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HUMAN PREFRONTAL LESIONS

by

Shulamit H. Verman

Dissertation presented to the Faculty of Graduate Studies

at the University of Manitoba

in partial fulfillment of

the requirements for the degree of

Doctor of Philosophy

in

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FACULTY OF GRADUATE STUDIES

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A STUDY OF LATERALITY EFFECTS IN HUMAN PREFRONTAL LESIONS

BY

SHULAMIT H. VERMAN

A thesis submitted to the Faculty of Graduate Studies of the University of Manitoba in partial fulfillment of the requirements of the degree of

DOCTOR OF PHILOSOPHY

ABSTRACT

Laterality effects in cognitive functioning were examined in 40 patients with unilateral, radiologically confirmed cortical lesions confined to frontal or postRolandic cerebral areas. Card sorting tasks were systematically designed so that the stimulus parameters and task demands reflected well known hemispheric differences and the sensitivity of the tasks to frontal deficits was maximized. Verbal comprehension and visuospatial tasks typically tapping deficits associated with unilateral post-Rolandic lesions were administered to facilitate meaningful anterior-posterior comparisons. Patients' ability to direct and alter ongoing behavior given verbal instructions, constraints and feedback was evaluated in terms of side and site of lesion.

The main findings were: _1._ Frontal lesioned patients as a group performed significantly more poorly than nonfrontal patients on both the verbal and nonverbal card sorting tasks. _2._ Left frontal patients were inferior to right frontal patients on verbal card sorting, and right frontal patients were inferior to left frontal patients on nonverbal card sorting. _3._ Left frontal patients were inferior to left postRolandic lesioned patients on verbal card sorting, and right frontal patients were inferior to right postRolandic lesioned patients on nonverbal card sorting. _4._ Left postRolandic lesioned patients were

inferior to left frontal patients on the tasks of verbal comprehension, and right postRolandic lesioned patients were inferior to right frontal patients on the task of visuospatial orientation. 5. The current battery discriminated frontal patients from postRolandic lesioned patients with 87.5% accuracy. It discriminated quadrant of lesion with 82.5% accuracy.

In summary, the study demonstrated a double dissociation between laterality effects in frontal and nonfrontal patients on frontal and nonfrontal tasks. The tasks which selectively tapped and underscored lateralized frontal deficits incorporated the dual requirements of 1. supramodal processing characteristic of frontal functioning and 2. processing associated with the functional strengths of each hemisphere. The format of the current study in terms of both procedure and design, was considered for its utility as a conceptual and experimental model for generating tests and designing research to further examine issues of laterality and localization of function within the human prefrontal cortex.

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Finally, I express my appreciation to the patients who participated in this study, and to their families. Their cooperation, the effort they invested and the invitation they extended to me to enter their private worlds taught me much more than can be apparent in this manuscript. They have helped ripen my holistic understanding of the experience of brain injury as a

personal and social process, as well as a medical and cognitive concern. I pray that I will continue to share with my patients the ways that these families have enriched me and the knowledge they have allowed me.

For the participating patients who died while this work was in progress, תהי"נה נשמתם צרורות בצרור החיים. [May their souls be bound in the skein of life.]

I humbly acknowledge G-d's grace in allowing me to reach this day.

סיימתי בחסד ה' יתברך ביום כ"ד לחדש אדר תשמ"ה לפ"ק:
תם ונשלם שבח לאל בורא עולם.

Shulamith H. Verman

15 March 1985
Jackson, Mississippi

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INTRODUCTION

The central role of the prefrontal cortex in the organization and regulation of complex behaviour has received increasing attention from neuroscientists over the past 20 years. Research on animals with experimentally induced prefrontal lesions has shown that while simple sensory and motor behaviour remains intact, deficits appear in the integration of multimodal sensory information, the selection of appropriate motor responses and the guidance of complex behaviour on the basis of changing environmental demands. For example, although prefrontal lesioned ani- mals may easily learn to respond alternately to two side-by-side, identical stimuli in order to obtain continuous reinforcement, the introduction of a delay results in significantly more errors relative to nonfrontal lesioned animals (e.g. Jacobsen, 1935).

Similar findings occur in studies of humans. Patients with radiologically demonstrable prefrontal lesions often show no abnormalities on neurological exam (Gilroy and Meyer, 1979; Tweedy et al., 1982) and no basic motor, sensory or intellectual deficits, even on formal neuropsychological assessment (e.g. Lezak, 1976; Kolb and Wishaw, 1980). However, on evaluation they do display characteristic changes in the modulation of complex motor and cognitive behaviour, and affective expression. For example, in the motor realm, although they can reproduce simple rhythms tapped with one hand, they may be unable to reproduce more complex alternating rhythms, or those requiring bilateral coordination (Luria, 1980).

Although some prefrontal lesions result in these relatively subtle deficits, more severe behavioural manifestations of prefrontal lesions -- such as perseveration and difficulty initiating and inhibiting activities or speech -- may present a clinical picture similar to emotional and functional disorders such as depression, apathy or malingering, and thus may go unnoticed as organic in origin. Alterations in behaviour such as attentive and mnemonic difficulties may look like dementia (Hecaen, 1964; Luria, 1980). These difficulties in correctly diagnosing frontal deficits highlight the importance of assessment techniques which reliably identify prefrontal cortex dysfunction.

A small number of neuropsychological tasks have consistently proven sensitive to prefrontal damage in humans. These include tests of oral and written verbal productivity -- such as Thurstone's Word Fluency Test (Thurstone and Thurstone, 1943) -- in numerous studies (e.g. Benton,1968; Milner, 1964; Perret, 1974), the Wisconsin Card Sorting Test (WCST) developed by Grant and Berg (Berg, 1948; Grant and Berg, 1948) which measures abstract conceptualization and the ability to maintain or change one's response set on the basis of feedback (Heaton, 1981), and a subset of tasks from Luria's neuropsychological examination (Christensen, 1975; Golden et al., 1981; Luria, 1980; McKay and Golden, 1980). Study of brain damaged patients' performance on these tasks (reviewed below) has increased our understanding of the functioning of the prefrontal cortex. However, well-controlled research on human prefrontal functioning has been limited, as elaborated in the Discussion section, below. Much remains to be learned regarding "the riddle of the frontal lobes" (Teuber, 1964).[1] The current study examined the influence of side of lesion on frontal functions, focussing on productivity and ability to shift response set, in frontal and postRolandic lesioned patients.

Historical Review

The scientific investigation of frontal lobe functioning has followed two paths since its beginning in the mid-1800's: 1. the physiological and psychological study of animal behaviour following frontal lobe extirpation, and 2. clinical case studies of behavioural changes in patients with wounds and tumours of the frontal lobes (Luria, 1980).

Animal Research

Early experimental studies yielded no apparent reaction to electrical stimulation of the frontal lobes. Furthermore, in animals with experimentally induced frontal lesions, simple sensory and motor behaviour remained intact. These results suggested that the frontal lobes lacked functional specificity and might represent superfluous or redundant brain tissue. Further examination of the behaviour of frontal-lesioned animals, however, revealed that goal directed, selective behaviour degenerated through distractability, arbitrariness and perseveration to the level of motor automatisms. For example, feeding behaviour became arbitrary chewing on any available object. Purposeful movement degenerated into walking in circles (Pavlov, 1949). Antilocalizationists (e.g. Loeb, 1902; Munk, 1881) attributed this breakdown to disturbances of the brain as a whole. Others adopted views of the frontal regions as the seat of the "regulating mind" (Gratiolet, 1861).

Bianchi (1920) postulated that reflex activity was organized hierarchically, with the frontal lobes responsible for the most complex coordination of motor and sensory elements into mental syntheses. Frontal lesions, by disturbing this integrative process, resulted in disorganized, fragmented behaviour. Other writers at the turn of the century emphasized the afferent aspects of frontal functioning and its role in inhibiting the functions of "lower divisions of the brain" (Luria, 1980).

Bekhterev (1907) extended the conceptualization of frontal functions to include a self-evaluative element. Hence he proposed that disintegration of goal-directed behaviour in frontal-lesioned animals resulted from a disturbance in their ability to evaluate and plan their own activity in relation to the results of their ongoing behaviour. While these authors advanced the understanding of frontal functioning, Luria (1980) notes that "the concept of the psychoregulatory role of the frontal lobes remained without a physiological basis" [p.251], resulting in a mentalistic concept of the frontal lobes directing activities initiated and carried out by the body.

The development of the reflex theory of behaviour and the physiological concepts of self-regulating systems provided a basis for advances in understanding the role of the frontal lobes. Pavlov (1949) introduced the concept of the motor analyzer. He postulated that in addition to directing actions, cortical areas involved in movement carried out afferent, analyzing functions in relation to sensory, motor and kinesthetic information from other areas, regarding the course of a movement and its effects. Pavlov regarded the frontal lobes as the most complex component of the cortical system of the motor analyzer involved in the selection, coordination and evaluation of goal -directed movements. Hence frontal lesions left relatively simple, conditioned reflex activity intact or only partially disorganized, while significantly disturbing complex motor syntheses.

Frontal lobe extirpation studies in the first half of the twentieth century provided an inventory of deficits associated with frontal lesions. In addition to the disruption of complex naturalistic behaviours, experimental investigation revealed the disruption of learning, following several simple paradigms. For example, while a conditioned response could be established to a single stimulus, frontal lesioned animals were unable to differentiate between two signals requiring two different motor responses. Differential reinforcement did not result in choice learning. The equivalent reinforcement of two approach behaviours led to aimless pendulum movements between the two goal areas with no claiming of the reinforcer. The establishment and maintenance of stable delayed reaction performance was disturbed, as was the ability to establish a discriminative stimulus (Fuster, 1980).

Jacobsen et al. (1935) concluded that these failures in learning represented disturbances in serial operations. Pribram (1959) concluded that frontal lesioned animals were unsuccessful in processing the effects of their own behaviour (i.e. analyzing and learning reinforcement contingencies). Luria (1980) summarized the deficits found in frontal lesioned animals as representing "a disturbance of the preliminary syntheses ... underlying the regulation of complex forms of motor operations and the evaluation of the effect of their own actions, without which goal-directed, selective behaviour is impossible [p.253]."

The basis for this disturbance is another area for speculation and hypothesis. It may be due in part to a marked increase in motor activity, through disinhibition and the emergence of elementary automatisms (e.g. Luria, 1980). Another hypothesis is that frontal lesions result in a heightened susceptibility to distractions, such that traces of previously established systems of connections do not persist long enough for stable response patterns to be established (e.g. Fuster, 1980; Luria,1980).

Human Research

Historically, data and ideas regarding the role of the frontal lobes in human functioning have followed an evolution similar to that of animal research. Early case studies consisted of clinical descriptions of patients with frontal lobe trauma (e.g. Harlow, 1848), disease and resection (e.g. Hebb and Penfield, 1940), and prefrontal lobotomy and leucotomy (e.g. Moniz, 1937; Watts and Freeman, 1938). No fundamental sensory or motor deficits were noted. Basic intellectual functioning remained intact. However, emotional changes involving disinhibition and failure in adaptation to changing circumstances were documented, as well as increased distractability, and deficits in planning and regulation of activities over the short and long term (e.g. Brickner, 1936; Hebb, 1945). These findings corresponded to the results of animal research, reviewed above, and led investigators to analogous and similarly diverse conclusions. Some concluded that the observed deficits were not dependent on specific frontal lesions but were related to disturbance of brain functioning as a whole (e.g. Pfeiffer, 1910; Schuster, 1902). Others conceived of the frontal lobes as a superior organ, essential to complex cognitive functioning (e.g. Goldstein, 1936; Halstead, 1947).

After World War II a trend toward more experimental group studies emerged. The orientation was to look at isolated deficits on specific tasks (e.g. Milner, 1963; Ramier and Hecaen, 1970). Deficits were demonstrated in a variety of areas associated with the planning, integration and regulation of behaviour, including productivity, abstract categorization, sequential ordering, sustained cognitive and motor activity and ability to shift response set (e.g. Drewe, 1974; Milner, 1964; Robinson, Heaton, Lehman and Stilson, 1980). In an independent line of research, a rich literature has emerged, describing the neuroanatomical connections of the frontal lobes with other cerebral areas (e.g. Damasio, 1979; Fuster, 1980). Although empirical evidence of anatomoclinical relationships is sketchy, current theories attempt to incorporate information regarding intracerebral connections with a knowledge of the functional neuroanatomy of the associated areas in elucidating frontal lobe functioning.

While the conceptualization of the frontal lobes as a super-regulatory agent has persisted and currently takes precedence in the theoretical literature, researchers now intimately relate function to structure. Damasio (1979) proposes that "knowledge of anatomy may well prove to be the vital step in the understanding of the roles of the frontal lobe [p.363]." This is affirmed in Fuster's heavily anatomical treatment of the topic in The Prefrontal Cortex (1980). Thus the modern study of the cytoarchitecture of the frontal lobes and their cortical and subcortical connections recalls and extends the promise of the functional-neuroanatomical approach of the earliest animal extirpation studies.

Damasio (1979) states that we can know the frontal lobe by "knowing the company it keeps". At present, however, this assertion is largely at the level of hypothesis. It brings neuroscientists to the threshold of a vast undertaking: to map the unique brain-behaviour relationships associated with specific areas of the frontal lobes. Given the current state of the art, this will require experimental study of behaviour using structured, analyzable tasks in patients with localized, circumscribed lesions. To date, experimental evidence regarding higher cortical functions indicates that frontal lesions do result in characteristic deficits (e.g. Luria, 1980; Malloy Webster and Russell, 1983). Case studies, isolated reports and theoretical formulations suggest the possibility of more specific functional-anatomic relationships within subdivisions of the frontal lobes. (e.g. Fuster, 1980; Luria, 1980; Stuss and Benson, 1983). Having confirmed specific frontal functions, a further step has been to investigate and describe possible hemispheric differences, so basic to our understanding of brain functioning and the division of labour within all other areas of the cerebral cortex. This was the purpose of the current study.

Cerebral Lateralization of Functions

Goodglass (in press) introduces the study of lateralization of function thus:

> The systematic investigation of the many ramifications of brain laterality dates back less than twenty years. It has entailed the development of non-invasive techniques through which lateral asymmetry of function could be studied in the intact brain in large normal samples as well as the introduction of controlled studies of unilaterally brain injured populations. Attention has been focused on the biological features of brain laterality, its heritability, its developmental course from birth to old age, and the appearance of sex differences. The major goals of experimental studies have been to define more precisely the operations for which the hemispheres have differing predilections, particularly to see whether they can be reduced to a basic dichotomy in modes of information processing, and to explore the interaction between the

hemispheres in complex tasks. [p. 276]

These investigations have yielded extensive empirical evidence that consistent differences exist between both the types of information, and the modes in which information is processed in the left and right cerebral hemispheres. The left hemisphere has been described as processing information in a verbal, analytic mode. The left hemisphere can be shown to demonstrate superiority in written and auditory language comprehension and calculation. The right hemisphere has been described as utilizing a gestalt, nonverbal mode of information processing. Right hemisphere superiority has been demonstrated for dealing with nonlinguistic, perceptual and musical functions including identification of emotion, facial recognition and visual-spatial relations (e.g. Bogen and Bogen, 1969; Kimura, 1973; Ley and Bryden, 1978).

Early evidence regarding cerebral lateralization of cognitive functions emerged from the study of clinical populations, particularly brain damaged and commissurotomized patients (e.g. Gazzaniga, Bogen and Sperry, 1962; Geschwind and Kaplan, 1962; Milner, Branch and Rasmussen, 1964; Penfield and Roberts, 1959). The validity of generalizing this data to the functioning of the intact brain was therefore suspect. Within the past decade, similar lateralization of cerebral functioning has been demonstrated in normal individuals for cognitive and emotional capacities using several techniques. These include dichotic listening (Kimura, 1967), reaction time (Filbey and Gazzaniga, 1969), tachistoscopic split-field presentation (Rizzolatti, Umilta and Berlucchi, 1971), electroencephalographic readings (e.g. Galin and Ornstein, 1974), evoked potentials (Galin and Ellis, 1975) and chimeric figures (Rappeport, 1978; Schwartz, 1978).

Since Broca's (1861) initial description of language deficit in left hemisphere lesioned patients, cerebral lateralization with regard to language and speech has been particularly well-documented. Disorders of both expressive and receptive language functions are commonly associated with lesions of the left cerebral cortex (e.g. Eccles, 1973; Penfield and Roberts, 1959; Zangwill, 1960). Investigations using the Wada test (Wada and Rasmussen, 1960) and the performance of commissurotomized patients on a variety of tasks suggest the predominant representation of verbal communication in the left cerebral hemisphere (e.g. Blakemore, Iverson and Zangwill, 1972; Milner et al., 1964). There is a consensus that a relationship exists between preferred hand use and hemispheric dominance for speech functions (e.g. Ley, 1974; Penfield and Roberts, 1959). Milner et al., (1964) concluded that while speech is typically represented in the left hemisphere regardless of handedness, for any individual, the probability is greater if he is right handed.

Sex Differences in Cerebral Laterality

There is evidence from both clinical and nonclinical populations that brain functions are less lateralized in females than in males (e.g. Kimura, 1966; Lansdell and Urback, 1968; McGlone and Davidson, 1973). There are "well established differences in proficiency between the sexes with regard to a number of those cognitive abilities (language, visuo-spatial skills, calculation) which have been shown to be mediated preferentially by the left or right hemisphere. Some of these differences have been shown to persist into the adult years." [Goodglass, in press, p. 173]. There is recent evidence that differences exist in the nature of behavioural effects of unilateral brain lesions: Right handed males are more likely than women to show selective cognitive deficits following damage to either hemisphere. That is, unilateral lesions in women are less likely to produce selective impairment of language functions with left hemispheric lesions, and deficits in nonverbal skills with right sided lesions, as they do in men (e.g. Lansdell and Urback, 1965; McGlone, 1978). For example, McGlone (1977) showed only 1/3 the incidence of aphasia in left brain damaged females as compared to males with comparable lesions. Lansdell (1962) and McGlone and Kersetz (1973) have shown comparable results regarding visuospatial functioning and unilateral right brain injury.

Studies employing stimulus presentation by dichotic listening and tachistoscopic visual half-field paradigms with non-clinical populations have generally found a significantly greater proportion of males than females showing an advantage for verbal stimuli presented to the <u>right</u> field (left hemisphere). They have similarly found a significantly greater proportion of males than females showing an advantage for visuospatial and visual perceptual material presented to the <u>left</u> visual field (right hemisphere) (e.g. Sasanuma and Robayashi, 1978).

Findings of demonstrable hemispheric disparity among males have been consistent under varying experimental conditions. While females sometimes demonstrate the field advantages described above, (e.g. Young and Willis, 1976), they may fail to demonstrate them, with only limited changes in the experimental task (e.g. Rizolatti and Buchtel, 1977).

Various explanations, including the demand characteristics of experiments, and genetic and sociocultural influences on behaviour, have been suggested to account for the sex differences in childhood skill proficiency, response to brain injury and experimental performance (Harris,1978; Maccoby and Jacklin,1974; McGlone, 1980). Goodglass (in press) suggested that in addition to a difference in extent of lateralization, "this disparity between the sexes may reflect some difference in the strategies used or a sex difference in conditions under which lateralization is activated [p. 279, in press]."

These considerations and the data on which they are based render it difficult to predict and interpret performance of female subjects with unilateral lesions. The study described below, because of its preliminary nature in the investigation of frontal lesions, therefore used only male subjects, for whom relationships between brain injury, behaviour and cerebral lateralization are better established.

Diagnostic Utility of Laterality Effects

Because of their essential role in localization of function, an understanding of laterality effects may prove diagnostically important: In a screening evaluation, observed assymmetrical deficits may suggest the presence and location of lesion. Conversely, when a lesion site is known, its location in the left or right hemisphere suggests which cognitive, sensory and motor functions are most likely to be spared or impaired.

Hence, lateralization of function is a basic conceptual constituent in our understanding of brain-behaviour relationships. It has been reliably demonstrated in all other cortical cerebral areas (e.g. Berent, 1981). Identification of possible laterality effects comparable to those described above, may thus be expected in frontal lobe functioning and lesions as well (e.g. Lezak, 1976)

In addition to our understanding of brain functioning, laterality differences have implications for the rehabilitation of frontal damaged patients. For example, if right frontal lesions selectively impair the ability to plan and organize in the nonverbal realm, with relative sparing of verbally mediated modulation of behaviour, patients with right frontal lesions may be trained to use linguistic strategies to aid in initiating and integrating typically nonlanguage activities. For example, one patient found himself unable to cook following a right frontal lesion. He would perseveratively repeat steps in food preparation, adding the same ingredients over and over. If verbal planning skills are spared in such a case, one might use such strategies as self-instruction and numbering the steps of the task to help compensate for the nonverbal dysregulation.

Laterality effects have been repeatedly described in clinical observations of patients with unilateral frontal lesions (e.g. Zangwill, 1966). Systematic, controlled investigation of this area using neuropsychological techniques, however, has been limited, with inconsistent results, as reviewed below.

Criteria for Studying Laterality Effects in Frontal Lobe Lesions

Ramier and Hecaen (1970), in a study of word fluency, found that frontal patients performed more poorly than nonfrontal lesioned patients, with left frontal patients more impaired than right frontal patients. Because of these performance differentials, they postulated two components to the task: a fluency one, sensitive to lesions of either frontal lobe, and a linguistic one, pertaining more specifically to the left hemisphere. In evaluating and generating tasks pertinent to lateralization of function in the frontal lobes, the current study adopted a general formulation based on Ramier and Hecaen's two-factor view. To test for laterality effects in frontal lesions, a task must require both of the following components: 1. supramodal types of processing characteristic of frontal lobe functioning (e.g. complex integration and coordination of multimodal information), and 2. processing conventionally associated with the functional strengths of each cerebral hemisphere (e.g. nonverbal/visuospatial for the right hemisphere and verbal/analytical for the left hemisphere).

A Review of Experimental Evidence of Laterality Effects in Frontal Lesions

Fluency

Observations of reduction in spontaneous speech in frontal lesioned patients have been made by Bonner et al. (1951), Luria (1966) and others. As noted above, this reduction in fluency has been demonstrated empirically on tests of both oral (Benton, 1968; Perret, 1974) and written (Milner, 1964; Ramier and Hecaen, 1970) verbal fluency, with frontal lesioned patients performing more poorly than nonfrontal lesioned patients and the left frontal lesioned patients yielding the poorest performances of all groups.

Jones-Gotman and Milner (1977) developed a nonverbal analogue to the word fluency task, asking subjects to draw as many different abstract designs as they could invent within a given time limit. Consistent with the two-factor formulation described above, this procedure combined task demands for right hemisphere modes of processing -- nonverbal, visuomotor -- with demands for supramodal processing characteristic of the frontal lobes -- productivity and inhibition of previously correct responses. They found that right frontal lesioned patients performed significantly more poorly than left frontal lesioned patients on their design fluency task.

Taken together, studies by Benton (1968), Milner (1964), Perret (1974), Ramier and Hecaen (1970) and Jones-Gotman and Milner (1977) suggest that a general frontal lobe deficit in productivity underlies poor performance of frontal patients on tests of fluency. Furthermore, a double dissociation -- "dissociation by task and by cortical area" (Fuster, 1980, p. 56) -- appears to exist such that right frontal damage leads to relatively worse performance on a task of nonverbal fluency, while left frontal damage results in relatively worse performance on tasks of verbal fluency.

To date, however, both types of fluency task have not been administered to comparable groups of right and left frontal patients and right and left posterior lesioned control patients. Since the fluency studies reviewed were performed on different subject populations, the dissociation remains to be definitively demonstrated.

Card Sorting

Investigations of the Wisconsin Card Sorting Test (WCST) have clearly demonstrated its sensitivity to frontal deficits. Successful performance depends on correct preliminary analysis of stimulus materials which vary in form, colour, configuration and number. The test requires subjects to discover the correct sorting principle, given feedback regarding the correctness of each response, and to switch principles on the basis of systematic changes in feedback. The WCST thus assesses the intactness of planning, maintaining and changing response set and inhibitory functions characteristic of frontal functioning.

While demonstrating sensitivity to frontal deficits, research using the WCST has yielded inconsistent findings regarding laterality. Milner (1963) found that patients with dorsolateral frontal excisions performed significantly more poorly on the WCST than did controls with lesions in other cerebral areas. In particular, frontal patients tended to have high perseverative error scores. That is, they continued sorting to a given category despite feedback that their responses were no longer correct. However, Milner demonstrated no laterality effects in groups of right and left frontal patients. Although Milner noted that left frontal excisions tended to be smaller than right frontal excisions in her patient groups, she stated that "both left and right superior-frontal removals were equally damaging to performance on the Wisconsin test (1963, p.97)." In contrast, Drewe (1974), in comparing WCST performance in patients with unilateral left and right frontal versus nonfrontal lesions, found that the right frontal group had the highest median perseverative error score. Left frontal patients performed more poorly on other WCST indices. Like Milner (1963) and Drewe (1974), Robinson et al. (1980) found that patients with focal frontal damage did significantly worse than nonfrontal brain damaged patients. Furthermore, consistent with Drewe's perseverative error findings, patients with focal right frontal damage performed significantly worse than those with focal left frontal damage. Hence the experimental evidence to date shows the WCST to be sensitive to frontal lesions and furthermore suggests that it may be most sensitive to right frontal brain damage.

The absence of clear and consistent hemispheric differences on the WCST may be due to its failure to meet the second criterion noted above to qualify as a test for laterality effects in frontal lesions. That is, it fails to meet the requirement for unilateral processing. The WCST requires patients to sort by the concepts of the colour, form and number of the shapes on the card. While the task is ostensibly nonverbal and visuospatial, the stimulus classes do not clearly maximize unilateral right hemispheric processing: The geometric forms are easily named, allowing left hemisphere processing. While the number of shapes on any card is confounded with the configuration of the display, suggesting right hemisphere processing, counting itself has been shown to be a left hemisphere task (Lezak, 1976). Modification of the stimulus materials would therefore be necessary to produce a genuinely nonverbal card sorting task sensitive to frontal laterality effects. To date no equivalent verbal, frontal/left hemisphere task has been developed.

Lurian Tasks

Luria's neuropsychological examination (1980) provides a wide variety of tasks to assess brain functions, including tasks which he felt to be sensitive to frontal deficits. As predicted, subsets of tasks from Luria's neuropsychological exam have been shown to be sensitive to frontal lobe lesions (McKay and Golden, 1980; Malloy et al., 1983). Luria's tasks include a wide range of variation along the dimensions of both complexity and the extent to which they demand right or left hemisphere modes of processing (Luria, 1980). Performance differences in frontal patients with lateralized lesions have not been extensively studied using Lurian tasks. Laterality effects have been demonstrated on a standardized version of Luria's tasks (Golden et al., 1981). While Malloy et al. (1983) demonstrated that tasks based on Luria's hypotheses could be used to discriminate frontal from nonfrontal patients with a high degree of accuracy, in a supplemental analysis they did not find significant differences between right and left frontal patients on most of the tasks. As with the WCST, these Lurian tasks apparently failed the second criterion for frontal laterality measures. They would require modification in order to maximize unilateral processing.

Mazes

Corkin (1965) found right frontal patients to be significantly more impaired than left frontal patients on tactually guided maze learning. While Milner (1965), studying the same patients, found deficits relative to normals in visually guided maze learning, she found no significant differences between the left and right lesioned frontal groups.

Integrative Studies of Laterality Effects in Frontal Lobe Lesions

The studies reviewed thus far have reported the performance of right versus left frontal lesioned patients on isolated tasks (see Table 1). Taken together they are suggestive of laterality effects in the frontal lobes, corresponding to well-documented hemispheric differences in the other lobes of the cerebral cortex. These unconnected findings on single tests in different subject groups are insufficient basis, however, for a general statement regarding lateralization of functions within the frontal lobes. They lack the integration of a range of lateralizing frontal tasks (i.e. tasks meeting both criteria cited above) tested within groups of unilateral frontal and nonfrontal lesioned patients.

To date, only Benton (1968) and Petrides and Milner (1982) have attempted to systematically study the extent to which interhemispheric differences are demonstrable on a range of typically "lateralizing" tasks, in patients with unilateral prefrontal lesions. Benton (1968) showed that left frontal lesioned patients were inferior to right frontal lesioned patients on a test of verbal associative fluency. Right frontal lesioned patients performed significantly more poorly than left frontal patients on nonverbal visuospatial tasks involving three-dimensional block construction and design copying. Benton concluded that

> ...for the most part, the interhemispheric differences in performance which are thought to be characteristic for patients with unilateral post-Rolandic disease may also be observed in patients with unilateral lesions confined to the frontal lobes. [Benton, 1968, p. 58]

While Benton's findings are suggestive, several aspects of his study preclude it as a definitive test of laterality effects in frontal lesioned patients. One serious difficulty involves task characteristics. Of the six tasks used in Benton's study, only the verbal associative fluency task meets both our criteria (frontality and hemisphericity) for a test of laterality effects in frontal lesions. Verbal paired associate learning, while it has a strong verbal/left hemisphere component, does not tap specifically frontal functions. Similarly, three-dimensional constructional praxis and design copying tap nonverbal, visuospatial right hemisphere modes of functioning, but do not rely heavily on specifically frontal types of supramodal processing. The remaining tasks, a mental status type evaluation of temporal orientation and a multiple choice test of proverb interpretation, are neither clearly frontal nor lateralizing tasks.

Equally important are the facts that the patient population was vaguely defined and the criteria used to localize lesions in the frontal lobes were not stated. Benton merely stated: "The sample is best viewed simply as comprising right handed patients without clinically evident motor impairment or dysphasia and with lesions apparently confined to one or both frontal lobes" [ibid, pp. 54ff]. He further noted the lack of surgical evidence of locus and extent of lesion. In addition, no radiological findings were provided. Hence there was no evidence that the lesions were located in, or restricted to, the frontal lobes. Furthermore, no posterior lesioned or non-brain-damaged comparison groups were studied.

In view of these limitations -- the not necessarily "frontal" nature of the tasks, the vague localization information and the absence of nonfrontal comparison groups -- no conclusions can be drawn about the contribution of specifically <u>frontal</u> damage in comparing the performance of right and left unilateral lesioned groups in Benton's (1968) study. Performance differences may reflect interhemispheric differences associated with nonfrontal cortical damage.

In a study of verbal and nonverbal self-directed organization and sequencing of responses, Petrides and Milner (1982) found that the left frontal group was significantly impaired relative to normal controls on the verbal tasks, whereas the right frontal group was not. The left frontal group was also significantly impaired on the nonverbal tasks. Right frontal lesioned patients were impaired only on the most complex of the nonverbal tasks. Thus a left frontal versus right frontal dissociation on these tasks was not consistently demonstrated. In addition, the significant impairment of the right temporal lobe lesioned group on both nonverbal tasks and the left temporal lesioned group on one of the two verbal tasks indicated that these tasks did not discriminate well between frontal and nonfrontal groups. It would therefore be important to know whether frontal lesioned patients and nonfrontal lesioned patients failed to different extents. The pertinent analyses comparing performance of frontal groups with that of nonfrontal groups were not presented. The impairment of the nonfrontal groups also brought into question the frontal nature of the experimental tasks, suggesting that they may not selectively tap frontal functioning and therefore fail to meet the first criterion for a test of laterality in frontal functioning (frontality). Tests known to tap skills associated with postRolandic functioning were not carried out. Hence comparisons evaluating possible performance differences on frontal and nonfrontal tasks could not be made.

Outline of Current Research

There is little empirical evidence concerning the functioning of specific zones within the frontal cortex in humans. Fuster (1980) notes that no double dissociations (by task and by cortical area) have been demonstrated in the frontal cortex. As reviewed above, even the dichotomy in functioning between the left and right hemispheres, basic to our understanding of brain-behaviour relationships, has not been clearly demonstrated in controlled investigation of lesions of the frontal cortex.

The purpose of the present study was to investigate laterality effects in unilateral, radiologically confirmed frontal lobe lesions, using a variety of tasks which meet both criteria outlined above. Tests previously demonstrated to be sensitive to frontal damage were selected (Benton, 1968; Jones-Gotman and Milner, 1977; Robinson et al., 1980). These tasks were then systematically adapted so that the stimulus parameters and task demands reflected well known hemispheric differences in processing and the sensitivity of the tasks to frontal deficits was maximized. Thus each task had two analogues in order to independently tap verbal and nonverbal strategies of solution. For example, both the verbal fluency (Benton, 1973) and design fluency (Jones-Gotman and Milner, 1977) tasks were administered to evaluate productivity and perseveration in both verbal and nonverbal response modalities. The specific tasks are described in the Method section, below. Tasks typically tapping deficits associated with unilateral postRolandic lesions were administered to facilitate meaningful anterior-posterior comparisons. Benton's Judgement of Line Orientation (JLO) was administered for sensitivity to right postRolandic lesions (Benton et al., 1977 and Benton et al., 1978) and the Western

Aphasia Battery "Auditory Verbal Comprehension" (AVC) subtests were used to tap left posterior deficits (Kertesz, 1982). These tasks are described in the Method section, below.

Experimental Predictions

The following were the predictions for the outcome of this experiment:

1. Frontal lesioned patients as a group will perform more poorly than nonfrontal comparison groups on the "frontal" tasks.
2. Left frontal lesioned patients will perform selectively worse than right frontal patients on the verbal/left frontal task, and right frontal patients will be inferior to left frontal lesioned patients on the nonverbal/right frontal task.
3. Left frontal lesioned patients will perform more poorly than left posterior patients on the verbal/left frontal task, and right frontal patients will be inferior to right posterior patients on the nonverbal/right frontal task.
4. Left posterior patients will be inferior to left frontal patients on the verbal AVC subtests, and right posterior lesioned patients will be inferior to right frontal lesioned patients on the visuospatial JLO.
5. Left hemisphere lesioned patients will perform more poorly than right hemisphere lesioned patients on the verbal frontal tasks and the AVC, and right hemisphere lesioned patients will perform more poorly than left hemisphere lesioned patients on the nonverbal frontal tasks and JLO.

METHOD

Subjects

All subjects were male patients in the neurology, neurosurgery, medical or surgical services of the Jackson VA and University of Mississippi Medical Centres. Subjects were selected on the basis of locus of lesion determined from CT head scan, using the mapping techniques developed by Mazzocchi and Vignolo (1978) and Luzzatti, Scotti and Gattoni (1979). Briefly, mapping consisted of measuring the extent of lesion on each cut of the scan, performing a proportional calculation, and plotting each cut on a standard lateral diagram of the brain taken from New and Scott (1975). Accuracy of the procedure was improved by first performing a scout scan, which allowed a more precise calculation of the angle and points of intersection of each cut. Examples of the plotted lesions of four of the patients studied are presented in Figure 1. Data on etiology of lesions are presented in Table 2.

Four groups of 10 patients each were compiled, having left frontal, right frontal, left postRolandic, and right postRolandic lesions. Only test protocols of patients who were able to attempt all tasks were included. Incomplete protocols resulted variously from rapid tumour growth, development of other cerebral disease (e.g. subdural haematoma) and progression of concurrent illnesses (e.g. pneumonia). Also excluded were patients who met the lesion selection criteria, but were illiterate or whose severe comprehension deficits precluded assessment and utilization of the complex language abilities requisite for the current testing. In the case of space occupying lesions, subjects were tested either after lesion excision or following courses of steroid and radiation treatment in order to minimize the remote effects of the lesions. A comparison group of 10 non-brain-damaged patients was selected from among medical and surgical inpatients with no history of cerebral neurological disease or psychiatric disorder. They were matched with the experimental groups for age and education. Subject selection and recruitment were carried out in consultation with neurology and neurosurgery personnel. Test administration and scoring procedures were then carried out.

Lesions in different cerebral areas differentially affect cognitive functioning and task proficiency. For a review, see Stuss and Benson (1983). Research has shown IQ performance to be relatively unaffected by frontal lesions (Luria, 1980), but often significantly impaired on selective tasks by more posterior lesions (Goodglass, in press), with the tasks affected depending upon the particular site of damage. As education has been shown to correlate with IQ (Matarazzo, 1972), in the present study "years of education completed" was used to match subjects for premorbid intellectual functioning.

Procedure

All subjects were first administered the posterior control tasks, JLO and AVC, according to their respective instruction manuals. Ss were then administered the frontal sorting tasks and fluency tasks, as described below. Half the Ss received the verbal version of each task first. Half received the nonverbal version first. This was determined by a randomized schedule, in order to randomize possible order effects.

Judgement of Line Orientation

In this nonverbal task, developed by Benton, Varney and Hamsher (1977), the patient is required to judge the spatial orientation of lines in relation to a set of standard references. The task is presented as a visual matching task, with five practice items and 30 test items. The bottom half of each page presents a standard semicircular array of 12 radiating numbered lines (sample). The top half of each page presents two lines (test items) whose angles of orientation correspond to those of two lines of the sample array. The patient must indicate which two of the numbered sample lines are at the same angle as the test items. This may be done either by pointing or by stating the numbers of the lines chosen. Performance is scored for number correct (Benton et al., 1977).

Auditory Verbal Comprehension

These tasks, developed by Kertesz (1982) require the patient to respond "yes/no" to simple and complex verbally presented questions (e.g. Are you wearing red pyjamas? Is a horse larger than a dog?); to point to named objects (e.g. a door, your left thumb); and to follow sequential commands (e.g. Point to the window, then to the door. Put the comb on the other side of the pen and turn over the book). Performance is scored for number correct for each subtest (Kertesz, 1982).

Card Sorting

Verbal

The word list consisted of 16 words belonging to four categories: vehicle, vegetable, animal and clothing. Each category had one word beginning with each of the phonemes "b", "p", "c" and "t". The four sample cards bearing the words "Boat", "Peas", "Cow" and "Tie" were laid on the table as illustrated in Figure 2a. The patient was then asked to read the word list from a typed sheet (Appendix 1). He was told, "These are the words in my deck of cards. The cards can be dealt in two ways."

Phonemic Sample. Pointing to the typed list and the samples on the table, E explained, "Boat, Bean, Bird and Belt all begin with the letter "b", so they go under Boat, which begins with a "b"." This pattern of instructions was repeated for the words beginning with each phoneme. E them said, "Now I want you to deal these cards according to the first letter, "b", "p", "c" or "t". Put them below the word that starts with the same first letter." S was then handed five cards, one at a time. Four were the same category (vegetable), each beginning with a different phoneme. One was a different category.

For all four sets of card sorting sample trials, E followed each correct match with "right". Any errors were corrected. If S erred on more than two matches, the entire sample sorting procedure was repeated once. On completion of the first sample, E said, "There is another way we can deal the cards."

Semantic Category Sample. Pointing to the typed list and the samples on the table, E explained, "Boat, Plane, Car and Truck are all vehicles, so they can go under Boat, which is a vehicle." This pattern of instructions was repeated for each word category. E then said, "Now I want you to deal these cards according to the category they belong to, whether it is a vehicle, a vegetable, an animal or clothing. Put them below the word that belongs to the same category, without paying attention to the first letter." S was then handed five cards, one at a time. Four were the same phoneme (b), each belonging to a different category. One card was a different phoneme. Feedback and practice were provided as described under A. above.

Experimental Task. The card deck consisted of 64 cards, with each of the 16 words in the word list being repeated four times. No two consecutive cards bore the same category or the same phoneme. E said, "First I want you to deal the cards according to the first letter. Put them below the word starting with the same first letter, "b", "p", "c" or "t"." Throughout card sorting, E handed S the cards one at a time. E said "yes" or "right" when S sorted correctly, and "no" or "That's not right" when S sorted incorrectly. After 10 consecutive correct responses, E said, "Good. Now I want you to switch to the other way of dealing the cards. Put them under the word belonging to the same category -- vehicle, vegetable, animal or clothing." Thereafter, following each 10 consecutive correct responses E said, "Good. Now I want you to switch to the other way of dealing the cards."

Nonverbal

The stimulus items consisted of 16 designs: Four patterns of lines, each presented at four different angles. After laying out the four sample cards as illustrated in Figure 2b, E said, "These cards can be dealt in two ways."

<u>Pattern Sample.</u> Pointing to the samples on the table, E explained, "Each of these cards has a different pattern of little lines on it: a different design. Can you see that each of the patterns is different?" S then examined the cards. If S did not understand, E explained further. "For example, this one has a lot of narrow lines (Fig. 2b, Sample 2) and this one has a thick black line in the centre (Fig. 2b, Sample 4). Each one is different. Now I want you to deal these cards according to the pattern. Put them below the card that has the same pattern of little lines." S was then handed five cards, one at a time. Four were the same angle, each bearing a different pattern. One card bore a different angle.

The sample trials proceeded as described under I.A. above.

<u>Angle Sample.</u> Pointing to the samples on the table, E explained, "Each of these cards has a different angle; the lines point in a different direction. This one points up and down. This one points up to the right. This one points up to the left, and this one lies flat across." E traced along each angle as it was described. "Now I want you to deal these cards according to their angle. Put them below the card with the same angle, <u>without</u> paying attention to the pattern of little lines." S was then handed five cards, one at a time. Four bore the same design, each oriented at a different angle. One card bore a different design.

The sample trials proceeded as described under I.A. above.

Experimental Task. The card deck consisted of 64 cards, with each of the 16 pattern/angle combinations repeated four times. No two consecutive cards bore the same pattern or angle. The nonverbal experimental task proceeded as did the verbal card sort described in I.C. above. E began with pattern first, then switched to angle.

Both the verbal and nonverbal card sorting tasks were scored for number of categories completed correctly and number of errors.

Fluency and Productivity

Verbal

Sample. S was instructed, "In the next minute, I want you to write as many words as you can think of; any words at all, like "dog", "cat", et cetera." The first word written was greeted with "That's right." If the patient wrote a proper name, E said, "Don't write proper names."

Experimental Task. This task was based on Milner (1964). S was instructed, "This time I want you to write as many different words as you can think of beginning with the letter "S"." E wrote a large "S" at the top of the response sheet. "They should not be proper names or the same word with a different ending." E crossed out examples of errors on the response sheet (Appendix 2) as each was described. "You can use any other words beginning with "S", like "soap" and "sharp"." E indicated these examples on the response sheet. "Make sure that each word is different, so that at the end I can count up how many different words you have written. You have five minutes."

Nonverbal

Sample. S was instructed, "In the next minute, I want you to draw as many different things as you can think of; anything at all, like a circle, square or any design." If S drew a scene, E said, "I want you to draw individual things." If S began to draw elaborately, E said, "Don't spend a lot of time on any one drawing. I want you to draw as many different things as you can."

Experimental Task. This task was based on Jones-Gotman and Milner (1977). E pointed to S's sample responses and said, "These are things that can be named, like [E named objects which S had drawn]." If S had drawn any objects which could not be readily labelled (as outlined in Jones-Gotman and Milner, 1977) E said, "These things don't have names. They are just designs." Turning to the response sheet, E said, "This time I want you to draw as many different designs as you can think of. The designs should be things you cannot name. They should not be objects, geometric shapes, letters, or numbers, or the same design turned around." E crossed out the examples of errors on the response sheet as each was described (Appendix 3). "You can draw anything else, like these designs which can't be named." E indicated examples of acceptable responses on the response sheet. "Make sure that each design is different, so that at the end I can count up how many different designs you have drawn. You have five minutes." If S had difficulty understanding the task, E elaborated: "Just designs, like when you're on the phone and you have a pencil in your hand and you're just doodling."

In both the verbal and nonverbal versions of the fluency and productivity task, the first two correct responses were greeted with "That's right." One warning was given for the first occurrence of each type of unacceptable response described above and for the first perseveration. If S stopped before the time elapsed, E did not enter into conversation, but said, "That's okay. I have to let the time run out. If you think of any other words/designs, just write them down."

Both the verbal and nonverbal versions of the task were scored for the total number of responses, the number of correct responses, the number of perseverative responses and the number of other unacceptable responses.

RESULTS

Demographic Variables

As patient groups were comprised of consecutive admissions to the neurology and neurosurgery services of the Veteran's Administration and University of Mississippi Medical Centres, demographic variables of age and education were analyzed to determine whether groups were of homogenous composition on these variables, or if systematic sources of variability existed among the groups on these dimensions. Demographic data are presented in Table 3.

Age

Univariate analysis of variance, with patient group as independent variable and age as dependent variable, showed no statistically significant differences in age composition among the groups ($F_{3,36} = 0.38$, $p < 0.77$). Results are presented in Table 4.

Education

Univariate analysis of variance, with group as independent variable and education as dependent variable, showed no statistically significant differences in educational level among the groups ($F_{3,36} = 0.29, p<0.84$). Results are presented in Table 5.

Thus no significant differences were found among the patient groups on the demographic variables of age and education.

Tests of Experimental Hypotheses

The experimental hypotheses were constructed in the form of predictions about specific directional differences in performance between pairs of groups on particular experimental tasks. For each hypothesis, the pertinent groups were therefore compared using planned comparisons (F statistic) within the framework of the General Linear Model (Ray, 1982).

Hypothesis One

It was predicted that frontal patients would be inferior to nonfrontal patients on all frontal tasks.

As predicted, frontal lesioned patients as a group (i.e. left frontal and right frontal combined) performed significantly more poorly than nonfrontal patients (i.e. left and right nonfrontal patients combined) on both the verbal and nonverbal card sorting tasks, which were designed to tap frontal functioning. This relationship was true for both measures of card sorting performance. Frontal patients achieved significantly fewer categories (M=4.2) than did nonfrontal patients (M=5.6) on the verbal card sorting task. Frontal patients made significantly more errors (M=8.7) than did nonfrontal patients (M=2.4) on the verbal card sorting task. Similarly, frontal patients achieved significantly fewer categories (M=4.4) than did nonfrontal patients (M=5.7) on the nonverbal card sorting task. Frontal patients also made significantly more errors (M=9.8) than did nonfrontal patients (M=2.2) on the nonverbal card sorting task. Results are presented in Table 6.

Hypothesis Two

It was predicted that left frontal patients would be inferior to right frontal patients on the verbal frontal task, and that right frontal patients would be inferior to left frontal patients on the nonverbal frontal task.

As predicted, left frontal lesioned patients performed significantly more poorly than right frontal lesioned patients on the verbal card sort task. This was true for both measures of card sorting performance: Left frontal patients achieved significantly fewer correct categories (M=3.5) than did right frontal patients (M=4.8). Left frontal patients made significantly more errors (M=12.0) on the verbal card sorting task than did right frontal patients (M=5.4). These results are presented in Table 7.

As predicted, right frontal lesioned patients performed significantly more poorly than left frontal lesioned patients on the nonverbal card sorting task. This was true for both measures of card sorting performance: Right frontal patients achieved significantly fewer correct categories (_M_=3.9) on the nonverbal card sort than did left frontal patients (_M_=4.9). Right frontal patients made significantly more errors (_M_=12.6) on the nonverbal card sorting task than did left frontal patients (_M_=7.0). These results are presented in Table 7.

Hence each frontal lesioned group performed more poorly on the particular task designed to selectively tap the specific skill deficits which were hypothesized to be associated with that lesion group, as predicted.

Hypothesis Three

It was predicted that left frontal patients would be inferior to left nonfrontal patients on the verbal frontal task, and that right frontal patients would be inferior to right nonfrontal patients on the nonverbal frontal task.

As predicted, left frontal lesioned patients performed significantly more poorly than did left nonfrontal lesioned patients on the verbal card sorting task. This was true for both measures of card sorting performance: Left frontal patients achieved significantly fewer correct categories ($\underline{M}$=3.5) than did left nonfrontal patients ($\underline{M}$=5.3). Left frontal patients made significantly more errors ($\underline{M}$=12.0) on the verbal card sorting task than did left nonfrontal patients ($\underline{M}$=3.0). These results are presented in Table 8.

As predicted, right frontal lesioned patients performed significantly more poorly than right nonfrontal lesioned patients on the nonverbal card sorting task. This was true for both measures of card sorting performance: Right frontal patients achieved significantly fewer correct categories ($\underline{M}$=3.9) on the nonverbal card sort than did right nonfrontal patients ($\underline{M}$=5.9). Right frontal patients made significantly more errors ($\underline{M}$=12.6) on the nonverbal card sorting task than did right nonfrontal patients ($\underline{M}$=1.9). These results are presented in Table 8.

As predicted, each frontal lesioned group performed more poorly than patients with nonfrontal lesions in the same cerebral hemisphere, on the particular task designed to selectively tap the specific skill deficits which were hypothesized to be associated with their area and side of lesion.

Hypothesis Four

It was predicted that left posterior lesioned patients would be inferior to left frontal lesioned patients on the tasks of verbal comprehension, and that right nonfrontal lesioned patients would be inferior to right frontal lesioned patients on the task of visuospatial orientation.

As predicted, left posterior lesioned patients were inferior to left frontal patients on each of the three components of the Western Aphasia Battery used to tap verbal comprehension skills. Hence, left posteriors achieved significantly fewer correct on Yes/No questions (*M*=54.9) than did left frontal patients (*M*=58.5). Left posteriors achieved significantly lower scores on Auditory Verbal Comprehension (*M*=56.2) than did left frontal patients (*M*=58.9). Left posteriors did more poorly on following Verbal Commands (*M*=68.0) than did left frontal patients (*M*=77.0). These results are presented in Table 9.

As predicted, right posterior lesioned patients were inferior to right frontal lesioned patients on the visuospatial task: Right posteriors achieved significantly lower scores on Judgement of Line Orientation (*M*=16.1) than did right frontal patients (*M*=21.3). These results are presented in Table 9.

As predicted, each nonfrontal lesioned group performed more poorly than patients with frontal lesions in the same cerebral hemisphere, on the particular task selected to tap deficits in postRolandic functioning associated with that cerebral hemisphere.

Hypothesis Five

It was predicted that left hemisphere lesioned patients would be inferior to right hemisphere lesioned patients on the verbal comprehension tasks and on the verbal frontal task, and that right hemisphere lesioned patients would be inferior to left hemisphere lesioned patients on the visuospatial task and on the nonverbal frontal task.

This hypothesis received partial support: As predicted, left hemisphere lesioned patients were inferior to right hemisphere lesioned patients on the verbal comprehension tasks. They achieved significantly lower scores on each of the subtests of the Western Aphasia Battery than did right hemisphere lesioned patients. These results are presented in Table 10. Furthermore, as predicted, right hemisphere lesioned patients were inferior to left hemisphere patients on the visuospatial task: Right hemisphere patients scored more poorly on Judgement of Line Orientation (M=18.7) than did left hemisphere patients (M=23.0). See Table 10.

On the frontal tasks, the target frontal group which was predicted to perform differentially poorly on a given task (e.g. left frontal group performing more poorly than right frontal group on the verbal card sort; cf. Hypotheses Two and Three), performed significantly more poorly than each of the other three brain lesioned groups. The only significant overall left hemisphere versus right hemisphere difference which emerged on the frontal tasks was that left hemisphere patients achieved significantly fewer categories on the verbal card sorting task ($\underline{M}$=4.4) than did right hemisphere patients ($\underline{M}$=5.3). Left-right comparisons are presented in Table 10.

Comparison with Normals

In each of the comparisons, the non-brain-lesioned group performed significantly better than the target brain-lesioned group which was predicted to perform differentially poorly on a given task. These results are presented in Tables 6, 7, 8, and 9.

Experimental Battery and Patient Classification

Multivariate discriminant analyses were performed using the six summary test scores to predict group membership. The summary scores used were:

1. verbal card sort, number of errors;

2. verbal card sort, number of categories;
3. nonverbal card sort, number of errors;
4. nonverbal card sort, number of categories;
5. Auditory Verbal Comprehension tasks, combined; and
6. Judgement of Line Orientation.

Multivariate discriminant analysis using these six summary scores correctly classified 87.5% of the patients on the anterior-posterior dimension.

Multivariate discriminant analysis using the six summary test scores correctly classified 82.5% of the patients by quadrant of lesion and group membership (i.e. including the non-brain-lesioned comparison group).

Multivariate discriminant analysis using four summary scores correctly classified 100% of the frontal lesioned patients by side of lesion. The scores used were:

1. verbal card sort, number of errors;
2. verbal card sort, number of categories;
3. nonverbal card sort, number of errors; and
4. nonverbal card sort, number of categories.

In summary, all experimental hypotheses related to laterality effects in unilateral frontal lesions were supported. The current task battery was found to be useful in discriminating frontal patients from nonfrontal patients with 87.5% accuracy. Furthermore, it discriminated quadrant of lesion with 82.5% accuracy, and side of frontal lesion with 100% accuracy.

Fluency and Productivity

The supplemental replication of Jones-Gotman and Milner's (1977) study of fluency in frontal lesioned patients did not yield results amenable to statistical analysis of group data.

Performance on both verbal and nonverbal fluency tasks was adversely affected (and sometimes precluded) by motor deficits of left hemisphere lesioned patients and motivational deficits of right hemisphere lesioned patients. Furthermore, both tasks elicited refusals and generated significant negativity and discontinuations. The verbal version, for example, was impaired by the pervasive deficits in this population in the area of written language: Misspelling and illegibility, combined with patients' inability to decipher their own written productions, rendered many protocols unscorable. Furthermore, self-consciousness about spelling appeared to be a factor in both refusals and some instances of low productivity, with patients taking time to select only the most simply spelled words from their vocabularies, requesting help with spelling, etc.

These general difficulties, in combination with the few cases of circumscribed lesion-specific deficits (e.g. dyslexia) resulted in such a prohibitive amount of missing and unscorable data as to preclude meaningful, valid and reliable statistical analysis of group data.

While the above qualitative observations were clinically interesting and often conformed to expectations based on Jones-Gotman and Milner and clinical experience, systematic data gathering on these process factors was not a planned component of the study. Hence systematic information on which to base evaluation and conclusions pertinent to the anterior-posterior and lateralization issues under consideration in the current study was unavailable from the fluency and productivity tasks.

The pervasiveness of difficulties on these tasks among all patient groups may have been related to task requirements. Jones-Gotman and Milner noted that the design fluency task "poses a difficult problem for any highly verbal subject" [1977, p.671]. This may have interacted with the the effects of low public education standards in Mississippi and the possibly related general reactivity to paper and pencil tasks observed in this patient population by various investigators (Nadeau, personal communication; Malloy, personal communication), perhaps contributing to their difficulties with both productivity tasks.

Other differences in patient population characteristics between Jones-Gotman and Milner and the current study may have further contributed to the lack of success with these tasks. Jones-Gotman and Milner's patients appeared to have relatively homogenous lesions, subjects being selected from among those being treated surgically for relief of epilepsy. Ninety-two percent of their subjects had preoperative epileptogenic lesions which were static and atrophic. Patients in the current study were primarily from the acute neurology and neurosurgery services, with largely preoperatively dynamic, metastatic lesions or recent cerebrovascular infarction.

Compliance with the test instructions itself has been described as a frontal function (e.g. Milner, 1964). Such general executive functions tend to become poorer with age (Jones-Gotman, personal communication; Kaplan, personal communication). The current group of patients was significantly older than those of the Jones-Gotman and Milner study. Their mean group ages ranged from 19.7 to 39.0, with ages ranging from 15 to 55 years. The current subjects ranged in age from 22 to 68 years, with group means ranging from 45.1 to 52.0 years. Thus their age may have further compromised their ability and inclination to comply with the relatively complex, multistep instructions and rules of these tasks.

DISCUSSION

Evidence has been presented that patients with unilateral frontal lesions demonstrated performance deficits indicative of lateralization of function within the frontal lobes. In the current study, the tasks which selectively tapped and underscored these lateralized deficits incorporated the dual requirements of 1. supramodal processing characteristic of frontal functioning and 2. processing associated with the functional strengths of each hemisphere. When compared with patients with unilateral postRolandic lesions, the frontal patient groups did significantly better on verbal and nonverbal tasks which typically or routinely tap deficits associated with unilateral postRolandic lesions (cf. Benton, 1969). Furthermore, while nonfrontal brain-lesioned comparison patients showed the expected deficits indicating laterality effects on the nonfrontal tasks, they performed significantly better than the frontal patients on the frontal tasks. Hence, the study demonstrated a double dissociation between laterality effects in frontal and nonfrontal patients on frontal and nonfrontal tasks. In combination, this pattern of results demonstrated that neither brain damage nor side of lesion alone accounted for the observed left-right differences among frontal patients, but rather a uniquely frontal laterality effect was in operation, dependent upon the frontal as well as the unilateral nature of the lesions and selectively tapped by specifically frontal tasks.

The sensitivity and specificity of the current set of tasks, with an accuracy of 87.5% in localizing damage to the frontal lobes and 82.5% in further localizing the quadrant of the lesion, demonstrated the clinical utility of these particular tasks in examining possible laterality effects as part of either experimental or functional analyses of patient deficits. The accuracy of 100% on the discriminant function analysis in classifying left and right frontal patients using card sorting scores, and the absence on any of the discriminant function analyses of any right frontal patients being classified as left frontal patients and vice versa, further attested to the value of these tasks in examining functional differences among unilateral frontal patients. The use of few summary predictors relative to sample size is consistent with Adam's proposals (1979) for discriminant analysis in exploratory neuropsychological research. While some variability in hit rates may be expected, the current results represent a clinically useful level of diagnostic and functional discrimination among left and right frontal patients and nonfrontal patients, given differing task demands.

The current findings lend experimental support to the hypothesis suggested by Lezak (1976) and the clinical observations described by Zangwill (1966) that frontal functioning, even with its supramodal qualities, incorporates lateralized verbal and nonverbal proclivities analogous to those which are characteristic of the organization of the rest of the cerebral cortex.

The current conceptualization of dual task requirements (i.e. 1. supramodal processing characteristic of frontal functioning and 2. processing associated with the functional strengths of each hemisphere) is valuable in designing further tasks to investigate lateralization within the functioning of the frontal cortex. Furthermore, the experimental design, with its format of comparisons which incorporate 1. both frontal and nonfrontal tasks and 2. both frontal and nonfrontal brain lesioned patients, further strengthens our ability to definitively demonstrate experimentally that lateralized deficits found in frontal patients are not primarily due to impairment in postRolandic cortical functions or to nonspecific factors associated with intracerebral damage and resulting generalized cortical dysfunction.

Stuss and Benson (1983) noted that "localization of psychological function in the prefrontal cortex has proven extremely difficult to document" [p. 429]. They reviewed impediments to studies of frontal-mediated functions in humans. While they described varying deficits depending on specific locus of lesion within the frontal lobes, historically there has been poor availability of patients with well-defined frontal pathology

(Stuss and Benson, 1983). Most cognitive psychological tests are insensitive to, or nonspecific for, frontal dysfunction (Lezak, 1976). Furthermore, manifestation of frontal-related deficits appears to be reactive to even minor modifications in administration and task demands (Milner, 1964). These difficulties obtaining groups and developing useful tasks, combine with multiple other clinical and research related factors to limit the experimental rigor of much frontal research. Poorly controlled procedural variables include practical difficulties in testing frontal lobe patients due to their attentional, motivational and information processing deficits (Stuss and Benson, 1983) and variability in administration and evaluation of tasks, as in the case studies of Luria and his colleagues (see Luria, 1980). Design limitations include inadequate or undefined methods used to localize brain damage (e.g. Benton, 1968), overinclusive selection criteria (e.g. Golden et al., 1981, described frontal patients as those patients for whom a majority of their lesion lay in frontal areas), and lack of nonfrontal brain-lesioned controls (e.g. Benson and Stuss, 1982; Benton, 1968). In summary Stuss and Benson (1983) call for more rigor in the definition of independent variables, and for construction of more specific tests.

The procedure and experimental design of the current study addressed the above issues. Patients with lesions limited to frontal and nonfrontal areas in each hemisphere were selected in consultation with neurology and neurosurgery personnel. All lesion sites were confirmed by careful mapping based on CT head scans. Nonfrontal brain-lesioned patients were used as comparison subjects. The experimental tasks were adapted from among those demonstrated by previous research to be selectively sensitive to frontal deficits. Their specific format was determined by both theoretical and practical considerations related to prefrontal cortical lesions. Simplification of tasks, tailoring of instructions and uniformity of feedback were based on pilot work in order to maximize their suitability to the dimensions being tested, while also maximizing their responsivity to clinical considerations (e.g. low motivation, memory deficits, concrete attitude, fatiguability) in evaluating a spectrum of brain-lesioned patients.

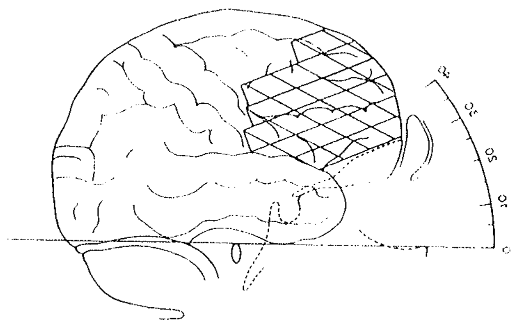
The detailed standard instructions, including explicit standard elaborations for common problem situations in administration, were designed to maximize the uniformity of the test situation across subjects. Nonetheless, subtle unintentional biasing influences, based on the examiner's foreknowledge of both the hypotheses and the group membership of each subject, remain a serious consideration in interpreting the results of this study. This is a practical problem common to exploratory neuropsychological studies of a similar scale (e.g. Benton, 1968; Drewe, 1974; Jones-Gotman and Milner, 1977; Milner, 1963). A more rigorous test of the current hypotheses will therefore require task administration by a technician blind to the diagnoses of the patients, to the extent that this is possible, and blind to the experimental hypotheses at the time of testing, followed by a similarly blind and anonymous scoring of test protocols.

The many remaining questions regarding frontal functioning, and the clinical challenge of evaluating these patients, makes frontal study an exciting and difficult area. As evidenced by the emphasis in recent writings on the specific neuroanatomical connections of frontal subareas, criterion groups precisely defined according to locus of lesion will remain a requirement of quality frontal research. In practice, most investigators will therefore require long term studies to accumulate a meaningful sample size. Useful refinements would be to analyze findings of patients with subcortical involvement separately from those with apparently strictly cortical lesions; replication and extension of exploratory studies to larger samples of patients; and development of a greater variety of both experimental and naturalistic tasks focussing on their clinical significance for functional adaptation.

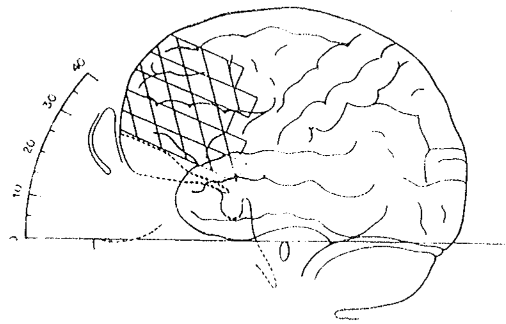
In conclusion, the current study provided clear support for lateralization of frontal lobe cortical functions consistent with well known hemispheric strengths and differences. The current format serves as a conceptual and experimental model for generating tests to further examine issues of laterality and localization of function within the human frontal lobes.

FOOTNOTE

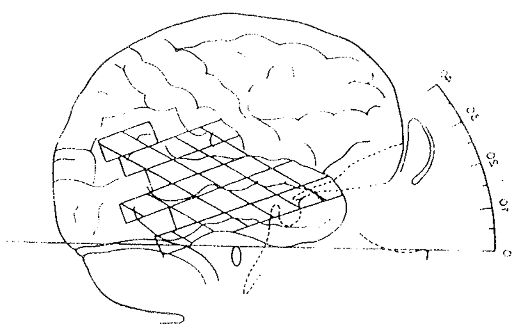
1. "The prefrontal divisions of the cerebral cortex are situated anteriorly to the motor (Area 4) and premotor (areas 6 and 8) areas, "having a distinctive neuronal structure and unique reciprocal vertical connections with the subadjacent divisions of the thalamus, particularly the mediodorsal nucleus, and "diverse connections with other divisions of the cerebral hemispheres" (Luria, 1980, p.258). In the neurological and neuropsychological literature (e.g. Milner, 1964; Reitan, 1964; Benton, 1968; Luria, 1980) the prefrontal cortex has typically been referred to as "the frontal lobes", "implicitly excluding the motor and premotor cortex" (Fuster, 1980, p.2). Usage in this paper conforms to this convention.



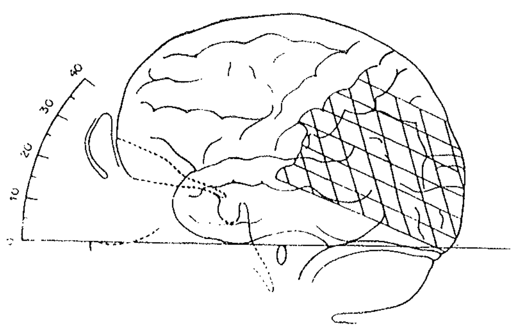
Right Frontal
Patient W.G.



Left Frontal
Patient K.W.



Right Nonfrontal
Patient F.S.



Left Nonfrontal
Patient B.B.

Brain schematics
From New & Scott:
COMPUTED TOMOGRAPHY
OF THE BRAIN AND ORBIT
(EMI SCANNING)

Figure 1. Examples of the plotted lesions of four of the patients evaluated in the current study. Shading indicates area of lesion.

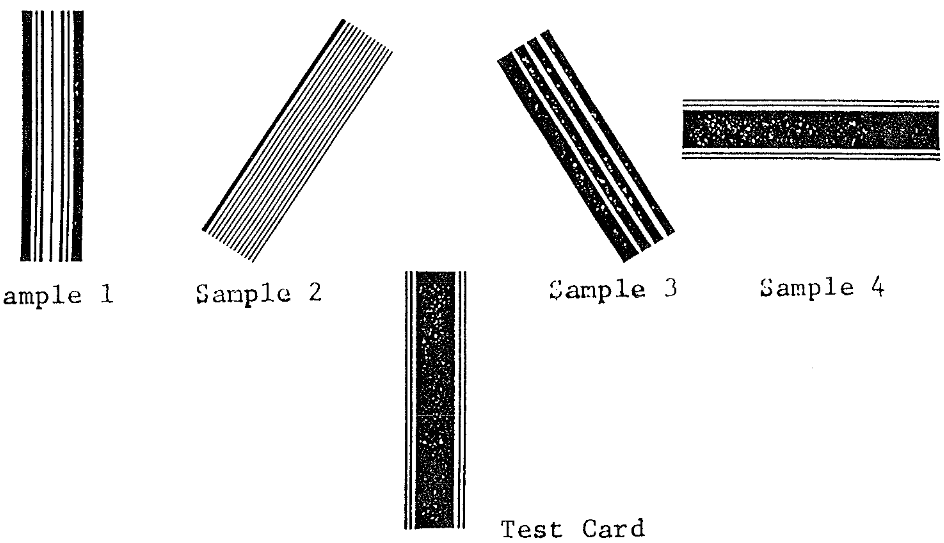
TIE PLANE CORN BIRD

Sample 1 Sample 2 Sample 3 Sample 4

TIGER

Test Card

2a. The test card can be matched to Sample 1 phonemicly and to Sample 4 semanticly



2b. The test card can be matched to Sample 1 by angle and to Sample 4 by pattern

Figure 2. Cards for the Card Sorting Task

Table 1

LATERALITY EFFECTS IN FRONTAL FUNCTIONING

Verbal Fluency	
Milner (1964)	L<R
Benton (1968)	L<R
Ramier and Hecaen (1970)	L<R
Perret (1974)	L<R
Design Fluency	
Jones-Gotman and Milner (1977)	R<L
Wisconsin Card Sorting Test	
Milner (1963)	L=R
Drewe (1974)	perseveration R<L; other indices, L<R
Robinson et al. (1980)	R<L
Lurian Tasks (from LNB)	
Malloy et al. (1983)	L=R
Mazes	
Corkin (1965)	R<L
Milner (1965)	R=L
Sequencing	
Petrides and Milner (1982)	
verbal	L impaired
nonverbal	L impaired; R mildly impaired
Conventionally Lateralizing Tasks	
Benton (1968)	
3-D block design and design copy	R<L
paired associate learning	L=R

Note. < indicates "did worse than".

Table 2

Demographic Data

Group	Age Mean[a]	Age Range	Education Mean[a]	Education Range
Left Frontal	47.1	22-68	11.3	0-18
Right Frontal	47.2	29-57	11.8	6-18
Left Posterior	52.0	40-66	12.6	8-16
Right Posterior	51.1	26-68	11.6	8-14
Non-brain-damaged	45.1	23-65	11.4	7-16

Note. All numbers represent years.
[a] n=10.

Table 3

Etiologies of Cerebral Lesions

Group	Neoplastic[a]	Vascular[b]	Traumatic[c]	Infectious[d]	?
Left Frontal	2	3	3	0	2
Right Frontal	6	3	0	0	1
Left Posterior	3	3	1	2	1
Right Posterior	1	7	0	0	2

Note. All numbers represent actual numbers of patients with a given etiology.
? indicates etiology of lesion seen on CT not definitively determined at the time of writing; neurological findings were consistent with site of lesion.
[a]Neoplastic: e.g. metastatic tumour, glioblastoma multiforme.
[b]Vascular: e.g. aneurysm, cerebrovascular infarction, arteriovenous malformation.
[c]Traumatic: e.g. cerebral contusion from blow to the head.
[d]Infectious: e.g. abscess.

Table 4

Analysis of Variance of Age comparing Side of Lesion and Anterior-Posterior Dimension of Lesion (AP)

Source	Sum of Squares	Degrees of Freedom	F	Tail Probability
Model	206.00	3	0.38	0.77
Side	2.50	1	0.01	0.91
AP	202.50	1	1.12	0.31
Side x AP	1.60	1	0.01	0.93
Error	6493.80	36		

Table 5

Analysis of Variance of Years of Education comparing Side of Lesion and Anterior-Posterior Dimension of Lesion (AP)

Source	Sum of Squares	Degrees of Freedom	F	Tail Probability
Model	9.48	3	0.29	0.84
Side	0.22	1	0.02	0.89
AP	2.02	1	0.18	0.67
Side x AP	7.22	1	0.66	0.42
Error	396.90	36		

Table 6

Performance of Frontal Patients versus Nonfrontal Patients on Frontal Tasks

	Verbal Card Sort		Nonverbal Card Sort	
	# categories[a]	# errors[b]	# categories[a]	# errors[b]
Frontal	4.2	8.7	4.4	9.8
Nonfrontal	5.6	2.4	5.7	2.2
Difference	1.4*	6.3*	1.3*	7.6*
F values for Frontal vs. Nonfrontal Comparison	14.65	8.52	12.50	12.93

Notes. All scores represent group means, n=20.
aMaximum possible categories=6.4.
bMaximum possible errors=64.
*p<0.01.
Df=1,45.

Table 7

Performance of Left versus Right Frontal Patients on Frontal Tasks

Group	Verbal Card Sort		Nonverbal Card Sort	
	# categories[a]	# errors[b]	# categories[a]	#errors[b]
Left Frontal	3.5	12.0	4.9	7.0
Right Frontal	4.8	5.0	4.0	12.2
Difference	1.3*	7.0*	0.9*	5.2*
Non-brain-damaged	5.9	1.5	6.0	1.3
F values for Left vs. Right Frontal Comparison	6.7	5.7	3.0	3.2

Notes. All scores represent group means, n=10.
[a]Maximum possible categories=6.4.
[b]Maximum possible errors=64.
*p<.05.
Df=1, 45.

Table 8

Anterior-Posterior Comparisons on Frontal Tasks by Side of Lesion

	# categories[a]	# errors[b]
Left	Verbal Card Sort	
Frontal	3.5	12.0
Nonfrontal	5.3	3.0
Difference	1.8*	9.0*
F value	12.2	9.4
Non-brain-damaged	5.9	1.5
Right	Nonverbal Card Sort	
Frontal	4.0	12.2
Nonfrontal	5.9	1.9
Difference	2.0*	10.3*
F value	14.1	12.4
Non-brain-damaged	6.0	1.3

Notes. All scores represent group means, n=10.
[a]Maximum possible categories=6.4.
[b]Maximum possible errors=64.
*p<.005.
Df=1,45.

Table 9

Anterior-Posterior Comparisons on Nonfrontal Tasks by Side of Lesion

	Task		
		Auditory Verbal Comprehension[a]	
Left	Yes/No[a]	Pointing[a]	Commands[b]
Frontal	58.5	58.9	77.0
Nonfrontal	54.9	56.2	68.8
Difference	3.6*	2.7*	8.2*
F value	8.7	9.9	13.1
Non-brain-damaged	59.3	59.5	80.0

Right	Judgement of Line Orientation[c]
Frontal	20.9
Nonfrontal	16.1
Difference	4.8**
F value	6.6
Non-brain-damaged	27.8

Notes. All scores represent group means, n=10.
[a]Maximum possible correct score=60.
[b]Maximum possible correct score=80.
[c]Maximum possible correct score=30.
*$p<.005$.
**$p<.01$.
Df=1,45.

Table 10

Left versus Right Lesioned Patients: All Tasks

Task	Left	Right	F value
Verbal Comprehension			
Yes/no (max.=60)	56.7	59.5	9.8*
Pointing (max.=60)	57.6	59.2	6.6**
Commands (max.=80)	72.9	79.8	18.5*
Judgement of Line Orientation (max.=30)	23.0	18.7	11.8*
Verbal Card Sort			
Categories (max.=6.4)	4.4	5.3	6.6**
Errors (max.=64)	7.5	3.6	3.8
Nonverbal Card Sort			
Categories (max.=6.4)	5.2	4.9	0.4
Errors (max.=64)	4.7	7.2	1.3

Notes. *p<.001.
**p<.005.

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Appendix 1

Verbal Card Sort: Word List

Boat	Bean	Bird	Belt
Plane	Peas	Pig	Pants
Car	Corn	Cow	Coat
Truck	Tomato	Tiger	Tie

Appendix 2

Word Fluency: Response Sheet

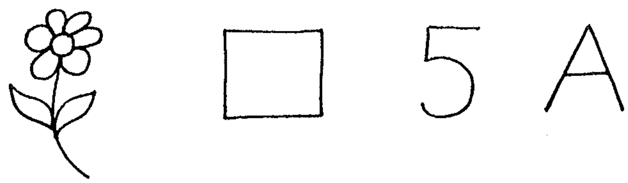
Wrong: Steven shoe shoes

Correct: soap sharp

Appendix 3

Design Fluency: Response Sheet

Wrong:



Correct: