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EXTRA-DIMENSIONAL VERSUS INTRA-DIMENSIONAL SET SHIFTING PERFORMANCE FOLLOWING FRONTAL LOBE EXCISIONS, TEMPORAL LOBE EXCISIONS OR AMYGDALO-HIPPOCAMPECTOMY IN MAN

ADRIAN M. OWEN,*† ANGELA C. ROBERTS,* CHARLES E. POLKEY,‡ BARBARA J. SAHAKIAN§ and TREVOR W. ROBBINS*

*Department of Experimental Psychology, University of Cambridge, Cambridge, U.K.; ‡Neurosurgical Unit, The Maudsley Hospital, London, U.K.; and §Section of Old Age Psychiatry, Institute of Psychiatry, University of London, U.K.

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Abstract—Attentional "set" shifting was assessed in a group of 20 neurosurgical patients with localized excisions of the frontal lobes, a group of 20 patients with unilateral temporal lobe lesions and a group of 11 patients who had undergone amygdalo-hippocampus removal. These three patient groups were compared with groups of both young (age-matched) and elderly normal control volunteers on a computerized test of visual discrimination learning involving both an intra- and an extra-dimensional shift. The frontal lobe group were selectively impaired in their ability to shift response set to a previously irrelevant dimension but not to shift attention to new exemplars of a previously relevant dimension. A similar pattern was observed in the elderly group of normal control volunteers. By comparison, both the temporal lobe patients and the amygdalo-hippocampectomy patients were unimpaired in their ability to perform either shift, although both groups had significantly prolonged selection latencies at the extra-dimensional shift stage of the task. These data are compared to previous findings from patients with idiopathic Parkinson's disease and are discussed in terms of a specific attentional set shifting deficit following frontal lobe damage.

INTRODUCTION

TESTS of sorting or "concept formation" appear to be particularly sensitive to frontal lobe pathology, especially when they are used to assess attentional set shifting ability [8, 16, 30, 34, 45, 47, 51]. However, these tests are not always differentially sensitive to frontal lobe dysfunction and generalized or diffuse brain damage can produce similar cognitive deficits [14, 28, 45]. In several studies, no impairment has been found in cases of known frontal lobe pathology [16, 17, 29] whilst in others, significant effects have been demonstrated following localized damage to specific non-frontal regions [7, 53]. Moreover, many studies have now established that patients with Parkinson's disease (PD) are also impaired on such tests of sorting or concept formation [5, 7, 9, 19, 20, 25, 40, 52]. Although some of these impairments closely resemble those commonly attributed to frontal lobe damage, the underlying neural substrates responsible have proved rather difficult to define.

We have recently compared the performance of medicated and non-medicated patients early in the course of PD on a test of visual discrimination learning culminating in an intra-

†To whom correspondence should be addressed: Section of Old Age Psychiatry, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, U.K.

and an extra-dimensional shift [15]. An intra-dimensional shift (IDS) occurs when a subject, trained to respond to a particular stimulus dimension, such as colour or shape, is required to transfer that rule to a novel set of exemplars of that same stimulus dimension. An extra-dimensional shift (EDS) occurs when a subject is required to shift response set to an alternative, previously irrelevant dimension (see [27, 50]). Both the medicated, and particularly the non-medicated patients with PD were selectively impaired in their ability to perform an extra-dimensional shift but not an intra-dimensional shift and this pattern has recently been replicated in an unrelated group of non-medicated patients (OWEN *et al.*, submitted). The pathological specificity of this effect has been confirmed by a parallel study in which a subgroup of elderly patients, in the mild to moderate stages of dementia of the Alzheimer type (DAT) were shown to be unimpaired on this test of visual discrimination learning despite having significant deficits in short-term visual recognition memory [48].

Whilst successful EDS performance is assumed to depend on the integrity of fronto-striatal mechanisms [15, 48] this issue has only been formally addressed in studies with non-human primates [38, 44]. In the present investigation, intra- and extra-dimensional set shifting ability was assessed in a young group of neurosurgical patients with localized excisions of the frontal lobes, a group of patients with unilateral excisions of the temporal lobes, a group of patients who had undergone unilateral amygdalo-hippocampectomy and a group of healthy volunteers matched for age and verbal IQ. A "total change" design was employed (as recommended by SLAMECKA [50], in which each shift was made in the presence of novel exemplars of the stimuli used as discriminanda.

It has been suggested that the cognitive functions associated with the frontal system are more vulnerable to the effects of normal aging than other "non-frontal" functions [1, 11, 55, 56]. In several previous studies, healthy elderly subjects have been shown to be impaired on traditional sorting tests such as the Wisconsin Card Sorting Test [4, 12, 22, 26]. However, although intra- and extra-dimensional set shifting ability has been assessed in elderly subjects [10, 33, 46] rather few studies have made specific comparisons with younger, normal controls. Accordingly, a separate group of elderly control volunteers (70 79 years) was included in the present study and their performance compared directly with both the neurosurgical patients and the younger group of normal controls.

METHOD

Selection of patient groups

The three groups of neurosurgical patients included in this study were consecutive referrals following frontal lobe, temporal lobe or amygdalo-hippocampus surgery at the Maudsley Hospital, Neurosurgical Unit, London. Among the frontal lobe cases, three patients were tested but later excluded from the analysis since examination of their CT scans revealed some damage to subcortical structures. Three (temporal lobe) referrals were not tested since they had histories of affective disorder (two patients) and substance abuse (one patient). Since the number of available patients in each group was limited, it was not possible to match the groups according to their preoperative pathology.

1. *Frontal lobe patients.* The twenty frontal lobe patients included in this study had all undergone unilateral or bilateral frontal lobe surgery at the Maudsley Hospital Neurosurgical Unit, London. Fourteen of these patients had right-sided frontal lobe excisions among which there were two cases of right frontal lobectomy, three cases where an aneurysm of the anterior communicating artery had been clipped, four cases where a right sided meningioma had been removed, two cases where a cranio-pharyngioma had been removed, two cases of arterio-venous malformation removal and one case of benign tumour removal.

Four patients had left-sided frontal lobe excisions. Among these there were three cases of unilateral lobectomy and one case where an astrocytoma had been removed. The remaining two patients had undergone bifrontal meningioma removal. Examples of the main lesion types for left- and right-sided cases are presented in Fig. 1.

A subgroup of 19 of these 20 patients has been shown to be impaired on a measure of verbal fluency [37] using the letters F, A and S of the Controlled Word Association Test [3] and the category "animals" with both right- and left-

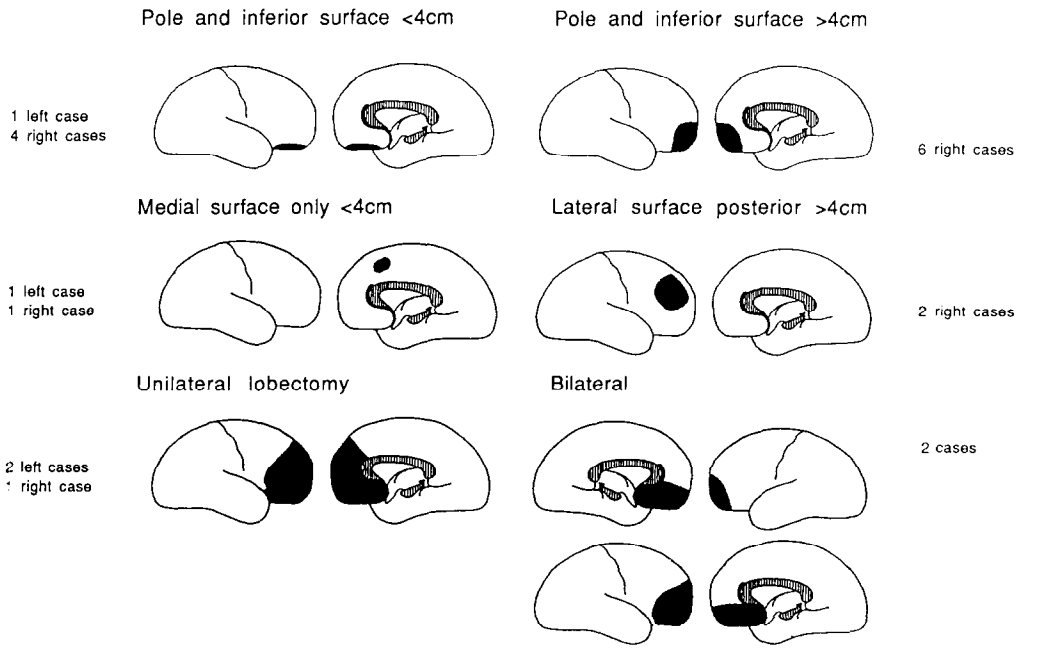

Fig. 1. Diagrams based on the neurosurgeon's drawings at the time of the operation showing the extent of the frontal lobe excision in several representative cases. The blackened areas define the lesion site.

sided cases being equally affected. Although this measure has been shown to be particularly sensitive to frontal lobe pathology when the damage is on the left side [30], significant impairments in right-sided cases have also been reported [41]. The frontal lobe group were tested on average 41 months postoperatively (range = 3–240 months). Fifteen were on anticonvulsant medication at the time of testing and all except two were seen as outpatients.

2. *Temporal lobe patients.* The 20 temporal lobe patients included in the study had all undergone unilateral temporal lobe surgery at the Maudsley Hospital Neurosurgical Unit, London, for the relief of intractable epilepsy. The standard "en bloc" temporal resection [18] involves the removal of between 5.5 and 6.5 cm of the temporal lobe measured from the pole and includes variable quantities of the medial temporal structures. Typically, a small amount (less than 3 cm) of hippocampus is removed and up to one half of the amygdala, although postoperative brain scans are necessary if precise measurements are to be made. This variable is not especially relevant to the current study since a standard operation is performed on the majority of patients and a relatively constant amount of hippocampus is removed. In the dominant hemisphere, only the anterior 1–2 cm of the superior temporal gyrus is removed to minimize the risk of postoperative speech problems.

In this group, there were 11 cases where left-sided surgery had been performed and these included one 4.5 cm resection, six 6 cm resections, three 6.5 cm resections and one 7 cm resection (mean = 6.09 cm). In seven of these cases the neuropathological report was sufficiently detailed to include an estimate of the length of hippocampal removal and the mean value was 17.4 mm (range = 5–28 mm).

Among the nine patients tested after a right temporal lobectomy there was one 5 cm resection, seven 6 cm resections and one 6.5 cm resection (mean = 5.94 cm). The mean length of hippocampal removal (reported in four of the patients) was 20.75 mm (range = 20–23 mm).

A typical left-sided (dominant) resection and a typical right-sided (non-dominant) resection are represented in Fig. 2. The 20 temporal lobe patients were tested on average 37 months (range = 8–121 months) after surgery. All were seen as outpatients and all were on anticonvulsant medication at the time of testing.

3. *Amygdalo-hippocampectomy patients.* A variant of the "en bloc" temporal resection is the selective amygdalo-hippocampectomy [57]. This operation is performed in patients who have a known structural lesion in or near the medial temporal structures or when other investigations have suggested a medial temporal focus for seizures. In most cases the amygdala and hippocampus are removed entirely on one side without any permanent damage to the overlying cortical structures. The 11 patients (seven left-sided, four right-sided) included in this group had all undergone unilateral amygdalo-hippocampectomy (AH) for the relief of intractable epilepsy and were tested on average 11.6 months (range = 5–24 months) after surgery. All were seen as outpatients and all were on anticonvulsant medication.

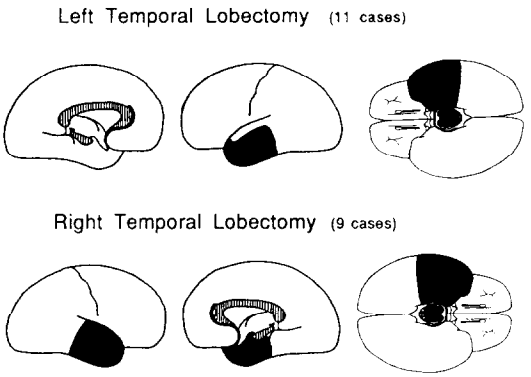

Fig. 2. A typical left-sided and a typical right-sided temporal resection based on the neurosurgeon's drawings at the time of the operation. The blackened areas define the lesion site.

4. *Normal controls. Subgroup* 1. Twenty healthy control subjects were chosen to match the frontal lobe group as closely as possible with respect to age and pre-morbid verbal IQ as estimated by the National Adult Reading Test (NART) [35]. These were drawn from a large pool of control subjects that have been assessed in the Cambridgeshire, Newcastle-upon-Tyne and London areas.

Subgroup 2. Twenty normal elderly control subjects between the ages of 70 and 79 were selected to match the frontal lobe group as close as was possible with respect to pre-morbid verbal IQ only. All of these volunteers were drawn from the North East Age Research Panel in Newcastle-upon-Tyne.

A summary of the main characteristics for the patient and control groups is presented in Table 1.

Table 1. Subject characteristics

	Age	Sex M:F	Handedness L:R	Education (school-leaving age)	V.IQ (NART)	Months since surgery
Frontal lobe	44.2 (4.33)	11:9	2:18	16.31 (0.50)	105.2 (2.99)	41.2 (4.33)
Temporal lobe	33.95 (2.07)	14:6	5:15	16.15 (0.23)	106.4 (2.57)	36.9 (6.43)
Amygdalo-hippocampal	31.54 (2.01)	5:6	4:7	16.81 (0.73)	104.8 (1.84)	11.63 (2.13)
Matched controls	43.05 (4.14)	12:8	2:18	15.61 (0.30)	110.1 (2.01)	
Elderly controls	73.05 (0.51)	15:5	4:16	15.78 (0.43)	117.7 (2.08)	

Standard errors in brackets.

One way analyses of variance confirmed that the frontal lobe group and the young control group (Group 1) were well matched in terms of age, $F(1, 38) = 0.039$, and pre-morbid verbal IQ, $F(1, 38) = 1.98$. Although the temporal lobe patients were slightly, but significantly younger than the frontal lobe group, $F(1, 38) = 4.79$, $P < 0.05$, the two groups were well matched in terms of pre-morbid verbal IQ, $F(1, 38) = 0.09$. The amygdalo-hippocampectomy group were also significantly younger than the frontal lobe group, $F(1, 30) = 4.59$, $P < 0.05$, but were well matched in terms of pre-morbid IQ, $F(1, 30) = 0.01$.

The second group of control subjects (Group 2) were considerably older than the frontal lobe group, $F(1, 38) = 46.05$, $P < 0.01$ and also scored significantly higher on the NART estimate of verbal IQ, $F(1, 38) = 12.19$, $P < 0.01$.

Materials and procedure

The main testing procedures were taken from the Cambridge Neuropsychological Test Automated Battery (CANTAB), a series of computerized paradigms designed to run on an Acorn BBC Master micro-computer with a high resolution Microvitec colour monitor and a Microvitec (Touchtech 501) touch sensitive screen. The computerized attentional set shifting paradigm has been described in detail elsewhere [15, 48] and only a brief description will be given here. The subject was required to learn a series of discriminations in which one of two

stimuli was correct and the other was not, using feedback provided automatically by the computer. The test comprised nine stages presented in the same fixed order (see [15] for detailed description), beginning with simple discrimination and reversal for stimuli varying in only one dimension (i.e. white lines or irregular purple filled shapes). In Fig. 3, example stimuli from various stages of the test are presented. A second, alternative dimension was then introduced and compound discrimination and reversal were tested (Fig. 3). To succeed, subjects must continue to respond to the previously relevant stimuli, ignoring the presence of the new, irrelevant dimension. At the intra-dimensional shift (IDS) stage new exemplars were introduced from each of the two dimensions and subjects were required to transfer the previously learned rule to a novel set of exemplars of the same stimulus dimension. Following another reversal of contingencies the extra-dimensional shift occurred and again, novel exemplars from each of the two dimensions were introduced. The subject was required to shift "response set" to the alternative (previously irrelevant) stimulus dimension (see Fig. 3).

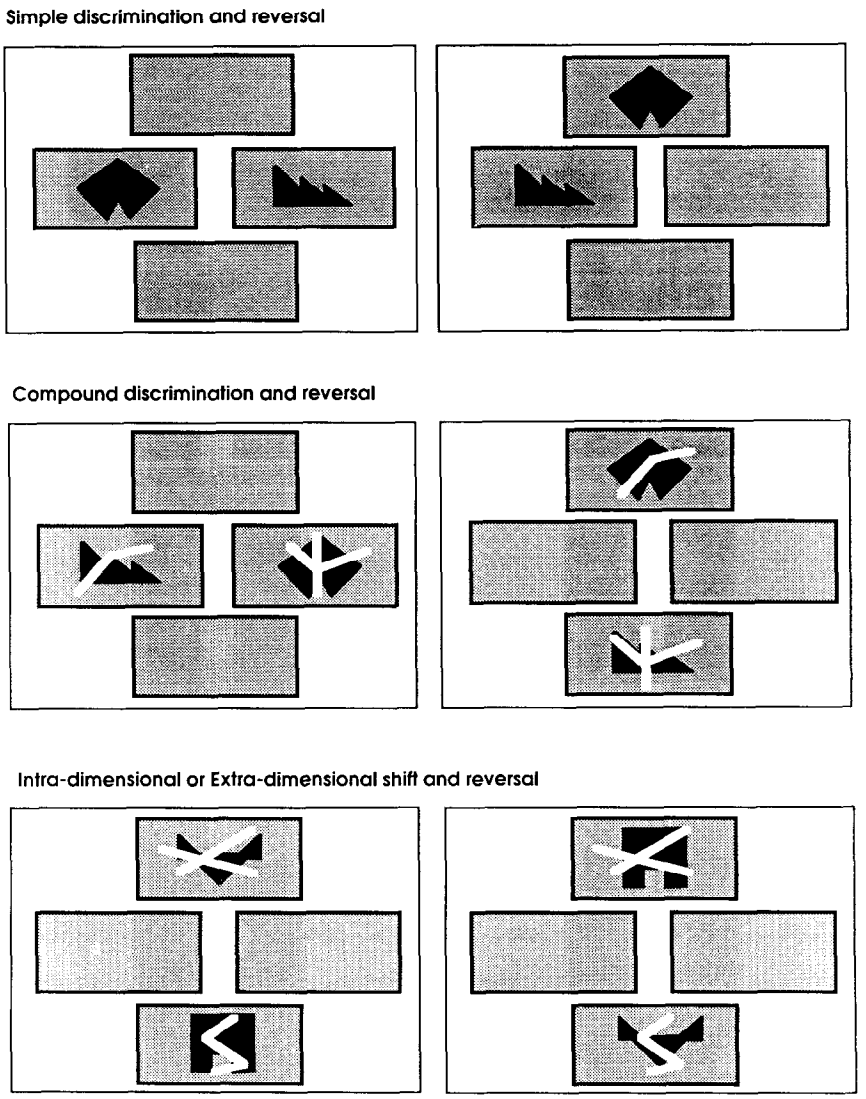

Fig. 3. Example stimuli from various stages of the attentional set shifting task. The "white line" and "purple shape" stimuli are presented exactly as they appear on the screen and at each stage, two *typical* trials are shown.

Thus, a "total change" design was employed in which both shifts were made in the presence of novel exemplars of the two dimensions.

At each stage, a change in contingencies would occur once the subject had learned the current rule to a criterion of six consecutive correct responses. Failure to achieve this criterion within 50 trials resulted in the premature discontinuation of the test.

Data analysis

In this study, two main methods of statistical analysis were employed. The five groups were initially compared in terms of the proportion of subjects succeeding or failing to reach criterion at each stage using a likelihood ratio analysis [24, 42]. This type of analysis allows the use of small cell frequencies and the partitioning of the contingency table into orthogonal contrasts. The resulting statistic, $2i$, is distributed as X^2. Trials to criterion at each stage and the mean response latency (measured to the nearest centisecond), were also measured, and specific comparisons were made between the IDS and EDS using a univariate analysis of variance (ANOVA) procedure from the Statistical Package For The Social Sciences (SPSS) [36]. Previous reports have highlighted the relative failure of patients with frontal lobe damage to eliminate irrelevant hypotheses following negative feedback ("lose-stay") [8]. The extent to which subjects were able to utilize the feedback provided at the EDS in the current paradigm was calculated in terms of the probability of failing to repeat a correct response ("win-shift") and the probability of immediately repeating an incorrect response ("lose-stay") to an identical stimulus configuration.

RESULTS

Initially, the five groups were compared in terms of the proportion of subjects reaching criterion (six consecutive correct responses) within the 50 trials allowed at each of the nine stages of the test (see Fig. 4). These data were analysed using the likelihood ratio method for contingency tables [24, 42]. Significant group differences emerged only at the extra-dimensional shift and reversal stages of learning [$2i(4)=16.46$, $P<0.005$]. There were no differences at the simple or compound discrimination and reversal stages or at the intra-dimensional shift and reversal stages. Further analyses using orthogonal contrasts (see [42]) established that both the frontal lobe group and the elderly control group (Group 2) were significantly impaired in terms of the proportion of subjects reaching criterion at the EDS stage when compared to the other three groups combined [$2i(1)=10.26$, $P<0.005$ and $2i(1)=10.26$, $P<0.005$, respectively]. In contrast, there were no differences between the frontal lobe group and the elderly control group [$2i(1)=0$] or between the young control group (Group 1), the temporal lobe group and the amygdalo-hippocampectomy group [$2i(2)=1.34$]. It is important to note that this significant pattern of differences between the groups does not change if only those subjects actually able to attempt the extra-dimensional shift stage are included in the analyses [main effect: $2i(4)=12.01$, $P<0.025$]. These results confirm that both the group of patients with frontal lobe damage and the elderly control group are specifically impaired in terms of the proportion of patients able to successfully complete the extra-dimensional shift.

The performance of the five groups on the intra- and extra-dimensional shift was analysed further in terms of the number of trials required to reach criterion at each of these stages. The raw data are shown in Fig. 5. There was a significant group by shift interaction, $F(4, 86)=2.73$, $P<0.05$, and a significant main effect of shift, $F(1, 86)=67.15$, $P<0.001$. This latter result confirms previous findings which have shown the EDS to be a more difficult shift than the IDS [15, 43]. Simple main effects were calculated separately for each shift and revealed no significant effect of group at the IDS stage, $F(4, 86)=0.43$, but a significant group effect at the EDS stage, $F(4, 86)=3.33$, $P<0.025$. Further between-group comparisons confirmed that both the frontal lobe patients and the elderly control sample were significantly impaired to the other three groups [$F(1, 69)=6.47$, $P<0.025$ and $F(1, 69)=12.84$, $P<0.001$, respectively]. These results confirm that both the group of

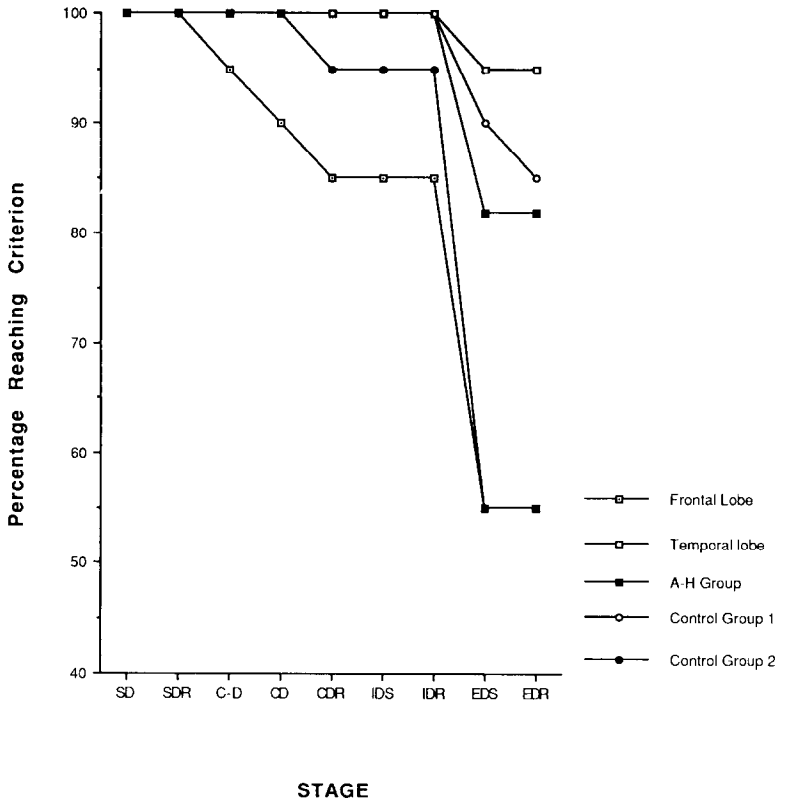

Fig. 4. The proportion of subjects reaching criterion at each of the nine stages of the discrimination learning paradigm.

patients with frontal lobe damage and the elderly control group required more trials to criterion than the other three groups specifically at the EDS stage of the test.

The five groups were also compared in terms of the mean latency to respond (corrected for number of trials) at the IDS and EDS stages (see Fig. 6). Latencies were recorded in centiseconds and then transformed into logarithms (base 10) to reduce skewness in the distribution. Both the main effects of group and stage were significant [$F(4, 73) = 4.02$, $P < 0.01$ and $F(1, 73) = 11.10$, $P = 0.001$, respectively] and there was a significant group X stage interaction, $F(4, 73) = 5.33$, $P = 0.001$. Simple main effects, calculated separately for each of the two shifts established that there was no difference between the groups at the IDS, $F(4, 73) = 0.68$, and a large group difference at the EDS, $F(4, 73) = 5.67$, $P < 0.001$. Further between-group comparisons confirmed that at this stage, both the temporal lobe patients and the amygdalo-hippocampectomy patients were significantly impaired compared to the other three groups [$F(1, 68) = 8.53$, $P < 0.01$ and $F(1, 68) = 24.38$, $P < 0.001$, respectively]. Importantly, there were no significant differences between any of the groups when the mean response latencies at each of the other seven stages of the test were compared, including the reversal stage *following* the EDS.

These results confirm that the amygdalo-hippocampectomy group and the temporal lobe

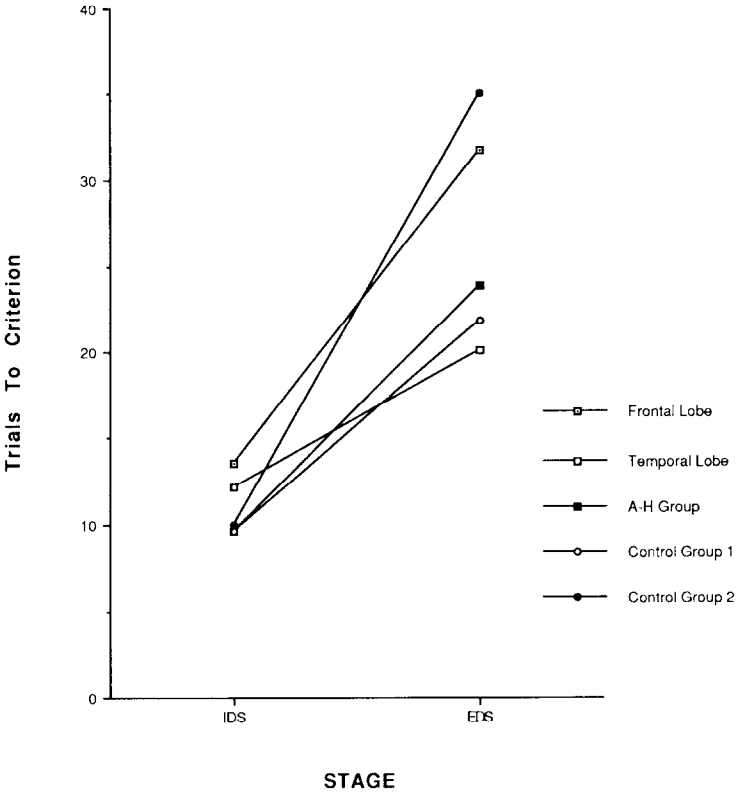

Fig. 5. The mean number of trials required to reach criterion at the intra-dimensional and extra-dimensional shift stages of learning.

group were significantly slower to respond than the frontal lobe group and both the normal control groups specifically at the extra-dimensional shift stage of the test.

The analysis of specific error types in terms of "win-shift" and "lose-stay" behaviour at the EDS revealed no significant differences between the groups. Since the majority of the unilateral frontal lobe patients were right-sided cases (14/18), it was not possible to assess the effect of laterality on performance. However, it is notable that the only three patients failing to reach criterion *before* the extra-dimensional shift stage of the test included the two cases of bifrontal lobe removal. Within the frontal lobe group, there was no obvious relationship between the incidence of success or failure on the test and aetiology, lesion site (lateral surface posterior, pole and inferior surface or medial surface only), or lesion size [<4 cm^2 ($N=7$) >4 cm^2 ($N=8$) or complete unilateral lobectomy ($N=3$)], with at least one failure occurring within each patient subcategory. Those frontal lobe patients failing to reach criterion at the EDS could not be distinguished from those passing on any other recorded variable, including age, sex, pre-morbid verbal IQ (NART), verbal fluency or time elapsed since surgery.

Within the temporal lobe and amygdalo-hippocampectomy groups a supplementary analysis was conducted on all data to investigate the effect of lesion laterality on performance. No significant effects of laterality were observed.

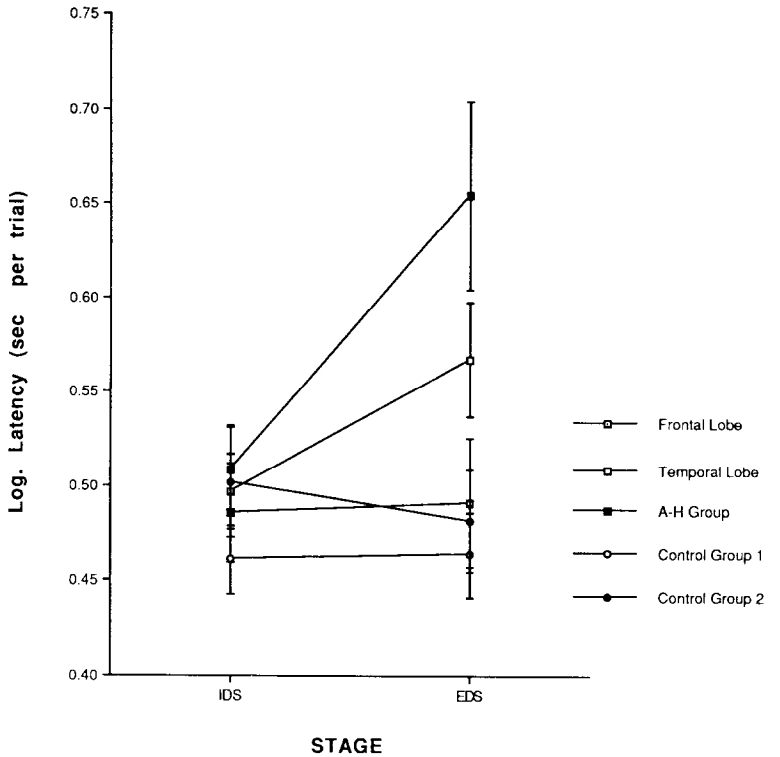

Fig. 6. The mean latency (per trial) at the intra-dimensional and extra-dimensional shift stages of learning.

DISCUSSION

This investigation has demonstrated that patients with localized excisions of the frontal lobes are significantly impaired in their ability to shift response set to a previously irrelevant dimension (EDS) but not to shift attention to novel exemplars of a previously relevant dimension (IDS). The proportion of frontal lobe patients failing to achieve criterion at the extra-dimensional shift stage (45%) was significantly greater than the proportion of temporal lobe patients (5%), amygdalo-hippocampectomy patients (18%) or normal control subjects matched for age and verbal IQ (15%) and this was reflected in the significantly increased number of trials for the frontal lobe group at this stage. There were no group differences at the simple or compound discrimination and reversal stages or at the intra-dimensional shift and reversal stages of learning.

The elderly group of normal controls was also selectively impaired at the EDS in terms of the proportion of subjects failing to reach criterion (45%) and there was a corresponding increase in the number of trials at this stage. In contrast, the temporal lobe and amygdalo-hippocampectomy groups who were unimpaired on all measures of performance accuracy had significantly prolonged selection latencies at the EDS when compared to the other three groups. There were no differences between any of the groups when the response latencies at each of the other seven stages of the test were compared, including the reversal stage *following*

the EDS. An error analysis in terms of "win-shift" and "lose-stay" tendencies revealed no differences between the groups in the extent to which feedback was appropriately used at the EDS stage.

The results of this study are consistent with previous reports in which groups of patients with frontal lobe damage have been shown to be impaired in tests requiring a shift of attention or response set [8, 16, 30, 45, 47, 51, 34]. Although failure at the EDS could not be related to any aetiological or anatomical variable within the frontal lobe group, it is notable that both the patients with bilateral frontal lobe excisions failed to reach criterion even before reaching this stage of learning. Therefore, whilst discrete lesions in one hemisphere clearly disrupt extra-dimensional set shifting ability, bilateral frontal lobe excisions appear to affect much simpler forms of discrimination learning.

The extra-dimensional shift is a core component of the Wisconsin Card Sorting Test [21] and the distinct pattern of deficits reported in patients with frontal lobe damage on this test may be explained in these terms. However, the Wisconsin Card Sorting Test (WCST) places demands on a number of other distinct cognitive processes which may be equally responsible for the deficits observed (for discussion, see [15]). The present study both confirms and extends NELSON'S [34] observations that the frontal lobe deficit can be elicited with "greatly simplified and less ambiguous material". Secondly, although the Wisconsin and Modified Card Sorting Tests [34] are popularly used to assess frontal lobe function, small but specific impairments have been observed following damage to posterior cortical areas, for example the right temporal lobe [7]. In the present study, both the temporal lobe patients and the amygdalo-hippocampectomy patients successfully reached criterion at every stage of the test. This confirms the findings of earlier studies in which patients with unilateral or bilateral temporal lobe damage and a patient with bilateral hippocampal damage have been shown to be unimpaired on the WCST [29, 32, 39]. However, in the present investigation, both the temporal lobe group and the amygdalo-hippocampectomy group exhibited prolonged response latencies at the EDS. Although bilateral removal of infero-temporal cortex in monkeys produces a severe discrimination learning impairment [6], these deficits cannot easily be interpreted in terms of impaired switching mechanisms [13]. Moreover, in the present study prolonged response latencies in these groups were not evident at any other stage of learning and therefore cannot be said to constitute a general impairment of discrimination learning. It is plausible that any slight difficulties experienced by these two groups at the EDS are overcome in the present study by prolonged consideration of the available hypotheses, a strategy not employed by the more severely impaired frontal and elderly control groups. Whilst corroborative evidence is lacking, response latencies are not routinely monitored during administration of traditional sorting tasks such as the WCST.

Although the differences in attentional set shifting ability between the patient group with frontal lobe damage and the groups with temporal lobe and amygdalo-hippocampus damage most likely result from their neurosurgical excisions they may also reflect differences in pre-operative pathology. In the frontal lobe group, several patients underwent operation for the removal of tumours and the clipping of aneurysms. In contrast, all the patients with temporal lobe and amygdalo-hippocampus removal (who were in general, less severely impaired than the frontal lobe patients) underwent surgery for the relief of intractable epilepsy and therefore, in general had much older pathology. Thus, it is difficult to see how these differences could have produced the pattern of results shown in this study.

Frontal lobe patients have previously been described as unable to eliminate irrelevant hypotheses following negative feedback ("lose-stay" behaviour) on a test of hypothesis

sampling during concept formation [8]. In the present study, both win-stay and lose-shift behaviour were assessed at the EDS and no group differences were observed. Therefore, although the positive and negative feedback were appropriately used on a trial to trial basis, those frontal lobe patients failing at the EDS appeared to be incapable of generating a global hypothesis based on this information. Several previous investigations have reported a striking dissociation between the ability of frontal lobe patients to verbalize the correct response in tests of sorting or concept formation and their ability to use this verbalization to guide their actions [29, 30, 34]. In contrast, in the present study the behaviour of both the frontal lobe group and those elderly subjects failing the EDS was observed to be characterized by a total disregard for the correct, previously irrelevant dimension. This trend may arise through differences in the requirements of the tasks employed. For example, in the WCST, a minimum of 10 correct responses (or six correct responses in the short form of the test) are required before the first shift takes place whilst in the paradigm employed here, the subject is required to make a minimum of 42 correct responses to the relevant dimension (i.e. in the previous seven stages) before the EDS is reached. Thus, the degree of bias shown to a particular stimulus dimension may depend in part, on the amount of previous positive feedback associated with that particular dimension as well as the amount of negative feedback associated with competing (irrelevant) dimensions. It would of course, be of interest to pursue this issue further by directly comparing this ED/ID shift test with the WCST in the same group of frontal lobe patients.

The pattern of deficits shown by the elderly control population in the current study is both qualitatively and quantitatively similar to that of the frontal lobe group. Whilst this impairment may represent a non-specific age related decline, it confirms earlier suggestions that the cognitive functions associated with the frontal system are particularly vulnerable to the effects of normal aging [1, 11, 55, 56]. Moreover, greater decreases in cerebral blood flow have been reported to occur in prefrontal vs more posterior regions in a healthy elderly population [49]. Several previous studies have demonstrated that elderly patients are impaired on traditional sorting tests such as the WCST [4, 12, 22, 26]. Although intra- and extra-dimensional set shifting ability has been previously assessed in this group [10, 33, 46], few studies have directly compared their performance with younger control subjects. The present findings confirm that compared to younger healthy controls, normal elderly subjects (aged 70+) are specifically impaired at extra-dimensional but not intra-dimensional set shifting.

In contrast, a subgroup of patients with mild DAT are not impaired despite showing deficits in a test of short term pattern recognition [48]. Patients who were much later in the course of DAT typically fail before even reaching the EDS. The group of patients with mild DAT are in general, younger than the elderly controls in the current study and the unimpaired performance of this group supports existing evidence from neuropathological, neurochemical [54] and imaging studies [23] that the cognitive deficits initially seen in DAT are due primarily to temporal lobe, and not frontal lobe dysfunction.

This test has previously been shown to be sensitive to idiopathic Parkinson's disease [15] particularly when patients are early in the course of the disease and non-medicated. With respect to PD, this impairment has been discussed in terms of a dysfunction of fronto-striatal mechanisms [15], although localization of function is complicated by the complex pattern of neuronal circuits connecting the frontal cortex to the basal ganglia [2]. Damage to sub-cortical structures will inevitably affect the expression of cortical functioning via defined cortico-striatal feedback loops. The present study demonstrates that in humans, critical

damage specific to the frontal lobes is sufficient, although may not be necessary, to produce a selective deficit in extra-dimensional set shifting ability.

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