# Changes in pupil diameter are correlated with the occurrence of pareidolias in patients with dementia with Lewy bodies

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**Pareidolias are visual illusions of meaningful objects, such as faces and animals, that arise from ambiguous forms embedded in visual scenes. Pareidolias and visual hallucinations have been suggested to have a common underlying neural mechanism in patients with dementia with Lewy bodies (DLB). The aim of the present study was to find an externally observable physiological indicator of pareidolias. Using a pareidolia test developed by Uchiyama and colleagues, we evoked pareidolias in patients with DLB and recorded the resultant changes in the diameters of their pupil. The time frequencies of changes in pupil diameters preceding pareidolic utterances and correct utterances by the patients, as well as correct utterances by healthy control participants, were analyzed by a fast Fourier transform program. The power at time frequencies of 0–0.46 Hz was found to be greatest preceding pareidolic utterances in patients with DLB, followed by that preceding correct utterances in control participants, followed by that preceding correct utterances in patients with DLB. When the changes in power preceding the utterance were greater than the median value of correct utterances by the control group, the frequency of pareidolic utterances was significantly greater than that of correct utterances and when the changes were the same as or lower than the median value, the frequency of correct utterances was significantly greater than that of pareidolic utterances. Greater changes in power preceding the utterance at time frequencies of 0–0.46 Hz may thus be an externally observable physiological indicator of the occurrence of pareidolias. *NeuroReport* 28:187–192 Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc.**

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## Introduction

Visual hallucinations are observed in more than 70% patients with dementia with Lewy bodies (DLB) [1]. Patients with DLB also frequently experience visual illusions, such as pareidolias. Pareidolias are visual illusions of meaningful objects, such as faces and animals, that arise from ambiguous forms embedded in visual scenes [2]. Uchiyama *et al.* [2] recently developed a tool that evokes and measures pareidolias, called the pareidolia test. Pareidolias and visual hallucinations have been suggested to have a common underlying neural mechanism in patients with DLB [3]. Uchiyama *et al.* [2] suggested that arousal and attention deficits mediated by abnormal cholinergic mechanisms, and dysfunction of occipitotemporal visual association cortical areas, are likely to be the common underlying mechanisms.

In the pareidolia test, patients are instructed to describe the objects shown in the stimuli. Thus, identification of pareidolias was dependent on only the subjective reports of participants. In this respect, there are challenges associated with carrying out research on the neural basis of pareidolias. If an observable physiological indicator that is not dependent on the report of patients could be found, it would considerably advance research on the neural basis of pareidolias.

The diameter of the pupil changes not only reflexively, as a function of the intensity of light reaching the retina, but also in response to other brain functions, such as arousal level [4], emotion [5], and attention [6]. Dysfunctions in arousal and attention systems are, reportedly, common mechanisms of pareidolias [2]. We hypothesized that fluctuation patterns in pupil diameter could serve as an

indicator of pareidolias. The use of an eye tracker facilitates ready access to information on pupil diameter and which part of the stimulus the participants are viewing.

The aims of the present study were to record pupil diameter, eyesight position, and saccadic eye movements of patients with DLB during the pareidolia test, and to elucidate the relationship between the occurrence of pareidolias and the characteristics of these indicators.

## Patients and methods

### Participants

We recruited eight patients with probable DLB from the dementia clinics at our hospitals. Nine healthy controls were recruited through an advertisement. The two groups were comparable in age, sex ratio, and educational level. The demographic characteristics of the participants are summarized in Table 1. All patients had stage-1 dementia according to the Clinical Dementia Rating [7]. Probable DLB was diagnosed according to the international workshop criteria [8]. The exclusion criteria were history of any other neurological, psychiatric, or severe ocular diseases; a best-corrected visual acuity of less than 20/40; and any error on the naming subtest in the Western Aphasia Battery [9]. At the time of examination, no patient was taking drugs that acted on the nervous system. All procedures in this study were approved by the Ethical Committee of the Yamagata Prefectural University of Health Sciences (#1103–18; 3 March 2011). All participants and main caregivers of the patients provided written informed consent after receiving a detailed explanation of the study.

### Behavioral assessments

The cognitive function of the patients with DLB and healthy controls was assessed using the Mini-Mental State Examination. The Neuropsychiatric Inventory [10] was administered to the caregivers of the patients with DLB.

**Table 1 Demographic and clinical profiles of the participants**

| Variables | DLB ($n=8$) | HC ($n=9$) | $P$-value |
|---|---|---|---|
| Age (years)[a] | 77.4 (6.9) | 71.4 (6.7) | 0.113 |
| Sex (female/male)[b] | 5/3 | 1/8 | 0.08 |
| Education (years)[a] | 10.1 (2.7) | 10.3 (1.6) | 0.385 |
| MMSE[a] | 22.0 (6.9) | 27.9 (1.8) | 0.04* |
| NPI | | | |
| Persecutory delusions | 1.6 (2.6) | | |
| Hallucinations | 2.1 (3.0) | | |
| Agitation/aggression | 0.3 (0.7) | | |
| Dysphoria | 0.3 (1.0) | | |
| Anxiety | 0.8 (1.6) | | |
| Euphoria | 0.3 (0.1) | | |
| Apathy | 2.7 (2.6) | | |
| Disinhibition | 0.4 (1.3) | | |
| Irritability/lability | 1.0 (1.6) | | |
| Aberrant motor behavior | 0.0 (0.0) | | |

The values in the second and third columns indicate the mean ± SD. The full scores for the MMSE is 30.
DLB, dementia with Lewy bodies; HC, healthy controls; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory.
[a]Mann–Whitney $U$-test.
[b]$\chi^2$-Test.
*$P<0.05$.

### Stimuli

The pareidolia test originally consisted of 25 blurred images of natural scenes. We used 10 such images (for instance, Fig. 1a). All images were $34^\circ \times 21^\circ$ in size and were shown on a display 57 cm from the participant.

### Apparatus

Eye movements, visual axis positions, and pupil diameters during exploration of the images were recorded with an eye tracker (EMR-8; nac Image Technology, Tokyo, Japan) with a 60-Hz sampling frequency, which detects infrared reflections from the cornea. The voices and behavior of the participants were recorded using a digital video camera.

### Procedures

On each trial, a blank screen was presented first for 3 s. Then, one of the blurred natural scene images was presented for 90 s. The participants were instructed to describe the objects shown in the image. No feedback was provided to them, irrespective of whether they gave correct or incorrect responses. Data were retrieved with the eye tracker and the video camera.

### Analysis of participants' responses

Participants' responses were classified into three types: correct utterances, in which the participant correctly identified objects that were on the images; pareidolic utterances, in which the participant falsely identified objects that were not on the images; and other utterances. Other utterances were excluded from further analysis. When a participant responded with a comment such as 'It looks like X', we excluded the response from the pareidolic utterances. Only responses that reported the presence of nonexistent objects without hesitation and remarks that presupposed the presence of nonexistent objects were considered pareidolic utterances.

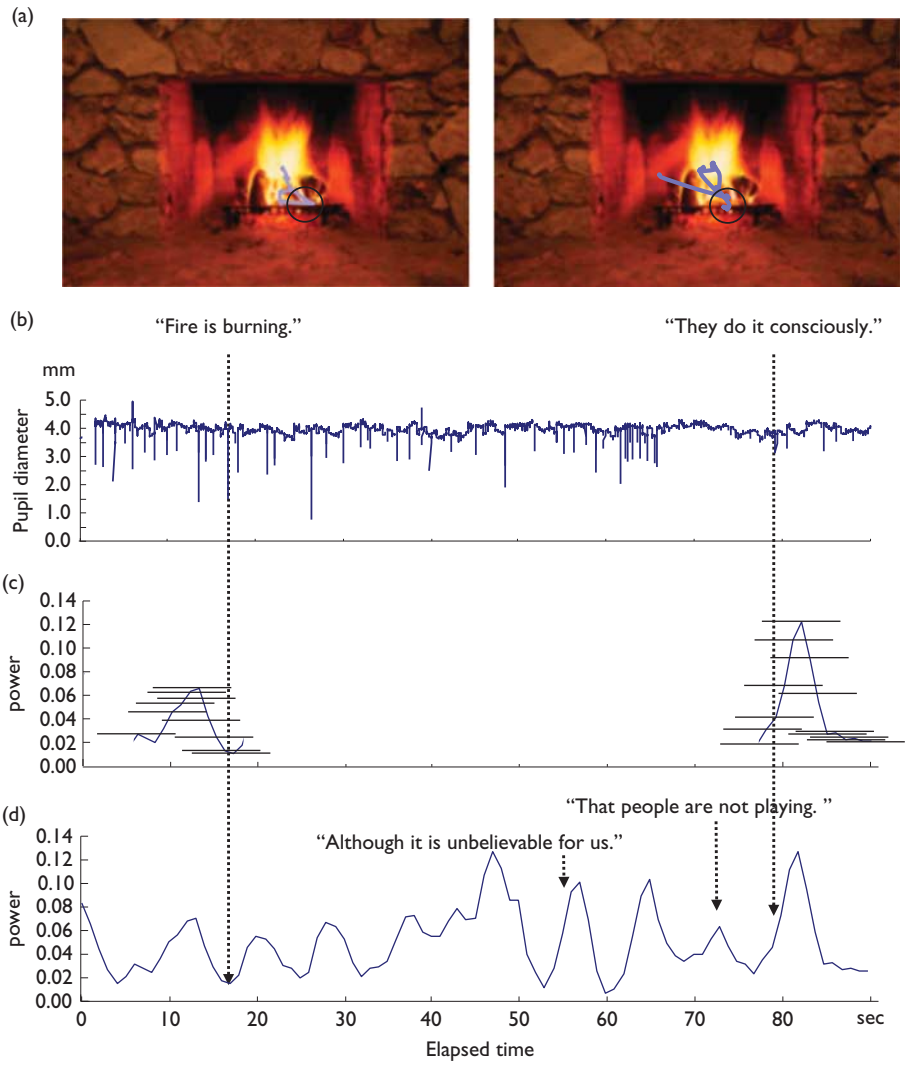
### Analysis of pupil diameters

Pupil diameters were analyzed using software (EMR-dFactory; nac Image Technology; an example of an analysis result is shown in Fig. 1b). Data from the first 3 s of presentation of the images were not analyzed because they could have been influenced by the change in luminance from blank to the images. The time frequencies of the changes in diameter were analyzed using a fast Fourier transform program (BINUTAS-Video; Kissei Comtec, Matsumoto, Japan).

#### *Analysis of time–frequency characteristics in the entire test*

We investigated the general tendencies in changes in pupil diameter in the presence or absence of pareidolic

**Fig. 1**




(a) An example of the blurred images of natural scenes by which we evoked pareidolias. (b) Pupil diameter changes in a patient with DLB while looking at the image. (c) Graphic representation of the overlapping Fourier analysis that we used to investigate changes in power at 0–0.46-Hz time–frequency. Horizontal linen segments indicate each 9-s analysis interval. (d) Changes in power at 0–0.46-Hz time–frequency in a patient with DLB while looking at the image. Black circles in the image indicate the ranges (circle radial visual angle of 1°) of fixation during the 1 s preceding the utterances. Gray lines indicate migration of the fixation point during the 2 s preceding the utterances. Phrases in quotation marks are utterances of the patient. Dashed arrows indicate the starting points of each utterance. The first and the last utterances occurred while the patient was viewing the image in the same position.

events to determine the time–frequency domain used in the examination of the onset of individual pareidolias. We collected all trials of patients with DLB in which at least one pareidolic utterance was observed, all trials of patients with DLB in which no pareidolic utterance was observed, and all trials of healthy control participants. We then calculated the power of time frequencies for 0.12-Hz width of each band for each of these three groups of trials. We set as the time–frequency domain of interest (TFDOI) the domain in which the power of the first group was different from the powers of the other two groups.

### *Analysis of pupil diameter preceding utterances*

In the most rapid cases, the change from a correct to a pareidolic utterance (or vice versa) occurs within a span of several seconds in patients with DLB. To extract the characteristics of pupil diameter in response to this change, it is necessary to divide the test into short temporal intervals and carry out Fourier analysis. However, the results of the Fourier analysis may not accurately reflect the conditions at the start and end of the intervals. Therefore, we used a method shown in Fig. 1c and summarized as follows: (a) one analysis interval was set at 9 s (540 samples). (b) We carried out a fast Fourier

analysis of the data in step 1 and calculated TFDOI power. (c) The subsequent analysis interval was set at 1 s after the previous analysis interval, and analysis as described above for steps 1 and 2 was carried out. (d) The process described in step 3 was repeatedly performed from 3 to 90 s following the start of presentation of images of scenes. (e) We selected the midpoint of each 9-s analysis interval as the representative time of the analysis interval and allocated TFDOI power to this time.

When pareidolias develop, patients with DLB may not necessarily make pareidolic utterances. Thus, when patients with DLB are silent, it cannot be known whether they are experiencing pareidolias. We can at least say, however, that pareidolias occur immediately before the start of pareidolic utterances and pareidolias do not occur immediately before the start of correct utterances. We therefore analyzed changes in TFDOI power during the 1-s period before each utterance (the power of the representative time 1 s before each utterance was subtracted from the power of the representative time of the utterance) for pareidolic and correct utterances of the patients as well as utterances of healthy participants. We subsequently determined whether there were any differences among these three groups of values.

We performed the following examination to determine whether differences in changes in TFDOI power during the 1-s period were predictive of pareidolias. Using the median variation in power change in healthy participants as a reference, we divided the changes in power in patients with DLB during the period into groups in which the values were either greater or lower than/equal to the reference values. Next, for each group, we counted the number of pareidolic utterances and correct utterances. Finally, we investigated whether the frequency of pareidolic utterances was significantly greater than that of correct utterances when the changes in power preceding the utterance were greater than the reference value, and whether the frequency of correct utterances was significantly greater than that of pareidolic utterances when the changes in power preceding the utterance were lower than or equal to the reference value.

#### *Comparison of changes in pupil diameter preceding correct and pareidolic utterances during fixation on the same objects*

Because pupil diameter is also influenced by changes in the brightness of the screen or fixation object, it is necessary to confirm that differences in pupil diameter preceding correct versus pareidolic utterances are not because of differences in brightness. If the fixation point was the same, it would appear that the brightness should be approximately the same. Therefore, we first collected cases in which the same patient produced correct utterances and pareidolic utterances while looking at the same images in the same positions, that is, the visual axis positions were in the same circle radial visual angle of 1° during the 1-s period before the utterances. Next, we compared the changes in the values of TFDOI power preceding these utterances.

#### Analysis of saccades

The positions of the visual axes were also analyzed with EMR-dFactory. We calculated and compared the frequency and angular velocity of saccades in patients with DLB during the 1-s period immediately preceding pareidolic utterances and correct utterances and the 1-s period immediately preceding correct utterances by the healthy participants. We defined a saccade as a shift of the visual axes faster than 30°/s.

#### Statistical analysis

Mann–Whitney *U*-test were used to compare the age and educational history between patients with DLB and healthy controls. The $\chi^2$-test was used to compare the sex ratios of the two groups. The Kruskal–Wallis test was used to compare the changes in TFDOI power during the 1-s period before pareidolic utterances and correct utterances by patients with DLB and correct utterances by healthy control participants. The $\chi^2$-test was used to compare the frequencies of pareidolic utterances and correct utterances by patients with DLB because of differences in the preceding change in TFDOI power. One-way analysis of variance was used to compare the frequencies and velocities of saccades and the Bonferroni procedure was used for post-hoc testing. In all cases, the threshold for statistical significance was set at *P* value is equal to 0.05.

## Results

### Demographic and behavioral data

The results are summarized in Table 1. There were no differences between the DLB group and healthy controls in age, sex ratio, or years of education. Patients with DLB had lower Mini-Mental State Examination scores than control participants. In the Neuropsychiatric Inventory, factors in which the mean of the total domain scores was more than 1.0 were persecutory delusion, hallucination, and apathy.

### Patients' responses

The patients with DLB made 123 pareidolic utterances and 146 correct utterances. The healthy participants made 323 correct utterances.

### Pupil diameter

#### *Time–frequency characteristics in the entire test*

The power of all trials from all patients with DLB in which at least one pareidolic utterance was noted was greater than that of the trials in which no pareidolic utterance was noted, and all trials of healthy participants only at the low time–frequency domain of 0–0.46 Hz. Approximately the same power was observed in all three groups at frequencies more than 0.46 Hz. On the basis of

these findings, we set TFDOI as the range of 0–0.46 Hz to carry out the subsequent analyses.

#### *Changes in pupil diameter preceding utterances*

The median value of the power changes at TFDOI of 0–0.46 Hz preceding pareidolic utterances by patients with DLB was 0.177 [interquartile range (IQR): −0.016–0.618], that preceding correct utterances by patients with DLB was −0.289 (IQR: −0.706–0.008), and that preceding correct utterances by control participants was −0.021 (IQR: −0.289–0.191). There were significant differences among these three types of utterances. The power changes were greatest before pareidolic utterances of patients with DLB, followed by changes before correct utterances of control participants, followed by changes before correct utterances of patients with DLB ($P < 0.001$).

Using the median value of the changes in TFDOI power before correct utterances by the control group (−0.021) as a reference value, we divided utterances of patients with DLB into two groups: a group in which the changes in TFDOI power during the 1-s period immediately preceding the utterances were greater than the reference value and a group in which the changes were lower than or equal to the reference value. In the former group, the number of pareidolic utterances was 121 and the number of correct utterances was 64, whereas in the latter group, the number of pareidolic utterances was 44 and the number of correct utterances was 104. When the changes in power preceding the utterance were greater than the reference value, the frequency of pareidolic utterances was significantly greater than that of correct utterances. When the changes were the same as or lower than the reference value, the frequency of correct utterances was significantly greater than that of pareidolic utterances ($P < 0.001$).

#### *Changes in pupil diameter preceding correct and pareidolic utterances during fixation on the same objects*

There were 13 cases in which a patient made correct utterances and pareidolic utterances while looking at the same image in the same position. In 11 such cases, the changes in TFDOI power preceding the pareidolic utterances were greater than the reference value, and the changes in TFDOI power preceding the correct utterances were the same as or lower than the reference value. Examples are shown in Fig. 1.

#### Frequency and angular velocity of saccades

The mean ± SD of the frequency and angular velocity of the saccades during the 1-s period immediately preceding pareidolic utterances by patients with DLB were 1.4 ± 0.3 times/s and 2.4 ± 1.2 cm/s, respectively. These values preceding correct utterances by patients with DLB were 1.4 ± 0.3 times/s and 2.5 ± 1.1 cm/s, respectively. In the control group, these values were 2.8 ± 0.4 times/s and 6.1 ± 4.1 cm/s, respectively. Although the frequency and angular velocity of saccades preceding pareidolic utterances and correct utterances in patients with DLB were smaller than those in healthy participants, no differences were noted between the frequency and angular velocity of saccades preceding pareidolic utterances and correct utterances in patients with DLB.

## Discussion

In this study, we compared the powers of pupil-diameters change at the low time–frequency domain of 0–0.46 Hz during the 1-s period immediately preceding utterances among the three groups (pareidolic utterances by patients with DLB, correct utterances by patients with DLB, and correct utterances by healthy control participants). The results showed that the change preceding pareidolic utterances by patients with DLB was greater than that observed in the other two groups. Furthermore, when the changes in power preceding the utterance were greater than the median value for the control participants, the frequency of pareidolic utterances was significantly greater than that of correct utterances; in addition, when the changes in power preceding the utterance were the same as or lower than the median value for the control participants, the frequency of correct utterances was significantly greater than that of pareidolic utterances.

We confirmed that the above-mentioned differences were observed in almost all cases in which patients viewed the same scene from the same position, with no differences in brightness or distance from the scene. Therefore, it appears that the differences in the changes in power observed before pareidolic utterances and correct utterances by patients with DLB are extremely unlikely to result from changes in brightness. Thus, the differences in changes in power in this low time–frequency domain may be an externally observable physiological indicator of the occurrence of pareidolias.

In the pareidolia test, identification of pareidolias is dependent only on the subjective reports of participants. In this respect, there are challenges associated with carrying out research on the neural basis of pareidolias. For example, when functional MRIs are used to measure brain activity during pareidolias and the patient is asked to explain the image that is seen, speaking itself causes brain activity. As the length and content of speech is highly variable, it is difficult to control for this confounder. Although participants may be asked to press a button to indicate the presence of pareidolias, it is difficult for DLB patients to follow directions such as 'If you see something that differs from what is presented in the image, please press the button'. This is because the patients do not see the image that is actually presented to them, but rather experience pareidolias. We suggest that changes in power at the low time–frequency domain may be used as an indicator of pareidolias during event-related functional MRI research to differentiate pareidolias from normal cognition.

The changes in pupil diameter observed in the low time–frequency domain may be associated with decreased arousal level [4], emotional changes [5], and attention changes [6]. Unfortunately, we could not investigate which of these factors was the background factor in determining the characteristic changes in pupil diameter in pareidolias.

Although clear differences in pupil diameter were noted when pareidolias occurred and when normal cognitive function was present in patients with DLB, no differences in saccades were noted. Assuming that the changes in pupil diameter during pareidolias are because of decreased arousal level, the frequency and velocity of saccadic eye movements similar to those during normal conditions remind us of rapid-eye-movement sleep. Some researchers have argued that the visual hallucinations experienced by patients with DLB while awake are similar to images seen in dreams during rapid-eye-movement sleep [11]. It is possible that a similar factor contributes toward the emergence of pareidolias.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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