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A new ERP paradigm for studying individual differences in the executive control of attention

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ABSTRACT

Event-related potentials (ERPs) provide valuable information about the fast brain dynamics subserving cognitive functions such as attention and working memory. Most ERP studies employ cognitive paradigms with a fixed task-set (i.e., press a button to named targets), but few have measured ERPs time-locked to shifts in set using a task-switching paradigm. The Madrid Card Sorting Test (MCST) is a dual task protocol in which feedback cues signal unpredictable shifts in set (i.e., from 'sort cards by colour' to 'sort cards by shape'). This protocol offers an integrated analysis of ERPs to both feedback cues and target card events, providing separate ERP indexes for the shifting, updating, and rehearsal of attention sets in working memory. Two of these ERP indices are the frontal and posterior aspects of the P300 response. Feedback cues that direct a shift in set also elicit both a frontally distributed P3a potential (300-400 ms), and a posteriorly distributed P3b potential (350-600 ms). In turn, target card events evoke posterior P3b responses whose amplitude increases as the new task set is gradually rehearsed. In line with current models about the role of prefrontal cortex in the executive control of attention, this P3a/P3b response system appears to reflect the co-ordinated action of prefrontal and posterior association cortices during the switching and updating of task sets in working memory.

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INTRODUCTION

Scalp-recorded event-related potentials (ERPs) provide a fine spatio-temporal analysis of brain activation in so-called ‘oddball’ target detection tasks. In these tasks, target events evoke a distinct long latency positive potential (350-600 ms; P3b) maximal over mid-parietal scalp. The P3b potential reflects task-relevant processes such as context updating [6] or closure of the event-encoding cycle in working memory [22]. An earlier latency positive potential (300-400 ms; P3a) indexes attention switching to non-target novel events [7]. Lesion, brain imaging and intracranial studies propose anatomical and functionally distinct neural sources for the switching (P3a) and updating (P3b) mechanisms [12]. For instance, the PFC plays a key role in triggering the P3a potential [10], but has a less critical involvement in P3b elicitation [11]. In spite of evidence about an implication of PFC in both task set-shifting and the detection of novel events [10, 14, 17, 18], to date there is no functional evidence that these two processes may be subserved by a common brain mechanism. However, one limitation of ERP studies on attention is that brain activity is measured under fixed task-set conditions (i.e., ‘press a button to named targets’). Further, even if the task’s rules change between successive trial blocks, ERPs are normally not recorded while the task’s rules are being changed. Thus, the critical brain potentials related to the shifting and updating of stimulus-response mappings (or task sets) in working memory still remain to be described.

In the last few years we have developed a task-switching paradigm, the Madrid card sorting test (MCST), inspired by a classic test of prefrontal impairment, the Wisconsin card sorting test (WCST) [9, 15, 17], to study the fast brain dynamics behind task-set switching [2-5]. Initially, we found a gradual modulation of P3b amplitudes across ‘shift’ and non-shift (‘stay’) trials time-locked to target card stimuli, but no clear evidence of a frontally distributed ERP activation [3]. Subsequent analyses revealed that the actual shift in set takes place at the feedback stage, that is, when a non-target ‘shift’ feedback cue instructs the subject to adopt a new rule for the task at hand. In turn, at the card-matching stage, the task-set is merely implemented or rehearsed [19-21]. This has led to a more comprehensive ERP analysis of both contextual processes time-locked to feedback events, and target-related

processes time-locked to the card-matching stage of task performance (see Fig. 1b). This novel ERP paradigm shows that task-switching consists of several cognitive processes, as reflected by a number of ERP components, the most conspicuous of which is the endogenous P300 response [4]. Therefore, the MCST task-switching protocol represents a new and promising tool for examining the putative relationship between attention set-shifting and the frontal (P3a) and posterior (P3b) components of the P300 response system. The interpretation of observed modulations in the frontal P3a and posterior P3b aspects of the P300 response system in terms of attention set shifting processes may benefit from the solid theoretical grounds yielded by current models about the role of prefrontal cortex in the executive control of attention [15, 16, 19]. To illustrate this new ERP paradigm, here we present a study designed to examine the involvement of the frontal and posterior components of the P300 response in switching (P3a) and updating (P3b) of task-sets in working memory.

METHOD

Subjects. Twenty-seven right handed subjects (15 females; mean age 23 ± 4 years, range 18 – 34 years), took part in the study. They all had normal or corrected visual acuity and no history of neurological or psychiatric disorder.

Behavioural procedures. We used a computer version of the WCST designed to assess attention set shifting using ERP recordings [3]. The task protocol used the 24 choice-cards of the original 64 WCST cards that can be matched unambiguously with the four WCST key-cards based on just one stimulus dimension (i.e., either colour, shape, or number of items in the card; Fig. 1a). Unambiguous cards are required for both a sensitive scoring of WCST errors and set-shifting ability [2]. These 24 choice-cards were repeatedly used in 137 trials arranged into 18 series (see Fig. 1). The correct sorting rule was initially unknown to the subject, and changed randomly from one series to the next. The length of each series varied randomly between 6 and 8 trials. Each trial began with the onset of a compound stimulus with the four WCST key-cards on top of one choice-card, all centred on a computer screen. The cards subtended a visual angle of 4° horizontally and 3.5° vertically, and remained on display until a response was given (Fig. 1b).

Subjects were instructed to match the choice-card with one of the four key-cards following one of three possible rules: number, colour, or shape. Likewise, subjects were informed that the correct sorting rule would change without notice after a variable number of card sorts, and hence, they would have to shift their sorting rule accordingly. The correct rule was to be

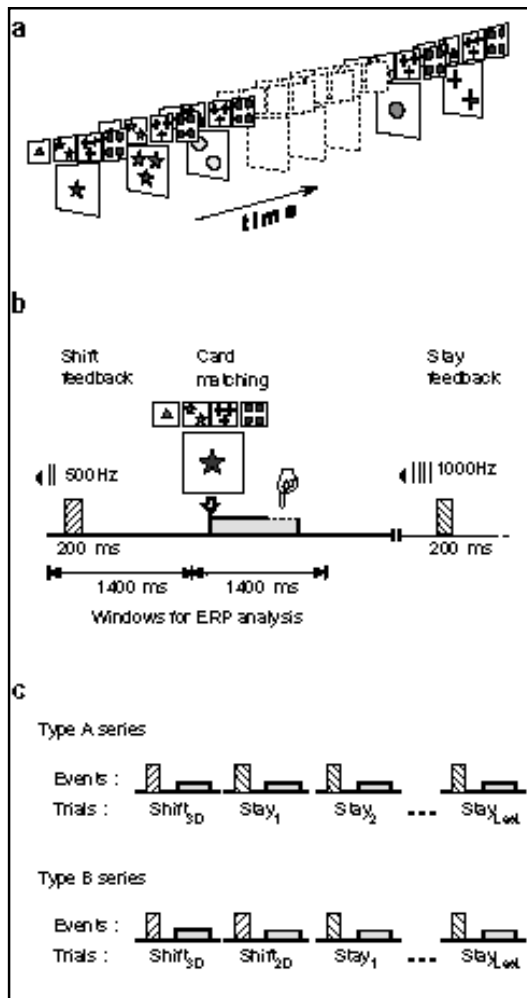
determined on the basis of an auditory feedback cue delivered within a variable interval of 1500-2000 ms after the response (200 ms duration, 10 ms rise/fall times; 65 dB SPL; 1000 Hz for 'stay' cues, 500 Hz for 'shift' cues).

Figure 1. Task design and ERP trial analysis.

a. Schematic example of one MCST series. Each choice-card could be unambiguously matched with each key-card based on just one stimulus dimension.

b. Feedback stage: A 'shift' feedback tone cued subjects to shift the task rule (sound frequency 500 Hz). A 'stay' feedback tone cued subjects to use the same rule again (sound frequency 1000 Hz). Card-matching stage: The choice-card remained on display until a response was given.

c. Trial analysis based on the subject's responses. In the first trial of a series (shift_{3D} trial), subjects inhibited the old rule and adopted



one of the remaining two for responding. In type B series, subjects had to shift set twice to find the correct rule (shift_{2D} trials). In the first stay trial (stay₁) the subject repeated his previous choice of rule. The last stay trial of a series (stay_{Last}) was preceded by another three to five stay trials (adapted from [1]).

Subjects used their thumbs for responding using a panel with four key-buttons aligned. Subjects performed two blocks of 137 trials each, with a 5 min rest period between blocks. The task was practised for about 5 min, or 5-7 series, to make sure that subjects had understood the instructions, and could sort cards efficiently (see operational criteria for efficiently completed WCST series below [2]). The sequence of trials used for practice was different from that in the main task. Therefore, in our adapted WCST protocol each correct card match was followed by a ‘stay’ feedback cue prompting the subject to use the same sorting rule again. After a variable number of correct card matches, the rule changed unpredictably and the subject had to adopt a new task rule upon hearing a ‘shift’ feedback cue (e.g., from shape to number, or to colour).

Following prior functional magnetic resonance imaging (fMRI) studies [14, 18], we defined three-dimensional shift trials (shift_{3D}) as those where subjects had to handle three task rules in working memory (i.e., inhibit the previous rule and consider the other two for responding; Fig. 1c). In two-dimensional shift trials (shift_{2D}), only two rules were handled, after having discarded one in the previous trial. In stay trials, a ‘stay’ feedback cue prompted the subject to use the same task rule again. This task design allowed us to carry out a separate analysis of attention switching (P3a) and memory updating (P3b) processes. After the first shift feedback cue of a new series (shift_{3D}), an ideal subject has 50% chance of choosing an incorrect task rule, and so needs to shift set again to achieve the remaining correct rule. This is an efficient trial-and-error process in normal subjects, who can use past contextual information to optimize task-set shifting. Here we considered data from efficient series only, with either no errors or just one such efficient error (shift_{2D}; Fig 1c).

ERPs and data analysis. The electroencephalogram (EEG) was recorded from 29 tin electrodes positioned at Fp1, Fp2, AF3, AF4, F7, F8, F3, Fz, F4, FC5, FC6, FC1, FC2, T7, T8, C3, Cz, C4, P7, P8, P3, Pz, P4, PO7, PO8, PO1, PO2, O1 and O2, and referenced to the left mastoid. The EEG signal was amplified (band pass, 0.01 - 30 Hz; 12 dB/octave roll/off), digitised at 250 Hz/channel and stored for off-line averaging. Electrode impedances

were kept below 5 k Ω . The averaging window was 1400 ms for the feedback and card matching epochs, including a 200-ms baseline in both cases (Fig. 1b). The electrooculogram (EOG) was also recorded for eye blink correction. Epoch trials with EEG exceeding $\pm 75\mu\text{V}$ in amplitude, muscle, or any other artifacts were discarded. ERP averages were obtained from completed WCST series only. A completed series was scored if (a) the new sorting rule was not anticipated (i.e., the first trial in a series was a shift_{3D} trial); (b) the subject shifted set efficiently and found the new rule in the second (type A series) or third trial (type B series, Fig. 1c); and (c) the rule was not missed thereafter. In the present sample of normal subjects, individual task performance ranged between 32-36 successfully completed WCST series [2]. ERPs were computed time-locked to both feedback cues and card onsets across both shift and stay trials. A linked-mastoid reference was obtained off-line. Mean ERP amplitudes were measured relative to the 200-ms pre-stimulus baseline. For feedback-locked averages, mean amplitude values were computed for the P3a component (375-400 ms post-stimulus onset) and P3b (550-600 ms post-stimulus onset). For card-locked averages, only mean P3b amplitudes were measured. The P3a potential was measured at Fz, and the P3b potential at Pz. A significance level of $P < 0.05$ was used in all contrasts.

RESULTS

Figure 2 presents the grand-average ERP waveforms evoked by feedback and card events from shift_{3D} trials as compared to stay_{Last} trials in the MCST series. Figure 3 displays the mean P300 amplitudes (Fig. 3, upper panel) and behavioural task performance (Fig. 3, lower panel) across shift and stay MCST trials. It can be observed that feedback cues signalling a shift to a new task rule evoked a distinct frontally distributed P3a potential that was absent after the first stay cue ($P < 0.0001$, for the main Trial effect; Figs. 2, 3). A sharp reduction in P3a amplitude was observed in response to the first ($P < 0.003$), and second stay cues ($P < 0.0001$; Fig. 3), but there was no decrement in P3a amplitude from shift_{3D} to shift_{2D} trials ($P > 0.2$; Fig. 3). In turn, shift_{2D} cues evoked larger P3a potentials than stay₁ cues ($P < 0.003$; Fig. 3). Stay₂ and later trials evoked similar brain responses in both type A and B series (Refs. [3, 4]). Finally, P3a amplitudes to shift_{3D} cues did not diminish over successive task blocks, consistent with behavioural evidence that set shifting costs do not decline with practice [20].

Feedback cues also elicited a distinct pattern of P3b activity across shift and stay trials ($P < 0.0001$, for the main Trial effect; Figs. 2, 3). There was a

reduction in P3b amplitude from shift_{3D} to shift_{2D} cues ($P < 0.003$), and between stay₁ and stay₂ cues ($P < 0.001$), but no P3b change was observed between shift_{2D} and stay₁ cues (Fig. 3). Thus, unlike the P3a, the P3b response to feedback cues was sensitive both to the number of rules held in memory, and to the subject's ability to predict the next task rule. Although the P3a and P3b components have never been compared in a similar task-switching paradigm, the present results reveal a significant interaction between the type of P300 component (P3a vs P3b) and the type of early task-set Trials (shift_{3D}, shift_{2D}, stay₁), suggesting their differential role in switching (P3a) and updating (P3b) of task-sets in working memory ($P < 0.03$, for the quadratic trend; see Fig. 3, upper panel).

At the card-matching stage, we observed the expected P3b response to visual targets, with a gradual P3b increment from shift to stay trials as revealed in the main Trial effect ($P < 0.0001$; Figs. 2b, 3), but no evidence of a P3a potential. However, the pattern of P3b responding at the card-matching stage differs substantially from that observed at the feedback stage, as revealed by a significant interaction between Stage and Trial ($P < 0.0001$; see Fig. 3). These results suggest that the posterior P3b response system accomplishes rather different functions during the feedback and card-matching stages of WCST performance [18, 21].

The analysis of behavioural responses confirmed the well established costs in speed and accuracy related to task-set shifting [19-21]. Response times were slower during shift as compared to stay trials (up to circa 500 ms; $P < 0.0001$; Fig. 3, lower panel), indicating a gradual speed-up in responding from shift_{3D} to shift_{2D} trials ($P < 0.02$), and from shift_{2D} to stay₁ trials ($P < 0.03$). The analysis of errors from failed series indicated that subjects were more likely to miss the task rule in shift_{2D} ($P < 0.001$) and stay₁ trials ($P < 0.01$), as compared to the last trial in the series ($P < 0.001$, for the main Trial effect; Fig. 3).

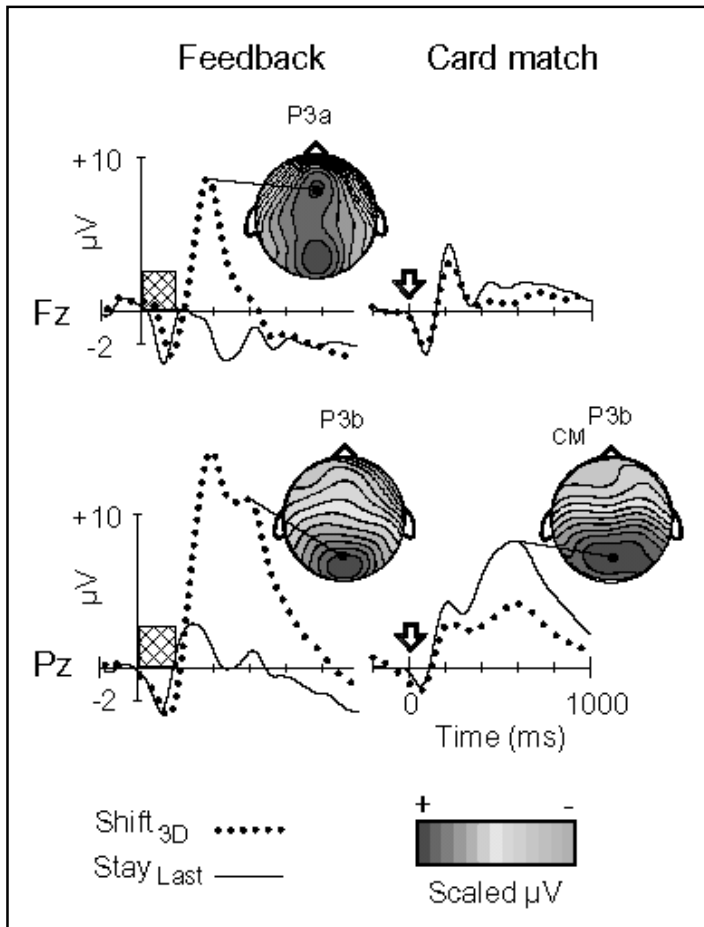


Figure 2. Brain responses to feedback and card events. Mean group-averaged ERPs to feedback cues and card stimuli are displayed for shift_{3D} and $\text{stay}_{\text{Last}}$ trials, at frontal (Fz) and parietal (Pz) midline electrodes. Voltages are in microvolts (μV). Scalp potential maps are displayed for mean P3a and P3b activity evoked by shift_{3D} feedback cues, and for mean P3b activity evoked by the last card-match in the series (CM P3b). The scale is in normalised units (adapted from [1]).

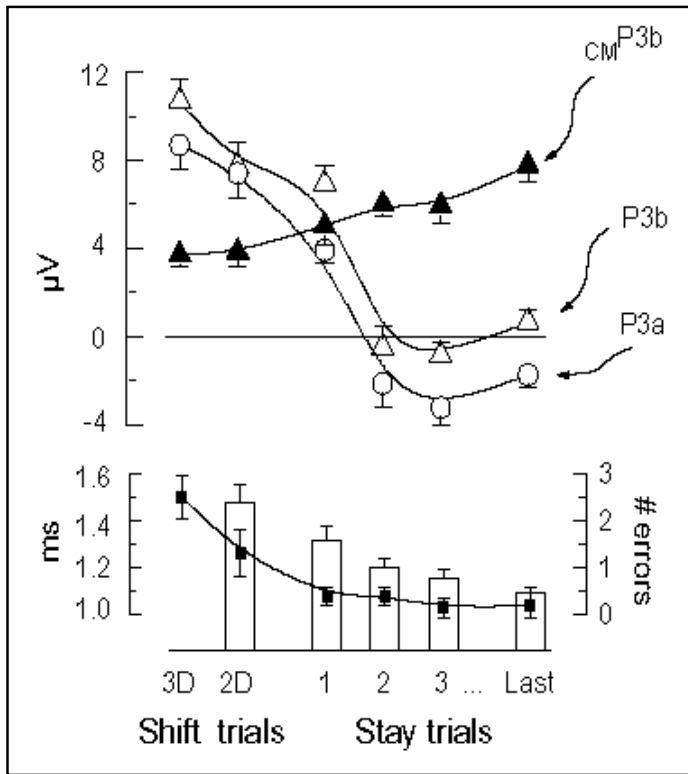


Figure 3. ERPs and behavioural responses across shift and stay trials. Upper panel: Group-averaged mean (\pm s.e.m.) amplitudes in microvolts of the P3a and P3b responses plotted across shift and stay trials in the MCST series. Mean P3a and P3b amplitudes were measured from the mid-frontal (Fz) and mid-parietal (Pz) scalp regions, respectively. P3a and P3b responses were time-locked to feedback events. $_{CM}$ P3b responses were time-locked to card-matching events. Lower panel: Mean (\pm s.e.m.) reaction times from completed MCST series (solid squares), and mean number of random of errors from failed series (bars), are plotted across shift and stay MCST trials (adapted from [1]).

DISCUSSION

This study represents the first evidence in the literature suggesting a role of the frontally distributed P3a response in the executive control of cognitive set shifting. Past ERP studies of attention set-shifting either focused on target events only, or failed to link the observed P3a-like activation to task-set switching. In our modified version of the WCST, feedback events that directed a shift in the subject's mental set to new task rules, also elicited P3a responses whose amplitude, latency and scalp topography closely resemble those elicited by non-target novel events in oddball tasks. However, our 'shift' feedback tone cannot be defined as a novel stimulus, as it had been learned to denote a shift in the task's rules, and the same tone was used along the practice and test sessions. Instead, the 'shift' tone prompted the subject to 'think differently', and to flexibly adopt a new solution (i.e., a new task set) for the same card sorting problem. Thus, our results indicate that the same brain system may subserve the processing of both stimulus and task novelty.

While 'shift' trials were infrequent relative to 'stay' trials (i.e., overall probabilities were 0.25 and 0.75, respectively), 'oddball' processes like uncertainty alone cannot explain the observed modulations of P3a brain potentials. First, oddball tasks with a fixed task-set and equally infrequent non-target tones elicit substantially smaller P3a potentials that decline rapidly with repetition. Second, task uncertainty cannot account for the functional dissociation of P3a responses to feedback and card events. Third, 'shift' trials from similar tasks evoke peak fMRI activation at PFC regardless of their relative frequency of occurrence. That said, brain responses to the first stay feedback cue revealed that task uncertainty did play a role in the early trials of each new WCST series. Indeed, our feedback cues did not make it explicit which task rule was to be used next. This ambiguity disrupts WCST performance in prefrontal patients, who cannot rely on internal representations to project future actions based on past stimulus-response contingencies. Even normal subjects who can anticipate the next set need to practice it at least once before reaching pre-shift levels of behavioural efficiency. Indeed, the brain responses observed to the first stay cue may reflect residual reorienting and updating to the newly established task set (Fig. 3). Activation in this P3a response system ceased completely at the second stay cue, after the new set had been rehearsed once. Rostral anterior cingulate (BA 24/32), mid-dorsolateral (BA 9/46), and mid-ventrolateral prefrontal cortices (BA 12/47) become simultaneously active in response to shift feedback cues in similar set-shifting tasks. In turn, the extant lesion,

fMRI and intracranial recording data from oddball tasks favours a lateral – rather than a medial– prefrontal source for the P3a potential.

The present results may help us resolve apparent inconsistencies in past brain imaging and clinical WCST research. First, an outdated model of prefrontal function, and the inherently limited temporal resolution of most metabolic brain imaging studies, had led us to expect maximal prefrontal ERP activation during the card matching stage rather than the feedback stage of WCST performance. In contrast, the observed P3a activation suggests that the shift in set actually takes place during the feedback period, and well before the next target card is on display. This new account is consistent with more recent fMRI and behavioural evidence, suggesting that the internal representation of task rules must be activated (i.e., updated) in anticipation of the behaviour they govern (i.e., card sorting). Second, our ERP results provide support for the view that PFC acts in concert with posterior association cortices for the executive control of cognitive set shifting. Indeed, Fig. 2 reveals instant widely distributed neural activation across both frontal and posterior brain generators in response to ‘shift’ feedback cues. This argues against the strict localizationist view conveyed by some studies that present isolated foci of prefrontal activation during WCST performance (i.e., see Fig. 5 in [14]). Third, an ERP index of set-shifting may help us integrate apparent inconsistencies in the anatomy reported by different metabolic studies. The stereotaxic coordinates of prefrontal regions with significant fMRI/PET activation during WCST performance show a good deal of variability across studies [14, 18]. One possibility is that different anatomical fMRI activation elicited by the same task reflects disparate cognitive processes. Another possibility is that these different fMRI patterns may be showing ‘tip-of-iceberg’ activation from different parts of the same neural network that gives rise to the P3a response [8]. The present ERP results support the latter alternative. Finally, the finding of feedback-locked frontally-distributed P3a activity helps to complete the picture offered by our previous ERP studies [3], suggesting that efficient WCST performance demands the activation of a widespread network of brain areas, with a key role played by prefrontal cortex. Further research will be necessary to map specific types of WCST deficits to specific anomalies in the frontal and posterior aspects of the P300 components reported here [2, 13, 17].

As in previous studies, a steady build-up in P3b activation to card onset was apparent as the new task set became established and gradually rehearsed. This was paralleled by a steady improvement in response speed and efficiency, indicating a growing degree of automaticity in task performance.

Unlike P3b responses to feedback cues, P3b activity during card matching was modulated neither by the number of task-sets in memory, nor by their predictability. This suggests a differential role of the posterior association cortices responsible for P3b elicitation during the updating (feedback) and rehearsal (card matching) of task rules in working memory. It could be argued that long-term memory networks at posterior association cortex need to be differentially engaged both for the rapid retrieval of new task rules during set-shifting and updating, as well as for the gradual rehearsal and consolidation of practised task-sets, leading to proficient task performance. Such a proposal could help us to integrate apparently contradictory accounts of the functional role of the P3b response in terms of either “context updating” [6], or “perceptual closure” processes [22]. Future ERP research with task-switching paradigms should explore further the double dissociation of P3b responses reported here, as well as its likely implication for current models of P300 function.

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