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EVENT related potentials (ERP) were recorded from 29 electrode positions in 10 normal subjects while they performed a simplified version of the Wisconsin Card Sorting Test (WCST). The design focused on ERP differences between early and late trials within each WCST series. Topographic and dipole analyses confirmed the reliability of two ERP signs: one conspicuous mid-parietal P3b wave and one asymmetrical frontal-temporal component. A three-dipole model accounted for these ERP signs with >90% accuracy even in individual subjects, and suggests a sub-second activation of temporal-parietal and medial temporal association areas during card sorting. The WCST-related P3b wave is proposed to reflect working memory operations such as template matching and template formation during card sorting.

Key words BESA; Event-related potentials; Frontal lobes; Wisconsin Card Sorting Test (WCST); Working memory

Non-frontal P3b-like activity evoked by the Wisconsin Card Sorting Test

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Introduction

The WCST originally earned its reputation as a test of frontal lobe function, and has long been adopted as an indicator of frontal dysfunction.^{1,2} Recent evidence from clinical and neuroimage studies has revealed that card sorting also involves activation of other brain areas.³⁻⁷ However, little is known about the relative contribution of frontal and non-frontal areas or their involvement in the underlying cognitive operations.

Event-related potentials (ERP) have proved useful for examining the functional relationship between brain physiology and the cognitive operations underlying behaviour. Barceló *et al.*⁸ recently described two ERP signs of brain activation associated with card sorting: one slow component centred in the left frontal-temporal area, and one conspicuous P3b wave centred over mid-parietal areas. In order to single out cognitive operations, ERPs were averaged from early and late trials within each WCST series. P3b amplitudes were significantly larger during late than during early WCST trials, which was attributed to working memory operations such as template matching and template formation.⁸

Intracranial and lesion studies suggest a plausible contribution to the scalp recorded P3b wave from structures as far as temporal-parietal,⁹ hippocampal,¹⁰⁻¹² or even frontal areas.^{13,14} However, in all these studies P3b waves were obtained during simple oddball tasks, and none used complex colour visual

stimuli as targets. Here we investigate whether the neural generators of WCST-related P3b waves correspond with the frontal or non-frontal generators suggested in the literature.

Another WCST-related ERP feature was described as a slow negative field potential centred over left frontal-temporal areas. This ERP asymmetry was more pronounced during early trials and was attributed to the activation of the left dorsolateral prefrontal cortex.⁸ However, the topographical distribution of this component was partly distorted by a concurrent positive frontal potential associated with visual scanning.¹⁵ Here we intend to examine the consistency of the frontal-temporal hemispheric asymmetry using WCST cards which subtend a much narrower visual angle.

The main purpose of the present study is to elucidate the frontal or non-frontal origins of these two WCST-related ERP signs through a combination of topographic and dipole analyses. Initial dipole models will take into account current physiological hypotheses and recent brain electrical source analysis (BESA) models about the neural generators of the P3b wave.¹⁶⁻²⁰

Materials and Methods

Ten right-handed young volunteers (five females, five males; mean age 23. 2 ± 3.7) with normal or corrected vision and no history of neurological or psychiatric problems were recruited from colleges in the

University campus. Subjects were informed of all aspects of the research and signed a consent form approved by the Ethical Committee of the Brain Mapping Unit. Subjects were paid for their participation.

A computerized adaptation of the WCST was designed with the Gentask module of the NeuroStim package (NeuroScan Inc). Each trial began with the onset of a compound stimulus containing the four WCST key-cards on top of one choice-card, all centred on the screen. The compound stimulus subtended a visual angle of 4° horizontally and 3.5° vertically. Subjects were instructed to match the choice-card with one of the four key-cards following one of three possible sorting principles: number, colour, or shape. The correct sorting principle could be determined on the basis of feedback which was delivered 1900 ms after each response through a computer-generated tone (2000 Hz for correct, 500 Hz for incorrect). Responses were made with a four-button panel. The length of the WCST series varied randomly between six and nine trials. The inter-trial interval varied randomly between 3000 and 4000 ms. The task consisted of two blocks of 18 series each. The order of choice-cards within the series was determined on a semi-random basis so that the first four sorts in the series could be made unambiguously. Elimination of ambiguity eased the correction of the test, and improved the signal-to-noise ratio in the ERPs. The average duration of each block was 12 min, with a 5 min rest period between blocks.

The electroencephalogram (EEG) was recorded from 29 tin electrodes positioned according to the extended 10-20 system²¹ and referenced to left mastoid. The EEG was amplified with a band pass from DC to 30 Hz (12 dB/octave roll-off), and digitised at 250 Hz over a 1700 ms epoch with a 200 ms baseline. Impedances were kept below 5 k Ω . The electrooculogram (EOG) was also recorded for blink correction. Trials with remaining muscle or movement artefacts were discarded. Separate averages were computed for early and late WCST trials. The second and third trials across series were averaged into a WIS23 waveform, and the last two trials were averaged into a WIS69 waveform. Both correct and incorrect trials entered the WIS23 averages, but only correct trials entered the WIS69 averages. A linked-mastoid reference was computed off-line for the averaged data.

Results

Subjects did not persevere, committed less than 2% random errors, and completed 35.4 out of 36 categories on average (cf. Appendix of Ref. 8). The

probability of finding the correct category in either the second or third trials was 0.93. The average reaction time was slower for early than for late trials ($t(8) = 5.36$, $p < 0.0007$; mean \pm s.e.m. = 2.12 ± 0.3 s and 1.4 ± 0.2 s, respectively). Thus, sorting a card typically took well over 1 s. In fact only 0.05% of trials were sorted in < 600 ms. This time limit was taken as an upper bound for subsequent ERP and dipole analyses.

As is apparent from Fig. 1, ERPs for early and late trials replicate those reported previously.⁸ In particular there was a large P3b centred over mid-parietal areas which was more conspicuous during late trials. A repeated-measures ANOVA with electrode (12 levels), hemisphere (two levels), and condition (WIS23 vs WIS69 trials) was performed for the mean area in four latency windows: N150 (120–180 ms), P200 (190–270 ms), P3a (280–360 ms) and P3b (450–600 ms). Significant main effects of condition appeared from the P200 window onwards ($F(1,9) > 6.5$, $p < 0.03$), but were largest in the P3b time range ($F(1,9) = 26.9$, $p < 0.001$). Only one interaction between condition and electrode reached significance in the P3b time window ($F(1,99) = 4.6$, $p < 0.04$], indicating that differences were larger at posterior rather than anterior electrodes. No other interactions reached significance.

Frontal effects were examined more closely with a second ANOVA which focused on data from electrodes F7, F8, T7, and T8. As before, the main effect for condition reached significance from 190 ms onwards. In the P3a window, a main effect of hemisphere ($F(1,9) = 9.0$, $p < 0.02$) indicated larger overall amplitudes in left than in right sites. Also in the P3a window, one significant interaction between condition and electrode ($F(1,9) = 6.84$, $p < 0.03$) indicated that differences between conditions were larger in temporal than in frontal leads. Two marginally significant interactions between condition and hemisphere appeared in the time ranges P200 ($F(1,9) = 3.8$, $p < 0.08$] and P3a ($F(1,9) = 3.6$, $p < 0.09$). These reflected larger differences between task conditions in the left rather than the right frontal-temporal leads. The third order interaction did not approach significance in any of the time windows.

Dipole analyses were performed on the difference waves resulting from subtracting WIS23 waves from WIS69 waves. The latency window 180–600 ms post-stimulus was chosen because it contains all significant ERP effects and remains largely free from motor processes, as denoted from response time data. At one initial stage, the sources proposed in the published literature served only as location co-ordinates and then dipole orientations were automatically refitted within the selected time interval. From all the models tested,^{17–20} the four-dipole model proposed

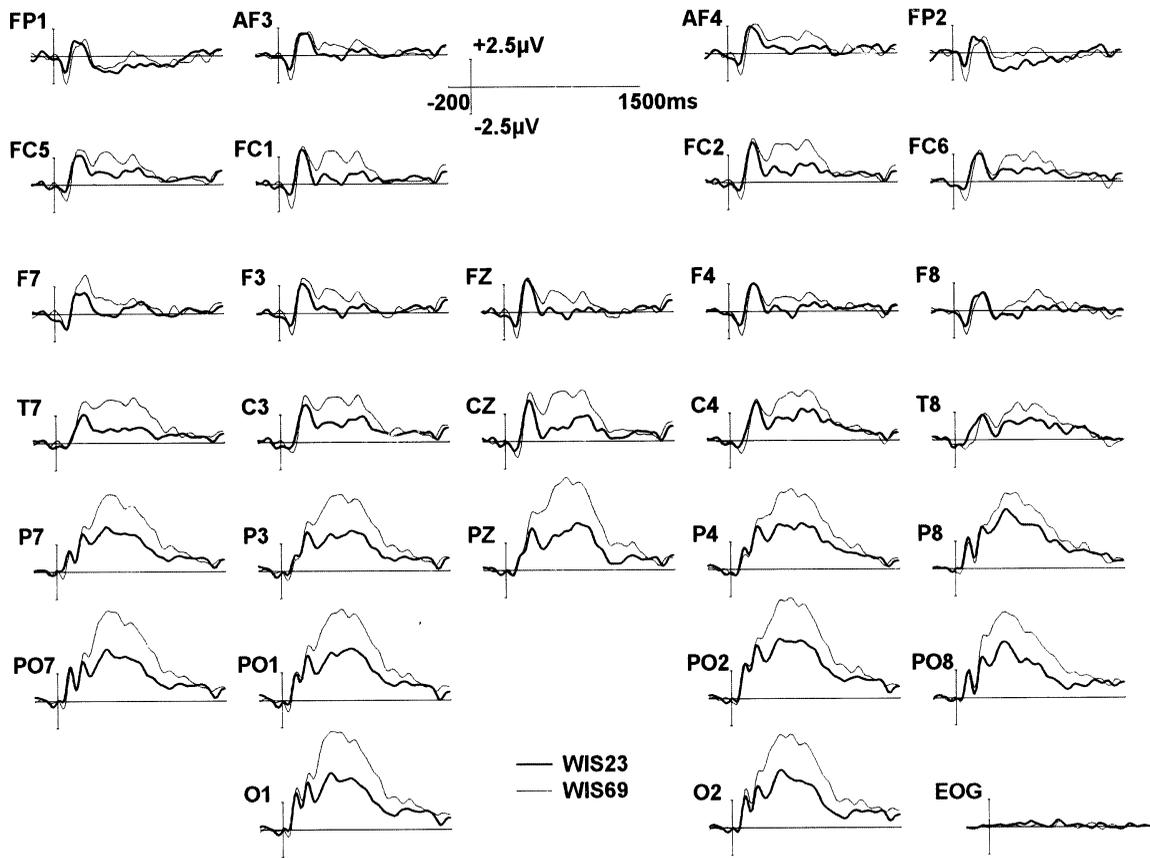


FIG. 1. Grand average ERPs for early (WIS23) and late (WIS69) WCST trials recorded from 29 electrode sites. The vertical bars indicate the onset of the four key-cards plus choice-card compound. Curves are linked-mastoid referenced averages from 10 normal subjects. The residual EOG activity is plotted in the lower right-hand corner of the figure.

by Tarkka *et al.*¹⁸ was the one which achieved the closest fit and explained the largest amount of variance in the data (see Fig. 2). The other models yielded percentages of residual variance (RV) ranging between 8.5% and 14.8% for those of Tarkka *et al.*¹⁹ and Mecklinger and Ullsperger,¹⁷ respectively.

Tarkka *et al.*¹⁸ estimated sources in two regions currently disputed as likely origins of the P3b, namely, the hippocampus and the temporal-parietal junction.^{9,11,14} Now the question was which of these structures made the largest contribution to WCST ERP difference waves. In a first approach, relative dipole weights were calculated from the increment in RV after switching off each dipole in turn. Increments in RV were then expressed as percentages of the contribution of each dipole to the model. Dipole weights thus obtained are listed in Table 1. In a second approach, two 2-dipole models were obtained by switching off either pair of symmetrical dipoles shown in Fig. 2. These two models were then tested by refitting orientations of the two remaining active sources. The hippocampal dipoles of Tarkka *et al.* accounted for 87.2% of the variance in the selected time window, whereas their two temporal-parietal dipoles accounted for 89.7% of the variance. Hence,

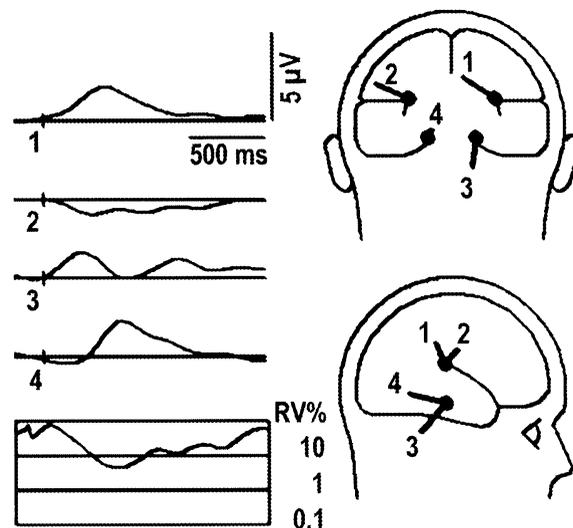


FIG. 2. The four-dipole model of Tarkka *et al.*¹⁸ after refitting orientations within the 180–600 ms interval of the average WCST ERP difference wave. Four temporal activity functions (left) and one residual variance (RV) function (bottom) are plotted over the whole recording interval. Positive voltage values are plotted upwards. The RV for the interval 180–600 ms post-stimulus was 7.27%.

Table 1. Total residual variance, residual variance at frontal electrodes, and partial contribution from individual sources to each model (in percentages)

	Model of Tarkka <i>et al.</i> ¹⁸ (see Fig. 2)	Final model (see Fig. 3)	Frontal model
Total residual variance	7.6	5.5	8.97
Frontal residual variance	9.5	5.8	5.5
Dipole 1	51.9	52.8	92.7
Dipole 2	10.2	35.3	0.9
Dipole 3	14.3	11.9	6.4
Dipole 4	23.6	–	–

despite the neat advantage for temporal-parietal dipoles in the first and second approaches, their hippocampal sources also managed to explain a substantial part of the average WCST ERP difference waves.

The final step was trying to find the simplest and most comprehensive model for the WCST ERP difference waves. To this end a third source was introduced in each of the 2-dipole models described above. After fitting the new source, all symmetry restrictions were released and all parameters re-fitted for each individual source in turn. The outcome was very similar regardless of the starting model. The final 3-dipole solution is presented in Fig. 3. The percentage of residual variance in the model, residual variance from frontal areas and dipole weights are listed in Table 1. This final model reveals activity near two of the areas proposed as neural sources of the P3b wave, and also suggests activation of the

visual association cortex.^{18,19} The model explained an acceptable amount of variance of the WCST ERP difference waves from individual subjects, with percentages of residual variance ranging between 3% and 10.5% across subjects.

None of the models attained so far includes sources at frontal areas. In order to explore further the possible contribution of the dorsolateral frontal cortex to WCST ERP difference waves, two symmetrical sources were constrained to prerolandic areas and had their location and orientation adjusted to their best fit. Then a third source was entered in the model. Frontal solutions proved highly unstable, as the third dipole systematically adopted a temporal-basal position and assimilated most of the variance. The best of such frontal models accounted for nearly 91% of total variance, but the joint contribution of the two frontal dipoles amounted to < 10% of variance in the data (see Table 1).

Discussion

The present results strongly suggest a non-frontal involvement during WCST performance within a fraction of a second of each card sort. This assertion needs to assume only gross accuracy of the BESA algorithm for appraising activity from broad brain areas.^{16,17} Moreover, the present dipole model is compatible with evidence from intracranial and lesion studies,^{9–14} and is rooted in recent P3b source models developed from ERP and neuroimage data.^{18,19}

Temporal-parietal dipoles made the largest contribution to the WCST-related P3b wave elicited during late trials. Lesions in the temporal-parietal junction are known to reduce the amplitude of the P3b,^{9,13} but it is unclear whether this is due to damage of lateral or medial regions. The present analyses suggest that medial structures of the temporal-parietal junction are more important than lateral ones in evoking the P3b wave. Attempts to fit the pair of temporal-parietal dipoles to more lateral locations led to large increases in residual variance (cf. Refs 18,19).

The present dipole results also suggest a contribution from medial temporal areas to WCST ERP difference waves. This agrees with reports that unilateral hippocampal lesions compromise WCST performance.^{4,6} Figure 3 shows that dipole 2 had a longer peak latency than dipole 1, which is consistent with evidence that the hippocampal P3b reaches its peak activation around 50 ms after the scalp-recorded P3b wave.^{10,11} On the other hand, it has been shown that hippocampal lesions do not totally abolish the P3b wave.^{22,23} Polich and Squire argue that the P3b wave is elicited within the time span of short-term memory, a capacity which remains intact following bilateral damage to the medial temporal

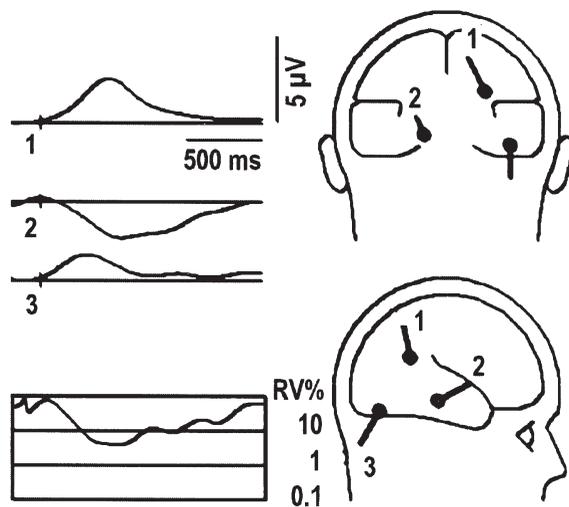


FIG. 3. Final three-dipole model for the grand average difference WIS69-WIS23 wave in the 180–600 ms interval. Three temporal activity functions (left) and one residual variance (RV) function (bottom) are plotted over the whole recording interval. Positive voltages values are plotted upwards. The RV for the interval 180–600 ms post-stimulus was 5.37%.

lobes.²² However, the WCST demands a good deal of interaction between the contents of working memory and long-term memory, and it is feasible that the WCST-related P3b reflects an interaction between generators at temporal-parietal and medial temporal areas.^{13,14} Future research should capitalize on the similarities disclosed here between the neural generators of oddball- and WCST-related P3b waves.

The asymmetry in WCST ERP difference waves has also been replicated. However, results from dipole analyses qualify the initial interpretation of this effect.⁸ First, the asymmetry is due to larger WIS69 amplitudes at left T7 and F7 sites rather than to more negative WIS23 values (Fig. 1). Second, WCST ERP differences were larger at left temporal than at left frontal leads. In fact, this was also the case in a previous study (cf. Ref. 8, Fig. 2). These data cannot be attributed to a larger activation of the left dorsolateral prefrontal cortex during early WCST trials.⁸ In turn, they are more consistent with an enhanced activation of left medial temporal areas during late trials (cf. Fig. 2 and Table 1).

Unilateral damage to temporal-parietal areas results in bilateral reductions in P3b amplitudes,⁹ which has been explained in terms of an interaction between left and right temporal-parietal areas as part of a larger network also involving hippocampal structures.¹⁴ The asymmetry in our dipole solution might precisely reflect this kind of interaction. Alternatively, the dipole in the left medial temporal area from our final model might be modelling some residual ERP activity from left dorsolateral frontal regions. It is possible that the WCST-related P3b may index working memory operations rather than shifts in attention.^{8,24} Sorting becomes progressively automated as the sorting rule becomes more consolidated towards the end of the series. Hence, the WCST-related P3b might reflect the degree of updating of the memory template for the ongoing sorting category.²⁵ This is compatible with the observation that correct sorts midway in the series (i.e. WIS45 trials), yield P3b waves midway those for WIS23 and WIS69 trials (data not shown). Memory operations such as template formation and template matching have been suggested as candidates for explaining these P3b effects.⁸

Conclusion

This study demonstrates that WCST performance evokes scalp-recorded P3b-like activity which can be best described in terms of a contribution from brain

sources in temporal-parietal and medial temporal regions. These areas are active within half a second of the onset of a choice-card and well before a response is made. This finding is consistent with recent reports that damage to hippocampal and medial temporal brain regions compromise WCST performance, as well as other clinical evidence which caution against the use of the WCST as a marker of frontal dysfunction.³⁻⁶ The present ERP approach to card sorting suggests that simple cognitive tasks induce activation of widespread neural networks. These data favour a functional neurocognitive approach rather than a strict localizationist approach to neuropsychological assessment. Even if the traditional WCST may be sensitive to certain types of frontal damage, it is less than adequate for localizing frontal lesions in absence of a more direct index of brain activation.

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