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Electrophysiological evidence of two different types of error in the Wisconsin Card Sorting Test

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THE specificity of the Wisconsin Card Sorting Test (WCST) for assessing frontal lobe pathology remains controversial, although lesion and cerebral blood flow studies continue to suggest a role for the dorsolateral prefrontal cortex in WCST performance. Inconsistencies might derive from the extended use of various WCST scores as equivalent indicators of frontal pathology. In this study, event-related potentials (ERPs) were recorded from 32 normal subjects who committed perseverative and non-perseverative errors. Both types of WCST errors evoked anomalous but distinct ERP patterns over frontal lobe regions. Perseverative errors were also associated with a dysfunctional extrastriate response to stimulation. This evidence suggests that perseverative and non-perseverative errors result from disruptions in two different prefrontal neural networks engaged during card sorting. *NeuroReport* **10:1–5 © 1999 Lippincott Williams & Wilkins.**

Key words: Evoked potentials; Frontal lobe; Selective attention; WCST; Working memory

Introduction

The Wisconsin Card Sorting Test (WCST) is one of the most widely used tests of frontal lobe function in clinical and research [1–7]. In recent years, however, the specificity of WCST scores as markers of frontal dysfunction have been questioned [8–13]. Among its various scoring norms, perseverative errors are regarded as the main signs of frontal dysfunction, with number of achieved categories, or category shifts, often referred to as an equivalent indicator [2,13–15]. This tendency to use several WCST scores as exchangeable indicators of frontal dysfunction may have added confusion and weakened the specificity of the test. Thus, for instance, non-perseverative errors may also bring down the total number of categories achieved. In this report I provide electrophysiological evidence that perseverative and non-perseverative errors reflect different types of disruption in frontal lobe function.

A perseverative error is committed early in the WCST series as the patient fails to shift to a previously irrelevant category. It reflects a failure to select a new perceptual category and to shift from the previously reinforced one [16,17]. These mental operations have been related to the function of the dorsolateral prefrontal cortex [6,16]. In contrast, a non-perseverative error results from a failure to maintain attention within the same perceptual category while inhibiting the distracting interference of co-existing stimuli. Thus, a non-perseverative error in late WCST trials can be regarded as a distraction, and has not been so often related to dorsolateral prefrontal damage [1,14]. Many neuroimaging studies have shown increased metabolic activation in both frontal and posterior brain areas during WCST performance [7,18,19]. However, no study to date has accomplished a direct measurement of brain activity associated with either type of WCST error.

Using event-related potentials (ERP), Barceló and collaborators have shown that early and late trials in the WCST series evoke distinct patterns of frontal and non-frontal brain electrical activation [20,21]. In the present study, I offer a topographical analysis of the brain electrical changes related to the commission of perseverative errors and distractions in a non-clinical sample of young volunteers. It is possible to make two predictions from our present state of knowledge. First, perseverative errors and distractions are expected to evoke ERP patterns which deviate from their respective normal counterparts, namely, efficient errors and non-distractions, respectively. Second, the scalp topography of these ERP differences is expected to hinge on frontal areas for perseverative errors, and on non-frontal areas for distractions.

Materials and Methods

Thirty-two right-handed young volunteers (12 females, 20 males; mean age 21.7 ± 2.4 years) with

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normal or corrected vision and no history of neurological or psychiatric disorder were recruited from the University campus. Subjects signed a consent form and were paid for their participation. This sample was screened from a larger pool of 45 college students on the basis that they had committed at least one perseverative error or one distraction while performing a simplified computer adaptation of the WCST for ERP research [20].

Each trial began with the onset of a compound stimulus containing the four WCST key cards on top of one sorting card, all centred on a computer screen. The compound stimulus subtended a visual angle of 4° horizontally and 3.5° vertically. Subjects were instructed to match the sorting card with one of the four key cards following one of three possible sorting principles: number, colour or shape. The correct sorting principle was to be determined on the basis of auditory feedback delivered 1900 ms after each response (65 dB tones; 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 the sorting cards within the series was determined on a semi-random basis so as to eliminate ambiguity from the series [2]. Elimination of ambiguity was critical for the accurate scoring of perseverative errors. The average duration of each block was 12 min, with a 5 min rest period between blocks.

The EEG was recorded from 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 in the international 10-20 system. The EEG signal was referenced to the left mastoid (0.01–30 Hz; 250 Hz digitisation rate), and a linked-mastoid reference was obtained off-line. Impedances were kept below 5 kΩ. The EOG was recorded for blink correction. Epochs with EEG exceeding ±75 μV were automatically rejected. Trials with residual muscle artefacts, or with response latencies >4 s, were also discarded. Mean amplitude values were computed for five components of the visual evoked potential [20,22]. The ERP components were P1 (100–130 ms), N1 (145–175 ms), P2 (195–225 ms), N2 (305–335 ms) and P3b (450–750 ms). Mean amplitudes were referred to a 200 ms prestimulus baseline.

A perseverative error was defined as a failure to change category in the second trial of a WCST series after having received negative feedback from the previous trial. In contrast, an efficient error was defined as a shift to the wrong category in the second WCST trial, and always led to a correct sort in the third trial. A distraction was defined as an error in the last trial of a clear WSCT series. Clear series were those with no errors, or with just one efficient error in the second trial. The selected sample of 32 young volunteers totalled 49 perseverative errors and 52 distractions. After rejection of EEG epochs contaminated with muscle or movement artefacts, 39 clean epochs from each type of error were used to form the grand ERP averages for perseverative errors and distractions. These were compared with the grand ERP averages of efficient errors (396 epochs) and non-distractions (385 epochs; see Fig. 1).

The statistical technique of bootstrapping was used to obtain normalized estimates of the sampling distributions of the mean reaction time (RT) for efficient errors and non-distractions [23,24]. The sampling distributions were estimated by drawing 100 random subsamples of 39 trials from a total population of 396 efficient error trials and 385 non-distraction trials, respectively. The samples were taken with replacement. This procedure yielded two normal distributions whose standard deviations were used for computing 95% confidence intervals around the mean RTs of efficient errors and non-distractions. The null hypothesis of these comparisons was that the mean RT of perseverative errors and distractions would not be significantly different from those of efficient errors and non-distractions, respectively. The same rationale was applied for the statistical test of differences of the mean amplitudes of each of the five ERP components studied (i.e., P1, N1, P2, N2, and P3b).

Results

Behavioural results: The mean reaction times (± s.d.) for perseverative errors and distractions were 1.73 ± 1.02 s and 1.06 ± 0.58 s, respectively. A 95% confidence interval around the mean of the respective sampling distributions did not reveal any significant difference in reaction time between perseverative error trials and efficient error trials, nor between distraction trials and non-distraction trials (see Table 1; Fig. 1).

Electrophysiological results: The mean ERP amplitudes evoked by WCST errors were compared with the sampling distributions of the mean ERP amplitudes of their normal counterparts at each of the five ERP components considered. Table 2 lists those ERP components and electrodes where differences in ERP amplitude were >2.5 s.d. of the corresponding sampling distribution ($p < 0.01$).

The earliest significant differences between perseverative errors and efficient errors were associated

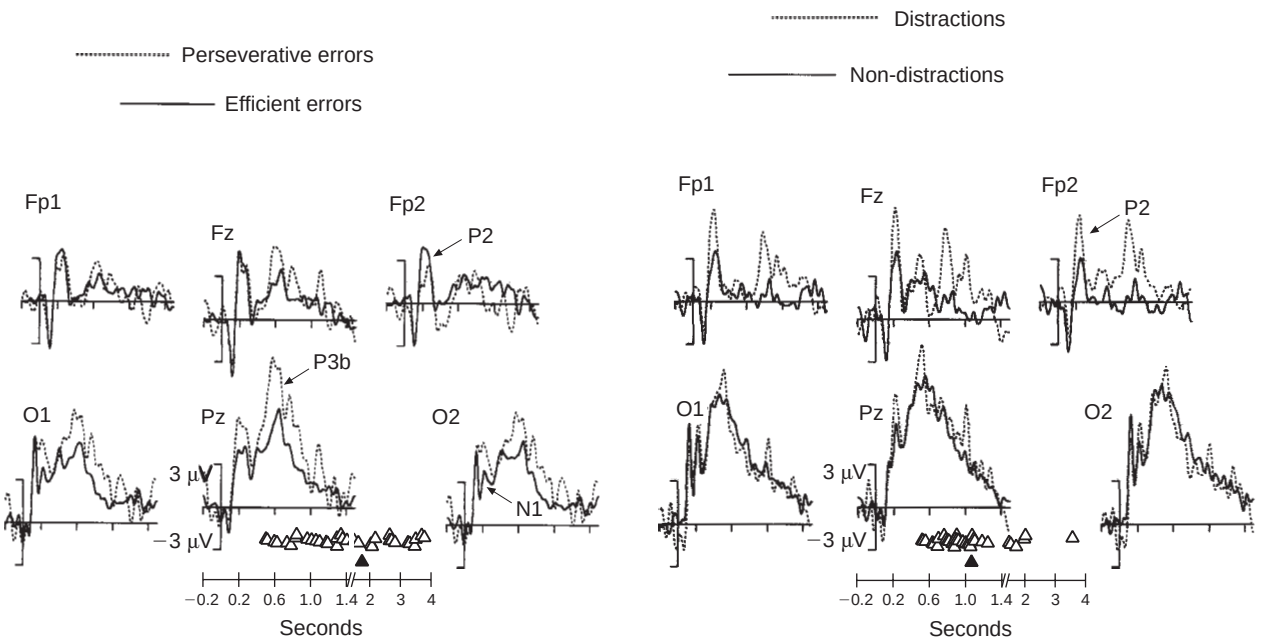

FIG. 1. Grand ERP averages evoked by perseverative errors and distractions and their respective normal counterparts at frontal, parietal and occipital electrodes. Upper panel: the ERP average of 39 perseverative errors compared with the grand ERP average of 396 efficient errors from the sample of 32 normal subjects. Lower panel: the ERP average of 39 distraction errors compared with the grand ERP average of 385 non-distractions. Open triangles represent reaction times for those WCST error trials included in the ERP averages. Solid triangles represent the overall mean reaction time for the population of functional trials.

Table 1. Bootstrap results and 95% confidence intervals for the mean reaction times of efficient errors and non-distractions

	Reaction times (s)			
	n	Mean	s.d.	95% Confidence interval
Efficient errors	100	1.56	0.15	1.27–1.82
Non-distractions	100	1.15	0.10	1.01–1.34

Table 2. Electrodes which showed statistically significant differences between the mean ERP amplitudes evoked by perseverative errors and distractions and their respective normal counterparts ($p < 0.01$)

ERP components	Perseverative errors *vs* efficient errors	Distractions *vs* non-distractions
N1	P4, O2, O1	–
P2	FP2, F4	AF3, AF4, F3, Fz, F4, FC1, FC2
P3b	PO1, Pz, PO2, P4	AF3, F3, Fz, F4, AF4

with both the parieto-occipital N1 and the frontal P2 components. The former was absent during perseverative errors when compared with efficient errors (Fig. 1), whereas the latter was significantly reduced at right frontal areas. Figure 1 and Fig. 2 show that such differences were not apparent at medial or left frontal sites. Finally, perseverative errors evoked a significantly larger P3b wave than efficient errors, with a maximal difference of 4.1 standard deviations at Pz (Fig. 1; Fig. 2).

The earliest significant ERP differences between distractions and non-distractions were apparent over central and frontal-central regions. Here distractions evoked significantly larger P2 waves than non-

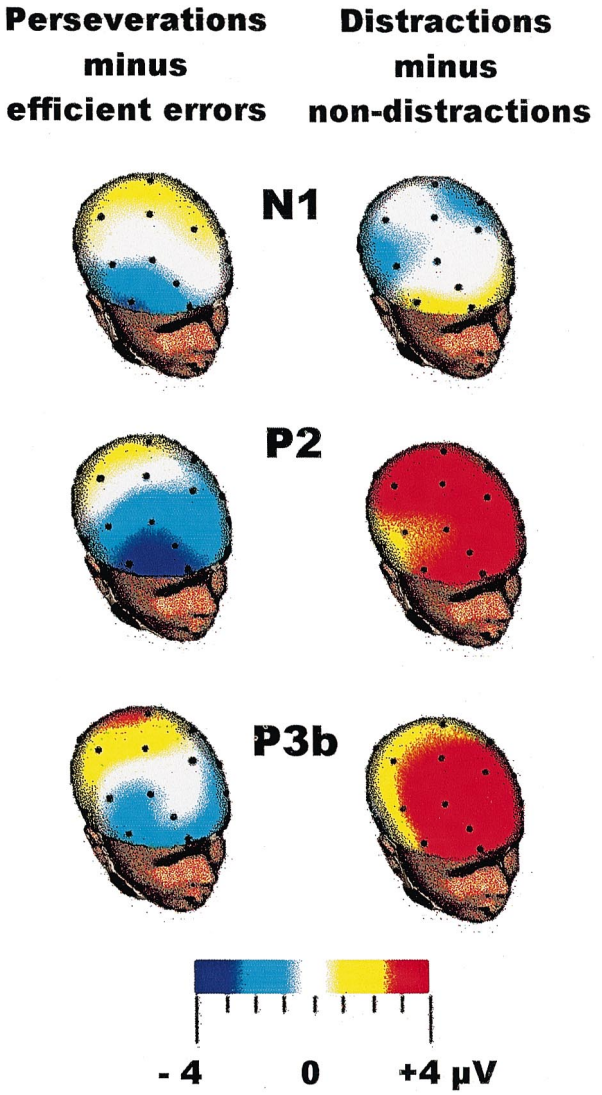

FIG. 2. Spherical spline topographical maps showing the mean difference in N1, P2 and P3b amplitudes evoked by each type of WCST error compared with their respective normal counterparts. Absolute voltage differences $>2\,\mu V$ are significant at $p<0.01$.

distractions, with a maximal difference of 3.5 s.d. at F4 (Fig. 1; Fig. 2). The next significant pattern of differences was linked to a late positive wave evoked by distractions over anterior frontal regions (Fig. 1; Fig. 2).

Discussion

The present data confirm the prediction that the patterns of brain activation evoked by WCST errors deviate from their functionally normal counterparts. Moreover, both perseverative errors and distractions were associated with distinct ERP anomalies encompassing frontal as well as non-frontal brain regions. This suggests that these two types of error result from different types of disruptions in the neural networks engaged during card sorting [5,6,16,17,20].

The present results can help us interpret recent conflicting clinical and neuroimage evidence. On the one hand, clinical reports suggest that WCST scores alone should not be regarded as markers of frontal dysfunction [10–12], since lesions in posterior brain regions may lead to increased rates of perseveration [8,9,15]. On the other hand, WCST performance is consistently related to bilateral metabolic activation of dorsolateral prefrontal regions [7,18,19]. Evidence from Fig. 1 and Fig. 2 suggests that perseverative errors may result from a functional disruption in a frontal-extrastriate network involved in the selection of visually relevant information. Unilateral prefrontal lesions are known to reduce extrastriate N1 amplitudes in visual attention tasks [22]. It has been shown that transient impairments in the feedback from extrastriate areas might lead to disruptions in the top-down modulation of this network [6]. Here, the anomalous absence of the extrastriate N1 component (Fig. 1) appears to precede in time a significant reduction in P2 activity over the right frontal region [7]. This explanation is consistent with claims that perseverative errors may result from disruptions in more than one mechanism of visual attention [16], as well as with mounting clinical evidence of increased rates of perseverative responses secondary to lesions in temporo-parietal visual association areas [8,12,15].

Figure 1 and Fig. 2 reveal that the ERP pattern evoked by distractions deviated from that evoked by non-distractions, and was clearly distinct from that evoked by perseverative errors. The locus of ERP differences between distractions and non-distractions hinged on frontal-central, rather than on posterior brain areas. Again, ERP differences affected the P2 component but neither the topography nor the sign of these differences resembled those of perseverative errors. A distraction error can be regarded as an untimely reset of the contents of working memory due to an inadequate inhibitory control of interfering stimuli. Such an inhibitory control of interference is complementary to the active selection of relevant information. These two attentional mechanisms have been related to the function of orbitomedial and dorsolateral prefrontal cortices, respectively [6,17]. Fuster [6] called this reciprocal action the Lebadean principle of prefrontal function. The widespread frontal-central distribution of P2 enhancements during distractions is consistent with a loss of inhibitory control from orbitomedial prefrontal cortices or interconnected subcortical structures [6,17].

Unlike perseverative errors, distractions did not evoke irregular P3b activity over posterior scalp

areas. This outcome suggests that the earliest frontal anomalies associated with either type of WCST error have very different consequences upon later stages of processing (i.e. in temporal-parietal association areas). Hence, the pattern of ERP responses evoked by WCST errors may help us understand the interactions between anterior and posterior association cortices (cf. [20–22]).

Conclusion

The present results suggest that perseverative errors and distractions result from disruptions of a distinct nature in the frontal mechanisms engaged during WCST performance. It is proposed that their distinct ERP patterns reflect separate but complementary mechanisms involved in the selection of relevant information and the inhibition of interference [6,17]. Although WCST errors have a lesser incidence in normal subjects, their more homogeneous causation makes them easier to pinpoint than in clinical samples. Conversely, WCST errors in non-clinical samples probably reflect transitory dysfunctions in the same neural mechanisms that are impaired by neurological or psychiatric disease. The present evidence should make clinicians cautious in taking different WCST scores as exchangeable indexes of brain pathology [5].

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