did not include the top of the frontal and parietal lobes and the inferior portion of the cerebellar hemispheres. Image preprocessing and statistical analyses were carried out using SPM5. The ventromedial prefrontal region was masked because of the presence of artefacts due to gas inhalation. The obtained images were reconstructed into 2 mm cubic voxels and then normalised to the SPM-PET template using affine transformation. The resultant images were smoothed with 12 mm full width at half maximum. Threshold masking was applied with a criterion of 80% of the mean global value. Proportional scaling was used to control the individual variation in the global CBF. Two-sample t-tests were used for a voxelwise group comparison between the patient and control groups. T-contrast maps were created with a height threshold of uncorrected $p<0.001$ and an extent threshold of 50 voxels (400 mm^3). As the small number of the subjects could cause underestimation of group difference in rCBF, we additionally analysed the PET data on individual subject basis using regions of interests (ROIs). Twenty-one pairs

Table 1 Results of the neuropsychological tests

Cognitive and behavioural domains	Tests		Patients 1	2	3	4	5	6	Normative data
General intelligence	MMSE (/30)		25	27	27	16*	24	22*	≥24
	WAIS-R[7]	VIQ	68*	78*	88	65*	81*	89	≥85
		PIQ	85	106	93	66*	91	91	≥85
Episodic memory	WMS-R[8]	Verbal memory index	<50*	64*	61*	<50*	50*	64*	≥85
		Visual memory index	72*	93	118	68*	114	100	≥85
		Attention/concentration index	66*	84*	94	55*	77*	97	≥85
		Delayed recall index	<50*	<50*	69*	<50*	71*	83*	≥85
	Retrograde amnesia		(−)	(−)	(−)	(−)	(−)	(−)	
Language/semantic knowledge	WAB[9]	AQ	69.2*	90.8*	86.4*	71*	83.6*	87.6*	97.7±3.0
		Spontaneous speech (/20)	13*	17*	17*	12*	16*	16*	19.7±0.6
		Auditory comprehension (/10)	7.2*	9.8	7.7*	7.2*	9*	9.5*	9.8±0.1
		Repetition (/10)	8.9*	9.6	9.9	9.2	9.9	10	9.9±0.3
		Naming (/10)	5.5*	9	8.6*	7.1*	6.9*	8.3*	9.5±0.6
		Reading (/10)	6.7*	10	8.9	4.1*	7.2*	7.7*	9.5±0.8
		Writing (/10)	6.4*	9.7	9.9	4*	9.1	8.9	9.6±1.0
	Animal fluency (/min)		4*	10	9	4*	4*	12	11.8±4.4
	Initial fluency (/min)		0*	3*	1*	1*	2*	7	6.8±3
	Picture Naming (/100)[10]		74*	97	84	66	86	89	98.2±2.3
	WAIS-R[7]	Information SS	6*	6*	10	5*	6*	8	≥7
		Vocabulary SS	5*	7	7	5*	6*	9	≥7
		Comprehension SS	2*	7	5*	2*	7	5*	≥7
		Similarities SS	4*	5*	8	4*	8	6*	≥7
Perceptual organisation/ construction	WAIS-R[7]	Picture completion SS	8	11	9	5*	8	9	≥7
		Block design SS	5*	13	9	4*	12	11	≥7
Concept formation	RCPM (/36)[12]		25	30	23	14*	32	26	26.9±5.4
	Weigl's colour-form sorting[13]		✓	✗	✓	✗	✓	✓	
Psychomotor speed	WAIS-R Digit symbol SS[7]		6*	8	9	4*	7	8	≥7
Executive/motor control	Fist-edge-palm[14]		✗	✗	✗	✓	✗	✓	
	2-1 tapping[14]		✗	✓	✓	✓	✓	✓	
	Alternative pattern drawing[14]		✓	✓	✓	✓	✓	✓	
Behaviour	Apathy		(++)	(+)	(+)	(++)	(+)	(+)	

*Score below −1 SD of the normative data.[8–12]
✓, passed; ✗, failed.
AQ, aphasia quotient; MMSE, Mini-Mental State Examination; PIQ, performance intelligence quotient; RCPM, Raven's coloured progressive matrices; SS, scaled score; VIQ, verbal intelligence quotient; WAB, Western Aphasia Battery; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised.

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of 8 mm spherical ROIs of each hemisphere were determined on the mean normalised PET image of the 12 subjects using the MarsBar toolbox (http://marsbar.sourceforge.net/). Left/right asymmetry indices (calculated as (mean voxel value of left ROI)/(mean voxel value of right ROI)) of each patient were compared to 95% CIs of that obtained from the six control subjects.[18 19]

RESULTS

Neuropsychology and behaviour

The results of the neuropsychological tests and behavioural observations are summarised in table 1.

General intelligence

The verbal intelligence quotient (VIQ) of the WAIS-R was less than 85 (−1 SD of the normative mean) in four of the six patients, whereas the performance IQ was within the normal range in all patients except Patient 4.

Episodic memory

All patients showed impairments in the verbal memory index (MI) of the WMS-R (<85, −1 SD). Their verbal MI was disproportionately lower than their VIQ in the WAIS-R (verbal MI − VIQ≥10)[8]. Retrograde memory was preserved in all patients.

Language/semantic knowledge

The spontaneous speech score was impaired in all patients due to poor information content and word-finding difficulties. Semantic paraphasias were occasionally observed in some patients. Articulatory errors and phonological paraphasias were not observed. All patients excluding Patient 2 showed anomia in the naming subtest of the Western Aphasia Battery and/or in the picture naming test of 100 words. Apparent reading and writing disabilities were observed in two patients (Patients 1 and 4). All the patients were impaired (<7) in at least one of the subtests of the WAIS-R: Information, Vocabulary, Comprehension and Similarities.

Perceptual organisation/construction

Five of the six patients performed at normal levels on the Picture Completion and Block Design subtests of the WAIS-R.

Executive function (concept formation, psychomotor speed and executive/motor control)

Although all patients excluding Patient 6 were impaired in at least one of the executive function tests, no consistent tendency in the test categories showing impairment was found in the patient group.

Behaviour

Apathy was observed in all patients. Lack of spontaneity, reduced emotional response and psychomotor retardation were observed in Patients 1 and 4. In the other four patients, their apathy was milder and consisted only of lack of spontaneity. Other behavioural alterations that have been associated with frontal lobe damage, such as disinhibition, irritability and repetitive behaviours, were not observed.

Stereotactic lesion localisation

The results are shown in figure 1 and table 2. Designations of the thalamic nuclei were according to Hirai and Jones.[20] The ventral anterior proper (VA proper; also referred to as the parvocellular VA or just the VA), magnocellular ventral anterior nucleus (VAmc), ventral lateral anterior (VLa), ventral lateral posterior (VLp), reticular (R) nuclei and mammillothalamic tract (MTT)

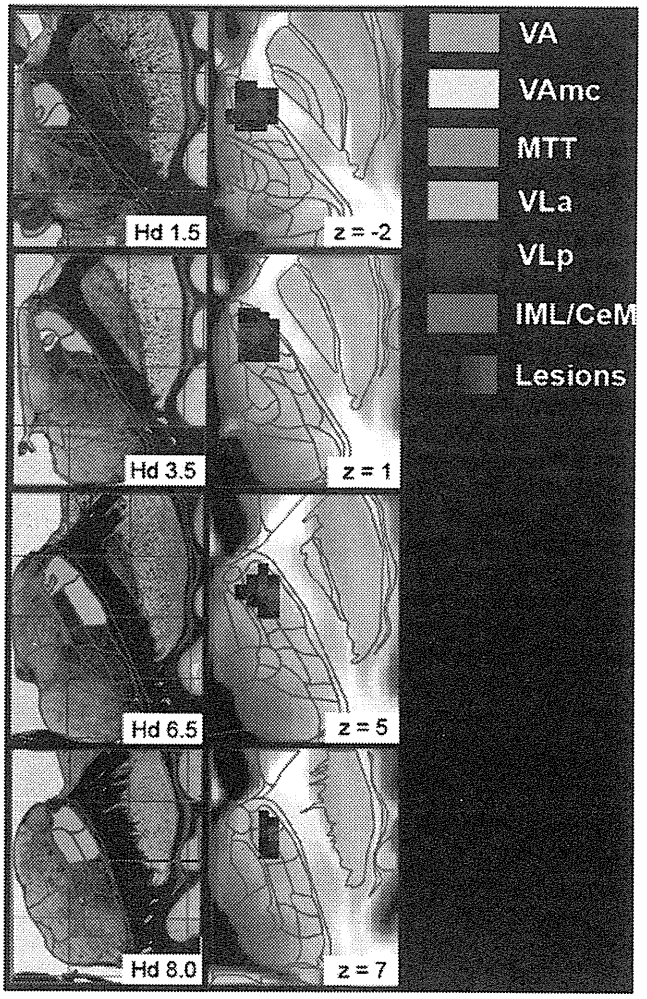


Figure 1 Transverse images from the Schaltenbrand–Wahren (S–W) atlas are shown in the left column. The structures involved in left anterior thalamic infarction are coloured. Images showing lesions (red) superimposed on the Montreal Neurological Institute (MNI) template are indicated in the right column. The voxels that overlapped in more patients are coloured in brighter red. CeM, central medial nucleus; IML, internal medullary lamina; MTT, mammillothalamic tract; VA, ventral anterior nucleus proper; VAmc, magnocellular ventral anterior nucleus; VLa, ventral lateral anterior nucleus; VLp, ventral lateral posterior nucleus.

were involved in all patients. The anterior nuclei (AN) were preserved in all patients. The mediodorsal nucleus (MD) was involved only in Patient 4. The internal medullary lamina (IML)/central medial nucleus (CeM) was affected in three patients with lesions that were located medially (Patients 2, 4 and 5). The genu of the internal capsule (ICg) was damaged at the site ventral to the thalamus in Patients 3, 4 and 5.

Positron emission tomography

A voxelwise group comparison revealed significant rCBF reductions in the anterior temporal lobe (ATL), thalamus, orbital frontal lobe (OFL) and middle frontal gyrus (MFG) of the left hemisphere in the patients with LATI compared to the control subjects (figure 2). A relative increase in rCBF was detected in the right precuneus and right lingual gyrus. An ROI analysis showed decreased left/right asymmetry index (lower rCBF in the left side compared to the right side) in the anterior cingulate gyrus, inferior temporal gyrus, inferior parietal lobule, calcarine

Table 2 The thalamic and adjacent regions affected in the patients

Thalamic regions		Patient No.						No. of patients
Hirai and Jones'	Hassler's	1	2	3	4	5	6	
VA proper	Lpo	(+)	(+)	(+)	(+)	(+)	(+)	6
VAmc	Lpo.mc	(+)	(+)	(+)	(+)	(+)	(+)	6
VLa	Zo	(+)	(+)	(+)	(+)	(+)	(+)	6
	Voa	(+)	(+)	(+)	(+)	(+)	(+)	
	Vop	(−)	(−)	(−)	(−)	(+)	(−)	
	Doe	(+)	(+)	(+)	(+)	(+)	(+)	
VLp	Voi	(+)	(+)	(+)	(+)	(+)	(+)	6
	Doi	(+)	(+)	(+)	(+)	(+)	(+)	
VM	Vom	(−)	(+)	(−)	(−)	(−)	(−)	1
MD	Mfa	(−)	(−)	(−)	(+)	(−)	(−)	1
IML/CeM	Lam	(−)	(+)	(−)	(+)	(+)	(−)	3
R		(+)	(+)	(+)	(+)	(+)	(+)	6
MTT		(+)	(+)	(+)	(+)	(+)	(+)	6
ICg		(−)	(−)	(−)	(+)	(+)	(+)	3
H		(−)	(−)	(−)	(+)	(+)	(−)	2
STN		(−)	(−)	(−)	(+)	(−)	(−)	1

The nomenclature for the thalamic nuclei is according to Hirai and Jones and Hassler. CeM, central medial nucleus; H, fields of Forel; ICg, genu of the internal capsule; IML, internal medullary lamina; MD, mediodorsal nucleus; MTT, mammillothalamic tract; R, reticular nucleus; STN, subthalamic nucleus; VA, ventral anterior nucleus; VAmc, magnocellular ventral anterior nucleus; VLa, ventral lateral anterior nucleus; VLp, ventral lateral posterior nucleus; VM, ventral medial nucleus.

gyrus and cuneus in addition to the ATL, thalamus, OFL, and MFG. Increased left/right asymmetry index was observed in the precuneus (table 3).

DISCUSSION

Clinical features of LATI

In agreement with previous reports of LATI, the symptoms of our patients were characterised primarily by memory impairment, language disturbances and apathy.[1 3 4 21] Although previous studies of acute LATI have reported a perseverative behaviour (palipsychism) and mild sensorimotor deficits,[21] we did not observe these symptoms.

The memory impairment was restricted to the anterograde domain and dominant in the verbal materials. Although the concomitant deficits in language, attention and executive function may partly explain the memory impairment observed in our patients, the dissociation between the verbal MI of the WMS-R and the VIQ of the WAIS-R suggested that our patients had deficits in the memory function itself. A hypothesis has been recently proposed that selective or predominant memory impairment of verbal materials in left temporal lobe pathology arises from concomitant deficits in semantic processing and protosemantic components of episodic memory.[22] The same perspective may be applicable to material-specific memory impairment in thalamic damage.

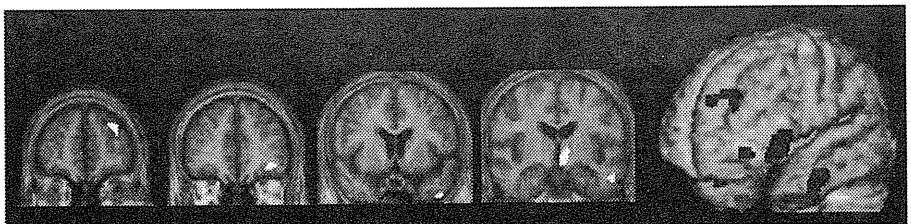
The language disturbances in our patients were characterised by word-finding difficulty and anomia. The articulation and phonological aspects were well preserved. Anomia and poor performance in the naming tests and the Information, Vocabulary, Comprehension and Similarities subtests of the WAIS-R suggested that the lexical-semantic impairment was the core deficit responsible for their language symptoms.[4] This interpretation is supported by previous reports investigating a variety of lexical-semantic deficits, including category-specific anomia, proper name anomia and degraded knowledge of object use, in patients with LATI.[5 23–25]

Cortical diaschisis in LATI

Using CBF diaschisis, we demonstrated that the connections of the thalamus with the dorsolateral, medial and orbital frontal lobes, the ATL, the inferior parietal lobule and the occipital lobe were disrupted in LATI. Compared to patients with paramedian thalamic infarction (PTI),[26] the extent of hypoperfusion regions in our patients was relatively restricted. This difference in PET findings is well correspondent with that in clinical manifestations; patients with PTI develop more severe behavioural symptoms compared with those that had anterior thalamic infarction (ATI), for example, coma, akinetic mutism and confusion.[3 26] The involvement of the intralaminar nuclei, which project broadly to the cerebral cortex,[20] and/or their projecting fibres probably causes extensive cortical dysfunction in PTI.[3 4] A previous single-case PET study of LATI reported restricted rCBF reductions in the ipsilateral amygdala and posterior cingulate cortex.[27] The disagreement between this and our studies is probably related to difference in affected thalamic structures and in neuroimaging analysis.

Neuroanatomical basis of memory impairment

The neural circuit that arises from the hippocampus via the fornix, mammillary body (MB), MTT, AN and posterior cingulate cortex and then projects back to the hippocampus is known



Contrasts	Regions	Cluster size (voxels)	Cluster-level corrected p values	T value	Voxel-level corrected p values	MNI coordinates x	y	z
LATI < Controls	Anterior temporal lobe L	223	0.103	6.58	0.465	−42	6	−40
	Thalamus L	235	0.090	5.39	0.828	−6	−12	−6
	Lateral orbital frontal lobe L	64	0.637	5.26	0.863	−36	42	−8
	Middle frontal gyrus L	84	0.514	4.71	0.964	−28	48	32
Controls < LATI	Precuneus R	104	0.409	5.34	0.844	4	−68	48
	Lingual gyrus R	56	0.691	5.04	0.912	12	−98	−14

Figure 2 Results of the voxelwise group comparison of positron emission tomography. Regions with regional cerebral blood flow (rCBF) reduction are superimposed on the mean normalised MRIs of the patients. The table indicates relative decrease and increase in rCBF in patients with left anterior thalamic infarction compared to controls. The height and extent thresholds were $p<0.001$ uncorrected and 400 mm^3, respectively. LATI, left anterior thalamic infarct.

Table 3 Left/right asymmetry indices obtained from the regions of interest- (ROI) based positron emission tomography analysis

	Patients						Controls (n=6)	
	1	2	3	4	5	6	95% CI	
Inferior frontal	**0.79**	1.03	0.91	**0.82**	**0.71**	0.88	0.84	1.37
Middle frontal	**0.80**	0.93	0.93	1.01	**0.76**	**0.82**	0.86	1.25
Frontal operculum	1.08	1.13	1.01	1.03	0.88	**0.85**	0.86	1.29
Lateral orbital frontal*	**0.80**	**0.92**	1.14	**0.90**	**0.69**	**0.85**	0.97	1.20
Anterior cingulate*	**0.78**	**0.87**	**0.94**	0.99	**0.80**	**0.79**	0.95	1.18
Central	*1.16*	0.97	1.04	**0.85**	**0.77**	**0.80**	0.87	1.11
Temporal pole*	**0.86**	**0.86**	**0.87**	**0.92**	**0.80**	**0.89**	0.95	1.17
Inferior temporal*	1.15	**0.92**	1.02	**0.94**	**0.93**	**0.81**	0.95	1.21
Middle temporal	1.05	0.86	0.87	1.03	*1.07*	1.02	0.85	1.05
Superior temporal	1.05	1.20	1.14	**0.77**	1.04	0.89	0.87	1.20
Medial temporal	*1.36*	1.00	*1.08*	*1.24*	0.83	0.90	0.89	1.05
Inferior parietal*	**0.84**	**0.88**	1.17	**0.89**	**0.67**	**0.87**	1.00	1.27
Posterior cingulated	0.94	1.04	1.03	1.00	*1.41*	0.93	0.86	1.10
Precuneus†	*1.17*	*1.18*	*1.17*	0.95	*1.16*	**0.84**	0.91	1.08
Cuneus*	**0.82**	**0.85**	1.12	**0.94**	**0.93**	1.07	1.05	1.25
Calcarine*	1.11	**0.79**	**0.81**	**0.87**	**0.85**	**0.82**	0.91	1.16
Lingual	1.24	1.14	0.96	0.94	1.12	0.96	0.88	1.38
Fusiform	0.95	0.98	**0.93**	1.02	0.97	0.95	0.95	1.09
Anterior striatum	1.07	*1.22*	0.90	**0.82**	0.85	0.98	0.83	1.13
Posterior striatum	1.18	1.19	1.14	0.94	**0.45**	0.94	0.92	1.21
Thalamus*	**0.66**	**0.80**	**0.86**	**0.77**	**0.57**	**0.75**	0.92	1.19

Indices lower and higher than 95% CI of the controls are shown in bold and italic, respectively.
*and † indicate ROIs in which laterality indices are lower and higher than 95% CI of the controls in four or more patients, respectively.

as the Papez or Delay–Brion circuit. This circuit has long been considered to play a central role in memory. In addition, the significance of the rhinal/parahippocampal-MD-prefrontal network has been recently recognised.[28] Because the AN and MD are spared in the majority of patients with ATI,[3 29] the disconnection of these neural networks at the intrathalamic white matter structures, namely the MTT and IML, have been considered critical in memory impairment in ATI.[5 29–31] In the present case series, the MTT was consistently involved, whereas the IML was affected only in half of the patients, suggesting the significance of Papez circuit disruption. In addition, we propose a possible role of lesions in the VA region, which is penetrated anteroposteriorly by the inferior thalamic peduncle, the bundle carrying the fibres from the rhinal/parahippocampal cortex to the MD.[20] In contrast with this view, however, our PET analysis did not detect diaschisis in the medial temporal lobe and other components of the Papez circuit. Two possible factors may be associated with this negative result: diaschisis is presumably hard to be observed in the disruption of polysynaptic connections,[26] for example, the connection between the MTT and the posterior cingulate cortex via the AN; rCBF reduction is an insensitive measure to detect medial temporal dysfunction.[32 33] This issue should be addressed using different neuroimaging modalities, such as fluorodeoxyglucose PET and diffusion tensor tractography, in future studies.

Neuroanatomical basis of language disturbance

It is noteworthy that diaschisis was observed in the ATL, which is a region that is putatively associated with the integration of lexical and semantic information.[34 35] Both LATI and left ATL damage have been linked to semantic-lexical deficits, including category-specific anomia and proper name anomia.[24 36 37] This symptomatic similarity suggests the presence of functional relationships between these two regions. Connectional anatomical studies in monkeys have shown anatomical connections between the VAmc, a thalamic structure consistently involved in ATI, and the anterior temporal neocortex.[38] We propose that thalamo-anterior temporal disconnection plays a significant role in the language disturbances observed in LATI. Some investigators have speculated that the disruption of the intralaminar nuclei-inferior thalamic peduncle-prefrontal system is critical in the language disturbances observed in LATI.[39] Although the IML was involved only in half of our patients, diaschisis in the dorsolateral prefrontal cortices was demonstrated in our PET analysis. The thalamo-dorsolateral prefrontal disconnection may also be related to the linguistic symptoms.

Behavioural symptoms and their relevance to cortical diaschisis

Apathy is the most common behavioural feature in the current and previously reported cases of LATI.[3 21] Although apathy can result from lesions in various locations,[40] it has been particularly associated with anterior cingulate damage. Consistently, rCBF reduction in the left anterior cingulated gyrus was observed in our patients. In the original formulation of the frontal-subcortical circuits,[2] disinhibited behaviour is linked to disruption of the orbitofrontal circuit. However, none of our patients developed such kind of behavioural alteration in spite of diaschisis in the OFL. Previous studies have suggested that disinhibition syndrome occurs after right-lateralised lesions.[41 42] The lack of disinhibited behaviour in our patients is presumably associated with the laterality of the lesions.

Limitations of the study

The first limitation of the study is the small sample size. Age, disease duration, subclinical neurodegenerative pathologies and individual differences in functional lateralisation among others, may have had a large effect on the clinical presentation and neuroimaging results. Clinical-PET correlation analyses were unavailable also due to the small number of subjects. Although much larger sample sizes are needed to overcome these problems, it would be quite difficult to recruit a sufficient number of subjects from a single institution due to the rarity of isolated ATI. A meta-analysis of studies that have performed detailed neuroimaging investigations would be valuable. Also, the probable selection bias on the neuropsychological and behavioural findings should be noted. Since we performed the study in a dementia department, only patients with cognitive problems mimicking dementia may have been referred to us. Lack of sensorimotor deficits and perseverative behaviours[21] and relatively long-lasting cognitive impairment may be associated with such kind of bias. Finally, as it took a long time, over 7 years, to recruit the patients, we failed to update the neuropsychological tests. Therefore, we could not incorporate new cognitive theories, such as the recollection/familiarity components of episodic memory.[43]

There are a number of methodological limitations to our neuroimaging investigations. The precision of lesion localisation on MRI is limited by image distortion due to magnetic field inhomogeneity, inaccuracy of spatial normalisation and image co-registration, difficulty in defining exact lesion boundaries and so forth. In the PET analyses, the proportional scaling probably led to underestimation of the spatial extent and strength of hypoperfusion and to spurious hyperperfusion. The ROI-based left/right asymmetry analysis is unable to detect bilateral rCBF changes.[19] Lastly, inhalation artefacts precluded the evaluation of the ventromedial frontal regions, which are reported to have dense interconnections with the thalamic structures.[20 44]

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RESEARCH ARTICLE

Illusory Misidentifications and Cortical Hypometabolism in Parkinson's Disease

Toshiyuki Ishioka, PhD,[1]* Kazumi Hirayama, MD, PhD,[1] Yoshiyuki Hosokai, PhD,[1] Atsushi Takeda, MD, PhD,[2] Kyoko Suzuki, MD, PhD,[1] Yoshiyuki Nishio, MD, PhD,[1] Yoichi Sawada, PhD,[1] Shoki Takahashi, MD, PhD,[3] Hiroshi Fukuda, MD, PhD,[4] Yasuto Itoyama, MD, PhD,[2] and Etsuro Mori, MD, PhD[1]

[1]*Department of Behavioral Neurology, and Cognitive Neuroscience, Tohoku University Graduate School of Medicine, Sendai, Japan*
[2]*Department of Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan*
[3]*Department of Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai, Japan*
[4]*Department of Nuclear Medicine and Radiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan*

ABSTRACT: Idiopathic Parkinson's disease (PD) is associated with documented impairments in various visual functions. However, there have been only a limited number of studies that have reported on the brain regions responsible for impairment of visual recognition in PD. In our study, we evaluated the performance of PD patients and 24 healthy controls on the Poppelreuter-type overlapping figure identification test to investigate the impairment of visual recognition. We also measured the PD patients' resting cerebral glucose metabolism using ^{18}F-fluorodeoxyglucose positron emission tomography and investigated the relationship between the impairment of visual recognition and cortical hypometabolism. The PD patients had substantial and frequent illusory responses in the overlapping figure identification test, and their illusory misidentifications were correlated with hypometabolism in the visual cortices, including the right inferior temporal gyrus and the bilateral temporo-parieto-occipital junction. These findings suggest that PD patients have impaired visual recognition characterized by illusory misidentifications of visual stimuli, which could be attributed to dysfunction of the visual cortices. © 2011 *Movement* Disorder Society

Key Words: Parkinson's disease; illusory misidentification; visual cortices; positron emission tomography; overlapping figure identification test

In addition to motor symptoms, idiopathic Parkinson's disease (PD) is associated with defects in visual function.[1] The various deficits in visual processing in PD patients are related to impairments of both retinal and cortical processing,[2] as shown by reports of a reduction in regional cerebral glucose metabolism or blood flow in the posterior brain regions, including the visual cortices, in PD patients.[3–6] It is widely assumed that the visual system is organized into 2 segregated pathways: the ventral visual stream, involved in object vision, and the dorsal visual stream, involved in spatial vision.[7,8] Although there is direct evidence indicating that dysfunction in the dorsal visual stream is responsible for impairments of visual recognition,[3,6] few neuroimaging studies have addressed dysfunction in the ventral visual stream.[9] To address this issue, we focused on the overlapping figure identification test, which was developed as a neuropsychological test to detect visual recognition disabilities.[10] Numerous studies have revealed that patients with retro-rolandic lesions have great difficulty with tests requiring identification of objects in overlapped, achromatic line drawings.[10–12] A previous positron emission tomography (PET) study demonstrated that perceptual segregation of overlapping simple geometric shapes activated a region of the lateral occipital visual cortex associated with the ventral visual stream.[13]

The overlapping figure identification test has been used to detect impairments in visual recognition in PD with dementia or dementia with Lewy bodies.[14–16] However, only 1 study focused on disabilities related

*Correspondence to: Toshiyuki Ishioka, Department of Occupational Therapy, School of Health and Social Services, Saitama Prefectural University, 820 San-Nomiya, Koshigaya, Saitama, 343-8540, Japan; t-ishioka@umin.ac.jp

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