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Cognitive Rehabilitation in a Visual Variant of Alzheimer’s Disease

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Alzheimer’s disease (AD) is commonly associated with marked memory deficits; however, nonamnestic variants have been consistently described as well. Posterior cortical atrophy (PCA) is a progressive degenerative condition in which posterior regions of the brain are predominantly affected, therefore resulting in a pattern of distinctive and marked visuospatial symptoms, such as apraxia, alexia, and spatial neglect. Despite the growing number of studies on cognitive and neural bases of the visual variant of AD, intervention studies remain relatively sparse. Current pharmacological treatments offer modest efficacy. Also, there is a scarcity of complementary nonpharmacological interventions with only two previous studies of PCA. Here we describe a highly educated 57-year-old patient diagnosed with a visual variant of AD who participated in a cognitive intervention program (comprising reality orientation, cognitive stimulation, and cognitive training exercises). Neuropsychological assessment was performed across moments (baseline, postintervention, follow-up) and consisted mainly of verbal and visual memory. Baseline neuropsychological assessment showed deficits in perceptive and visual-constructive abilities, learning and memory, and temporal orientation.

*These authors contributed equally to this work.

Informed consent was obtained from the patient, and an informed written consent was obtained from the patient’s next of kin.

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After neuropsychological rehabilitation, we observed small improvements in the patient’s cognitive functioning, namely in verbal memory, attention, and psychomotor abilities. This study shows evidence of small beneficial effects of cognitive intervention in PCA and is the first report of this approach with a highly educated patient in a moderate stage of the disease. Controlled studies are needed to assess the potential efficacy of cognition-focused approaches in these patients, and, if relevant, to grant their availability as a complementary therapy to pharmacological treatment and visual aids.

Key words: Alzheimer’s disease, cognitive intervention, cognitive rehabilitation, posterior cortical atrophy

INTRODUCTION

In the most typical clinical presentation, early stages of Alzheimer’s disease (AD) are usually marked by memory deficits. However, other nonamnestic clinical profiles/syndromes of AD can also be observed and have been consistently described as affecting predominantly language or visuospatial skills (Galton, Patterson, Xuereb, & Hodges, 2000).

One of the most frequently referred AD variants is posterior cortical atrophy (PCA), which has been described as the visual variant of AD, in which most cases show AD neuropathology (Victoroff, Ross, Benson, Verity, & Vinters, 1994) and similar amyloid-b burden (de Souza et al., 2011). Distinctively, patients with this visual variant show a marked array of visuospatial symptoms, such as apraxia, alexia, and spatial neglect (Caprile et al., 2009; Kas et al., 2011; McMonagle, Deering, Berliner, & Kertesz, 2006), reflecting a widespread impairment in occipital- and parietal-related visual functions (Metzler-Baddeley, Baddeley, Lovell, Laffan, & Jones, 2010).

A concomitant pattern of posterior cerebral impairment, structural and/or functional, has been found: hypoperfusion and hypometabolism (Kas et al., 2011; Nestor, Caine, Fryer, Clarke, & Hodges, 2003), marked amyloid load in the occipital and parietal regions (Formaglio et al., 2011), and a pattern of atrophy in posterior regions (Whitwell et al., 2007). On the contrary, when compared with patients with the visual variant, those with typical amnestic AD display greater atrophy in the hippocampi and the left medial temporal lobe (Feldmann et al., 2008; Whitwell et al., 2007).

Despite recent increasing clinical evidence for this visual variant of AD, only a few studies are currently available, particularly in the area of cognitive intervention. However, as shown by a recent review/meta-analysis (Alves et al., 2013), there is current evidence of cognitive intervention for improving global cognitive functioning in AD. To the best of our knowledge, there are only two other previous studies assessing the effects of non-pharmacological intervention specifically for PCA (Roca, Gleichgerrcht, Torralva, & Manes, 2010; Weill-Chounlamountry et al., 2012). However, intervention approaches in these two works were different from one another. Whereas Roca and colleagues (2010) developed a compensatory neuropsychological intervention that resulted in better perception of difficulties and improvements in visuoperceptual tasks, Weill-Chounlamountry and colleagues (2012) developed a multidisciplinary approach (including speech therapy, occupational therapy, and physiotherapy) allowing the patient to reach his/her functional objectives.

Here we report a case of cognitive intervention in a patient (diagnosed with a visual variant of AD), who, although similar to patients reported in previous studies (Roca et al., 2010; Weill-Chounlamountry et al., 2012), had higher formal education and more advanced deficits.

CASE REPORT

A 57-year-old male patient who was a native speaker of English, bilingual, and highly educated (master’s degree) was referred to our clinic for neuropsychological assessment and cognitive intervention. Two years earlier, the patient had been diagnosed with a variant of AD of early onset associated with a progressive decline in visuospatial functioning (without visual loss) starting with difficulties in driving, writing, and reading.

The patient met the criteria (Kas et al., 2011) for PCA, which is characterized by progressive decline in visuospatial, visuoperceptual, literacy, and praxic skills (Crutch et al., 2012). The patient remained aware of his impairments since the onset of the symptoms. Additionally, an existence of mild depressive symptoms was reported at the time of the first complaints. Depression and the absence of anosognosia are two characteristics commonly reported in this visual variant (Mendez, Ghajarania, & Perryman, 2002). Magnetic resonance imaging performed at diagnosis showed a slight enlargement of the sulci and ventricles, which was more evident in the posterior regions (Figure 1).
Both patient and caregiver reported worsening of initial visuoperceptive and visuospatial symptoms. Posteriorly, cognitive deficits progressed toward memory loss (mainly visual memory and face recognition, subsequently progressing to naming abilities and autobiographical semantic memories). Furthermore, at the time of the study, the patient was receiving a stable dose of three medications (memantine, sertraline, and buspirone). As assessed through clinical interview with the patient and caregivers, current major depression symptoms were not evident.

Neuropsychological assessment was performed at baseline (Month 0), postintervention (Month 3), and follow-up (Month 12) by the same clinicians across all moments, who were not blinded to the different assessment moments nor to intervention goals. Assessment sessions were approximately 1.5 hr to 2 hr long, with breaks provided as needed and without violating test norms. English tests and available normative data were used for testing (the only exception was the Wechsler Adult Intelligence Scale Vocabulary, for which only the Portuguese version (Rocha, 2008) was used because we did not have the English version; see Table 1 for full list of tests across different moments). Due to practical constraints (e.g., time, fatigue), it was not possible to administer all tests across all moments.

Baseline assessment showed deficits in perceptive, visuoconstructive, learning and memory, and temporal orientation.

Formal evaluation of executive functioning was not possible because most of the available tasks required visual abilities, and application of those tests was not possible when tried. However, informal (through clinical interview) assessment showed relatively preserved abstract reasoning (e.g., metaphor understanding). No signs of anosognosia were present.

### Table 1

<table>
<thead>
<tr>
<th>Neuropsychological Tests</th>
<th>Baseline Raw Score</th>
<th>z Score</th>
<th>Postintervention Raw Score</th>
<th>z Score</th>
<th>Difference Postintervention—Baseline (z score)</th>
<th>Significant Change (Preintervention to Postintervention)</th>
<th>Follow-Up Raw Score</th>
<th>z Score</th>
<th>Difference Follow-Up—Baseline (z score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE (max. 30)</td>
<td>18</td>
<td>-7.33</td>
<td>22</td>
<td>-1.63</td>
<td>1.33</td>
<td>12.86</td>
<td>11</td>
<td>-2.97</td>
<td>0.00</td>
</tr>
<tr>
<td>Word List Recall (WMS-III) Total Score</td>
<td>2</td>
<td>-2.97</td>
<td>7</td>
<td>1.30</td>
<td>2.33</td>
<td>N/A</td>
<td>4</td>
<td>-0.37</td>
<td>0.67</td>
</tr>
<tr>
<td>Word List Learning Slope (WMS-III)</td>
<td>0</td>
<td>N/A</td>
<td>6</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>3</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Word List Short Delay (WMS-III)</td>
<td>2</td>
<td>-0.3</td>
<td>7</td>
<td>0.70</td>
<td>1.00</td>
<td>3.07</td>
<td>4</td>
<td>0.03</td>
<td>0.33</td>
</tr>
<tr>
<td>Word List Long-Term Recall (WMS-III)</td>
<td>20/24</td>
<td>-0.65</td>
<td>22/24</td>
<td>0.00</td>
<td>0.65</td>
<td>1.03</td>
<td>19/24</td>
<td>-1.29</td>
<td>-0.65</td>
</tr>
<tr>
<td>Visual Reproduction Recall Total Score (WMS-III)</td>
<td>20/104</td>
<td>-2.94</td>
<td>17</td>
<td>-2.94</td>
<td>0.00</td>
<td>-2.59</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Spatial Span (WMS-III) Score</td>
<td>2</td>
<td>-2.67</td>
<td>6</td>
<td>-2.33</td>
<td>0.33</td>
<td>2.48</td>
<td>0</td>
<td>-2.94</td>
<td>-0.27</td>
</tr>
<tr>
<td>TMT-A</td>
<td>612 s</td>
<td>-57.23</td>
<td>281</td>
<td>-24.58</td>
<td>32.64</td>
<td>N/A</td>
<td>621</td>
<td>-58.11</td>
<td>-0.89</td>
</tr>
<tr>
<td>TMT-B</td>
<td>988 s</td>
<td>-43.73</td>
<td>691</td>
<td>-29.60</td>
<td>14.13</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>COWAT</td>
<td>22</td>
<td>-2.03</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Vocabulary (WAIS-III)</td>
<td>43</td>
<td>0.69</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>7</td>
<td>-2.21</td>
<td>N/A</td>
</tr>
<tr>
<td>Digit Span (WMS-III)</td>
<td>N/A</td>
<td>N/A</td>
<td>10</td>
<td>-1.52</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A = not available; MMSE = Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975); WMS-III = Wechsler Memory Scale-Third Edition (Wechsler, 1999); WAIS-III = Wechsler Adult Intelligence Scale Third Edition; COWAT = Controlled Oral Word Association Test (Strauss, Sherman, & Spreen, 2006); TMT-A, TMT-B = Trail-Making Test-Parts A and B (Reitan, 1955).
Neuropsychological tests for which postintervention versus baseline changes surpassed 1.5 standard deviations based on normative data were considered to exceed cognitive changes due to disease course variations and test–retest and practice effects, similar to the criteria used in previous studies (Roca et al., 2010). This criterion was considered the primary endpoint.

To improve cognitive functioning, the patient was enrolled in an individual cognitive rehabilitation program delivered by a clinical psychologist with training in neuropsychology who was not blinded to the assessments or to the objective of the intervention. A detailed description of the rehabilitation program exercises is shown in Table 2. The program included reality orientation, cognitive stimulation, and cognitive training exercises, according to the approaches established by Clare and Woods (2004). A set of training exercises was prepared for the individual cognitive rehabilitation program; none of these comprised materials from neuropsychological assessment instruments. There were 30 sessions, 2 hr each, with a frequency of 3 sessions per week. The ultimate goal was to improve the patient’s cognitive functioning.

During rehabilitation, the patient showed evidence of improvement in some of the trained tasks illustrated in Table 2. Although no quantitative improvements were noted in the exercises of verbal fluency, number and letter identification, and word reading, small qualitative improvements were observed (note that response times were not registered). These qualitative improvements possibly contributed to quantitative improvements in tasks such as word and phrase writing and math exercises. No follow-up data were collected on performance in trained tasks.

After the completion of the rehabilitation program, neuropsychological assessment showed evidence of small improvements in temporal and spatial orientation, verbal learning, attention, and psychomotor abilities. Although performance on the Trail-Making Test-Parts A and B (TMT-A, TMT-B) was still far from the normative range, aforementioned outcomes of TMT-A and TMT-B were considered to be considerable improvements. Nevertheless, visuoperceptive and visuospatial domains remained severely impaired (Table 1).

A clinically significant change is often difficult to assess. Therefore, we complemented our primary analysis, which was based on improvement of at least 1.5 standard deviations relative to baseline, with calculation of the clinically significant change (Reliable Change Index adopted from Christensen & Mendoza, 1986), which was adopted as a secondary endpoint. Specifically, when the value of significant change was greater than 1.96, it was interpreted as a pretest to posttest change probably due to an experimental treatment effect rather than measurement error. The latter mentioned

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Objectives and Conceptualization of the Cognitive Rehabilitation Program</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective of the Cognitive Rehabilitation Program: Improve Patient Cognition</strong></td>
<td><strong>Patient Evolution (Preintervention vs. Postintervention)</strong></td>
</tr>
<tr>
<td>Written reproduction of auditorily and visually presented numbers</td>
<td>Patient was unable to write numbers at baseline but was able to write numbers in Arabic numerals and in written numbers postintervention. At baseline, patient needed a mean of eight tries to correctly reproduce a word; at postintervention, patient needed a mean of four tries. Also, at postintervention, correctly reproduced words were longer (e.g., baseline, rice; postintervention, octopus)</td>
</tr>
<tr>
<td>Word writing</td>
<td></td>
</tr>
<tr>
<td>Phrase writing</td>
<td>Patient improved from writing simple sentences with four words (e.g., <em>It’s cold outside</em>) to longer sentences (e.g., <em>I like to walk in the garden</em>).</td>
</tr>
<tr>
<td>Temporal and spatial orientation (routinely ask the patient to recall present, past, and future dates; use of activities as clue of day of the week, etc.)</td>
<td>Temporal orientation: At postintervention, patient was able to allocate his routines to specific days of the week. Spatial orientation: At postintervention, patient was able to describe places and to independently travel to the coffee shop.</td>
</tr>
<tr>
<td>Adding exercises (to improve autonomy when going to coffee shops or stores)</td>
<td>Baseline: Patient was unable to perform daily simple mathematical calculations. Postintervention: Patient was able to do adding exercises reaching results in the order of 10th (e.g., 5 + 6 = 11)</td>
</tr>
<tr>
<td>Sequential adding</td>
<td>Patient improved from series of adding 2 + 2 to series of 3 + 3.</td>
</tr>
</tbody>
</table>
| Psychoeducational and compensatory strategies | Examples: 
- Basic notion of time (24-hr day; 1 hr = 60 s). 
- Promotion of healthy sleep routines. 
- Adapted watch was built for allowing patient to manipulate the hands of the clock. 
- Use of daily tasks as clues for time orientation (e.g., night and day; meals). |
calculation was performed only on tests for which we had available measurement error data. Using this method, significant improvements were observed at postintervention on the following neuropsychological tests: Word List Recall Total Score, Word List Long-Term Recall, and Spatial Span Total Score. No change was observed in Word List Recognition. A significant level of deterioration was observed in the Visual Reproduction Total Score. In sum, there was no agreement between changes detected with the 1.5-standard deviation criteria and the clinical significant change criteria.

Although not formally evaluated, a modest improvement in daily functionality was reported by the patient and caregivers (e.g., the patient was able to resort to environmental cues, such as daylight, for temporal orientation).

At the 9-month postintervention/follow-up assessment (Month 12), all cognitive domains displayed a decline when compared with postintervention. However, overall cognitive functioning at follow-up assessment did not decline when compared with baseline.

DISCUSSION

In this study, we reported a cognitive intervention program delivered to a patient diagnosed with an AD visual variant. This cognitive intervention resulted in small benefits particularly right after the intervention, in accordance with the only two previously published studies (Roca et al., 2010; Weill-Chounlamountry et al., 2012).

Although there are a growing number of studies describing the neuropsychological profile of atypical variants of AD (Galton et al., 2000; Lambon Ralph, Patterson, Graham, Dawson, & Hodges, 2003), research on cognitive intervention in atypical variants of AD remains considerably scarce. In the previous cognitive intervention study (Roca et al., 2010), a 64-year-old patient underwent a cognitive rehabilitation program. This program included psychoeducation, compensatory strategies, and cognitive training exercises, respectively, aimed at improving disease and symptom understanding, diminishing difficulties in finding things and pouring drinks, and improving the reading of written messages. Small improvements were observed in visuo-perceptual tasks and in the patient’s perception of difficulties. In the present case report we had comparable clinical goals with a similar, but more intensive, cognitive rehabilitation approach; however, our patient had higher formal education and presented a more extensive impairment. In accordance with previous literature (Liberati, Raffone, & Olivetti Belardinelli, 2012), we hypothesize that even when neuropathology is present, it is possible to build on cognitive reserve with a tailor-made cognitive intervention.

Some limitations need to be considered. This is a clinical case report; therefore, our data do not clearly demonstrate the efficacy of the cognitive intervention. Moreover, although there was no agreement between changes detected with the 1.5-standard deviation criteria and the clinical significant change criteria, we should highlight that the former is based on a comparison to a normative group. Considering the severe cognitive dysfunction present in patients with dementia, the clinical significant change criteria are probably a more meaningful way of assessing change in cognitive intervention settings. Alternatively, the attainment of a stable course (no further cognitive decline) could be a reasonable outcome criterion for future studies, because we are considering a neurodegenerative condition.

Also, our patient showed more extensive deficits than those previously reported in other studies (as shown by the Mini-Mental State Examination score), so cognitive intervention might prove to be beneficial also in moderate stages of PCA.

Additionally, it should be mentioned that the present intervention format was relatively intensive and time-consuming (60 hr), which could be difficult to implement in some clinical settings. Nevertheless, it should be acknowledged that in countries such as the United Kingdom, individual cognitive rehabilitation is an available therapy option for dementia, and small-group cognitive stimulation (fourteen 1-hr sessions) is recommended by UK health guidelines (National Institute for Health and Clinical Excellence, 2006). It is relevant to consider that 16 additional weekly maintenance sessions (totaling 30 sessions) were shown to sustain cognitive benefits for about 6 months (Orrell, Spector, Thorgrimsen, & Woods, 2005). Taking into account costs and cognitive benefits, the relative value of brief versus long intervention formats has yet to be thoroughly addressed in this condition.

Overall, we believe that this report adds to the sparse literature justifying the development of controlled studies of nonpharmacological interventions for this population. Further controlled studies are needed to explore the effects of cognition-based approaches for enhancing mood, functionality, cognition, and quality of life of patients with visual variants of AD. Additional topics need to be investigated such as differential benefits for patients according to their levels of education (and cognitive reserve) and their cognitive profiles (e.g., typical amnestic AD vs. visual variant of AD), differential effects of each cognitive intervention approach (cognitive stimulation, cognitive training, cognitive rehabilitation), and the impact of parameters such as frequency and duration. Comparison between different parameters and type of approach might also be useful to provide a cost-effective nonpharmacological approach to PCA.
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