Capgras-like visual decomposition in Lewy body dementia with therapeutic response to donepezil

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Deffects in visual/spatial cognition, including hallucinations and Capgras syndrome, are common in Lewy body dementia (LBD).¹ In Capgras syndrome, a person holds a delusion that a friend, spouse, parent, or other close family member has been replaced by an identical-looking impostor. These visual phenomena frequently induce anxiety and agitation, and the only treatment currently available is neuroleptics. Neuroleptics have severe side effects in LBD as well as a black box warning for increased risk of death and stroke in elderly patients with dementia. We report 2 cases of LBD where visual phenomena including Capgras-like syndrome responded favorably to the use of a cholinesterase inhibitor.

Case reports

Case 1 A 79-year-old man presented with a 3-year history of progressive word-finding difficulties and memory decline. His symptoms fulfilled criteria for probable LBD including cognitive impairment, fluctuating attention/concentration, and REM sleep behavior disorder.² Neuropsychological testing was consistent with LBD (table e-1 at Neurology.org/cp). He alleged that his wife was an intruder with similar facial features. He did not recognize his wife during these periods and was uncooperative with her efforts to assist him. He was started on donepezil 5 mg, which was subsequently titrated to 10 mg daily after 4 weeks, and it was well-tolerated. These episodes became less frequent within 2 weeks of initiation of treatment parallel to improvement in cognitive function (Mini-Mental State Examination [MMSE] 19–28). He then was able to reconstruct the image of her face, starting with a unique mole on her cheek. Within a year, severe depression necessitated psychiatric admission, during which donepezil was discontinued. He developed paranoia and experienced visual hallucinations of

Practical Implications

Consider cholinesterase inhibitors for visual hallucinations or Capgras syndrome first.

Supplemental Data

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small animals within 2 weeks of discontinuation of donepezil; these visual hallucinations resolved when donepezil was restarted, while cognitive status remained stable (MMSE 26–28). He later developed rigidity and parkinsonian tremor requiring treatment with dopamine agonists, which he tolerated without recurrence of hallucinations at low dose. Over 2 years, he continued to tolerate donepezil and remained relatively stable with minimal decline in his dementia.

Case 2 A 69-year-old woman presented with a 1.5-year history of reported cognitive decline. Clinical features met criteria for probable LBD including new-onset REM sleep behavior disorder and visual hallucinations.² Neuropsychological testing was consistent with LBD (table e-1). The visual hallucinations mainly consisted of a familiar or an unfamiliar face projecting onto the face of her husband. She experienced severe anxiety and agitation because of the perceived intruder during these episodes, occurring several times a day, lasting up to 2–3 hours. She endorsed problems with visual/spatial orientation, reporting that the alignment of furniture was off or experiencing her surroundings as unfamiliar due to altered proportions. Empirical treatment with donepezil 10 mg was initiated and the visual phenomena resolved within 2 weeks of initiation of therapy parallel to improvement in cognitive function (MMSE 19–24). She had recurrence of the Capgras syndrome after several weeks on donepezil 10 mg and again remitted with escalation of the dose to 23 mg daily while MMSE remained stable.

DISCUSSION

We elected to use Capgras-like syndrome to reflect on the unusual features in each case, namely the ability to reconstruct the image starting with a unique mole on the cheek, and the phenomenon of projecting the son's face onto the face of the husband. Visual hallucinations and misidentification are key features of LBD and are often the most distressing. Dysfunction of the visuo-amygdaloid pathway has been implicated in the visual misidentification and visual hallucinations.³ The inferior longitudinal fasciculus projects from the occipital lobe visual association cortex to the medial and anterior temporal lobe and carries modulatory projections back to the visual cortex from the amygdala. The inferior longitudinal fasciculus is disrupted in LBD with visual hallucinations compared to LBD without visual hallucinations as measured by diffusion tensor imaging.³

LBD is associated with widespread cholinergic dysfunction as demonstrated by PET using radiolabeled acetylcholine analogues MP4A and MP4P.⁴ The maximum deficits are measured in the posterior cortical regions, the inferior temporal gyrus, the supramarginal gyrus, and the posterior cingulate.⁴ The cholinergic deficit in LBD is more marked than in Alzheimer disease (AD),⁵ suggesting that cholinesterase inhibitors may be more effective in LBD than in AD. Although the cholinergic component of the visuo-amygdaloid pathway is unknown, the PET images demonstrating the cholinergic deficits in LBD overlap with this pathway. Furthermore, in a group of patients with LBD, the preservation of the hippocampal volume predicted favorable response to cholinesterase inhibitors.⁶ Although clinical trials are limited, cholinesterase inhibitors are frequently used in this group.⁷

Currently, evidence-based treatment to treat visual hallucinations in LBD is lacking. Antipsychotics have severe risks and side effects in this patient group. Brain cholinergic dysfunction may contribute to visual phenomena including visual hallucinations, visual misidentification, and Capgras-like visual decomposition of faces in LBD. The presented cases suggest that cholinesterase inhibitors may be useful to target the visual phenomena in LBD with superior safety when compared to neuroleptics. While the initial response was concomitant with cognitive improvement, the subsequent response was uncoupled from it. Further double-blind studies are needed to evaluate the role of cholinesterase inhibitors in the treatment of visual symptoms in LBD.

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Practical Implications

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