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Supplementary Data

Lost and Found: Bespoke Memory Testing for Alzheimer's Disease and Semantic Dementia

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1. Introduction

The effect of potential confounding factors, such as mood, sex, age and educational achievement was examined.

While depression is associated with memory complaints, and is often the main alternative diagnosis with respect to isolated memory impairment, TM has been reported to be insensitive to depression [1], in contrast to conventional memory tests (e.g. word-list learning). Furthermore, patients with subjective memory complaints performed normally at the Four Mountains short-term TM test [2]. This suggests that clinical tests of TM may have a role in separating these groups.

There is debate in the literature with respect to the effect of sex in navigational ability. Some authors claim to find sex-specific differences [3,4] while others do not [5,6]. Others focus on the fact that men and women employ or favour different strategies with which to navigate [7], or even that other factors, such as previous experience (by men) of virtual environments [8] are driving such differences.

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2. Methods

An independent samples t-test of male versus female controls was performed for each TM task to look for any sex-specific differences in performance.

To assess potential relationships of age, intelligence and mood with TM, Pearson product-moment correlation coefficients (or Spearman's , if the data were not normally distributed) were performed in controls.

3. Results

3.1. Sex differences in TM performance

Women performed less well in the HOT ($p = 0.0009$) but there was no difference in the VRLT, 4M-PP or the 4M-PM task (Supplemental Fig. 3). Therefore, the HOT results were re-analysed in a two-way ANOVA [Sex (2) x Subject Group (4)]. There was a significant effect of group [$F(3,80) = 14.18$, $p < 0.0001$] (which, as before, was driven only by AD impairment) and of Sex [$F(1,80) = 21.35$, $p < 0.0001$], with men outperforming women, but not a group by sex interaction [$F(3,80) = 0.85$, $p = 0.47$)].

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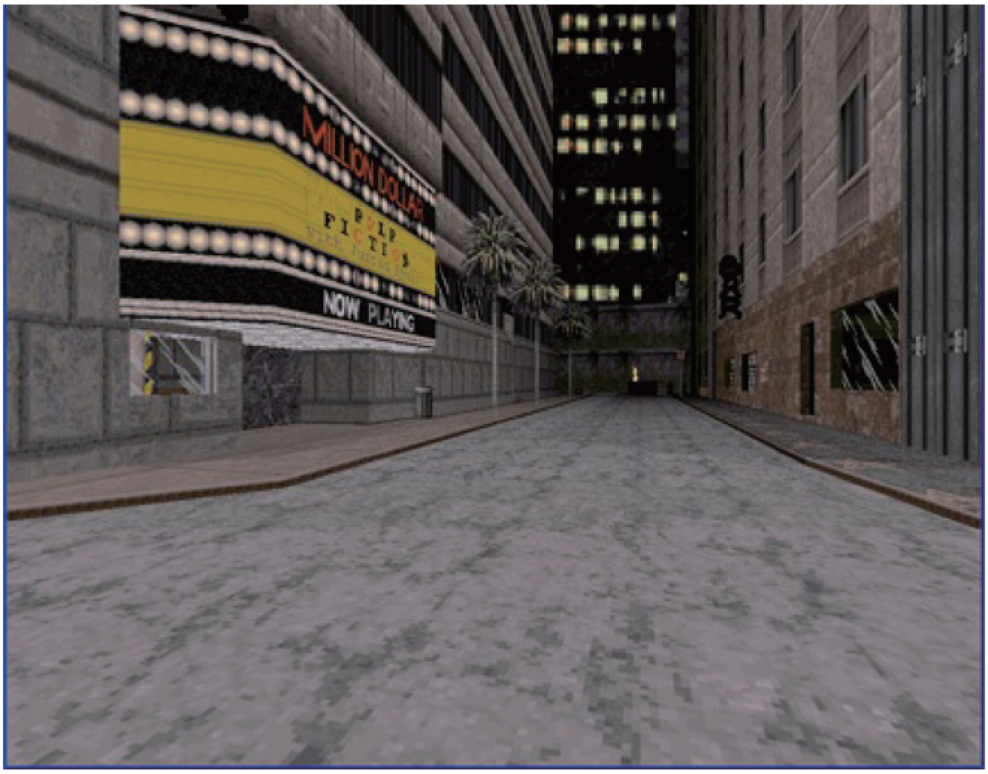


Supplemental Fig. 1. View of the cinema in the virtual town. This exact position and facing is the starting point for all tasks.

3.2. The effect of age

Correlation analyses revealed a small but significant effect of age-related decline in performance of the 4M-PM task in controls ($p < 0.05$, Pearson R $= -0.38$). There was no relationship to age on the VRLT, HOT or 4M-PP task.

3.3. The effect of education

There was no correlation between any of the TM tests and years of education.

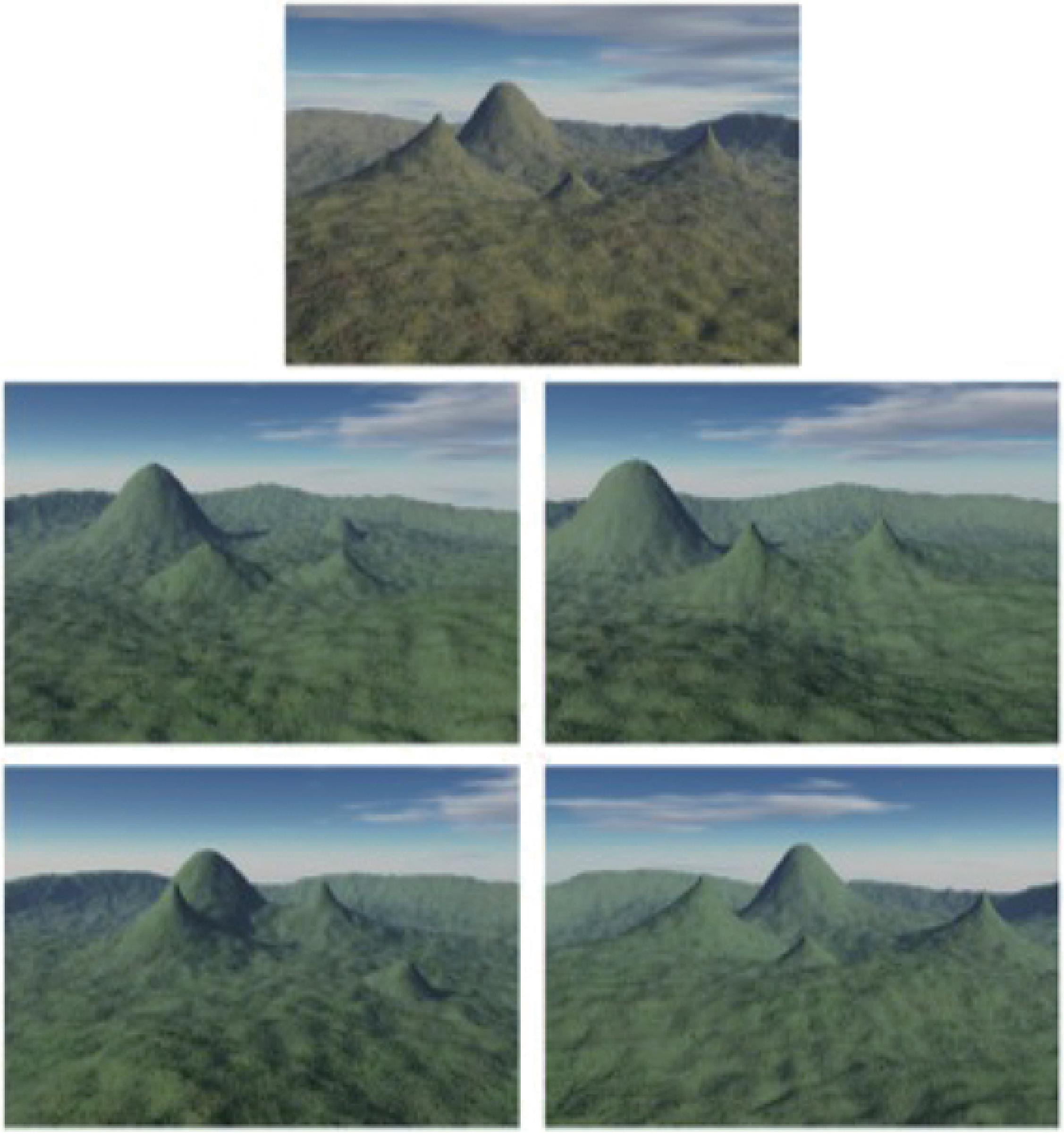
3.4. The effect of mood

The 4M-PM test correlated weakly with the GDS (p(1-tailed) $= 0.03$, $= -0.34$) but not the HADS-Depression or Anxiety scores. There was no relationship of anxiety or depression with the 4M-PP, VRLT or HOT.

4. Discussion

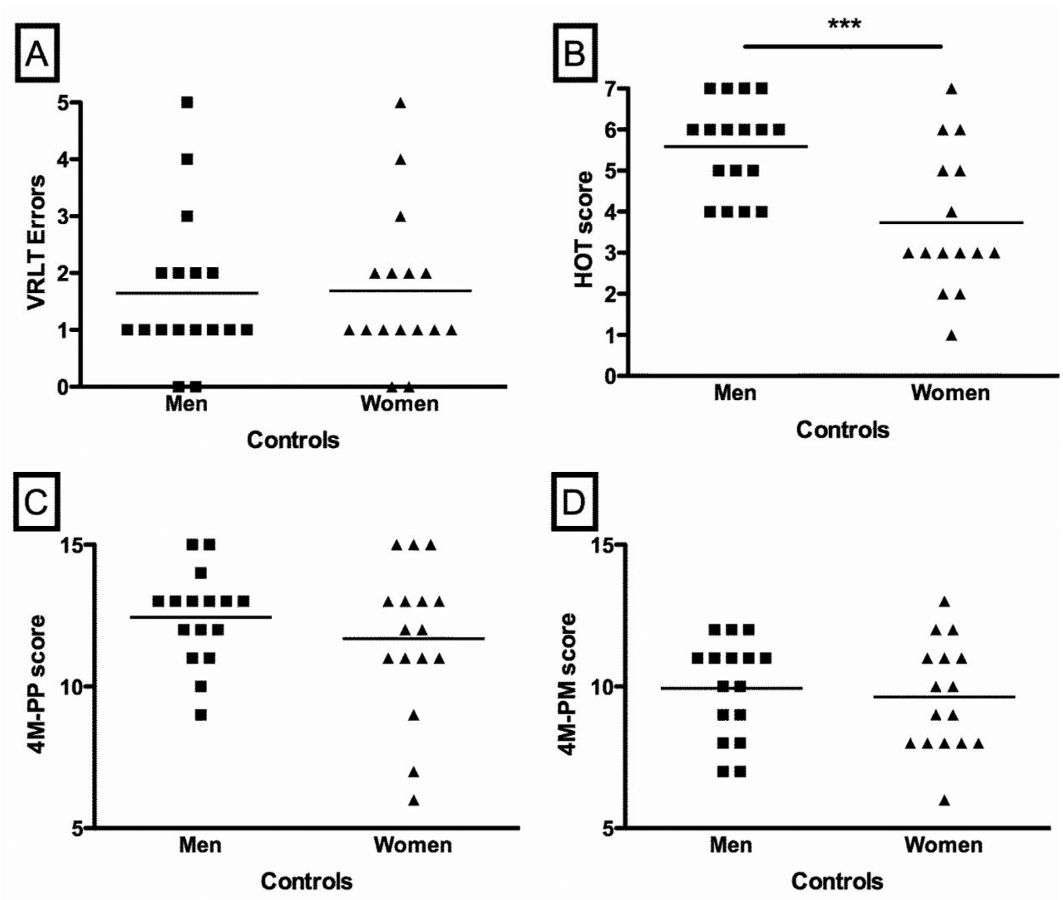
In this aged control cohort, TM performance was unrelated to education level, or anxiety. The 4M-PM correlated weakly with depressive symptoms (using the GDS but not HADS) and age; the VRLT, HOT and 4M-PP task did not. It is important to acknowledge, however, that the absence of correlation was with depressive symptoms in a dementia cohort; it does not necessarily follow that this would be the case where depression is severe and the primary diagnosis, as in the study by Gould et al. [9]. As this study aimed to examine TM performance in dementia, the controls' age range (59–79) was matched to that of the patient groups. As such, although the VRLT, HOT and 4M-PP test performance was independent of age in this control group, it is quite possible that there is an age effect over a wider range, as has been demonstrated in TM tasks when young versus aged healthy volunteers were contrasted [5,10]. Importantly for the current study's purpose, however, the tests remained stable in controls across the age range in which patients typically present with neurodegenerative dementias.

The was no sex difference in performance of the VRLT and Four Mountains tasks, but women were sig-



Supplemental Fig. 2. The Four Mountains Test. In the 4M-PP (control) condition, the target (top picture) was presented concurrently with four possible responses, whereas in the 4M-PM condition, the target was presented alone first and then hidden. The answer in this exemplar is the bottom right hand landscape.

nificantly worse than men at the HOT. Female controls were as good as males at learning routes in a virtual town, contrary to suggestions that men have an inherent advantage in virtual environments [8]. In the same environment, however, women were significantly less accurate at pointing to the direction of a landmark. Routes taken were often long, with multiple turns, so path integration, or tallying the number of turns taken, was not an efficient strategy; a more allocentric representation [11], including translation between allocentric and egocentric space, was necessary to perform this task accurately. It has been suggested [7], that women favour different strategies than men, e.g. that men use both landmarks and vectors to navigate whereas women favour mainly landmarks [8]. Thus a plausible explanation could be that there is a different weighting to certain strategies between the sexes in navigation (VRLT) but either is adequate for task success. If, however,



Supplemental Fig. 3. Gender differences in TM. ***, $p < 0.0001$.

one probes a specific determinant of task performance (in this case heading orientation), then sex differences emerge.

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