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The occipital white matter lesions in Alzheimer's disease patients with visual hallucinations

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Abstract

Purpose: Investigators have suggested that lesions responsible for visual hallucinations (VHs) are situated in the visual association cortex. The aim of this study was to assess the relationship between occipital white matter lesions and VHs in Alzheimer's disease (AD) patients. **Methods:** AD patients with a history of VHs (AD+VH) and those without (AD−VH) were retrospectively studied. The two groups of patients were matched by sex and mental state. All subjects underwent brain magnetic resonance image (MRI) scans. The periventricular hyperintensities (PVHs) and deep white matter hyperintensities (DWHs) on MRIs were rated by two raters using a semiquantitative scoring method (0=absent; 6=confluent). **Results:** Five AD+VH patients and five AD−VH patients were enrolled into this study. The occipital PVH score was higher in the AD+VH patients than in the AD−VH patients. The occipital DWH score was zero in both groups. **Conclusion:** The presence of VHs in AD was associated with increased occipital PVHs and an absence of occipital DWHs on brain MRIs, implying that structural lesions in the geniculocalcarine region and preserved subcortical connections with visual association areas are involved in the genesis of VHs in AD.

Keywords: Alzheimer's disease; Visual hallucinations; Magnetic resonance image; White matter hyperintensities; Occipital lobe

1. Introduction

Psychotic symptoms (e.g., delusions and hallucinations) are common in patients with Alzheimer's disease (AD) and impose a considerable burden on the caregivers of such patients [1–3]. More and more studies have disclosed that delusions and hallucinations differ in their predisposing factors and etiopathogenesis [4,5]. Delusions and hallucinations may be best approached separately, with hallucinations being more indicative of a psychotic syndrome and delusions being indicative of either a psychotic disturbance or an affective disturbance [6].

Visual hallucinations (VHs) are the most common type of hallucinations in AD. Most investigators suggested that lesions responsible for VHs are situated in the visual cortex, with the visual association cortex being extraordinarily important [7–9]. Few studies have been carried out to describe the structural brain imaging of AD patients with VHs (AD+VH) [10]. For example, AD+VH patients have been shown to have a significantly smaller occipital/whole brain ratio as compared with those without VHs [11], inferring the role of pathologic changes in the occipital cortex in the occurrence of VHs in such patients.

White matter changes seen on magnetic resonance images (MRIs) had been reported to be related to cerebrovascular hyalinization of the arteriolar bed in pathologic series and to occur more frequently as an individual ages [12–14]. The hyperintense white matter lesions in MRIs can be divided into those immediately adjacent to the ventricles [periventricular hyperintensities

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(PVHs)] and those located in the deep white matter hyperintensities (DWHs). PVHs and DWHs may result from different pathologic processes, and the possible contributions of these lesions to the pathogenesis of AD, as well as its psychotic symptoms, remain to be clarified. Howanitz et al. [15] claimed that there is no correlation between the presence of white matter lesions and the occurrence of hallucinations in AD, whereas Barber et al. [16] reported that the presence of VHs in patients with dementia, including AD, dementia with Lewy bodies, and vascular dementia, is associated with the absence of occipital DWHs, suggesting that a disease-free occipital subcortical area is necessary to develop VHs. PVHs were not associated with psychotic symptoms in these patients. In the same article, however, AD patients were not examined distinctly and separately from those with dementia forms other than AD. Only 3 of the 11 AD patients experienced VHs, and these 3 patients accounted for 10.3% of the total 29 dementia patients with VHs.

The present study aimed to investigate the relationship between occipital white matter lesions on MRIs, regarding PVHs and DWHs separately, and the occurrence of VHs in AD patients.

2. Participants and methods

2.1. Patients

The AD+VH patients came from a dementia clinic of a medical center located in southern Taiwan. Their diagnosis of probable AD was made by a senior behavioral neurologist according to the criteria of the National Institute of Neurological Disorder and Stroke and the Alzheimer Disease and Related Disease Association [17]. A VH was defined as present if the subject reported seeing a perception in the absence of an external stimulus or if the caregiver, by history, or the examiner had observed the patient to interact by verbalization or action with a nonexistent person or object. Patients with the following characteristics were excluded from the study: the VH occurred exclusively in the context of delirium; the VH occurred only once before this study; or the recorded history of neuropsychiatric disorder is of one other than AD.

The control group consisted of sex- and Mini-Mental State Examination (MMSE) [18] score-matched AD patients without a history of VHs (AD−VH). Matching on cognition was done because it is known that hallucinations in AD are associated with lower cognitive scores [19].

2.2. MR imaging

All scans were performed on a 1.5-T GE Signa CVi MRI scanner. Whole brain axial images of 5-mm thickness (0.5-mm gap) were obtained by fluid-attenuated inversion recovery imaging technique to allow for detailed visualization of white matter lesions. The matrix size was 256×192. The acquisition time was 3 min.

2.3. Hyperintense white matter lesion rating

The white matter signal hyperintensities were rated by a neuroradiologist and a neurologist, both of whom were experienced in rating white matter lesions in brain imaging and were blinded to the age and diagnosis of the subjects, with the use of semiquantitative regional scoring (Table 1) [20,21]. In this rating scale, the size and number of foci with an increased signal hyperintensity were assessed. The scores of PVHs and DWHs were made when a consensus was reached between the two raters.

2.4. Statistical analysis

The differences in the mean values between groups were analyzed using Student's t test. Associations between hyperintense white matter lesions and clinical variables were examined using the Mann–Whitney U test. All statistical tests were two tailed; findings were regarded as significant if $P<.05$.

3. Results

Ten patients, including five AD+VH and five AD−VH patients, completed the study. No difference was observed in age and MMSE score between groups. The manifestations of VHs are listed in Table 2. One patient had hallucinated about a waterwheel, which was related to his previous job as an aquafarm keeper. Another patient who is a faithful Buddhist experienced VHs of Buddha. Concurrent vascular risk factors, including hypertension and diabetes mellitus, are also shown in Table 2. In addition, three of the five AD+VH patients suffered from

Table 1
The visual and semiquantitative ratings of regional hyperintense white matter lesions on brain MRIs

	Rating
PVHs (0–6)[a]	
Caps	
Occipital	0/1/2
Frontal	0/1/2
Bands	
Lateral ventricles	0/1/2
DWHs (0–24)[b]	
Frontal	0/1/2/3/4/5/6
Parietal	0/1/2/3/4/5/6
Occipital	0/1/2/3/4/5/6
Temporal	0/1/2/3/4/5/6

[a] Ratings are defined as follows: 0=absent; 1=≦5 mm; 2=>5 mm but <10 mm.

[b] Ratings are defined as follows: 0=absent; 1=≦3 mm (n≦5); 2=≦3 mm (n≧6); 3=4–10 mm (n≦5); 4=4–10 mm (n≧6); 5=≧11 mm (n≧1); 6=confluent.