Semantic information alters neural activation during transverse patterning performance

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ABSTRACT

Memory tasks can be performed using multiple cognitive strategies, which are mediated by different brain systems. The transverse patterning (TP) task is dependent upon the integrity of the hippocampal system, however, we previously demonstrated successful TP following hippocampal damage using meaningful stimuli and relations (Moses, S.N., Ostreicher, M.L., Rosenbaum, R.S., Ryan, J.D., 2008. Successful transverse patterning in amnesia using semantic knowledge. Hippocampus 18, 121–124). Here, we used magnetoencephalgraphy (MEG) to directly observe the neural underpinnings of TP, and the changes that occur as stimuli and relations become more meaningful. In order to optimize our ability to detect signal from deep, non-dominant, brain sources we implemented the event-related synthetic aperture magnetometry minimum-variance beamformer algorithm (ER-SAM; Cheyne, D., Bakhtazad, L., Gaetz, W., 2006. Spatiotemporal mapping of cortical activity accompanying voluntary movements using an event-related beamforming approach. Human Brain Mapping 27, 213–229) coupled with the partial least squares (PLS) multivariate statistical approach (McIntosh, A.R., Bookstein, F.L., Haxby, J.V., Grady, C.L., 1996. Spatial pattern analysis of function brain images using partial least squares. NeuroImage 3, 143–157; McIntosh, A.R., Lobaugh, N.J., 2004. Partial least squares analysis of neuroimaging data: Applications and advances. NeuroImage 23, S250–S263). We found that increased meaningfulness elicited reduced bilateral hippocampal activation, along with increased activation of left prefrontal and temporal cortical structures, including inferior frontal (IFG), as well as anterior temporal and perirhinal cortices. These activation patterns may represent a shift towards reliance upon existing semantic knowledge. This shift likely permits successful TP performance with meaningful stimuli and relations following hippocampal damage.

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Introduction

Memory tasks can be performed using multiple cognitive strategies, which are mediated by different brain systems. The transverse patterning (TP) task requires memory for relations among stimuli, and is dependent upon the integrity of the hippocampal system (Alvarado and Rudy, 1995; Driscoll et al., 2003; Driscoll et al., 2005; Reed and Squire, 1996; Rickard and Grafman, 1998; Rickard et al., 2006). We demonstrated intact TP performance following bilateral hippocampal damage using meaningful stimuli and relations, such as playing cards and the childhood game rock–paper–scissors (RPS; Moses et al.,

2008). We suggested that a proposition-based cognitive strategy that relies on pre-existing semantic knowledge could be mediated by extra-hippocampal structures.

Here we asked specifically how the relational TP task with meaningful stimuli and relations can be mediated by extra-hippocampal structures. We used magnetoencephalgraphy (MEG) to directly observe the neural underpinnings of TP, and the changes that occur as stimuli and relations become more meaningful. Previous work shows that TP with abstract stimuli elicits hippocampal activation that is detectable with MEG (Hanlon et al., 2003, 2005, 2007), and this activation is found less reliably for TP with RPS stimuli (Hanlon et al., 2005). However, these studies focused predominantly on activation within the hippocampus. We sought to examine the dynamic neural activity across hippocampal and cortical regions supporting TP with abstract stimuli, and the subsequent changes elicited by increased meaningfulness of stimuli and relations. We

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expected that meaningfulness would recruit extra-hippocampal structures involved in processing semantic information, such as left prefrontal and temporal cortex (Davies et al., 2004; Mummery et al., 2000; Taylor et al., 2006; Wagner et al., 2001), with a concurrent reduction in hippocampal activation.

The sensitivity of MEG to signals from deep neural structures, such as the hippocampus, has been debated because: 1) magnetic field strength decreases with increasing distance between neural sources and MEG sensors and 2) the "spiral" or "spherical" shape of the hippocampus could theoretically lead to cancellation of magnetic signal (for in depth discussions see Stephen et al., 2005; Riggs et al., 2009). However, an increasing body of empirical evidence demonstrates that, although hippocampal activation may be more difficult to detect than superficial sources, it can be reliably detected with a range of experimental paradigms and analysis techniques (Breier et al., 1998, 1999; Hanlon et al., 2003, 2005, 2007; Ioannides et al., 1995; Kirsch et al., 2003; Martin et al., 2007; Mikuni et al., 1997; Nishitani et al., 1999; Papanicolaou et al., 2002; Stephen et al., 2005; Riggs et al., 2008; Tesche, 1997; Tesche and Karhu, 1999, 2000; Tesche et al., 1996).

In order to optimize our ability to detect signal from deep, non-dominant, brain sources we implemented the event-related synthetic aperture magnetometry minimum-variance beamformer (ER-SAM; Cheyne et al., 2006) coupled with the partial least squares (PLS) multivariate statistical approach (McIntosh et al., 1996; McIntosh and Lobaugh, 2004). The ER-SAM algorithm permits detection of weaker sources, as it uses information from all MEG sensors, and does not require *a priori* assumptions about number or location of sources. The entire brain volume is covered by a grid, and at each grid node, the beamformer enhances sensitivity for the signal from that node and suppresses the signal from other nodes (Huang et al., 2004). The mean-centred PLS analysis is ideal for detecting non-dominant or weaker neural sources. Activation patterns that are unique to individual conditions become enhanced, and patterns that are similar across all conditions (such as strong primary sensory sources) are removed. Further, PLS is more sensitive to distributed signals than traditional univariate statistical approaches. Thus, the application of PLS to ER-SAM source-space solutions is a powerful method for localizing weaker sources that are unique to specific cognitive processes, and reducing contributions from dominant sensory responses that are similar across all conditions.

Materials and methods

Participants

Participants consisted of 22 right-handed individuals (14 female) with no known pathology from the volunteer pool at the Rotman Research Institute. Ages ranged between 20–35 (mean = 26).

Post-experimental questionnaires revealed that 18/22 participants were able to correctly report the relationship among the stimuli for all four TP blocks. The remaining participants were unable to correctly report the relationship either on the first block, or the first two blocks. These four participants were considered non-learners, and their data were not included in any of the analyses. Of the 18 remaining participants, 9 participated in the "Progressively meaningful" condition, and 9 participated in the "All abstract" condition.

Stimuli and procedures

Participants performed four independent TP blocks during MEG recording. Three different achromatic stimuli (A, B, and C) were used in each of the four blocks (Fig. 1). Within each block, the stimuli were grouped into three completely overlapping pairs in which A was correct when paired with B, B was correct when paired with C
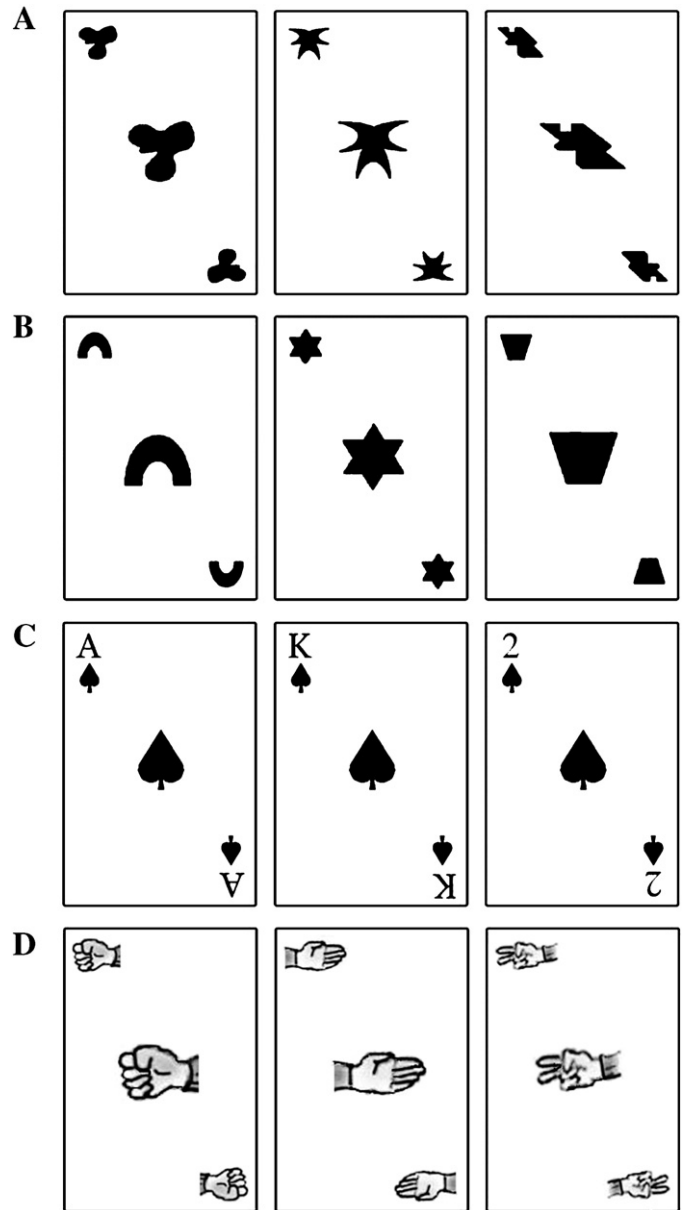
Fig. 1. Stimuli used for the four TP blocks in the Meaningful condition. A, *Abstract Objects*: abstract stimuli with arbitrary relations; B, *Geometric Shapes*: meaningful stimuli with arbitrary relations; C, *Playing Cards*: meaningful stimuli with meaningful relations; D, *Rock–paper–scissors*: meaningful stimuli with meaningful relations. For the All abstract condition, each block contained a unique set of three abstract stimuli.

and C was correct when paired with A (A + B−, B + C−, C + A−). Participants were not informed of any relationship among the stimuli, and were required to use button presses to learn the computerized task by trial and error. For each trial, stimuli were presented in pairs, counterbalanced for right and left side presentation. Pairs of stimulus were presented in random order. Stimuli remained on the screen until participants responded, and the inter-trial interval following stimulus termination was jittered between 2000–2500 ms (mean 2250 ms). Correct responses were followed by a pleasant chime sound, and incorrect responses were followed by an unpleasant buzz sound. MEG recording continued until participants made 100 or 120 correct responses[1]. Only correct responses, in which participants responded within 3 s, were retained for analysis.

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[1] Accuracy was similar regardless of whether 100 or 120 trials were administered (*F* > 1); therefore, all participants were combined.