A NOVEL VISUAL PAIRED ASSOCIATES TASK DETECTS OBJECT AMBIGUITY AND SEMANTIC FAMILIARITY IMPAIRMENTS IN LEARNING AND RECOGNITION IN VERY EARLY ALZHEIMER’S DISEASE

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Background

• Alzheimer’s disease (AD) neurofibrillary pathology associated with cognitive impairments begins in the perirhinal cortex (PRC) before spreading to the rostral anteromedial temporal lobe (aMTL) and beyond (Fig. 1).

• A hierarchical model of meaningful object processing in the ventral stream (Desimone & Ungerleider, 1989) (Fig. 2):
  - Increasingly more complex features are coded from posterior to anterior sites
  - PRC at apex of stream
  - Processes most complex object representations required to disambiguate between visually and semantically familiar objects (Saksida, Bussey & Murray, Bussey & Saksida, 2007; Tyler et al., 2004)

• Receives information from other sensory modalities (Suzuki & Amaral, 1994), possibly supporting long-term memories of familiar (sematic) objects (Kivisaari, Tyler, Monsch & Taylor, in press; Murray & Richmond, 2001; Taylor et al., 2006).

Methods

1. To develop a novel visual paired associates (VPA) task stressing PRC function (object confusability, semantic familiarity) for use as a cognitive marker of very early AD.
2. To test the validity of this task in patients with this syndrome.

AIMS:

Behavioral task

Stimuli

- We constructed two visual paired associates subtasks, one with less and one with highly confusable object stimuli, i.e. tools and fruits.
- Each learning trial presented nine pairs of grayscale object pictures representing semantically unfamiliar (n=4), semantically familiar (n=5) and paired unfamiliar-familiar (n=3) objects (see Table 1).

Table 1. Task design and example stimuli.

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>Confusability</th>
<th>Familiarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfamiliar</td>
<td>Less Confusable (tool VPA)</td>
<td>Confusable (fruit VPA)</td>
</tr>
<tr>
<td>Mixed</td>
<td>first fender</td>
<td>park tool</td>
</tr>
<tr>
<td>Familiar</td>
<td>hailstone</td>
<td>thread cutter</td>
</tr>
<tr>
<td></td>
<td>bolt cutter</td>
<td>spruce</td>
</tr>
<tr>
<td></td>
<td>lemon</td>
<td>nectarine</td>
</tr>
</tbody>
</table>

Tasks:

Immediate pair recognition: 3 learning (i.e., viewing) trials were each immediately followed by a recognition task with the original and completely novel (familiar and unfamiliar) object pairs from the same semantic category for OLD/New pair decisions.

Delayed object recognition: Individual objects from the VPA learning phase and novel (familiar and unfamiliar) objects from the same semantic categories were individually presented for OLD/new object decisions.

Participants

Healthy controls (NC) and patients with AD and its purported prodromic amnestic Mild Cognitive Impairment (aMCI) completed both VPA subtests (fruit and tool task presentation order counterbalanced over participants; see Table 2).

Table 2. Demographic characteristics and Mini-Mental State Examination scores of the participants.

<table>
<thead>
<tr>
<th></th>
<th>NC</th>
<th>aMCI/AD</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>68</td>
<td>68</td>
<td>1.535</td>
</tr>
<tr>
<td>Education</td>
<td>12.9±2.8</td>
<td>13.4±3.3</td>
<td>1.016</td>
</tr>
<tr>
<td>Gender (m/f)</td>
<td>41:27</td>
<td>35:33</td>
<td>0.861</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.2±1.0</td>
<td>27.6±2.2</td>
<td>1.581</td>
</tr>
</tbody>
</table>

Statistical analyses:

- VPA-learning % correct: ANOVA with the factors diagnostic category, confusability (fruits vs. tools), familiarity and learning trial
- VPA-recognition % correct: ANOVA with the factors diagnostic category, confusability (fruits vs. tools), familiarity and learning trial
- Both analyses used counterbalancing and gender as covariates.

Immediate pair recognition (learning)

- Both controls and patients performed more poorly on the confusable fruit compared to the less confusable tool task, but this difference was more pronounced in the control group, contrary to our prediction (F(1, 127) = 3.197, p = .001; see Fig. 3):
  - Patients’ performance was not significantly modulated by the familiarity of the VPA pairs (F(2, 127) = .003, p = .96).
  - However, patients’ learning curve was flatter than controls’ (F(2, 127)=9.917, p = .05), an effect which interacted with the confusability of the VPA pairs (F(2, 127)=7.336, p < .01) (Fig. 4 and 5, respectively):

Delayed object recognition

- Similar to learning, there was a trend for poorer performance with confusable fruits compared to less confusable tools over both groups (F(1, 127) = 3.452, p = .07, see Fig. 6):

- Significantly, patients were less able to benefit from item familiarity than controls (F(1, 127) = 4.226, p < .05), an effect which was slightly more pronounced during the recognition of confusable fruit stimuli (F(1, 127) = 3.610, p < .06) (see Figs. 7 and 8, respectively):

- Finally, while both groups performed more poorly with distractors compared to targets (F(1, 127) = 15.864, p < .0001), this effect was significantly more pronounced in patients with familiar stimuli (F(1, 127) = 20.567, p < .00001) (Fig. 9 and 10).

Conclusions:

1. Patients with early Alzheimer’s disease showed learning and memory impairments for highly confusable and semantically familiar objects, especially those in the distractor condition (see 194.29), processes presumably undermined by the PRC.
2. Since AD neurofibrillary pathology begins in the medial PRC, these impairments may characterize the pre-dementia stage of AD.