Brain and Cognition 86 (2014) 90–97

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Neuromagnetic correlates of intra- and extra-dimensional set-shifting

Anna Oh [a], Julie Vidal [a,1], Margot J. Taylor [a,b,c], Elizabeth W. Pang [a,c,d,*]

[a] Neurosciences and Mental Health, SickKids Research Institute, Toronto, Ontario, Canada
[b] Diagnostic Imaging, Hospital for Sick Children, Toronto, Ontario, Canada[2]
[c] University of Toronto, Toronto, Ontario, Canada[2]
[d] Neurology, Hospital for Sick Children, Toronto, Ontario, Canada[2]

ARTICLE INFO

Article history:
Accepted 12 February 2014
Available online 5 March 2014

Keywords:
Cognitive flexibility
MEG
Executive function
Frontal lobes
Dorsolateral prefrontal cortex (dlPFC)

ABSTRACT

Set-shifting is essential to cognitive flexibility and relies on frontal lobe function. Previous studies have mostly focused on feedback processes following shifting rather than set-shifting itself. We designed an MEG paradigm without feedback to directly investigate the neural correlates of set-shifting. Adults ($n = 16$) matched one of two coloured images with a third stimulus, the target, by either the colour or shape dimension of the target. Half of the shift trials involved colour-to-colour or shape-to-shape (intra-dimensional: ID) shifting and the other half involved colour-to-shape or shape-to-colour (extra-dimensional: ED) shifting. MEG was continuously recorded on a 151 channel CTF system. We used beamforming to analyze responses to the first (shift) and the third (repeat) trials in each set. These trials were contrasted separately for ID and ED sets. Shift versus repeat trials showed larger MEG activations for intra-dimensional shifting in the right inferior frontal gyrus (BA 47), left medial frontal gyrus (BA 10) and right superior frontal gyrus (BA 9) as early as 100 ms, and in left middle frontal gyrus (BA 11) between 250–500 ms. Activations related to extra-dimensional shifting were detected in left inferior frontal gyrus (BA 44), left middle frontal gyrus (BA 11), and right middle frontal gyrus (BA 46) between 100 ms and 350 ms, followed by superior frontal gyrus (BA 8/BA 10) between 250–500 ms. Intra-dimensional and extra-dimensional shifting also activated bilateral and right parietal areas, respectively. This study establishes the location and timing of frontal and parietal activations during an intra-dimensional versus extra-dimensional shifting task.

1. Introduction

Set-shifting is an important cognitive function that permits the updating of cognitive strategies in response to changing goals or environments. As a core component of executive functioning, set-shifting is governed primarily by the frontal lobes (Shallice, Stuss, Picton, Alexander, & Gillingham, 2008). The most widely used experimental set-shifting paradigm is the Wisconsin Card Sorting Task (WCST) (Milner, 1963). In this paradigm, subjects match a given card to four key cards according to one of three perceptual categories (colour, form or number). The subject must sort the cards according to the correct principle (set), based on trial and error with feedback. As the test progresses, the sorting principle will change, requiring a shift in set. However, this task involves many processes of executive control.

Several neuroimaging techniques have been employed to examine the neural correlates of set-shifting abilities. Many of these studies have used both traditional and modified versions of the WCST task and functional magnetic resonance imaging (fMRI) to localize brain regions activated during set switching. Identified neural areas include a distributed network involving prefrontal and frontal cortical regions, (e.g., Konishi et al., 1998; Monchi, Petrides, Petre, Worsley, & Dagher, 2001; Nagahama et al.,1998; Rogers, Andrews, Grasby, Brooks, & Robbins, 2000), as well as associated posterior cortical regions (e.g., Konishi et al., 2002; Lie, Specht, Marshall, & Frink, 2006; Nagahama et al., 2001).

While fMRI has localized brain regions involved in set-shifting, it does not capture the millisecond timing of neurocognitive processes. Magnetoencephalography (MEG) is a modality that provides good spatial and temporal resolution and is excellent for examining the timing of activations across brain regions during cognitive tasks. Previous studies have employed MEG to examine the spatiotemporal dynamics of set-shifting in typical adults. Using a traditional WCST paradigm, Wang, Kakigi, and Hoshiyama (2001) found MEG differences during shift cues compared to non-shift cues

* Corresponding author at: Division of Neurology, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada. Fax: +1 416 813 6334.
E-mail address: elizabeth.pang@sickkids.ca (E.W. Pang).

[1] Present address: Paris Descartes University and UMR CNRS 3521, Paris, France.
[2] Work performed at the Hospital for Sick Children.

http://dx.doi.org/10.1016/j.bandc.2014.02.006
0278-2626/

in dorsolateral prefrontal cortex (dlPFC), specifically middle frontal gyrus (BA 9), within 460 ms to 640 ms post-cue onset. Perianez et al. (2004) used a modified version of the WCST to examine the preparatory stages of set-shifting. Greater activations occurred during shift trials at the inferior frontal gyrus (BA 45, 47/12) within 100–300 ms post-cue onset, as well as in the anterior cingulate cortex within 200–300 and 400–500 ms. MEG activations were also seen at the supramarginal gyrus (BA 40) within the latency periods of 300–400 and 500–600 ms. More recently, Henaff, Bayle, Krolak-Salmon, and Fonlupt (2010) characterized the dynamics of frontal regions using a modified WCST paradigm with emotional face stimuli. Significant differences in source activities were seen in the superior frontal gyrus within 350–450 ms during the shift trials. Thus, MEG evidence suggests that a distributed network of frontal and posterior regions is activated during shifting with the MEG activations starting at 100–200 ms post-switch cue, peaking at 300–500 ms.

Neuroimaging evidence suggests that the WCST task activates prefrontal as well as parietal and/or temporal lobes; however, the WCST paradigm is complex and thus it is difficult to dissociate the neural underpinnings of set-shifting from other cognitive processes that may also be involved. For example, adequate performance on the WCST also requires working memory, inhibition, decision making and reasoning. This issue was addressed in a previous fMRI study that examined brain activations associated with distinct stages of the WCST by separating feedback from card matching components (Monchi et al., 2001).

Most MEG studies on set-shifting have investigated the response to feedback (e.g., visual feedback in Bayless, Gaetz, Cheyne, & Taylor, 2006 and Henaff et al., 2010; auditory cues in Mulas et al., 2006 and Perianez et al., 2004). However, in everyday life, situations which require a change in behaviour do not consistently entail a feedback signal. For example, when a professor shifts topics in a lecture, or re-directs attention to another aspect of the lecture, the student is required to shift and track with the professor; however, a failure to shift would not necessarily be noticed. In a PET study, Sawada et al. (2012) used a paradigm without feedback in patients with Parkinson's disease. As we aimed to explore the fine temporal characteristics of shifting, we also chose a task without feedback so as to reduce the likelihood of confounding from overlapping processes involved in feedback processing and error monitoring.

An alternative to the WCST that places fewer cognitive demands on subjects is the attentional set-shifting, Intra-Extra Dimensional Set Shift (IED) test, from the Cambridge Neuropsychological Test Automated Battery (CANTAB®, Cambridge Cognition). Like the WCST, the IED requires that subjects maintain a set and select a response within that set, and at some point, the subject is required to shift sets. Unlike the WCST which has many choices per trial, the IED only has two choices per trial; thus, it is less complex. The IED has a lengthy testing protocol but has been used for behavioural assessments in many different clinical populations including Alzheimer's disease (Dorian et al., 2002), schizophrenia (Pantelis et al., 2009), fetal alcohol spectrum disorders (Green et al., 2009), fragile X syndrome (Van der Molen et al., 2012), ADHD (Gau & Shang, 2010), as well as in monkeys (Dias, Robbins, & Roberts, 1996).

Thus, similar to the CANTAB® IED set-shifting test, we designed an attentional set-shifting task targeting both intra-dimensional and extra-dimensional shifting. However, our set-shifting task did not require feedback to be performed, and the participant did not need to be cued for shifts as there was no ambiguity in the choices; only one option was correct on each trial. We were interested in the ability to shift attention within the same dimension of sensory attributes or from one dimension to another one, as previous studies have shown anatomical dissociations of these two cognitive processes in the prefrontal cortex (Bissonnette et al., 2008; Dias et al., 1996). We therefore included, in our paradigm, two types of shifts: (1) intra-dimensional (ID) shifts: from one colour to another colour, or from one shape to another shape, and (2) extra-dimensional (ED) shifts: from colour to shape, or from shape to colour, as in the IED test (see detail in Luciana & Nelson, 1998).

2. Materials and methods

2.1. Subjects

Sixteen right-handed adults (7 males and 9 females; mean age 27 years ±4) took part in this study. Subjects had normal or corrected to normal vision and reported no history of learning disabilities, neurological or psychiatric disorders. All subjects gave informed written consent. This study was approved by the Hospital for Sick Children Research Ethics board.

2.2. Stimuli and task

A set-shifting task was used in which subjects had to match one of two images with a third image, the target, by either the colour or shape dimension of the target. Stimuli were 6 geometric shapes in 6 different colours (36 bi-dimensional images) centered on grey squares. The stimuli were displayed side by side above the target image (see Fig. 1). Images were back-projected onto a screen with a black background. A white cross was displayed in the middle of the screen between trials. Subjects were instructed to select whether the left or right image was in the same set as the target and to indicate their response as quickly as possible by pressing a button that corresponded to the right or left image. No trial was presented in which both dimensions were possible matches. When a shift in set occurred, subjects acquired a new rule of matching by either colour or shape. A rule shift occurred after a minimum of three to four successive correct trials; sets included a maximum of eight trials. Half of the sets involved extra-dimensional colour-to-shape or shape-to-colour shifting (ED shifts) and the other half involved intra-dimensional colour-to-colour or shape-to shape shifting (ID shifts). ED and ID shifts were presented in random order. Stimuli duration was self-paced with a maximum duration of 4 s and a variable ISI of 1.0–1.5 s. All subjects completed two runs of 51 ± 3 sets on average, each lasting 6 min.

2.3. Data acquisition

MEG data were recorded (625 Hz sampling rate, DC-100 Hz band pass, third-order spatial gradient noise cancellation) using a 151 channel whole-head CTF system (MISL Ltd., Canada) at the Hospital for Sick Children. Three localization coils were placed on the nasion, left and right pre-auricular points. Head movement was recorded before and after each run. For each subject, head movement was <0.5 cm. Localization coils were replaced with radiological markers before MRI acquisition. Co-registered anatomical T1-weighted MRI images (3D SPGR) covering the whole brain (TR/TE/FA = 9 ms/4.2 ms/15°, 116 slices, voxel size = $0.9375 \times 0.9375 \times 1.5\ mm^3$, 2 NEX, 7 min) were obtained from each subject, acquired on a 1.5T Signa Advantage System (GE Medical Systems, Milwaukee, WI USA) with a quadrature head coil.

2.4. Behavioural analysis

Reaction time (RT) was measured from the onset of stimulus presentation to the button press for correct responses only. RTs were calculated for the first, second, and third trials separately for both ID sets and ED sets.