Naturalistic fMRI of Clinical Computerized Paired Associate Learning Test with Visual Feedback of Hand Position

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Introduction: Neuropsychological (NP) tests are behavioural tasks that have been used widely to probe human cognition, and to characterize abnormal brain function as part of patient management. However, the relationship between NP test performance and neuropathology is complex, partly because the underlying brain activity is regionally distributed in networks. Impaired test performance can potentially arise from damage to one or more nodes in such networks, or to their connections. One way to investigate these brain/behavior relationships, and potentially improve NP test sensitivity and specificity, is to study NP test performance during non-invasive brain activity measurements using fMRI [1]. Many newer NP tests are computerized and involve complex movements of the hand. For example, the Cambridge Neuropsychological Test Automated Battery (CANTAB) is a comprehensive, widely used set of NP tests that are administered on a touch screen computer to improve quantification of behavioural responses [2]. Recently, our laboratory has developed an fMRI-compatible tablet touch screen system and stylus that enables brain activation studies of CANTAB tests, as well as many other NP tests that involve writing and drawing [3].

The fMRI-compatible tablet prototype is activated when the user depresses a microswitch at the stylus tip, which triggers writing and drawing movements to be recorded on a computer display for viewing purposes. Because the user is lying in the magnet bore, they cannot view their hand during this process and must rely on their sense of proprioception, associated with muscle movements. Visual feedback of hand position while performing complex hand movements is extremely desirable, reducing learning requirements and improving motor performance, especially in patients with neurological impairment [4,5]. The purpose of the present work is to augment our fMRI-compatible tablet prototype to integrate visual feedback of hand position (VF), and to assess the influence of VF on fMRI tablet measurements involving the CANTAB Paired Associate Learning (PAL) test applied to young healthy adults. The CANTAB PAL test is known to be sensitive to memory impairment in patients with early probable Alzheimer's Disease (AD). This test probes visual memory using 6 boxes evenly spaced on computer screen. The boxes are opened and closed in random order. One or more boxes contain a pattern. The patterns are then displayed in the middle of the screen, one at a time, and the subject must touch the box where each pattern was originally located [2]. It is hypothesized that using the tablet with VF to perform the PAL test produces sparser brain activity in healthy young adults, consistent with reduced motor control demands, compared to using the tablet without visual feedback of hand position (without VF).

Method: An fMRI-compatible video camera (MRC Instruments) was mounted on the tablet to record color video of hand position during PAL task performance. A widely used skin color detection algorithm was used to extract (segment) the hand and stylus from the tablet background colors in each video frame [6]. The segmented hand and stylus were then superimposed in real time with computerized NP test presentation and stylus responses, on a computer screen at 30 Hz frame rate (33 ms maximum time lag). The tablet computer was programmed to administer the PAL test [2] with increasing difficulty levels (judgements involving 1 to 6 patterns). Eight young healthy adults performed fMRI of PAL in a 3T GE MR750 system with 8 channel head coil, and spiral in-out k-space acquisition. Four subjects performed PAL with VF, and another four performed PAL without VF of hand position. Each task repeated 2 times in a mixed fMRI design interspersed with baseline visual fixation and a simple reaction task (SRT) involving tapping a flashing box as quickly as possible. Each run lasted approximately 6 minutes. The fMRI data were analyzed using "Analysis of Functional Neuroimages" (AFNI) freeware [7].

Results: The fMRI results for the two groups of individuals with and without VF are shown in Fig. 1. The color overlay depicts brain activation from one of the recall phases of PAL undertaken (judgements involving 3 patterns) contrasted with the SRT condition. (a) With VF: Compared to the Without VF condition, brain activity is sparser, with less volume activated. While more activity is observed in visual and medial temporal areas, much less is observed in areas involved in motor control. (b) Without VF: A more extensive brain network is observed, with stronger engagement of cortical sensorimotor, basal ganglia, and parietal regions.

Discussion and Conclusion: These results suggest that use of the new fMRI-compatible tablet with VF produces more naturalistic behavioral performance, and a sparser network of brain activity that is more reflective of PAL task performance outside the magnet. Less reliance on proprioception reduces engagement of the sub-network of motor regions. Activity in visual regions is larger in extent, associated with more salient visual input relevant to task performance. Activity within medial temporal lobe regions is more extensive, consistent with the memory component of the PAL task. These observations are preliminary given the small sample size, and additional fMRI of subjects is ongoing. Nevertheless, the findings are sufficiently strong to consider future fMRI using the tablet with VF and the PAL applied to patients with early AD, and to healthy elderly controls.

Fig.1.a. with VF

Fig.1.a. without VF

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