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Wisconsin Card Sorting Test performance in patients with focal frontal and posterior brain damage: effects of lesion location and test structure on separable cognitive processes

D.T. Stuss[a,*], B. Levine[a], M.P. Alexander[a,b,c], J. Hong[a], C. Palumbo[b], L. Hamer[a], K.J. Murphy[a], D. Izukawa[d]

[a]*Rotman Research Institute, Baycrest Centre for Geriatric Care, University of Toronto 3560 Bathurst Street, Toronto, ON M6A 2E1, Canada*
[b]*Boston University School of Medicine (Neurology), USA*
[c]*Harvard Medical School (Neurology), USA*
[d]*Mississauga Hospital, Division of Neurosurgery, Mississauga, ON, Canada*

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Abstract

Forty-six patients with single focal lesions (35 frontal, 11 nonfrontal) were administered the Wisconsin Card Sorting Test (WCST) under three conditions of test administration. The three conditions varied in the amount of external support provided via specificity of instructions. The WCST, while a multifactorial test, is specifically sensitive to the effects of frontal lobe damage if deficits in language comprehension and visual–spatial search are controlled. There is also specificity of functioning within the frontal lobes: patients with inferior medial frontal lesions, unilateral or bilateral, were not impaired on the standard measures although they had increased loss of set when informed of the sorting categories. Verbal instructions may provide a probe to improve diagnosis and prognosis, assessment of the potential efficacy of treatment, and the time frame of plasticity of specific cognitive operations.

Keywords: Card sorting; Frontal lobes; Localization of process

1. Introduction

1.1. Wisconsin Card Sorting Test

The Wisconsin Card Sorting test (WCST) has been considered a key measure in the diagnosis of frontal lobe dysfunction [6,7,15,27,39,40]. This view of the WCST as a specific measure of impairment in the frontal lobes has also been seriously questioned. Reviews and published research stressed that some patients with definite frontal lobe damage performed well on the WCST, or that impairment on the task could be found after lesions in many regions of the brain [1–3,10,16,19,24,43,46,52,56,70,71]. As the WCST remains one of the most widely used of neuropsychological tests [50], investigation of its usefulness as a measure of frontal lobe dysfunction is highly relevant. Furthermore, the WCST is often used as a correlative index of 'frontal functions' in studies with neurologically intact individuals [11,30,49]. Validation of this relationship is required.

Understanding the brain-behavior relationships tapped by the WCST requires careful analysis of patients with brain disease. In particular, the comparison of patients with focal frontal to those with focal nonfrontal lesions is essential. Only a small number of studies have done this [2,40]. While such a complex multifactorial test as the WCST is unlikely to be sensitive only to the functions of the frontal lobe, analysis of the cognitive processes involved can be helpful in

* Corresponding author. Fax: +1-416-785-2474.
E-mail address: rotman@rotman-baycrest.on.ca (D.T. Stuss).

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understanding why and how individuals with lesions in different brain regions may be impaired on this test. A corollary of this process analysis is that the WCST may indeed be a reasonable index of frontal lobe functioning, if there is control of some of the 'nonfrontal' processes involved in the performance of the WCST. The study of patients with different lesions may dissociate how different brain regions are involved during the completion of this complex task. Imaging research has already suggested that multiple regions are active during the performance of the WCST [5,44] but such studies cannot normally analyze the different processes required for such a complex task. Studies of lesion patients serve as an important validation for such imaging studies, but more importantly, they extend the localization results. Dissociation of processes and lesion location within the frontal lobe would also provide greater evidence for the separation of frontal lobe processes that has been postulated [33,56,61,62,65,67].

The studies demonstrating that patients with frontal lobe damage were impaired on the WCST have not been consistent in their designation of the most relevant region within the frontal lobes. Drewe [15] suggested the importance of medial frontal cortex and Stuss et al. [63] noted the sensitivity of the WCST to orbitofrontal lesions (although the deficit in the latter patients was not reflected in an increased number of perseverations but in loss of maintenance of set). These results are in apparent contrast to Milner's original emphasis on the dorsolateral prefrontal cortex and the subsequent supporting evidence for this localization [9,35,40,51,74].

How the test is administered is also important. Stuss et al. [63] reported that the frontal lobotomy patients became impaired after they were told the three sorting criteria necessary to complete the task. It was possible that the provision of information made these patients reflect on what they were automatically doing, making the task more 'supervisory' in nature. This finding, though fortuitous, could not be fully explored because there was inadequate control over several factors, such as comparison of lesion location, and the length of test administration. The use of additional instructions may also provide information as to the potential value of external support provided by the instructions as a rehabilitative tool in patients with focal frontal lobe lesions [34,36,73]. This notion is supported by the fact that several studies have demonstrated that instructions of various kinds had improved the performance of schizophrenics on the WCST [4,18,21,37,57,72,76]. Manipulating WCST instructions might also be useful in differentiating the sensitivity of the test for patients with pathology in different brain regions. For example, in schizophrenic patients performance improved with additional instructions but remained in the impaired range [54]. Comparison of individuals who did and did not improve with additional instruction would indicate the severity of a particular patient's deficit.

In the present study we examined WCST performance in a large sample of patients with focal single lesions in frontal and nonfrontal regions of the brain, and compared their performance to age- and education-matched control subjects. In addition to extending previous work, we sought to analyze separable cognitive processes required to complete the task, differentiate patients according to intra-frontal lesion location, and assess the effect of test structure (environmental support) on performance. Each subject was administered the full 128 cards with the standard administration [20,40]. Following this, two sets of 64 cards were administered, each proceeded by different instructions. For the first set of 64 cards (64A), each subject was told the three sorting criteria. For the second set of cards (64B) (not administered to the normal control subjects), each patient was told that the sorting criterion changed after 10 correct responses. The first criterion was verbalised, and the patient was told WHEN the change occurred, but not what the new sorting criterion was. To replicate Stuss et al. [63], in addition to standard measures of categories and perseverative errors, we analyzed 'set loss', defined as the number of times the subject obtained at least three correct sorts in a row, followed by an error. We also included a measure of perseveration reflecting consecutive repetition of incorrect sorts.

2. Method

2.1. Participants

Focal lesion participants were recruited from neurosurgery, neurology, and rehabilitation centres in Ontario and Massachusetts, and control participants from the Rotman Research Institute control subject database. All focal lesion participants had a single focal lesion, verified by CT or MRI, confined to frontal, striatal or nonfrontal structures. Patients with unilateral striatal lesions were included because previous research had indicated similarity in performance to patients with dorsolateral lesions [60]. In a few patients a minor overlap of frontal and nonfrontal structures or a minor secondary lesion was observed but allowed. Focal lesion participants were at least (with one exception) 2.5 months post-onset. Two raters (CP and MPA) who were blind to experimental results analyzed all scans. Lesions were localized with standard atlases and transferred to template according to the method of Damasio and Damasio [12]. Patients with frontal pathology were assigned to one of four lesion groups as detailed in Stuss et al. [60]. This method of grouping patients takes into account the possibility of mul-

Table 1
Etiology, lesion location and extent, and months post onset within patient groups

Participant no.	Etiology	Lesion location	Months post onset	Lesion extent
Right dorsolateral frontal				
1067	Stroke	Dorsolateral	20.9	Right frontal
1068	Stroke	Dorsolateral, striatal	7.5	Right frontal
2001	Stroke	Dorsolateral, striatal	5.3	Right frontal
2024	Stroke	Dorsolateral, striatal	2.5	Right frontal
1043	Stroke	Dorsolateral, striatal	15.1	Bilateral frontal
1064	Stroke	Striatal	14.7	Right frontal
Left dorsolateral frontal				
1053	Trauma	Dorsolateral	291.1	Left frontal
1081	Hemorrhage	Dorsolateral	10.0	Left frontal
2056	Tumor	Dorsolateral	10.4	Left frontal
1042	Stroke	Dorsolateral, lateral temporal (small)	17.8	Left frontal
1071	Stroke	Dorsolateral, parietal	12.8	Left frontal
1079	Stroke	Striatal	10.7	Left frontal
Superior medial frontal				
2011	Stroke	Superior medial, ACG[a]	3.6	Right frontal
2044	Tumor	Superior medial, ACG	3.6	Right frontal
1055	Infarct	Superior medial, dorsolateral	10.9	Right frontal
2012	Tumor	Superior medial, striatal, ACG	3.9	Left frontal
1060	Stroke	Medial, ACG	6.2	Bilateral frontal
1075	Hemorrhage	Medial, ACG	22.1	Bilateral frontal
2039	Hemorrhage	Medial, ACG	1.8	Bilateral frontal
2002	Infarct	Medial, dorsolateral, ACG(L)	4.6	Bilateral frontal
2005	Tumor	Medial, dorsolateral, ACG	3.6	Right frontal
2058	Tumor	Medial, dorsolateral	74.6	Left frontal
2100	Stroke	Medial, septal	9.8	Left frontal
2045	Stroke	Medial, septal, ACG	59.8	Bilateral frontal
2049	Hemorrhage	Medial, polar	3.4	Left frontal
Inferior medial frontal				
1056	Stroke	Inferior medial, ACG	33.1	Left frontal
1065	Trauma	Inferior medial	15.7	Bilateral frontal
1070	Stroke	Inferior medial, ACG(R)	2.6	Bilateral frontal
1077	Trauma	Inferior medial	10.3	Bilateral frontal
2047	Stroke	Inferior medial	3.5	Right frontal
1054	Tumor	Inferior medial, dorsolateral, ACG	24.6	Right frontal
2102	Trauma	Inferior medial, dorsolateral	4.3	Left frontal
2053	Trauma	Inferior medial (R), dorsolateral (L), ACG(R)	3.4	Bilateral frontal
2104	Trauma	Inferior medial, dorsolateral (L), lateral temporal (small, L)	3.9	Bilateral frontal
2013	Stroke	Inferior medial, septal, ACG	8.8	Bilateral frontal
Right nonfrontal				
2040	Lobectomy	Temporal	89.3	NA
2055	Hemorrhage	Temporal	55.4	NA
2057	Lobectomy	Temporal	134.6	NA
2103	Stroke	Parietal	34.6	NA
2043	Stroke	Occipital	36.3	NA
Left nonfrontal				
1058	Stroke	Parietal	3.5	NA
2028	Stroke	Temporal, occipital	31.3	NA
2032	Lobectomy	Temporal	49.6	NA
2036	Lobectomy	Temporal	91.4	NA
2038	Lobectomy	Temporal	144.8	NA
2054	Lobectomy	Temporal	142.6	NA

[a] ACG = Anterior Cingulate Gyrus.

tiple brain regions being involved, allowing greater specificity of lesion location-behavior relations within the frontal lobes. There were 35 frontal and 11 nonfrontal patients. Those with unilateral dorsolateral frontal and/or lenticulostriate damage were classified as left and right dorsolateral frontal (RDL, $N = 6$; LDL, $N = 6$). Those with lesions in the medial frontal regions were classified as superior (Brodmann areas 6, 8, 9, dorsal 10 and 24 on the medial surface with possible inferior medial extension) or exclusively inferior medial frontal (Brodmann areas ventral 10, 11, 12, 25, and 32 on the medial surface) (SM; $N = 13$; IM, $N = 10$). The superior and inferior medial frontal groups included patients with left, right, or bilateral damage. While subjects in the SM group possibly had extension of the lesion into the IM area, none of the IM group extended into the SM area, suggesting for the SM group that the SM region was the most relevant area of brain pathology (hence the label). Patients with severe aphasia (as indicated by the language tests), or clinically detectable neglect, were excluded. Thus, we classified nonfrontal patients into right ($N = 5$) and left ($N = 6$) nonfrontal groups. The lesion location and etiology of the patient participants are detailed in Table 1. Fig. 1 depicts the lesion overlap for each frontal group.

Control participants ($N = 16$) were matched as closely as possible to the focal lesion participants according to age, education, gender, and handedness, and were screened for history of significant neurological or psychiatric disorders. The demographic data, estimated IQ, and limited neuropsychological testing for all

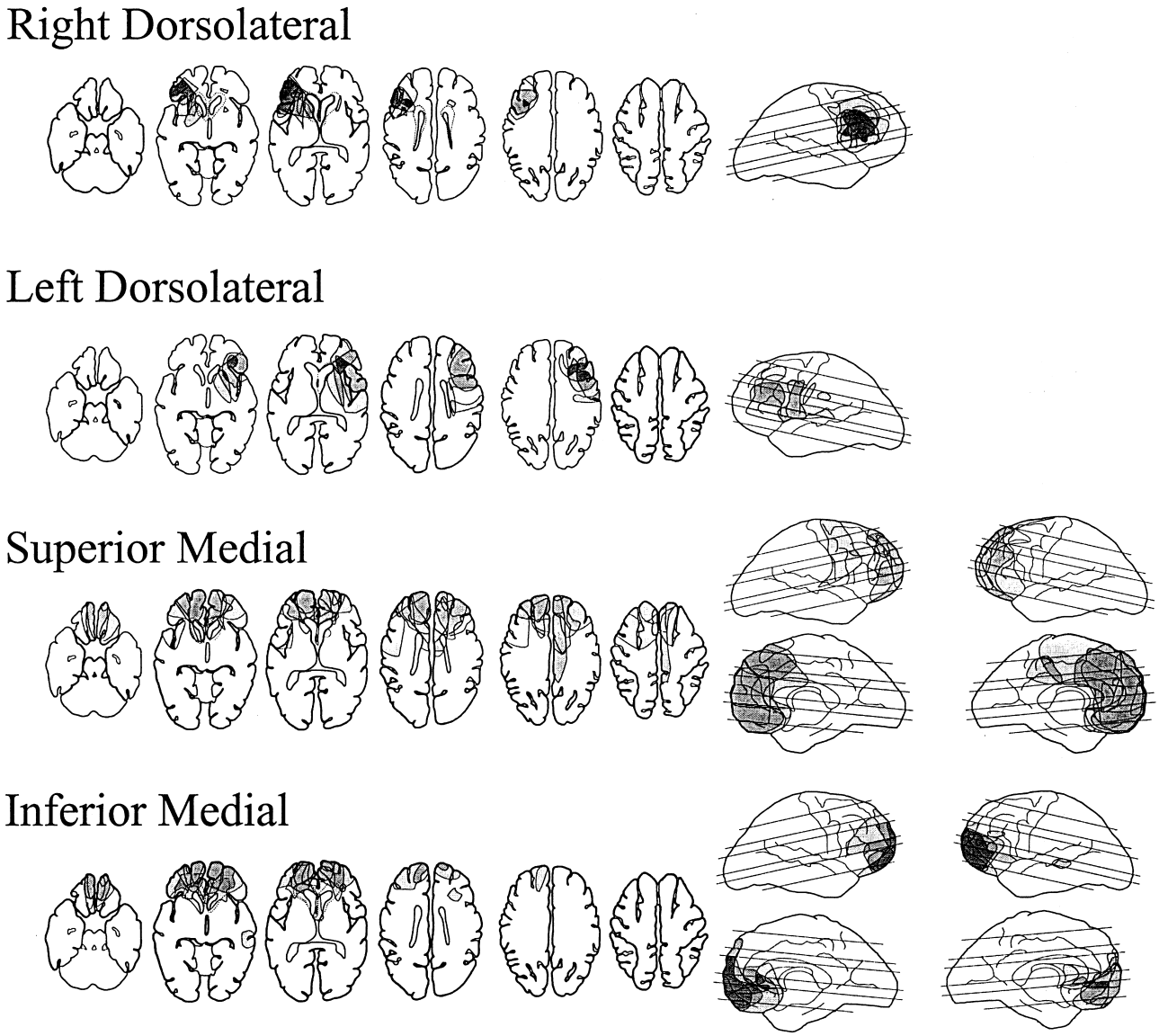

Fig. 1. Overlap of the lesions for each of the four frontal groups.

Table 2
Demographic data, estimated IQ, and neuropsychological test results for the participant groups

	Right dorsolateral		Left dorsolateral		Superior medial		Inferior medial		Right nonfrontal		Left nonfrontal		Control	
Variable	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD
Age	62.0	9.7	51.0	9.0	53.6	10.8	49.6	10.2	43.0	16.4	40.8	10.2	48.9	15.9
Education	10.7	2.7	12.8	3.2	11.8	3.5	11.9	2.0	12.0	3.2	13.0	1.3	13.4	2.2
Boston Naming Test	46.0	18.2	46.6	8.5	47.2	10.5	50.9	9.7	56.0	3.2	43.2	8.7	55.6	3.7
Digit Span forward	5.4	1.5	6.0	1.2	5.8	1.3	6.5	1.1	6.8	0.8	6.0	1.5	7.1	1.3
NART	103.6	8.9	102.1	9.4	101.0	10.9	103.3	9.5	107.7	6.3	102.2	9.3	113.2	6.4
Token Test	41.5	4.4	41.0	5.2	38.4	9.7	43.5	0.8	44.0	0.0	42.2	1.5	43.1	0.9
Number males	3		4		8		6		3		0		6	
Number females	3		2		5		4		2		6		10	

groups are presented in Table 2. There were no significant group effects for age or education. The Digit Span forward and the NART presented information on basic abilities of each group. There was no significant difference for Digit Span forward. There was a significant group difference on the NART ($F(6,52) = 3.07$, $P = 0.05$), with the control group's score significantly higher than that of the SM and IM groups. There were no group differences for the Token Test or the Boston Naming Test (BNT).

2.2. Administration

The WCST was administered in three sequential conditions within the same testing session. The entire administration lasted between 20 and 40 minutes, depending on the patient. In condition 1, the administration procedures of Grant and Berg [20,40] were followed. In contrast to standard clinical procedures, in which cards are administered until 6 sorting categories (*C*olour, *F*orm, *N*umber twice) have been achieved [22], we administered all 128 cards regardless of performance. This assured equivalent exposure to the test across subjects and maximized our assessment of set loss.

After the first 128 card administration (WCST128), each participant (regardless of how they performed or what they said) was then informed that there were three ways to sort the cards correctly: by colour, number of shapes, and the type of shape itself. Condition 2, involving an additional 64 cards (64A), was then administered as described above.

Following the 64A condition, a third condition involving another set of 64 cards (64B) was administered to the patient groups only. Participants were reminded of the three sorting criteria, then asked to sort by colour. After 10 correct sorts, the examiner said, 'Now I'm changing how you sort beginning with the next card.' This warning was given each time the criterion changed, but the actual sorting criterion was not mentioned. This method is similar to the Nelson [45] procedure for the modified card sorting test administration. The 64B condition was not administered to control subjects, who were at ceiling on performance of condition 2.

2.3. Measurements

The following measurements were obtained for each condition — WCST128; 64A; 64B.

1. Number of correct categories: the number of categories sorted with 10 consecutive correct responses.
2. Perseverations of the preceding criterion (PPC): all incorrect responses that contained a match to the preceding (no longer valid) sorting category. Sorts that were correct but which also corresponded to the preceding criterion were scored as correct. The PPC measure is similar to perseverative errors as scored by Heaton et al. [23]. PPCs in our study were defined by the preceding criterion with one exception. In cases of subjects who were so perseverative that they never attained the first category, a situation that occurred in nine of our focal frontal participants, Heaton et al.'s perseverative error score was substituted for PPC. The subject 'establishes' the 'perseverated to' criterion at the start of the test with their first unambiguous incorrect response. This allowed us to establish the 'preceding' criterion by a string of consecutive responses to a single incorrect criterion.
3. Perseveration of the preceding response (PPR): exact repetitions of the immediately preceding incorrect response were designated perseverations of the preceding response (PPRs). Only exact matches to the preceding incorrect response were included. For example, if form (F) was the correct criterion and the subject sorted F, N, N, N, two PPRs would be scored. If the sorts were F, CN, CN, then one PPR would be scored. PPR was considered a more pathognomonic kind of repetition than PPC, as the participant had just been informed that the exact

same response was incorrect. This error type is not tallied in Heaton et al's system, but was used by Nelson [45]. It is possible that an error could be scored as both a PPC and a PPR, according to our definitions. For example, if form was the correct sorting criterion and colour the preceding criterion, the following responses would be scored as indicated.

Response	Scoring
F	Correct
FC	Correct
C	PPC
CN	PPC
FN	Correct
CN	PPC
CN	PPC, PPR
N	Incorrect (other)
N	PPR

4. Set Loss: the number of times an incorrect response occurred after three or more consecutively correct responses [63]. This contrasts with system of Heaton et al., where set loss is scored after five or more correct responses. For example, if number was the correct criterion, the sequence NC, NC, N, NF, *F*, N, NC would include one set loss error (italic) [58]. To ensure that the participant was sorting to the correct criterion, at least one of the three or more correct responses had to be an unambiguously correct sort (i.e. a single match to the correct criterion, in this case number). Considering set loss as a percentage of correct responses did not affect the results. Therefore, raw set loss scores are reported. Because set loss was significantly positively skewed (i.e. many subjects with low scores and a few subjects with very high scores), additional analyses were conducted using cut-off scores. For WCST128, subjects with two or more set loss errors were classified as having high set loss and those with fewer than two were classified as low set loss. As the 64A and 64B conditions had half as many cards as the WCST128 condition, this cut-off score was reduced to one.
5. Other: this category is for non-perseverative errors and unique errors that do not match any sorting criterion.

2.4. Statistical analyses

First, the main effects of group and condition on the various scores were analyzed in mixed design ANOVAs. Then, for each condition (WCST128, 64A, 64B) the effect of group was examined using ANOVAs for each measurement score (categories, PPC, PPR, and set loss). Finally, based on past research, categories and set loss for the SM and IM groups were compared directly in mixed design ANOVAs with condition and group as factors. All group differences were evaluated in post hoc analyses with the Newman–Keuls test. Unless otherwise indicated, all differences were considered statistically significant at $P < 0.05$.

3. Results

Although the control group had a NART score significantly greater than the SM and IM groups, the results are unaffected if the NART score was used as a covariate. Moreover, there was no pattern of WCST results that was commensurate with IQ level. For example, while the two nonfrontal groups had somewhat lower IQ, their WCST scores were as good if not better than the control group. While the SM and IM groups both had significantly lower IQ scores than the control group, their WCST profiles were noticeably different from each other. There was no significant group difference in lesion size ($P = 0.26$).

We first tested the main effects of condition and group and possible interactions by comparing for all measures the first two conditions (128 and 64A), the latter doubled across all groups, and then 64A and 64B. This latter analysis was done as the control group had not received the 64B condition. There were significant main effects of group and condition with no significant interactions, with one exception noted below. These main effects are summarized as follows: the two dorsolateral frontal groups and the superior medial groups were significantly impaired compared to the control group on the measures of categories obtained, PPCs and PPRs for all conditions, with minor variations. All groups improved with instructions for all measures, again with minor variations. The effects of groups analyzed separately for each condition are presented below.

3.1. Condition 1 — WCST128 (Fig. 2A–2D)

There was a significant group effect for the number of categories obtained ($F(6,55) = 10.14$). As seen in Fig. 2A, the RDL, LDL, and SM groups attained significantly fewer categories than the two nonfrontal and control groups. The performance of the IM frontal group was not impaired relative to nonfrontal and control groups, and was significantly better than the RDL and SM groups.

The three frontal groups with low categories also had significantly more PPCs than the control group ($F(6,55) = 9.52$) (Fig. 2B). The SM group committed

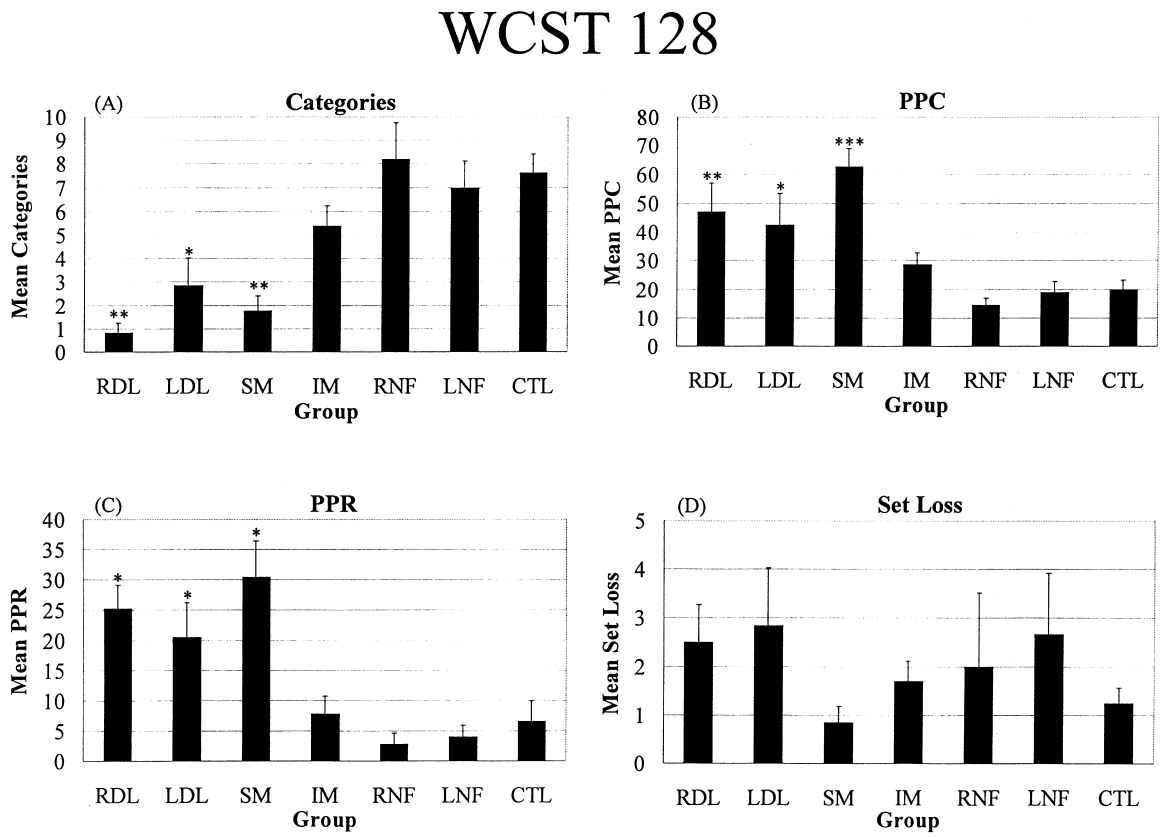

Fig. 2. Means and standard errors are presented for the performance of each of the participant groups on the four measurement scores, obtained in condition one, WCST128. (A) — number of correct categories achieved; (B) — PPC — perseverations of the preceding criterion; (C) — PPR — perseverations of the preceding response; (D) — Set Loss. RDL — right dorsolateral frontal; LDL — left dorsolateral frontal; SM — superior medial frontal, IM — inferior medial frontal, RNF — right nonfrontal; LNF — left nonfrontal; CTL — age and education matched control participants; $^{***}P < 0.001$; $^{**}P < 0.01$; $^{*}P < 0.05$.

significantly more PPCs than all groups with the exception of the RDL and LDL. The RDL group was significantly more impaired than the right nonfrontal and control groups, and the LDL was significantly more impaired than the control group only. The profile for PPRs ($F(6,55) = 11.31$) was similar to that for PPCs (Fig. 2C); the SM, RDL, and LDL groups were significantly impaired relative to posterior groups, the control group, and the IM group.

Means for set loss errors are presented in Fig. 2D. In contrast to the other performance indices where the SM group was among the poorest performing groups, the SM group was least impaired among all groups on the set loss measure. This may be related to their inability to attain the string of three or more correct responses that define set loss errors. When high set loss was defined as two or more set loss errors, the RDL group had the highest percentage of subjects with high set loss (67% — compared to 25% of controls), but there were no statistically significant group differences. There was no group effect for other (non-perseverative, unique) errors.

3.2. Stage 2 — 64A (Fig. 3A–3D)

The structure provided in the 64A condition (where subjects were informed what the three criteria were) differentially affected performance across groups. As in WCST128, SM, RDL, and LDL groups attained fewer categories than the nonfrontal or CTL groups ($F(6,55) = 11.33$) (Fig. 3A). The IM group was again the least impaired of the frontal groups, attaining significantly more categories than the SM and RDL groups. Unlike the WCST128 condition, however, the IM group was impaired relative to the control and right nonfrontal groups.

The group differences for PPCs in the 64A condition ($F(6,55) = 8.96$) were similar to that of the WCST128 condition (Fig. 3B). Again, the SM group had the highest number of PPCs, followed by the RDL group, both of which were significantly higher than the posterior and control groups. The LDL group was also impaired relative to control participants. The IM group was not impaired. As in the WCST128 condition, the IM group had sig-

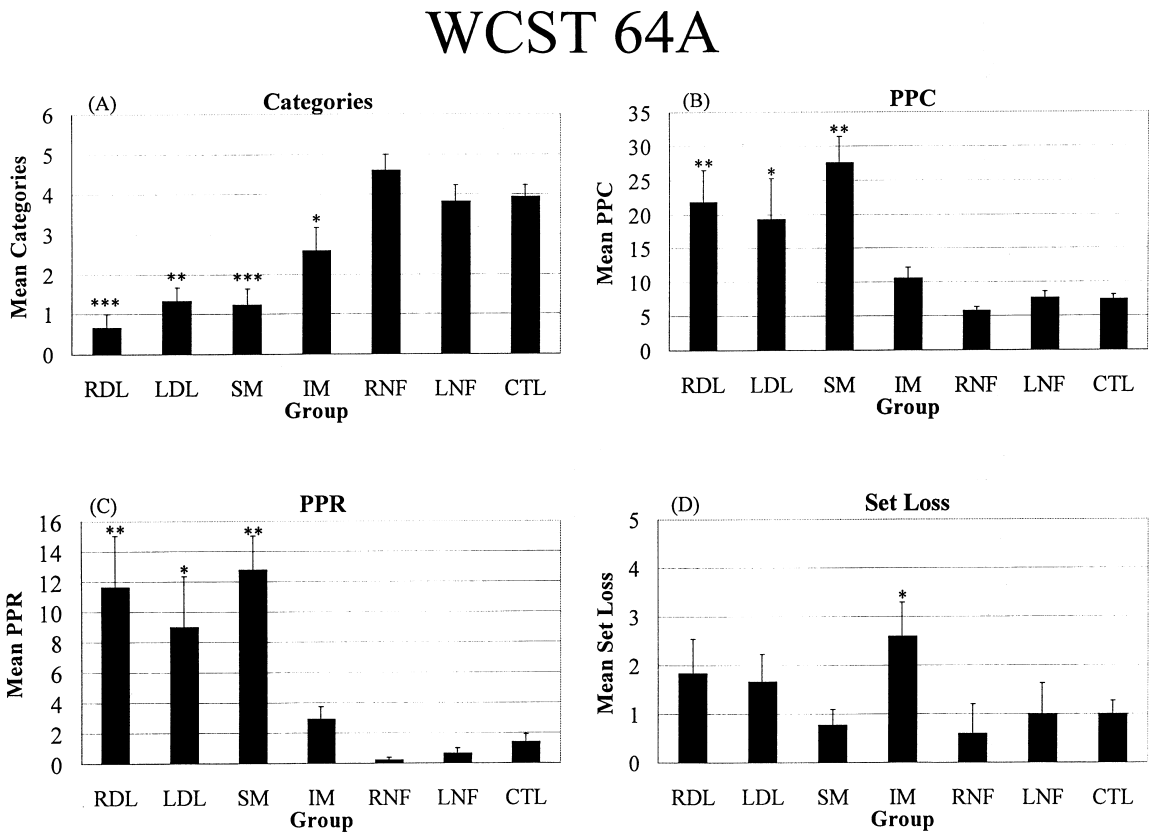

Fig. 3. The four scores for the second condition, consisting of 64 cards, are depicted. For this condition, participants were informed of the three categories. All other definitions are as in the legend for Fig. 2.

nificantly fewer PPCs than the SM group. Unlike the WCST128 condition, they also had significantly less PPC errors than the RDL group. The SM, RDL, and LDL groups again had elevated PPR scores compared to all other groups ($F(6,55)=9.02$) (Fig. 3C). Whereas these differences attained significance for the SM and RDL, the comparison between the LDL and nonfrontal groups fell short of significance, possibly due to variance differences across the groups.

Although the omnibus test for group differences in set loss in the 64A condition fell short of significance ($F(6,55)=2.06$, ($P < 0.08$)), there were significant differences among the group means. The IM group was significantly impaired relative to controls ($P < 0.05$). As in WCST128, the SM group had low set loss, again probably because of the inability to attain set. When analyzed in terms of percentages of subjects at or above the cut-off score of 1 set loss error, both the IM and RDL groups had high percentages (80 and 83%, respectively, compared to 56% of control subjects), although these differences were not statistically significant. There was a significant effect of group ($F(6,53)=3.65$) on the 'other' errors, with the RDL and LDL groups significantly greater than the control subjects, but the IM and SM groups did not differ from the control group on this measure.

3.3. Stage 3 — 64B (Fig. 4A–4D)

The SM, RDL, and LDL groups were impaired in the 64B condition, in which subjects were told when the sorting criterion changed (as well as being apprised of the three criteria prior to the start of the condition). Although these three groups improved in the 64B condition, they still achieved fewer categories than the other groups ($F(5,39)=4.14$) (Fig. 4A), although the difference reached significance only in comparison to the IM group. The lack of difference in comparison to the nonfrontal groups was due to the restricted ranges in these groups, which similarly affected the other 64B analyses. (The 64B condition was not administered to controls.)

The SM group continued to have high PPCs in the 64B condition ($F(5,39)=3.80$) (Fig. 4B), with significant differences in comparison to the IM and left nonfrontal groups. RDL, and to a lesser extent LDL, showed non-significant trends towards high PPC scores. The significant effect for PPR ($F(5,39)=3.80$) (Fig. 4C), involved the SM and RDL groups, with the

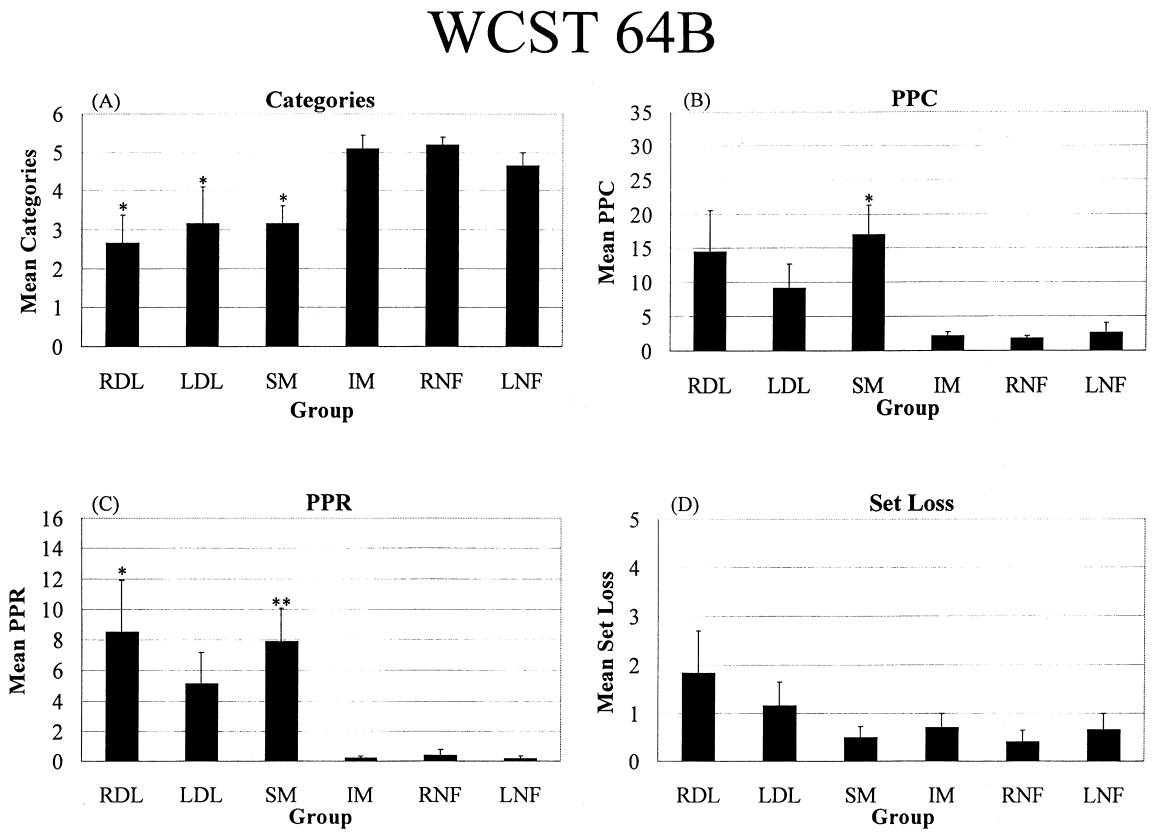

Fig. 4. The four scores for the third condition, consisting of 64 cards, are illustrated. For this condition, all participants were reminded of the three categories, and warned each time the sorting criterion would change. The control group did not receive this condition. All other definitions are as in the legend for Fig. 2.

SM group significantly different from the posterior and IM groups, and the RDL group significantly different from the IM group only. Unlike WCST128 and 64A, the LDL group did not commit a significantly greater number of PPRs than other groups, although their score for this measure was elevated.

There were no significant differences for set loss, although the RDL group was the most prone to this error type in the 64B phase (Fig. 4D).

3.4. Comparison of the SM and IM groups

Supplemental analyses of the effect of condition on the set loss and categories for the SM and IM groups were motivated by previous research suggesting a set loss deficit for patients with IM lesions when additional instructions are provided [63]. Furthermore, SM and IM patients are often grouped together in a single medial frontal group even though these areas are functionally and architectonically distinct. There was a significant group by condition interaction for set loss ($F(2,40) = 5.20$). A significant group difference was found only for the 64A condition, in which the IM group were significantly impaired (Fig. 5). The interaction for categories was not significant. The IM group performed significantly better than the SM group except for a significantly greater set loss in the 64A conditions.

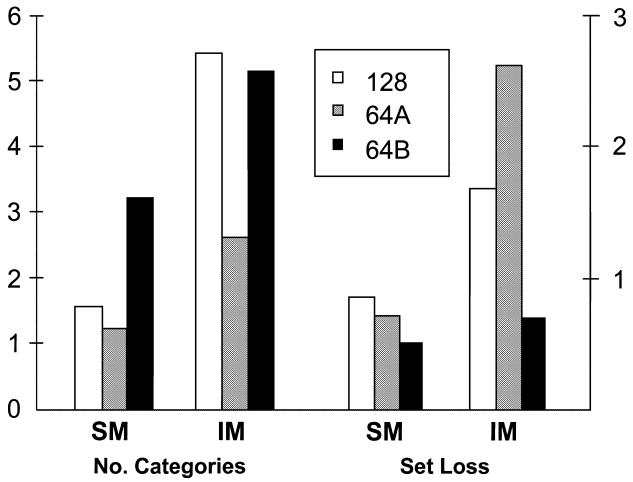

Fig. 5. Interrelationship between the number of categories achieved, and set loss for the patients in the inferior medial and superior medial frontal lesion groups. For 64A and 64B, the scores are doubled to allow comparison to condition one with 128 cards.

4. Summary

As can be seen in Figs. 2 and 3 the patients with nonfrontal lesions were not impaired compared to the matched control group on any measure. Further, there were no significant differences between the two nonfrontal groups on any of the measures. The frontal effects were due to perseverative errors and set loss errors. Non-perseverative and unique errors were not indicative of frontal dysfunction. One exception was the 64A condition, where RDL and LDL patients made more of the other errors. However, even in this condition, errors of this sort were not elevated in the IM and SM groups, who were nevertheless impaired on the other measures.

Of the four frontal groups, three groups, SM, RDL, and LDL were the most consistently impaired. In particular, the SM group was the most impaired on nearly every measure. One exception was set loss. Although the SM patients' low set loss scores in the WCST128 condition could be accounted for by a failure to achieve the requisite string of correct responses, this does not account for their low set loss in the 64B condition, where their number of categories increased twofold over the 64A condition. In contrast, the RDL group had high set loss in the context of decreased category shifts, and was the only group to maintain high set loss across all three conditions.

The IM group was least impaired of the frontal groups, but appeared to have a selective problem that was related to the context provided by the instructions. In the WCST128 condition, there were no significant differences between the IM frontal and nonfrontal or control groups. In the 64A condition, the IM group remained superior to the other frontal groups, but was impaired relative to control subjects in the number of categories attained. This appears to be due to a high degree of set loss. The degree of set loss for the IM group increased 50% from 1.7 in the WCST128 condition to 2.6 in the 64A condition — which had half as many cards. Importantly, this increased set loss occurred in the absence of an increase in PPC and PPR errors. With additional increased instruction (64B), this set loss deficit diminished.

The set loss measure differentiated the IM and SM groups. The SM group showed minimal set loss for both 64A and 64B. The IM group had the highest set loss of all frontal groups, revealed in the 64A condition, but this was virtually eliminated in 64B.

5. Discussion

5.1. The WCST as a measure of frontal lobe functioning

The presented data support the widely held assumption that the WCST is sensitive to focal frontal brain damage, and that this effect is specific to patients with focal frontal brain damage. There are, however, qualifications. The sensitivity of the WCST depends on which measure is used, reflecting a differentiation of processes/lesion location relationships within the frontal lobes. For the standard measures such as perseverations of the preceding criterion and number of categories achieved, there is minimal effect of damage to the inferior medial frontal region. In addition, test administration plays a role in the sensitivity of the test.

In our nonfrontal patients, we excluded those with notable aphasia or neglect. We wanted to understand distinct processes that are necessary for the performance of the WCST, and it was important to test patients who could do the basic aspects of the task. Since chronicity of lesions has been suggested to have an effect on WCST performance [2,53,68], we tested patients with circumscribed lesions, who were in a chronic stage of recovery after injury. There was no significant correlation of chronicity with any WCST measure, the highest correlation being 0.23 in the wrong direction. Nevertheless, our frontal patients were tested at a somewhat earlier phase (mean of 13.4 months after injury — excluding 1053 with close to 300 months — with 65% less than one year) than those in the Anderson et al. [2] study (mean of 27 months, with over 50% over one year), who did not find a specific sensitivity of the frontal lobes to the WCST. It may be that at least one year is necessary for spontaneous improvement in this type of task.

5.2. Left and right dorsolateral frontal lobe

The sensitivity of the dorsolateral prefrontal cortex to the demands of the WCST proposed in lesion and imaging studies [9,35,38,40,51,74] is confirmed by our results. Lesion and imaging studies have demonstrated the involvement of both right and left dorsolateral frontal lobes [5,15,40,44,47]. The results of hemispheric laterality (regardless of the within hemisphere location) on the WCST can be grouped into three categories: greater deficit with left hemisphere damage [17]; a greater effect with right hemisphere damage [10,25,70]; or no lateralizing effect [6,25,45,69,71]. In our study, impairment on the number of categories achieved and number of perseverations was observed after left and right dorsolateral damage. However, there were differences in how severe the impairment was. Thus, patients with LDL, RDL and SM lesions were all impaired relative to controls, but the LDL patients were impaired to a lesser degree. For the 64B administration, the LDL group was not significantly impaired on PPR, while the RDL and SM groups were. Several previous studies had suggested that the right frontal

patients made more perseverative errors than the left frontal group [15,22,47]. This may be reflective of the greater sustained attention and monitoring role of the right frontal lobe [55,75]; however, this was found only in the 64B condition.

5.3. Set loss and the inferior medial frontal region

At first blush, sparing of performance of the IM group on the commonly used WCST measures of number of categories achieved and number of perseverations seems inconsistent with the monkey literature, where inferior prefrontal lesions have been reliably associated with perseveration [41]. In recent monkey studies, however, this discrepancy has been resolved [13]. The extra-dimensional shifting that corresponds to PPC's is specifically affected by lateral frontal lesions (and not by orbitofrontal lesions) in the monkey [14]. This attentional disinhibition can be contrasted with affective disinhibition (assessed by reversal of stimulus-reward associations), affected by orbitofrontal lesions (and not by lateral frontal lesion) [14], but not specifically assessed by WCST measures. Moreover, this good performance of patients with inferior medial frontal lesions on at least certain 'frontal lobe' measures parallels other findings in our lab on letter fluency and conditional associative learning [31,60].

The inferior medial patients (bilateral, left or right unilateral lesions), however, were not free of deficits. They showed increased loss of cognitive set in the 64A condition. The profile of results in which the increased set loss in the IM group occurs in the absence of an increase in PPC and PPR errors stresses that lesions in this region produces a pattern of deficits distinct from that of patients with frontal damage in other regions. This increased set loss in patients with orbitofrontal or inferior medial lesions is consistent with other research. Stuss et al. [63] reported increased set loss in frontal leucotomy patients. Nagahama et al. [44] demonstrated in a PET study that controlling for maintenance of set reduced orbitofrontal activation, leading to the suggestion that the orbitofrontal cortex might play a role in maintenance of set. Berman et al. [5] also showed orbitofrontal activation during the WCST, but they did not specifically focus on maintenance of set. These results are not inconsistent with Milner's [38,40] claim that the WCST is sensitive to dorsolateral prefrontal cortical dysfunction, since she did not assess loss of set.

What may be the cause of the set loss in the IM patients? A single, unitary factor, such as a 'working memory' deficit proposal, cannot account for these WCST results. Both loss of set and perseverations would seem to require working memory, yet different frontal groups are impaired on these measures in different ways. For the dorsolateral groups, there appears to be some relationship between set loss and perseverative errors. The SM group, on the other hand, reveals dissociation between the number of perseverative errors and set loss score. The IM group has primarily set loss difficulty. The fact that the IM patients could manage and use the information provided argues against a working memory deficit. The deficit cannot be due to boredom, since boredom would result in an even worse set loss in 64B (in which condition performance was normal).

Two possible reasons for set loss are proposed, derived from a comparison of IM and RDL groups who demonstrated a different profile of problems with set loss. The same leucotomy patients with orbitofrontal (IM) lesions who demonstrated set loss on the WCST [63] were significantly impaired on the Brown–Petersen test of 'short-term memory', despite *normal* memory on the Wechsler Memory Scale [66]. In a separate study, IM patients were impaired on a strategy application task requiring the suppression of responses to irrelevant (but salient) stimuli [32]. The additional information given in the instructions, the additional efforts required in counting backwards while trying to remember letters, or the inhibitory processing of irrelevant stimuli, may have evoked additional 'supervisory' reflective efforts interfering with more automatic processing, as earlier hypothesised [63].

The disturbed process underlying set loss in the RDL group (which had a trend to be more resistant to the instruction manipulation) may be different from that of the IM group. The right frontal lobe is involved in sustaining attention and monitoring [29,75]. Sustained attention deficits would be expected to produce loss of set. We have already demonstrated loss of set in a subset of these patients in a different task, conditional associative learning [31]. In a study of memory, right frontal patients tended to repeat words previously recalled, as if they were not monitoring their output [59]. Mizuno [42], in a study of the WCST performance of 126 patients, also suggested that the difficulty in maintaining set reflected a sustained attention problem, although the set loss deficit was attributed to general right hemisphere damage, with no indication of rostral-caudal specificity. Our hypothesis — that set loss in the IM group is related to a disruption of automatic processing, and the set loss in the RDL group to a sustained attention deficit — is suggested by our results. More direct examination of the above hypothesis is warranted in future research.

5.4. The role of the superior medial frontal lobes

While there clearly was some overlap of lesion area involvement in the different groups, the patients with superior medial involvement (including patients with unilateral right OR left SM as well as bilateral

damage) performed as badly as the patients with dorsolateral lesions. Few previous studies have identified the involvement of the SM area in WCST performance. Kawasaki et al. [28] reported less activation in the left medial prefrontal cortex in schizophrenic patients. Nagahama et al. [44] observed blood flow activation in bilateral rostral areas 10 and 11, left SMA, and bilateral cingulate. In our study on verbal fluency with many of the same individuals, patients with left dorsolateral and bilateral SM lesions were impaired, but not those with right dorsolateral lesions [60]. In this present study, the performance of the SM group was most similar to the right frontal DL group. Taking the verbal fluency and WCST results together, one might consider that the SM region is functionally continuous with the dorsolateral region that is involved in a specific cognitive process. This is consistent with Pandya and Yeterian's [48] assertion that these two regions emerge from the same archicortical (hippocampal) evolutionary trend. We are uncertain what specific brain region within the SM is most necessary, since we could not dissociate the effects of SMA, rostral areas 10, 9, and 8, and superior anterior cingulate damage. We also could not differentiate any lesion laterality or size effect.

5.5. Perseveration measures

The different measures of perseveration may assess different cognitive processes. PPCs have been interpreted as extradimensional shifting, requiring a release from a previously relevant dimension and eventually a move to a previously irrelevant dimension [47]. While Owen and colleagues found no obvious relationship between the degree of perseveration and the precise location of the frontal lobe excision (all patients in their study were surgical excision patients), our data suggest some relationship, with the IM group not demonstrating perseverative impairments. Our measure of PPR represents the immediate repetition of a response that was just identified as being erroneous. Such errors have been reported to be more related to the right hemisphere, particularly the right frontal region [8,55]. Our results implicated the right frontal and superior medial regions. PPRs would appear to be a true pathognomonic sign of frontal (with the exception of the IM area) lobe disturbance. Very few nonfrontal patients exhibited these, particularly when instructions had been given.

5.6. Our experimental manipulations: the value of instructions and external support

The deficit on the WCST in the frontal lobe patients is not secondary to a conceptualization or category deduction deficit. Many of the patients spontaneously verbalised what the three sorting categories were, and there were no group differences (with the exception of set loss for the IM group) between 128 and 64A. Stratta et al. [57] had demonstrated that, in 62% of schizophrenics who had performed poorly on the WCST, mere statement of the criteria before sorting improved performance. For the rehabilitation of frontal lobe patients, our data indicate that this would not be the case. In most patients with focal frontal lobe damage, *it is not the lack of knowledge but the use of knowledge* that is most detrimental.

A major observation for the 64B condition is the effect of alerting participants to the impending category shifts (in addition to the practice effects). These instructions brought performance to ceiling in the nonfrontal and IM groups. Performance also improved for the other frontal groups (SM, LDL, and RDL), where the number of categories achieved increased more than two-fold and the number of perseverative errors decreased. Highly structured verbal instructions providing explicit direction do improve test performance of frontal lobe patients on the WCST, suggesting that this may be a worthwhile rehabilitative avenue to pursue. It would be necessary to see if such an effect generalizes, can be internalized [64], or if any improvement is retained over a period of time. There is some suggestion in the schizophrenia literature that instructions on how to complete the WCST results in some retention of benefit over time [4,21,37,76], although this may depend on the type of patient tested [18]. An additional implication from the 64B condition is that modifying the WCST by announcing impending category shifts, as employed in the Modified Card Sorting Test [45], makes the test less sensitive to frontal lesions, a conclusion suggested earlier by Teuber [68].

Despite the general improvement on 64B, performance of the SM, RDL, and LDL groups remained impaired compared to the other patient groups, although this was not significant for all measures. One implication of this finding relates to the assessment and diagnosis of individual patients. The use of this level of instruction may be one way of narrowing the number of classification outliers, at least for the nonfrontal lesioned patients. Documenting that a patient who performs poorly on the WCST is able to understand general task demands, and does significantly improve after this level of instruction, may provide useful functional information about the individual patient. Conversely, this method identifies those individuals who have difficulty even when provided with considerable external support.

6. Conclusion

This is one of a few studies on the WCST that has been completed on patients with documented focal lesions in various regions of the brain. The current data, along with previous lesion data research on WCST performance, provide a framework for understanding the value of the WCST for the assessment of brain-damaged individuals. Certain themes are constant. The WCST is a multifactorial test that requires a distributed neural network. Performance can be impaired on this test for various reasons, and not all of these are related to the functions associated with the frontal lobes. Nevertheless, in patients who meet certain conditions related to a basic ability to address the demands of the task, the WCST can be sensitive to the effects of frontal lobe damage.

Our results, in conjunction with other published data, suggest functional dissociations between superior and inferior medial regions and between dorsolateral and orbitofrontal/inferior medial areas. The patients with superior medial frontal lobe involvement were most impaired on the standard WCST measures (with the exception of set loss). The IM group displayed somewhat of an opposite profile. The left and right dorsolateral involvement groups were comparable on almost all measures, with the exception of continuing set loss problems in the RDL group, even after the highest level of additional instruction had been given. Whereas the IM group had high set loss and low PPC in 64A, the DL groups were characterized by perseveration.

The possibility that recovery could take place at a late stage, and that verbal instructions can be used as a probe for improvement of behavior, might provide a window for prognosis, timing of rehabilitation efforts, assessment of efficacy of treatment, and for scientific understanding about the time frame of plasticity of specific operations [26].

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References

[1] Anderson CV, Bigler ED, Blatter DD. Frontal lobe lesions, diffuse damage, and neuropsychological functioning in traumatic brain-injured patients. Journal of Clinical & Experimental Neuropsychology 1995;17:900–8.

[2] Anderson SW, Damasio H, Jones RD, Tranel D. Wisconsin Card Sorting Test performance as a measure of frontal lobe damage. Journal of Clinical and Experimental Neuropsychology 1991;13:909–22.

[3] Axelrod BN, Goldman RS, Heaton RK, Curtiss G, Thompson LL, Chelune GJ, Kay GG. Discriminability of the Wisconsin Card Sorting Test using the standardization sample. Journal of Clinical & Experimental Neuropsychology 1996;18:338–42.

[4] Bellack AS, Mueser KT, Morrison RL, Tierney A, Podell K. Remediation of cognitive deficits in schizophrenia. American Journal of Psychiatry 1990;147:1650–5.

[5] Berman KF, Ostrem JL, Randolph C, Gold J, Goldberg TE, Coppola R, Carson RE, Herscovitch P, Weinberger DR. Physiological activation of a cortical network during performance of the Wisconsin Card Sorting Test: A positron emission tomography study. Neuropsychologia 1995;33:1027–46.

[6] Bornstein RA. Contribution of various neuropsychological measures to detection of frontal lobe impairment. The International Journal of Clinical Neuropsychology 1986;8:18–22.

[7] Braff D, Heaton RK, Kuck J, Cullum M, Moranville J, Grant I, Zisook S. The generalized pattern of neuropsychological deficits in outpatients with chronic schizophrenia with heterogeneous Wisconsin Card Sorting Test results. Archives of General Psychology 1991;48:891–8.

[8] Brugger P, Monsch AU, Johnson SA. Repetitive behavior and repetition avoidance: the role of the right hemisphere. Journal of Psychiatry and Neuroscience 1996;21:53–6.

[9] Catafau AM, Parellada E, Lomena FJ, Bernardo M, Pavia J, Ros D, Setoain J, Gonzales-Monclus E. Prefrontal and temporal blood flow in schizophrenia: resting and activation technetium-99 m-HMPAO SPECT patterns in young neuroleptic-naive patients with acute disease. Journal of Nuclear Medicine 1994;35:935–41.

[10] Corcoran R, Upton D. A role for the hippocampus in card sorting? Cortex 1993;29:293–304.

[11] Craik FIM, Morris LW, Morris RG, Loewen ER. Relations between source amnesia and frontal lobe functioning in older adults. Psychology and Aging 1990;5:148–51.

[12] Damasio H, Damasio AR. Lesion analysis in neuropsychology. New York: Oxford University Press, 1989.

[13] Dias R, Robins TW, Roberts AC. Dissociable forms of inhibitory control within prefrontal cortex with an analog of the Wisconsin Card Sort Test: restriction to novel situations and independence from 'on-line' processing. Journal of Neuroscience 1997;17:9285–97.

[14] Dias R, Robins TW, Roberts AC. Dissociation in prefrontal cortex of affective attentional shifts. Nature 1996;380:69–72.

[15] Drewe EA. The effect of type and area of brain lesion on Wisconsin Card Sorting Test performance. Cortex 1974;10:159–70.

[16] Eslinger PJ, Damasio AR. Severe disturbance of higher cognition following bilateral frontal lobe ablation: Patient EVR. Neurology 1985;35:1731–41.

[17] Ettlinger G, Teuber HL, Milner B. The seventeenth international symposium of neuropsychology. Neuropsychologia 1975;13:125–33.

[18] Goldberg TE, Weinberger DR, Berman KF, Pliskin NH, Podd MH. Further evidence for dementia of the prefrontal type in schizophrenia? A controlled study of teaching the Wisconsin Card Sorting Test. Archives of General Psychiatry 1987;44:1008–14.

[19] Grafman J, Jonas B, Salazar A. Wisconsin card sorting test performance based on location and size of neuroanatomical lesion

in Vietnam veterans with penetrating head injury. Perceptual and Motor Skills 1990;71:1120–2.
[20] Grant DA, Berg EA. A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a weight-type card-sorting problem. Journal of Experimental Psychology 1948;38:404–11.
[21] Green MF, Satz P, Ganzell S, Vaclav JF. Wisconsin Card Sorting Test performance in schizophrenia: remediation of a stubborn deficit. American Journal of Psychiatry 1992;149:62–7.
[22] Haut MW, Cahill J, Cutlip WD, Stevenson JM, Makela EH, Bloomfield SM. On the nature of Wisconsin Card Sorting Test performance in schizophrenia. Psychiatry Research 1996;65:15–22.
[23] Heaton R. A manual for the Wisconsin Card Sorting Test. Odessa, Florida: Psychological Assessment Resources, 1981.
[24] Heck ET, Bryer JB. Superior sorting and categorizing ability in a case of bilateral frontal atrophy: An exception to the rule. Journal of Clinical and Experimental Neuropsychology 1986;8:313–6.
[25] Hermann BP, Wyler AR. Effects of anterior temporal lobectomy on language function: A controlled study. Annals of Neurology 1988;23:585–8.
[26] Hetherington CR, Stuss DT, Finlayson MAJ. Reaction time and variability 5 and 10 years after traumatic brain injury. Brain Injury 1996;10:473–86.
[27] Janowsky JS, Shimamura AP, Kritchevsky M, Squire LR. Cognitive impairment following frontal lobe damage and its relevance to human amnesia. Behavioural Neuroscience 1989;103:548–60.
[28] Kawasaki Y, Maedo M, Urata K, Higashima M, Kiba K, Yamaguchi N, Matsuda H, Hisada K. SPECT analysis of regional cerebral blood flow changes in patients with schizophrenia during the Wisconsin Card Sorting Test. Schizophrenia Research 1993;10:109–16.
[29] Knight RT. Evoked potential studies of attention capacity in human frontal lobe lesions. In: Levin HS, Eisenberg MH, Benton AL, editors. Frontal lobe function and dysfunction. New York: Oxford University Press, 1991. p. 139–53.
[30] Kopelman MD. Frontal dysfunction and memory deficits in the alcoholic Korsakoff syndrome and Alzheimer-type dementia. Brain 1991;114:117–37.
[31] Levine B, Stuss DT, Milberg WP. The effects of aging on conditional associative learning: Process analyses and comparison with focal frontal lesions. Neuropsychology 1997;11:367–81.
[32] Levine B, Stuss DT, Milberg WP, Alexander MP, Schwartz M, Macdonald R. The effects of focal and diffuse brain damage on strategy application: Evidence from focal lesions, traumatic brain injury, and normal aging. Journal of the International Neuropsychological Society 1998;4:247–64.
[33] Lhermitte F. 'Utilization Behavior' and its relation to lesions of the frontal lobes. Brain 1983;106:237–55.
[34] Luria AR. The working brain. An introduction to neuropsychology. New York: Basic Books, 1973.
[35] Marenco S, Coppola R, Daniel DG, Zigun JR, Weinberger DR. Regional cerebral blood flow during the Wisconsin Card Sorting Test in normal subjects studied by xenon-133 dynamic SPECT: comparison of absolute values, percent distribution values, and covariance analysis. Psychiatry Research 1993;50:177–92.
[36] Meichenbaum D, Biemiller A 1990. In search of student expertise in the classroom: a metacognitive analysis. Paper Presented at the Conference on Cognitive Research for Instructional Innovation, University of Maryland, College Park, Maryland.
[37] Metz JT, Johnson M, Plishkin N, Luchins JS. Maintenance of training effects on the Wisconsin Card Sorting Test by patients with schizophrenia or affective disorders. American Journal of Psychiatry 1994;151:120–2.
[38] Milner B. Interhemispheric differences in the localization of psychological processes in man. British Medical Bulletin 1971;27:272–7.
[39] Milner B. Some effects of frontal lobectomy in man. In: Warren JM, Akert K, editors. The frontal granular cortex and behaviour. New York: McGraw-Hill, 1964. p. 313–34.
[40] Milner B. Effects of different brain lesions on card sorting: The role of the frontal lobes. Archives of Neurology 1963;9:100–10.
[41] Mishkin M. Perseveration of central sets after frontal lesions in monkeys. In: Warren JM, Akert K, editors. The frontal granular cortex and behavior. New York: McGraw-Hill. p. 219–41.
[42] Mizuno M. Neuropsychological characteristics of right hemisphere damage: investigation by attention tests, concept formation and change test, and self-evaluation task. Keio Journal of Medicine 1991;40:221–34.
[43] Mountain MA, Snow WG. Wisconsin Card Sorting Test as a measure of frontal pathology: a review. The Clinical Neuropsychologist 1993;7:108–18.
[44] Nagahama Y, Fukuyama H, Yamauchi H, Matsuzaki S, Konishi J, Shibasaki H, Kimura J. Cerebral activation during performance of a card sorting test. Brain 1996;119:1667–75.
[45] Nelson HE. A modified card sorting test sensitive to frontal lobe defects. Cortex 1976;12:313–24.
[46] Oscar-Berman M, McNamara P, Freedman M. Delayed-Response tasks: Parallels between experimental ablation studies and findings in patients with frontal lesions. In: Levin HS, Eisenberg HM, Benton AL, editors. Frontal lobe function and dysfunction. New York: Oxford University Press, 1991. p. 256–72.
[47] Owen AM, Roberts AC, Hodges JR, Summers BA, Polkey CE, Robbins TW. Contrasting mechanisms of impaired attentional set-shifting in patients with frontal lobe damage or Parkinson's disease. Brain 1993;116:1159–75.
[48] Pandya DN, Yeterian EH. Comparison of prefrontal architecture and connections. Philosophical Transactions of the Royal Society of London, Part B 1996;351:1423–32.
[49] Parkin AJ, Walter BM. Aging, short-term memory, and frontal dysfunction. Psychobiology 1991;19:175–9.
[50] Retzlaff P, Butler M, Vanderploeg RD. Neuropsychological battery choice and theoretical orientations: a multivariate analysis. Journal of Clinical Psychology 1992;48:666–72.
[51] Rezai K, Andreasen NC, Alliger R, Cohen G, Swayze V, O'Leary DS. The neuropsychology of the prefrontal cortex. Archives of Neurology 1993;50:636–42.
[52] Robinson AL, Heaton RK, Lehman RAW, Stilson DW. The utility of the Wisconsin Card Sorting Test in detecting and localizing frontal lobe lesions. Journal of Consulting and Clinical Psychology 1980;48:605–14.
[53] Rosvold HE, Mishkin M. Evaluation of the effects of prefrontal lobotomy on intelligence. Canadian Journal of Psychology 1950;4:122–6.
[54] Rothke S. The role of interpersonal feedback in group psychotherapy. International Journal of Group Psychotherapy 1986;36:225–40.
[55] Sandson J, Albert ML. Perseveration in behavioral neurology. Neurology 1987;37:1736–41.
[56] Shallice T, Burgess PW. Deficits in strategy application following frontal lobe damage in man. Brain 1991;114:727–41.
[57] Stratta P, Mancini F, Mattei P, Casacchia M, Rossi A. Information processing strategy to remediate Wisconsin Card Sorting Test performance in schizophrenia: a pilot study. American Journal of Psychiatry 1994;151:915–8.
[58] Stuss DT. Contribution of frontal lobe injury to cognitive impairment after closed head injury: Methods of assessment and recent findings. In: Levin HS, Grafman J, Eisenberg HM, editors. Neurobehavioral recovery from head injury. New York: Oxford University Press, 1987. p. 166–77.

[59] Stuss DT, Alexander MP, Palumbo CL, Buckle L, Hamer L, Pogue J. Organizational strategies with unilateral or bilateral frontal lobe injury in word list learning tasks. Neuropsychology 1994;8:355–73.
[60] Stuss DT, Alexander MP, Hamer L, Palumbo C, Dempster R, Binns M, Levine B, Izukawa D. The effects of focal anterior and posterior brain lesions on verbal fluency. Journal of the International Neurological Society 1998;4:265–78.
[61] Stuss DT, Benson DF. Neuropsychological studies of the frontal lobes. Psychological Bulletin 1984;95:3–28.
[62] Stuss DT, Benson DF. The frontal lobes. New York: Raven Press, 1986.
[63] Stuss DT, Benson DF, Kaplan EF, Weir WS, Naeser MA, Lieberman I, Ferrill D. The involvement of orbitofrontal cerebrum in cognitive tasks. Neuropsychologia 1983;21:235–48.
[64] Stuss DT, Delgado M, Guzman DA. Verbal regulation in the control of motor impersistance: a proposed rehabilitation procedure. Journal of Neurologic Rehabilitation 1987;1:1–6.
[65] Stuss DT, Eskes GA, Foster JK. Experimental neuropsychological studies of frontal lobe functions. In: Boller F, Grafman J, editors. Handbook of neuropsychology. Amsterdam: Elsevier, 1994. p. 149–85.
[66] Stuss DT, Kaplan EF, Benson DF, Weir WS, Chiulli S, Sarazin FF. Evidence for the involvement of orbitofrontal cortex in memory functions: an interference effect. Journal of Comparative Physiology and Psychology 1982;96:913–25.
[67] Stuss DT, Shallice T, Alexander MP, Picton T. A multidisciplinary approach to anterior attentional functions. Annals of the New York Academy of Sciences 1995;769:191–212.
[68] Teuber HL. Comment on 'Some Effects of Frontal Lobectomy in Man' by Brenda Milner. In: Warren JM, Akert K, editors. The frontal granular cortex and behaviour. McGraw-Hill, 1964. p. 332–3.
[69] Trennerry MR, Jack CR, Cascino GD, Sharbrough FW, Ivnik RJ. Gender differences in post-temporal lobectomy verbal memory and relationships between MRI hippocampal volumes and preoperative verbal memory. Epilepsy Research 1995;20:69–76.
[70] Upton D, Corcoran R. The role of the right temporal lobe in card sorting: a case study. Cortex 1995;31:405–9.
[71] van den Broek MD, Bradshaw CM, Szabadi E. Utility of the modified Wisconsin Card Sorting Test in neuropsychological assessment. British Journal of Clinical Psychology 1993;32:333–43.
[72] Vollema M, Geurtsen G, van Voorst A. Durable improvements in Wisconsin Card Sorting Test performance in schizophrenic patients. Schizophrenia Research 1995;16:209–15.
[73] Vygotsky LS. Thought and language. Ed and transl. Hanfmann E, Vakar G. MIT Press, Cambridge, Massachusetts, 1962.
[74] Weinberger DR, Berman KF, Zec RF. Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia: I. Regional cerebral blood flow evidence. Archives of General Psychiatry 1986;43:114–24.
[75] Wilkins AJ, Shallice T, McCarthy R. Frontal lesions and sustained attention. Neuropsychologia 1987;25:359–65.
[76] Young D, Freyslinger M. Scaffolded instruction and the remediation of Wisconsin Card Sorting Test deficits in chronic schizophrenia. Scizophrenia Research 1995;16:199–207.