TESTS OF CORPUS CALLOSUM AND HEMISPHERE FUNCTION AND THEIR RELEVANCE TO SCHIZOPHRENIC DISORDERS

By

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TABLE OF CONTENTS

Chapter 3 cont.../

Page

LIST OF TABLES

Page

* * *

LIST OF FIGURES

Page

(i) Acknowledgements and Statement of Personal Contribution

I was supported by the Medical Research Council (UK) from 1987-1990 on a project grant to myself and Dr John Cutting. The bulk of the work was carried out while I was a Lecturer at the Institute of Psychiatry in the section of Neuropsychiatry. Throughout this time, I was privileged to work under the direction of Professor Alwyn Lishman, who provided me with the perfect environment, the physical and mental space, in which I could develop the ideas and techniques described in this thesis. He offered advice when asked, criticism when necessary and support continuously. The other main source of guidance and inspiration was John Cutting who was generous enough to share his immense knowledge of the psychology of schizophrenia and his unique creativity in this field.

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The design of the studies, the preparation of materials, the recruitment of patients and their testing, diagnosis and clinical assessment, was carried out by me alone. The analysis of the data, literature review and preparation of the thesis was also done entirely by me.

Parts of this thesis have been published in peer reviewed journals.

Chapter 2 is based on:
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(ii) SUMMARY

Study of the neuropsychological functioning of the cerebral hemispheres and the transfer of information between them, can be achieved by presenting visual stimuli for processing, to one or other (or both) visual field(s), using a tachistoscope. Research of this kind has been applied to the study of schizophrenic disorders but the results remain inconclusive because of methodological problems in the execution of such studies. In this thesis, three novel tests were devised in an attempt to build upon and clarify this work. The tests were designed to have useful properties such as feasibility in the testing of psychotic patients and the ability to elicit clear lateralised asymmetries in performance by normal subjects. A series of experiments were undertaken to examine the effect that psychiatric disorders had on the performance of these tests. The bulk of the subjects who participated in this research included 52 normal controls, drawn mainly from the nursing, technical and ancillary staff of the Maudsley Hospital. The patients comprised of 46 schizophrenics at various stages of their illness, most of whom were in-patients. A psychiatric control group was also included and this consisted of 22 patients with affective disorder, 10 of whom were bipolar. Again, the majority were in-patients. All the patients were assessed using standardised semi-structured interviews and questionnaires, and diagnoses were made according to agreed international criteria. Essentially, all of the patients did all of the tests. A sub-group of 30 schizophrenics had CT scans and of these, 21 had magnetic resonance imaging (MRI).

The first test involved the processing of pictorial stimuli. The test had two components: one required the classification of the item depicted as being either living or non-living, which produced a left hemisphere (LH) advantage. The other, using the same stimuli, required a judgement of size in comparison with a standard referent using mental imagery; this produced a right hemisphere (RH) advantage provided the size comparison was sufficiently taxing. When the patients performed these tasks, they showed the expected RH advantage for the size comparison, although their reaction time was slowed, presumably due to non-specific effects of illness and medication. However, the schizophrenic group, while showing no abnormality of

mental imagery in the RH, failed to demonstrate an LH advantage on the categorisation task and this was particularly so for those who had experienced visual hallucinations. This was interpreted as a deficit in visual semantic memory in the LH.

The second test employed chimeric face drawings in which half of the face looked happy and the other looked sad. It was shown that normal right handers were biased in their judgements of whether the composite face looked happy or sad by the affective valence of the half-face to their left. The effect was highly significant, robust and reliable. This was not found in non-right handers. The perceptual bias evoked by the stimuli was interpreted as a function of the normal RH's role in directing spatial attention. The influence of affect, also thought to involve the RH, was examined by inducing different moods in a sub-group of normal subjects and found to be insignificant. When the same stimuli were presented tachistoscopically, to a different group of normal controls, the same perceptual bias was elicited. Patients with manic or depressive illness showed an increase and decrease in the strength of the bias, respectively. Schizophrenic patients showed a significantly reduced bias suggesting RH impairment in attentional processes. A proportion of the subjects also performed on a test of selective attention. The normal pattern of correlations between this, and bias and reaction time on the chimeric faces test, appeared to break down in the schizophrenics, suggesting widespread disruption of attentional systems. Distinct patterns of inter-correlations were observed for each of the subject groups.

The third test was designed to determine the extent and nature of interhemispheric transfer of information, across the corpus callosum. A tachistoscopic version of the Stroop colour-word test was used in which the 2 elements were separated across the mid-line. A "control", intrahemispheric version was also administered. In normals subjects, interference and facilitation of colour naming by colour-words was reduced in the interhemispheric condition relative to the intrahemispheric condition. This situation was exaggerated in subjects with agenesis of the corpus callosum. When patients with schizophrenia were administered this test, they showed a unique pattern of results. As a group, the amount of Stroop interference and facilitation which occurred across the corpus callosum was greater than within the hemispheres. Otherwise, their performance was comparable to the controls. This did not appear to be related to clinical variables including, age, IQ, the severity of psychotic symptoms or a positive family history, although there was a trend for recovered patients to show the effect to a greater degree. The interhemispheric Stroop effect was positively correlated with anterior callosal width, as measured from mid-sagittal MRI scans when the appropriate corrections were made for intracranial volume, but was unrelated to ventricle:brain ratio. Anterior callosal width was also found to be inversely related to auditory hallucinations.

It may be concluded that there is a specific abnormality of corpus callosum (interhemispheric) function in schizophrenia, in the form of increased transfer or perhaps decreased filtering of high-level information. This appears to be related to a relative increase in anterior callosal size. The finding is consistent with previous psychological studies and recent MRI data. However, there may be other neuropsychological deficits in other brain areas. The RH's attentional system also appears to be dysfunctional in schizophrenia and, to a lesser extent in affective disorder. Furthermore, while the RH imagery mechanism would seem to be intact, there is evidence of impairment in the LH visual semantic system. Further research should aim to clarify more precisely the structural basis of these functional abnormalities and also their relationship to important clinical and phenomenological variables.

PART I

CHAPTER 1

INTRODUCTION AND REVIEW OF THE LITERATURE

1.1 INTRODUCTION

In 1844, Arthur Ladbroke Wigan (see Clarke, 1987), a general practitioner working in the South of England, suggested that insanity might be due to the failure of the two cerebral hemispheres to work in together in harmony. He believed that the hemispheres were essentially duplicates and, in keeping with the knowledge of the day, had little concept of cerebral localisation, other than that provided by phrenology. After all, this was some 20 years before Paul Broca's landmark description of a disturbance of speech consequent upon lesions of the left but not right side of the brain. Wigan's thesis remained ignored until the early 1970's when questions were raised as to whether this idea might be relevant to the understanding of abnormal mental phenomena (Lishman, 1971; Galin, 1974). This was facilitated thanks to advances in psychology and the growth of a new branch, namely neuropsychology. These advances included an impressive body of research illuminating the role of the corpus callosum (CC) from studies of individuals who had undergone commissurotomy or the "split-brain" operation (Gazzaniga et al., 1965; Sperry, 1968) or who had become "disconnected" by naturally occurring lesions (Geschwind, 1965). The function of this the CC, a broad band of more than 200,000,000 myelinated fibres, was inferred from the effects of its transection and this in turn led to speculation regarding the cerebral basis of the unity of conscious experience, the unconscious, and other questions related to the mind-body problem (see Sperry, 1968). Furthermore, the activity of the right hemisphere was "unlocked" from the domination by its partner on the left and this too fuelled the imagination of neurophilosophers and psychologists alike.

Psychopathology entered the stage with a report of thickening of the CC in the post-mortem brains of 10 chronic schizophrenics (Rosenthal & Bigelow, 1972). This provided the impetus to study interhemispheric transmission in patients with schizophrenia. Neuropsychologists Stuart Dimond and Graham Beaumont were the first to apply the sort of divided visual field (DVF) techniques used in split brain research to psychiatric patients (Beaumont & Dimond, 1973). Their paper, brief and inconclusive as it was, (see later) provoked a minor explosion of studies using these and other techniques. By the 1980's this sort of work began to fade with several reviewers expressing frustration at the lack of consistency to the results (Walker & McGuire, 1982; Colbourn, 1982; Gruzelier, 1981; Cutting, 1985; Robertson & Taylor, 1987). The main reasons for this were methodological and can be placed into 3 broad categories:

a) technical problems

- in DVF (tachistoscopic)/dichotic listening/haptic techniques

b) subject factors

- inadequate care over psychiatric diagnosis
- clinical heterogeneity, especially with regard to schizophrenia
- medication effects
- lack of control subjects and failure to take into account such variables as IQ, education and psychopathology etc.

c) experimental design

- failure to separate intra-hemisphere effects from inter-hemisphere effects
- failure to match subjects on a control task

This thesis deals with studies in the visual domain so the following discussion will be limited to DVF techniques and their application in psychiatric research.

1.2 (a) Technical problems

The basic principle underlying DVF studies is that visual information in one hemifield is projected entirely to the opposite cerebral hemisphere. This is unlike the auditory and tactile pathways which have ipsilateral as well as contralateral projections. To take advantage of the anatomical arrangement, presentation duration must be short (<150 msec) so as to avoid reflex visual scanning, and stimuli should be outside the foveal region (<1.2°) where there may be bilateral cerebral connections (see Young, 1982 for review).

Accurate fixation can be achieved in a variety of ways from simply urging the patient to look straight ahead (Clooney & Murray, 1977; David, 1987), to requiring the subject to recall a central digit (Gur, 1978; Magaro & Page, 1983) or by visual monitoring (Eaton et al., 1979). Though ensuring fixation is important in preventing information entering the "wrong" visual field, the use of a central stimulus may add to the cognitive load and so interfere with the cognitive processing of the test stimulus. Electro-occulographic measures or video monitoring are precise methods for ensuring fixation but these are intrusive and cumbersome and may reduce a patient's willingness to cooperate with testing. Direct observation is a perfectly acceptable method and has the added bonus of being inexpensive and relatively free from technical failure (Young, 1982). Poor fixation will result in unreliable "noisy" data, though it should not give rise to errors in one visual field rather than the other, unless asymmetries in the direction of gaze exert an effect.

Numerous studies (see Beaumont, 1982; Bradshaw & Nettleton, 1981; Beaton, 1985) have shown that verbal stimuli (e.g. letters, words, letter strings) are better recognised, named and matched when presented to the right visual field/left hemisphere (RVF/LH). Non-verbal stimuli (e.g. dot location, line orientation, form and facial recognition) tend to produce a left visual field/right hemisphere (LVF/RH) advantage, but results are less consistent. However, human experimental psychology cannot be reduced to a simple stimulus-response equation and must take into account such factors as cognitive strategy, response bias, attention and task demands. When this is not done, many "left hemisphere tests" turn out to produce left visual field advantages under some circumstances, and similarly, "right hemisphere tests" may produce unexpected right visual field advantages. For all but the most rudimentary task, both hemispheres cooperate in subtle complex ways, involving many synapses (Moscovitch, 1986). Sergent (1983) has examined the effects of psychophysical properties of visual input (e.g. stimulus duration, luminance, retinal eccentricity, stimulus size) as well as task difficulty and familiarity. All these have been shown to exert a profound influence on hemispheric asymmetries.

1.3 (b) Subject factors

Subject differences including sex, age, handedness and intelligence are potentially confounding variables. These variables are especially relevant when DVF techniques are applied to a psychiatric population since such factors are not distributed evenly among patients in comparison to the normal population.

Controls

Selection of control groups is highly problematic. Chapman and Chapman (1977) have argued cogently that psychiatric controls as well as normals should be used in this kind of work so that factors pertaining to hospitalisation may be controlled. However the matter does not end there. Cognitive tests should be given to subjects (including normals) matched for IQ; for schizophrenics this often means "low-normal". The deleterious effect schizophrenia has on IQ (Goldstein, 1986) may be obviated by using tests which to tap premorbid abilities (Nelson & O'Connell, 1978), or by including data on educational attainment. Despite taking pains to select appropriately matched controls, it may still prove difficult design a test which avoids reaching the schizophrenics' performance "ceiling" whilst remaining firmly on the controls' "floor". One appealing way round this, is to determine a threshold level for each subject by altering the presentation time (Gur, 1978; Colbourn & Lishman, 1979) or some other stimulus parameter. While this enhances the sensitivity of the test in question, alteration in for example, exposure duration may have, as previously mentioned, differing effects on each hemisphere's efficiency, so confounding the results.

Which psychiatric patients should be used as controls? The study of "typical" hospitalised affective disorder patients may be fruitful in its own right but in comparison to schizophrenics they will tend to be older, predominantly female (inpatient schizophrenics are more often male) and are likely to have been in hospital for a shorter time (Wing & Wing, 1982). Therefore, accurate matching may lead to the inclusion of atypical cases which may reduce the generalisability of any findings. Also, attempts to match groups for degree of psychopathology creates another problem due to the lack of reliability and validity of clinical diagnosis. As non-schizophrenic controls approach schizophrenics on degree or even nature of psychopathology, for example schizoaffectives, so they are bound to include "true" schizophrenics wrongly classified. As a result, the control group's performance will begin to approximate that of the schizophrenics. This emphasises the need to improve the reliability of diagnoses by using standardised assessments and criteria, supplemented by quantitative and qualitative ratings of symptoms.

An alternative strategy may be to compare groups on the basis of specific symptoms alone rather than their diagnoses, such as hallucinations or thought disorder. This may prove rewarding in determining possible psychological mechanisms for those symptoms. Along the same lines, dividing schizophrenic patients into subgroups according to symptoms (e.g. with or without Schneiderian first rank symptoms (David, 1987)) may be informative, given the accepted heterogeneity of "the schizophrenias" (Bleuler, 1911). Another subdivision might be between cases with predominantly "positive symptoms" versus those with "negative symptoms" (Andreasen, 1987; see also Liddle, 1987). Care must be taken that "severity" is independently controlled. In addition, these groupings are not mutually exclusive. Nevertheless, some of these clinically familiar categorisations may yet prove to reflect lateralised cerebral dysfunction (Gruzelier, 1984; Weiner et al, 1990).

Subdivisions in terms of acute and chronic may reveal qualitative differences in hemispheric function but the latter group of patients tend to have more severely and globally impaired performance (see Cutting, 1985). Changes in the pattern of test performance over time may cloud the differences between groups, although these differences will be of interest in themselves.

Medication

Medication is a potential source of unsystematic bias in studies of psychiatric populations. Most schizophrenics available for testing will be on neuroleptic drugs. Those who are not, are by definition atypical and are likely to be less severely disturbed or so disturbed as to be untestable. There are exceptions such as those admitted to specialised research units. Some chronically ill patients with affective disorder may be treated with neuroleptics but these too are somewhat atypical. Although parkinsonism and other neuroleptic induced extrapyramidal side effects may significantly hamper motor speed, overall performance, including speed of visual information processing (Braff & Saccuzzo, 1982; Spohn & Strauss, 1989) is improved by neuroleptics. Eaton et al., (1979) found that neuroleptics improved both left and right hemisphere performance but not uniformly for different cognitive tasks. Hammond & Gruzelier (1978) showed that left hemisphere functioning was differentially improved compared to right. Caution must be exerted in interpreting these claims: if an experimental design has revealed an LH deficit, it is predictable that after treatment, it may be attenuated, due to regression to the mean. Also, "state dependant" abnormalities may disappear with clinical improvement regardless of whether the improvement is spontaneous or pharmacologically mediated. Testing patients during the acute illness and again after a period of treatment, whether or not they have responded, might shed light on this (see Wexler, 1986; Johnson & Crockett, 1982; Tomer & Flor-Henry, 1989).

1.4 (c) Experimental design

There is a truism: "give any test to a schizophrenic and he will perform it more poorly than a normal control." Further, the more difficult the test the worse he will do. This leads to the so-called "differential deficit problem" whereby an apparently specific deficit is in fact due to a failure to match tests on difficulty and hence discriminating power (Chapman & Chapman, 1973). A spurious deficit may not only emerge in a comparison of schizophrenics and controls, but also between hemispheres within the patient group if say, the "LH task" is more difficult than that of the RH.

In neuropsychological research, the aim is often to reveal a deficit in one hemisphere as opposed to the other. Commonly, two roughly equivalent tasks are chosen, one designated a LH and the other, a RH task. Ensuring equivalence at the perceptual level for example between letters and shapes, is necessary and may be difficult. One way round this is to use the same stimuli but alter the task instructions, thus producing in effect two, different but matched tests, each producing opposite hemisphere advantages. Internationally agreed criteria for what constitutes a reliable, hemisphere-specific test do not exist. At the least, it is necessary to show that normal subjects produce the expected, statistically significant asymmetries using the identical stimuli and apparatus intended for the psychiatric patients. Ideally, data from subjects with known unilateral brain lesions on the same or similar tests should show the predicted lateralised deficits that are predicted from normal data.

When the corpus callosum is the target of investigation, the experiment must be designed in such a way that performance can be related to interhemispheric transfer alone and not to an intra-hemispheric processing stage. One method is to compare matching across the visual fields with matching within a visual field. Again, concurrent validity may be provided by work done on patients with callosal sections or agenesis.

Table 1.1 summarises the results and methodologies of all the published divided visual field studies on schizophrenic patients.

Table 1.1. Summary of divided visual field studies of schizophrenic patients

Investigators	*Subjects (Medication) Diag criteria*	*Controls*	*Task (dependant var - response mode)*	*Results*	*Comment*
Beaumont & Dimond (1973)	12 Sz (M) "active" No criteria	12 mixed psych pts 12 general hospital pts	Matching:letters shapes and digits Across & within VFs (accuracy - vocal)	Poor Xmatching of shapes & letters Sz vs Cs	Poor LH letter matching Sz vs Cs; poor RH digit/ shape matching, Sz vs psychiatric patients
Clooney & Murray (1977)	12 para Sz 12 non para (M) No criteria	12 normals	Matching; letter combinations (LJU) Across & within VFs (R & L manual RT)	Poor matching across & within, Sz vs Cs LH=RH	Para Sz ↑ RT with ↑ number of letters for 'same' judgment only (R hand response)
Gur (1978)	12 para Sz 12 nonpara (M) No criteria	24 normals	Dot location & syllable recognition within Vfs (accuracy - vocal)	Sz ↓ on syllable test vs Cs; Sz RH advantage for dots	Sz ↓ on dot location vs Cs. RH verbal task scores relatively good vs Cs
Colbourn & Lishman (1979)	13 Sz (M) PSE	9 affectives 11 psych pts-non-psychotic 19 normals	Word & complex shape recognition within Vfs (accuracy - vocal)	No LH ↓ word task in male Sz only. No RH deficit	No RH ↓ in Sz or Cs in non-verbal task. Only 5 male Sz showed abnormal laterality
Connolly et al (1979)	15 Sz (M) PSE	6 affectives 14 psych pts-non-psychotic 20 normals	Dot pattern & alpha-numeric recognition in R or L VF (vocal RT)	LH deficit for lexical & spatial tasks, Affs & Sz vs other Cs	Sz and Affs poor overall. Lexical task failed to produce LH advantage in Cs
Hillsberg (1979)	5 Sz (M)	10 normals- 5 students 5 hospital workers	Matching of arrow directions Across & within VFs (bimanual RT)	LH ↓ vs RH in Sz. All ↓ in bilateral vs single VF match	Sz much slower vs Cs. Trend for Sz 'across' VFs match to be most ↓ of all
Eaton (1979) & Eaton et al (1979)	51 Sz RDC 24 Sz Feighner	18 normals (pre/post treatment)	Matching: letters digits & shapes Across & within VFs (manual RT/accuracy)	Sz less accurate on verbal task. Poor Xmatching of shapes	General improvement posttreatment. LH ↑ more for digit task, RH ↑ for verbal task
Pic'l et al (1979)	10 para Sz 10 nonpara Chronic (M) No criteria	10 psych in-patients 10 normals	Dot enumeration & identification of 4 letter strings (accuracy - vocal)	LH↑ for lexical task all groups Nonparas RH ↓ for on dot task	All pts poorer vs normals on LH (& RH) tasks Nonparanoids worst of all
Schweitzer (1982)	16 Sz (M) DSM-III	16 normals	Shape/word STM matching, within R or L VF (accuracy - vocal)	LH shape-task performance=Cs RH shape-task↓ vs Cs	Word task accuracy Sz=Cs, regardless of VF

Table 1.1. Summary of divided visual field studies of schizophrenic patients (cont).

Investigators	*Subjects (Medication) Diag criteria*	*Controls*	*Experimental Task (dependant var - response mode)*	*Results*	*Comment*
Connolly et al (1983)	12 Sz (no M)	16 normals	Identification of dot patterns and letters, R or L VF (R & L manual RT)	LH↓ (RH ↑) for letters, Sz vs Cs RH↑ for dots Sz & Cs; Normal IHTT time	Sz ↓ on all tasks. R hand ↑ for dots. Weak LH advantage on Verbal task in Cs
Magaro & Page (1983)	8 para Sz 8 nonpara (M) DSM-III/RDC	8 mixed psych in-pts 8 normals (accuracy - vocal)	Matching: letters shapes and faces Across & within VFs	Nonpara ↓ for all RVF stimuli & Xmatching of letters	Para Sz poor at X matching of shapes. RH ↑ for matching in all subjects
Shelton & Knight (1984)	12 Sz (M) DSM-III	12 mixed psych in-pts	Identification of inverted U R or L VF (R & L manual RT)	Sz=Cs for IHTT No VF or hand advantage in either group	No reliable estimate of IHTT obtained in Sz or Cs. RHd response poor in Sz
Schwartz et al (1984)	10 Sz Chronic (M) DSM-III & Feighner	9 normals	Temporal discrimination of 2 dots (SOA) Across & within VFs (vocal)	LH↑, Sz & Cs Slower IHTT in Sz vs Cs	Sz responses slower throughout; No difference for bi vs uni-lateral, Sz & Cs
George & Neufeld (1987)	14 para Sz 14 nonpara (M) RDC	14 mixed psych in-pts 14 students 14 normals	Matching: target (face/word) followed by stimulus in VF (manual RT/accuracy)	LH↑ on words RH↑ for faces, Sz and Cs; Sz ↓ generally vs Cs	Nonpara Sz most ↓ affected by increased cognitive load. Effect different in R & L Vfs
Merriam & Gardner (1987)	16 Sz Chronic (M) DSM-III	16 normals	Matching: bilateral word/dots followed by same in R or L VF (manual RT/accuracy)	Poorer matching X Vfs, Sz & Cs Sz slow & less accurate than Cs	LH↑ for word & dot matching accuracy in Sz & Cs. Within VF matches, Sz ↓ vs Cs
David (1987)	22 Sz (M) RDC	14 affectives 16 normals	Naming of colours in R or L VF. Matching Across & within VFs (vocal - accuracy)	Poor LVFcolour naming Sz vs Cs. Sz↓ colour matching X Vfs	R & L VF matching and RVF colour naming not ↓ Sz vs Cs. suggests ↓ callosal transmission

Table 1.1. Summary of divided visual field studies of schizophrenic patients (cont).

Investigators	*Subjects (Medication) Diag criteria*	*Controls*	*Experimental Task (dependant var - response mode)*	*Results*	*Comment*
Eccleston & Eccleston (1988)	36 Sz DSM-III (?M)	15 Normals	Dot & syllable localisation (accuracy)	↓RH for both stimuli in Sz	Main deficit was loss of normal lateralisation
Posner et al (1988)	12 Sz (9 M, 3 non-M) DSM-III	30 normals	Detection of star valid/invalid cues (manual RT)	↓RT for target in LH when not cued	Failure to make use of valid cues in RH. Second expt showed↑ bias to non-language cues (arrows)
Schwartz et al (1990)	19 Sz (M) DSM-IIIR	6 schizoaffs 12 depressives 11 normals	Gratings of low/high spatial freq. R, L & foveal (detection of dis-continuity between successive gratings	↑ visible persistence in Sz & schizoaffects	No asymmetries in any group. Sz more susceptible to high spatial freqs
Min & Oh (1992)	33 Sz (drug free for 5 days) DSM-IIIR	33 affectives 33 normals	Matching Hangul words in R/L VF with central target (manual RT/accuracy)	↓LH RT in Sz ↓RH RT in Affs ↑RH errors in affs	No LH↑ in normals Sz RT > aff > Cs

Key to abbreviations:

Sz: schizophrenics
VF: visual field
RDC: Research Diagnostic Criteria (1975)
(M): medication
X Matching: matching across visual fields
RH: right hemisphere
nonpara: non paranoid schizophrenics
para: paranoid schizophrenics
Cs: controls
pts: patients
DSM-III: Diagnostic and statistical manual
IHTT: interhemispheric transmission time

RT: reaction time
Feighner: Feighner diagnostic criteria (1972)
PSE: Present State Examination (1974)
LH: left hemisphere
SOA: stimulus onset asynchrony
Rhd: right hand
↑: superiority
↓: impairment
Affs: affectives
psych: psychiatric
Schizoaffects: schizoaffectives
STM: short term memory

RESULTS

1.5 Clinical Variables

Of the 20 studies reviewed (see Table 1.1), only 9 included a psychiatric control group. Explicit, standardised diagnostic criteria were used in 15 studies. Handedness and sex were usually controlled for. Few studies attempted to match individuals on an estimate of IQ in addition to a record of length of schooling. Of those that did, 2 were able to match the schizophrenics with the normal controls (George & Neufeld, 1987; David, 1987) against 2 that did not (Colbourn & Lishman, 1979; Magaro & Page, 1983). Only 2 projects recruited unmedicated patients (Eaton et al., 1979; Connolly et al., 1983) the results of which do not point to dramatic drug-induced lateralised differences of cerebral function as they are consistent with similar studies of medicated patients.

1.6 Left Hemisphere Abnormality

The results of DVF studies in schizophrenia have been interpreted as showing hemisphere overactivation, underactivation and/or dysfunction; altered or reduced asymmetry, lack of integration or impaired interhemispheric transfer. Sometimes a superiority in one hemisphere is interpreted as abnormal overactivation in that hemisphere or an abnormal underactivation of the opposite hemisphere. Such explanations may suit almost any hypothesis and are therefore irrefutable. At this stage in our understanding of models of hemisphere interaction, it is perhaps wiser to resist unbridled speculation on the basis of equivocal data and instead confine ourselves to modest statements about the nature of the abnormality we believe we have uncovered.

An LH abnormality in the broadest sense has been found in the majority of DVF studies to date (see Table 1.1). This has manifested in: 1) impaired RVF matching of letters (Beaumont & Dimond, 1973; Magaro & Page, 1983); 2) impaired RVF identification of letters, in schizophrenics and manic depressives (Connolly et al., 1979) and unmedicated schizophrenics (Connolly et al., 1983); 3) impaired RVF identification of 3-letter syllables, arranged vertically (Gur, 1978), and 4-letter nouns in European (Colbourn & Lishman, 1979) and Korean scripts (Min & Oh, 1992). Posner et al., (1988) described slower RT to targets in the RVF when preceded by an invalid visual cue or no cue at all, similar to the performance of patients with known LH damage.

However, the remaining studies which claim to show an RH abnormality or no lateralised deficit, also show generally poor performance on tasks including those presented to the RVF/LH. The Posner study (Posner et al., 1988) is open to the interpretation that the most striking deficit is a failure of the schizophrenics, especially those unmedicated, to benefit from the valid cue when presentation was to the LVF/RH. Also, in a subsequent experiment, a sub-group of the schizophrenics were more susceptible to verbal direction cues (i.e., *left* or *right*) than symbolic cues (arrows), which the authors interpret as further evidence for LH dysfunction because RT was slower with verbal cues. Equally, the failure of the arrows to influence performance could be taken as evidence for RH dysfunction. In other words, the LH abnormality has not been an isolated finding. The pattern of asymmetry was the same in both schizophrenics and controls in Clooney & Murray's study, (1977), and schizophrenics showed the anticipated LH advantage for verbal tests in studies by Pic'l et al., (1979), George & Neufeld, (1987) and Merriam & Gardner, (1987). In an effort to be more specific about the nature of the LH abnormality workers have examined the accuracy and/or speed of processing of "non-verbal" stimuli presented to the RVF/LH. There is a hint that RVF/LH performance on non-verbal tasks may be less impaired than on verbal tasks (Pic'l et al., 1979; Connolly et al., 1979; Connolly et al., 1983; Gur, 1978; Eaton et al., 1979). Connolly et al., (1979) argue that this indicates intact RH along with CC functioning, in that spatial percepts must be transferred to the RH for processing. Given the dimensional nature of hemisphere asymmetries already mentioned (Bradshaw & Nettleton, 1981) relative sparing of LH non-verbal processing is an equally plausible explanation. Hillsberg (1979) found an RVF/LH deficit in a non-verbal matching task which is somewhat contradictory, but her schizophrenic group were considerably slower than controls overall, so that this plus the small sample size raises the possibility of a Type II error.

Failure to find an expected hemisphere advantage in normal controls has undermined the basic assumptions of many studies since the presence of just such an asymmetry or its opposite in the patient group is almost impossible to interpret. In 3 studies, the "lexical" task revealed only minimal or absent asymmetry in normal subjects (Connolly et al., 1979; Connolly et al., 1983; Magaro & Page, 1983; Min & Oh, 1992), in this case LH superiority, and in other studies, an RH advantage for shapes (Colbourn & Lishman, 1979) and faces (Magaro & Page, 1983) was not elicited in controls. Merriam & Gardner (1987) in an across VF matching paradigm found an LH advantage for both words and dots, the latter being contrary to prediction. One reason for the inconsistency in determining lateral advantages may be that the "verbal" and "non-verbal" tasks may differ considerably in difficulty (see Gur, 1978; Connolly et al., 1979) as discussed earlier.

In summary there is support for a left sided intrahemispheric abnormality in most schizophrenics but further comparisons with psychiatric controls and more careful matching of tasks on level of difficulty is required before definitive statements can be made.

1.7 Right Hemisphere Abnormality

A degree of impairment in the processing of stimuli presented to the LVF/RH is shown in the majority of DVF studies though, as in the case of RVF/LH stimuli, this has been a reflection of generalised deficit (see Table 1.1). Three studies have found RH abnormalities to be more significant than those pertaining to the LH. Pic'l et al., (1979) and Eccleston and Eccleston (1988), demonstrated poor RH performance on a dot enumeration experiment in at least some schizophrenics, which was in contrast to LH performance on a verbal task, which may also have been impaired. Schweitzer (1982), using a complicated design which consisted of a single stimulus (shape or word) followed at differing intervals by an additional stimulus for matching, found that schizophrenics' RVF/LH accuracy approximated that of a normal control group whereas the patients' performance on shape matching was impaired. Finally, Schwartz et al (1990) found generalised slowing in schizophrenic and schizoaffective patients in a test which required them to decide whether there was a time gap between the presentation of linear gratings. There were no hemisphere differences and furthermore, the expected RH superiority for low spatial frequencies was not seen in any of the groups including normals.

Some authors (e.g. Gur, 1978; Connolly et al., 1983; Magaro & Page, 1983) have stressed the relatively preserved RH superiority for spatial tasks although it must be remembered that Gur (1978) showed the stimuli for a longer duration to schizophrenic subjects compared to controls and Connolly et al., (1983) subtracted "response time" from "processing time" which exaggerated the similarity between patients and controls.

A combination of right and left hemisphere dysfunction, or an imbalance between the two sides of the brain, forms the basis of theories explaining many of the typically schizophrenic features described by Bleuler (1911) including thought disorder and emotional disturbance (see Cutting, 1985; Gur, 1979).

1.8 Corpus Callosum Abnormality

Experimental designs which present visual stimuli to both Vfs simultaneously and require the subject to make a same-different judgement depend on a degree of cooperation between the cerebral hemispheres and ipso facto communication between them (see Table 1.1). Beaumont & Dimond (1973) used this paradigm in their original study and found that the matching of shapes and letters was performed significantly more poorly across Vfs than within them, though within VF matching was also defective. This mixed picture of less accurate matching within and across Vfs was also found in other studies (Clooney & Murray, 1977; Eaton et al., 1979; Hillsberg, 1979; Magaro & Page, 1983). Merriam & Gardner (1987) modified the matching procedure by beginning with bilateral stimuli followed 2 seconds later by a single lateralised stimulus, with the subject asked to decide whether the latter matched the former in either the right or left VF. Matches where the single stimulus was the same as the one of the pair in the opposite VF were more difficult for all subjects and so the schizophrenics' impairment on this task could not have been due to a "differential deficit". In contrast, a colour matching task (David, 1987) revealed superior "across" as opposed to "within" VF matching in affective and normal controls, compared to schizophrenics who found the "across" matching more difficult.

From the studies available, there appears to be a slight trend towards cross matching of non-verbal stimuli to be most impaired in schizophrenia (Eaton, et al., 1979; Hillsberg, 1979; David, 1987) with one study showing this tendency in paranoid schizophrenics only (Magaro & Page, 1983). These authors also found a cross matching deficit for verbal stimuli in nonparanoid schizophrenics which they attributed to poor LH verbal functioning rather than a CC abnormality.

Interhemispheric transmission time (IHTT) has been estimated by subtracting manual reaction time (RT) obtained when stimulus and response involve different hemispheres (e.g. RVF/left hand) (crossed), from RT following stimulus and response in the same hemisphere (e.g. RVF/right hand) (uncrossed) (Bashore, 1981). Using this method, Connolly et al., (1983) failed to demonstrate increased IHTT in schizophrenics. As a group, they produced a faster RT for the hand ipsilateral to the VF of stimulation compared to the contralateral hand by approximately the same margin as controls (≈4 msec). However as individuals, this was not a consistent finding pointing to unreliability of the method and the confounding effect of (in this study) generally slow left hand responses. Shelton & Knight (1984) using a more simple visual stimulus did not show prolonged IHTT in their schizophrenic sample. Again this conclusion is suspect since the expected IHTT delay was not found in the normal group, and considerably slower right hand responses regardless of VF in the schizophrenics, may have obliterated the IHTT component of the total RT.

Response hand may be employed as an independent variable in laterality research with central presentations of visual stimuli. Simple studies of RT for different hands provide an indirect measure of hemisphere functioning. Fishman et al., (1991) compared simple RT to a central light flash and RT on the same task but with a concurrent short-term auditory memory load, in 20 schizophrenics with 26 affectively ill patients. They found no right-left differences. Psychotic symptom scores negatively correlated with left dual-task RT and positively with right dual-task RT. This might be interpreted as showing LH hyperfunction and RH hypofunction, a pattern suggested by Cutting (1990).

A novel procedure was utilised to measure IHTT in schizophrenia by Schwartz et al., (1984) in which 2 dots were flashed in either one or both Vfs with a small delay between them. The authors marshal previous work which suggests that the LH is responsible for temporal analysis and detection of successive stimuli. Therefore, information from the LVF/RH must be transferred via the CC to the LH for analysis. By delaying the RVF/LH stimulus until the subject reports apparent simultaneity, a measure of IHTT is obtained. The authors found that the LH advantage for temporal sequential analysis was present in both schizophrenics and normal controls, though the schizophrenics' response time was slower overall, but that IHTT was significantly longer (10 msec vs 4 msec) in the patient group. This is another example of a non-verbal stimulus revealing a CC defect. No study published to date has attempted to discover qualitative disturbances in callosal transfer and how these might relate to schizophrenic symptoms (for reviews see Doty, 1989; Coger & Serafetinides, 1990).

1.9 Other Studies

A more sophisticated approach to specifying the nature of information processing dysfunction in schizophrenia using DVF techniques has been attempted (Clooney & Murray, 1977; Pic'l et al., 1979; George & Neufeld, 1987). By increasing the size of array of letters, Clooney & Murray, (1977) found that paranoid schizophrenics' RT increased (for "same" judgements only). This was interpreted as reflecting a reliance on LH serial processing as opposed to RH parallel processing. Increasing the display size (number of dots) seemed to impair paranoid schizophrenics performance more than non-paranoids (as classified by the Maine Scale (Magaro et al., 1981)) and this too was said to indicate an inappropriate reliance on serial processing by the paranoids. Since the non-paranoids' performance was less influenced by the size of the array, the authors proposed that this indicated parallel processing. A more parsimonious explanation would be that the non-paranoids, who were the most impaired sub-group, were performing at ceiling even with low cognitive loads and hence their performance could hardly get worse. George & Neufeld (1987) increased the cognitive load by introducing 4 levels of complexity to each of their hemisphere-specific tasks. They found that the schizophrenics, especially non-paranoids, declined in their performance as the attentional demands increased but there was no obvious pattern with respect to the differential sensitivity of the hemispheres. Exceptions to this were that non-paranoids responded significantly more slowly than paranoids only at the fourth level for RVF stimuli and displayed a marked increase in response latency at the third load level for LVF stimuli.

Research of this kind has not so far been particularly rewarding but is more likely to yield useful data than more tests showing that schizophrenics are slow and make mistakes. Longitudinal rather than cross-sectional data has led to interesting hypotheses from dichotic listening (Johnson & Crockett, 1982; Wexler, 1986) and non-lateralised visual information processing experiments (Nuechterlein & Dawson, 1984; Holzman, 1987) and there is no reason why these methods should not apply to DVF studies. Questions relating to whether the abnormalities detected are a consequence of a "trait" or "state" could be tackled by testing first degree relatives of schizophrenics as well as patients who have recovered.

1.10 CONCLUSIONS

A review of DVF studies in schizophrenia has revealed a bewildering mass of contradictory results. Many projects, none of which have exactly replicated their predecessors, each with their own methodological flaws, have contributed to an undifferentiated pool of data. Nevertheless, certain consistencies emerge:

1) Schizophrenics' performance is impaired in comparison to normal controls on tasks which present stimuli to the right or to the left visual fields.
2) Cognitive tasks presented tachistoscopically to the LH have been performed less well more often than those involving the RH, but dysfunction in both has been recorded.
3) Verbal tasks presented to the LH give rise to the largest performance decrement compared to non-verbal tasks, though both types are impaired.
4) Experiments requiring integration of stimuli presented across the VFs, which presumably relies on an efficient CC, show impairment in schizophrenics, and this is especially so for non-verbal stimuli.

What then, remains to be done in this field? First of all researchers need to refine their techniques in terms of subjects selection, matching and evaluation. Second, the test materials need a firmer grounding in terms of cerebral localisation. Third, the psychological processes contained within these tests need to be specified in terms of current information processing models. For example, rather than the test being labelled, say, "right hemisphere", it would be more informative if it could be described as a "right hemisphere imagery task". Similarly, it is insufficient to assume a non-verbal test is also a RH test. Fourth, tests of interhemispheric transfer should attempt to specify the nature of the information to be transferred, since this seems to be an important variable in studies done to date. Fifth, more attention should be paid to the functional significance of any intra- or inter-hemispheric abnormalities detected. For example, do they relate to current psychotic symptoms or persistent disabilities (see lpert et al., 1976)? Finally, the power of neuropsychological research can now be enhanced by advances in functional and structural neuroimaging techniques. Neither X-ray computerised tomography and magnetic resonance imaging (MRI), nor single photon and positron emission tomography were imaginable when the first experimental neuropsychology studies were being carried out. The author has already demonstrated tentatively, a relationship between cerebral atrophy and tests of callosal function as well as characteristic symptoms of schizophrenia (David, 1987). It is now possible to map almost any aspect of psychological functioning onto the size and activity of specific brain areas. Nevertheless, such a combination could just as easily magnify the methodological inadequacies of the neuropsychological and imaging approaches.

This thesis describes the attempt to examine interhemispheric (corpus callosum) and intrahemispheric functioning in schizophrenia while avoiding the pitfalls evident in the foregoing review of the literature.

Tests were conceived on the basis of a contemporary understanding of the information processing differences within the cerebral hemispheres, and the nature of information transfer between them. These tests were devised and validated on normal subjects. The limitations inherent in the testing of psychiatric patients was taken into account in the design of the materials. Three tests were employed in order to examine left, right and interhemispheric or corpus callosal function. One was a non-verbal imagery test intended to show both left and right hemisphere advantages under different test instructions. The other intra-hemispheric test used chimeric faces, and reliably taps into RH functioning. The interhemispheric test, which forms the core element to the thesis, is a new version of the Stroop paradigm, designed so as to allow the measurement of semantic inhibition and facilitation across the CC. As well as preliminary studies on normals, the Stroop procedure was used on 3 cases of callosal agenesis.

The patients were diagnosed using international criteria and their psychopathology assessed using standardised rating scales. Schizophrenic subjects were compared with patients with affective disorder and also normal controls. Background variables such as IQ and education were recorded and taken into account in the analyses. In a proportion of schizophrenic patients, ventricle:brain ratio was calculated from CT scans and in a smaller sub-sample, corpus callosum dimensions were obtained from MRI scans. These structural measures were related to neuropsychological test results.

The format of this thesis is as follows. Part I (chapters 1 to 4), comprises this introduction plus the description of each of three tests given alongside its application on normal control subjects. Part II (chapters 5 to 9), describes the test results in schizophrenic patients all of whom performed on all of the neuropsychological tests, with psychiatric and normal controls for comparison. Chapter 6 also includes the relationship between two of the tests since both examine aspects of a single psychological function (namely, attention). Chapter 8 contains results on the relationship between psychological test data pertaining to interhemispheric transfer, and structural measures from MRI scanning of the corpus callosum as well as CT measures of cerebral atrophy. The summary and conclusions are given in chapter 9. An appendix is added which charts the number of subjects used in each experiment.

CHAPTER 2

CATEGORICAL-SEMANTIC AND SPATIAL-IMAGERY JUDGEMENTS OF NON-VERBAL STIMULI IN THE CEREBRAL HEMISPHERES

2.1 INTRODUCTION

A frequent preoccupation of neuropsychology has been to discover the fundamental difference between information processing in the two cerebral hemispheres. Beginning with the dominant - non-dominant and later, verbal - non-verbal, to the analytic - holistic dichotomies, the search has been for the most parsimonious division of faculties (see Bradshaw & Nettleton, 1981). Kosslyn in 1987 moved the debate forward significantly by attempting to relate the necessary properties of a useful, computational visual system to observations on human object recognition, normal and disordered. He concluded that a minimum of two distinct sub-systems exist: one for categorical representations, that is how elements are arranged topographically in relation to each other. The other sub-system operates upon dimensional characteristics, and is necessary to determine where an entity or its elements lie in terms of spatial coordinates. Kosslyn (1987) was the first to propose that these 2 operations underlie the processes of the left and right hemispheres respectively on the basis of clinical and experimental evidence.

To test this theory, Kosslyn et al., (1989) devised a series of tachistoscopic divided visual field tests using novel stimuli consisting of simple shapes or lines with adjacent dots. Groups of subjects were required to decide whether the dot was on or off the line/blob - a categorical task, or, whether the dot was near to or far from the same, a task requiring a metric computation. The experiments confirmed the cerebral laterality predictions and have been replicated using a within subjects design (Hellige & Michimata, 1989).

The purpose of the present study was to extend Kosslyn et al's findings by examining whether meaningful stimuli are processed in a similar way and whether the categorical *versus* dimensional distinction can be generalized to a broader range of cognitive operations. Cutting (1990) has recently argued that the left hemisphere (LH) is particularly adept at determining whether or not an entity belongs to a category or class, while the right hemisphere (RH) is specialized in judgements concerning individual members within a class. This view is arose from the pattern of deficits observed in brain damaged patients and might explain various psychopathological phenomena. One motivation for the current study was to develop tests which could be readily applied to psychiatric patients so that these ideas could be tested empirically.

At this point it may be instructive to retrace some of the experimental evidence which led Kosslyn to formulate his model. Early interest grew out of rather more naturalistic studies on mental imagery (see Kosslyn, 1984). The idea of an "internal psychophysics" was invoked by Moyer (1973) who found that when subjects were asked to judge, from their names, which of two animals was the larger, reaction time (RT) increased systematically by an inverse log-linear function of the estimated difference in size between them. Paivio (1975) later produced evidence in support of an imagery basis for this example of mental chronometry, including relatively faster responses to size comparisons from pictures versus words; and an interference effect with pictures but not words, when the physical size of the presented stimulus conflicted with its size in real life (e.g. a large lamp compared to a small zebra). Kosslyn et al (1977) developed this research further in a series of experiments in which size comparisons between 2 classes of items, designated "big" and "small", were made by a group of subjects, half of whom had had the opportunity to memorize the correct class of the item. Predictably, the memorization manipulation improved performance generally. However, of more note, the results showed that prior learning of the size category abolished the usual relationship between size-difference and RT, only in comparisons *between* these categories but not within them. This work was interpreted in relation to a functional model in which the question "Which is larger?" is answered by 2 systems working in parallel, one using propositional or categorical representations and the other making use of imagery to calculate dimensions. Whichever system comes up with the answer first wins the race to the output stage. The result is a flexible and efficient operation which uses all the information available in the best possible way.

The notion that memory can be encoded visually or verbally and that these have different anatomical locations, has been accepted for several years (e.g. Milner, 1971). However, there has been little interest in attempting to further separate the 2 processes described above in terms of hemisphere asymmetries (c.f. Warrington &

Taylor, (1978) for discussion on object recognition; Paivio & Te Linde, (1982)). On this theme, Farah (1984) reappraised published reports in which specific deficits in the various sub-components of mental imagery could be inferred. She concluded that the ability to generate images was the exclusive domain of the left hemisphere (though this has been challenged by Sergent, (1990a)) and this was confirmed in a test requiring the generation of lower case letters from their upper case equivalents in callosotomy patient, J.W. (Farah et al, 1985). The same subject was tested for the ability to "generate multipart images", i.e. deciding on whether an animal's ears protrude above its head, and was found to be able to do so only with his left hemisphere (Kosslyn et al, 1985). Processes involving the calling up of visual representations from memory for inspection, such as those required to decide which of two animals is the larger, could be carried out by either disconnected hemisphere (Kosslyn et al, 1985). Data from commissurotomy patient, L.B., is somewhat contradictory since his right hemisphere appears to be superior on most imagery tasks (Corballis & Sergent, 1988; Corballis & Sergent, 1989; see also Nebes, 1972) though his left hemisphere could generate images accurately (e.g. lower case letters from upper case and a clock face from a time presented digitally) but considerably more slowly than the right.

Data from normal subjects is less clearcut still (see Ehrlichman & Barrett (1983) for a review). Corballis & McLaren (1984) suggest that for normals especially, the nature of the stimulus may influence the hemisphere advantage in imagery tasks, with non-linguistic stimuli favouring the RH. This might go some way in explaining the opposite pattern of visual field advantage seen in a large sample of normal subjects who showed a LH, compared with L.B.'s substantial RH superiority on the same letter rotation test (Corballis & Sergent, 1989; see also Fischer & Pellegrino, 1988). However, generation of letter images produced a LVF/RH advantage in one study (Sergent, 1989), and the clock face task a RVF/LH advantage in another (Hatta, 1978).

Sergent (1989; 1990a) has attempted to explain some of these discrepancies on the basis of hemisphere differences concerning the psychophysical properties of the stimuli used. Another interpretation might be that, if Kosslyn's competitive parallel model operates, with the propositional route housed in the left hemisphere and the coordinate system in the right, the resultant hemisphere advantage might be less predictable than at first thought, depending as it does upon whether a given stimulus is processed faster by one system or the other, which in turn will be exquisitely sensitive to such idiosyncratic factors as familiarity, ease of image formation and cognitive style, etc (Voyer & Bryden, 1990). Indirect support for this dual route model comes from the speed/accuracy trade-off seen in L.B. (Corballis & Sergent, 1988), the more rapid increase in error rate with angle of orientation on LH compared with RH presentations in a visual rotation experiment involving shapes in normals (Jones & Anuza, 1982), and loss of the LH accuracy advantage in rotating nonsense figures compared to alphanumeric stimuli (Fischer & Pellegrino, 1988).

In view of this frustrating lack of consensus it was decided to look for cerebral asymmetries on one of the more traditional non-rotation imagery experiments in normals, namely size comparison. It was predicted that such a task would not require left hemisphere processes of defining and manipulating categorical relationships between parts of multipart images, so would *not* produce an LH advantage (after Kosslyn, 1987; Kosslyn et al, 1985), or, taking into account data from L.B. and given the use of non-linguistic stimuli, it would favour the right hemisphere. On the other hand, should the LH preference for categorical judgements involve wider aspects of cognition: the decision as to whether an entity belongs to a superordinate category, should hence produce an LH advantage (see Hatta, 1977; Wilkins & Moskovitch, 1978).

The particular categorization chosen in the present study was "living" versus "non-living". This was not arbitrary since it seems that it is a distinction which may have a strong neuropsychological basis. For example, Warrington & Shallice (1984) have found patients with bilateral brain lesions, with dissociable abilities in naming and recognising foodstuffs and animals (broadly speaking "living") and inanimate (mostly non-living) entities. The prosopagnosic patient with bilateral (right more than left) hemisphere damage described by Farah et al., (1989) also had a particular difficulty answering questions pertaining to living things using "visual semantic memory", such as, "Are the hind legs of a kangaroo larger than the front legs?"

The studies reported here used picture stimuli and required subjects to i) classify items according to living/non-living categories, and ii) carry out a size judgement - perhaps using a mental imagery routine.

2.2 EXPERIMENT 1

This experiment consisted of i) a categorical-semantic task - (living/non-living) and ii) a spatial-imagery task - (bigger/smaller). Judgements were made on standardized pictorial stimuli, presented tachistoscopically to the right or left visual field. Left and right hemisphere advantages respectively, were predicted for the two tasks.

Materials and Method

Subjects

Twenty-two normal subjects drawn from academic and ancillary staff of the Institute of Psychiatry were tested. 12 were male; all were right-handers according to Annett's classification (1970). Mean age was 34.8 years (range 26-58). IQ was estimated using the National Adult Reading Test (NART) (Nelson & O'Connell, 1978): mean IQ=118, (range 100-125).

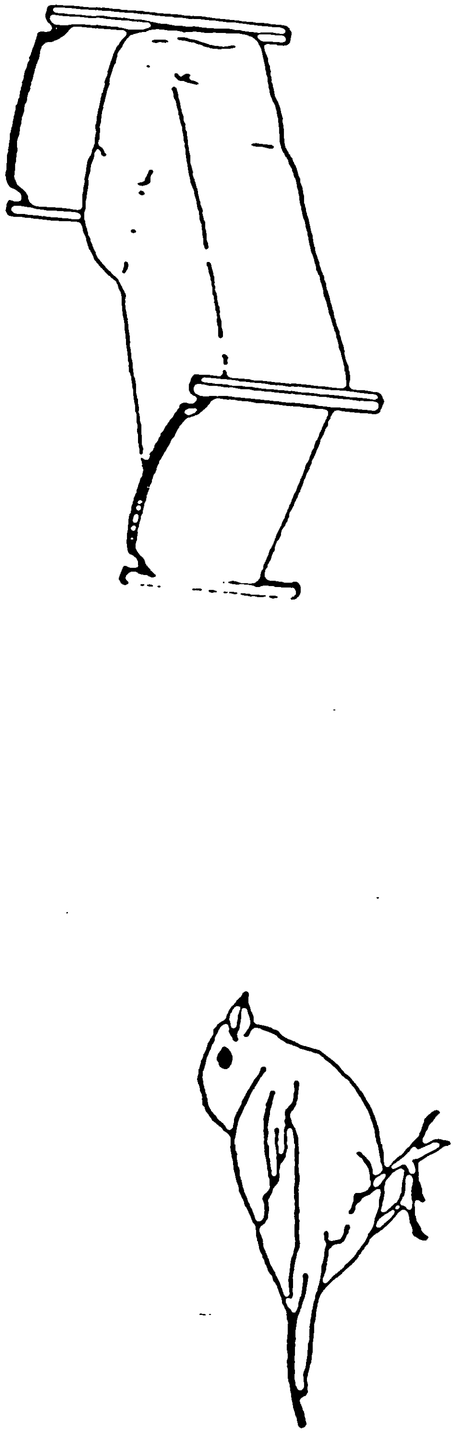
Stimuli

These consisted of 24 items from the Snodgrass and Vanderwart (1980) line drawings, standardized for familiarity and complexity. High complexity items were avoided given the brief duration of presentation to be employed. A previous study (Davidoff & Ostergaard, 1988) had shown that these pictures are eminently suitable for living/non-living judgements and decisions concerning relative size (in that instance, bigger or smaller than a trumpet) [see Figure 2.1]. A more familiar referent was chosen for comparison, namely the (domestic) cat (see Warrington, 1975). A panel of 6 colleagues classed the 24 items in free vision, as bigger or smaller than a cat and living or non-living, with unanimous agreement. The "bigger" items were (in descending order of size): mountain (Non-Living), windmill (NL), house (NL), tree, sailing boat (NL), truck (NL), camel, zebra, cow, bed (NL), lion, leg. The "smaller" items were (in descending order of size): bird, glass (NL), envelope (NL), spoon (NL), comb (NL), bulb (NL), ear, mouse, leaf, mushroom, whistle (NL), snail.

Each of the stimuli was presented to the left or right visual field, with the medial edge 3° lateral to a fixation cross. Pictures were between 2 cm and 6 cm across on the screen (approx 2° to 7°). Each stimulus was presented a total of 4 times, once to each visual field for each condition: bigger/smaller and living/non-living. Hence there were 96 presentations in all. The number of stimuli was kept low so as not to introduce the confounding effects of practice and fatigue but also with a view to using the same tests on clinical populations. The 2 conditions were done in blocks, the order of which was balanced across subjects. 8 practice stimuli were shown prior to each block.

The stimuli were presented in the form of slides for use with the back-projection tachistoscope, at a rate of approximately 1 every 2.5 seconds, as determined by the experimenter.

Figure 2.1



Pictorial Stimuli examples. Bird and bed. i) bigger/smaller than a cat?

ii) Living/non-living?

Apparatus

This consisted of a Kodak S-AV 2050 projector with custom built shutter attachment, controlled by an Electronic Developments tachistoscope timer panel. Slides were projected onto a perspex screen with a central fixation spot. Subjects were seated with their chins resting on a padded support, a fixed distance from the screen (50 cm). Responses were made by pressing one of two circular buttons separated by 15 mm, mounted on a box, between the subject and the screen. Each button was 20 mm in diameter and was supported by a spring. A weight of 270 grams was required to depress the button and produce a response. Reaction time in milliseconds was recorded and entered directly into a personal computer for analysis. The maximum time allowed for a response was 2500 msec after which an error was recorded for that stimulus. The projector beam was passed though a polaroid filter to reduce glare. A constant background illumination was maintained throughout the testing sessions.

Procedure

Subjects were instructed to look at the central fixation spot at all times. A warning tone would sound over the subject's headphones, followed 500 msec later by the visual stimulus which would remain for 120 msec. Prior to testing, subjects were given a standard set of instructions.

i) Living/non-living task: "You are going to see pictures of common things flashed up on either side of the screen. I would like you to decide as quickly and as accurately as possible whether the picture is of a living thing, such as an animal, plant, or part of the body or a non-living thing, such as a car, table etc."

ii) Size task: "You are going to see pictures of common things flashed up on either side of the screen. I would like you to decide, as quickly and as accurately as possible whether the thing in real life is bigger or smaller than a domestic cat. Imagine the thing next to a cat and decide whether it would be bigger or smaller."

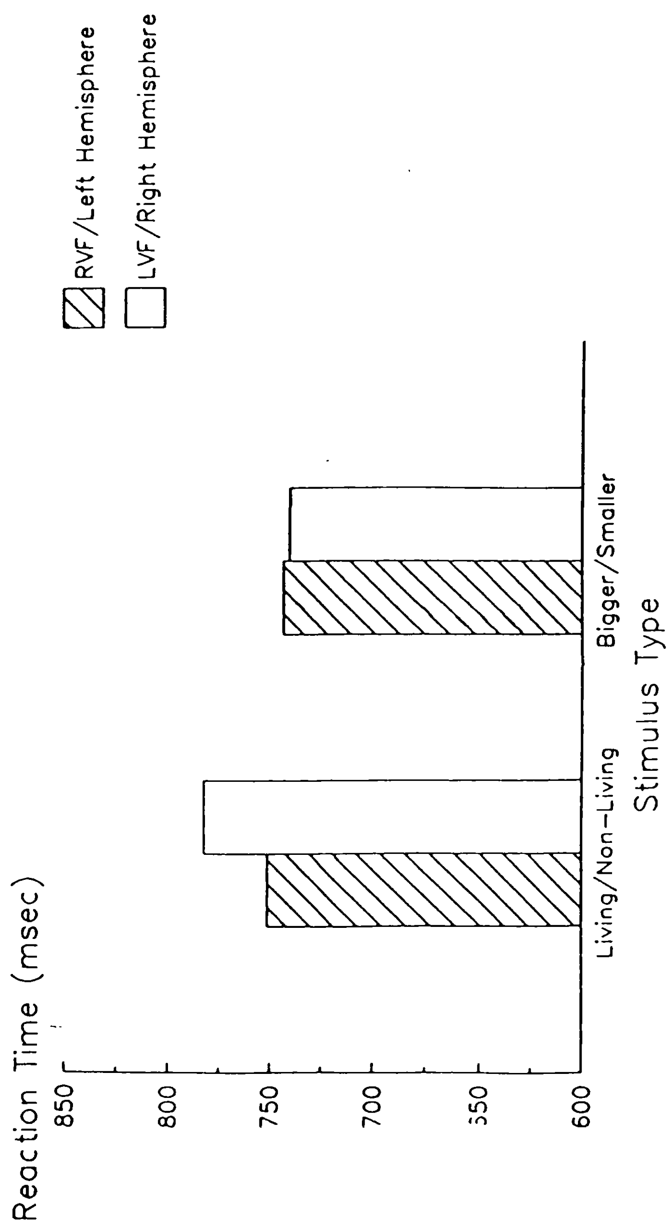
Subjects were then instructed to press one of two buttons marked appropriately, with the middle or forefinger of one hand. Response hand was changed after every 24 stimuli, the order balanced across subjects.

2.3 Results

Statistical analyses were carried out using SPSS/PC software. The data from one subject for part (ii) of the experiment were lost due to a technical error. Subject-based analysis of variance (ANOVA) was performed with reaction time (RT) as the dependent variable.

The analysis was 3-way with condition (category or size), and visual field (VF) as the within-subject variables and sex as a between-subject variable. There was no main effect for condition [$F_{1,20}=2.04$; $p=0.17$]: the mean RT for the categorization or semantic task (living/non-living) for the 22 subjects was 765.9 msec, S.D. 148 msec; and for the dimensional or imagery task (bigger/smaller than a cat), 740.7 msec, S.D. 150 msec, though the trend is for quicker RT on the dimensional task. Nor were there main effects for visual field or sex. There was a suggestion of an interaction between field and condition [$F_{2,20}=2.32$; $p=0.14$], but none between sex and the other factors. Figure 2.2 shows RTs for each visual field (VF). Analyzing RT for each condition separately employing planned comparisons using t-tests (2 tailed) does, however, suggest that there may be a LH advantage on the categorization task as predicted [751.1 msec vs 782.3 msec, $t=1.42$; $df=20$, $p<0.05$] but there is clearly no difference between the Vfs for the size judgement task [742.8 msec vs 740.1 msec, $t=0.16$; $p=0.87$].

Figure 2.2


Reaction Time (msec)
850
800
750
700
650
600
Living/Non-Living
Bigger/Smaller
Stimulus Type
RVF/Left Hemisphere
LVF/Right Hemisphere

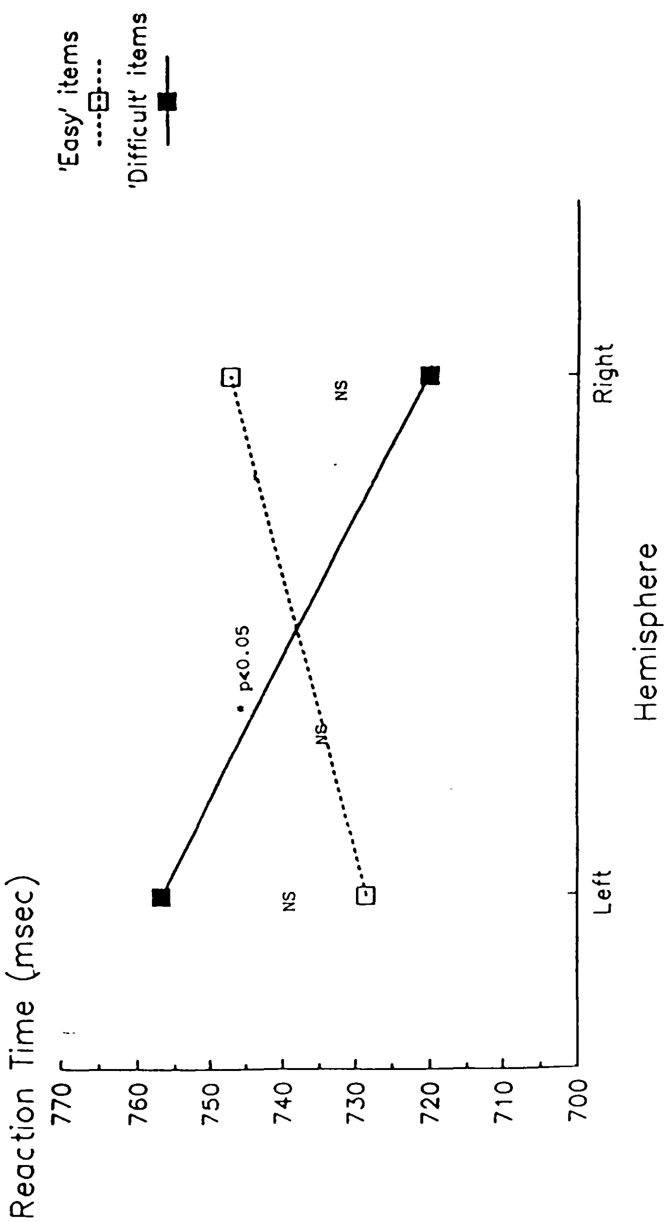
There was a weak negative correlation between the LH advantage - speed of RH minus LH presentations - on the semantic categorization task and age (Pearson's r=-0.32), and a weak positive one between LH advantage and IQ (r=0.34), suggesting that verbal intelligence but not experience of the world may be factors which might enhance performance.

While no clear hemispheric advantage emerged for the dimensional (size) task, it seemed plausible that the nature of some of the judgements such as "Is a mountain bigger (or smaller) than a cat?" or "Is a snail smaller (or bigger) than a cat?" may have been too easy, thereby calling upon readily accessible semantic information without the necessity to call upon the RH's putative imagery system. It was therefore decided to re-analyze the data comparing, on the one hand those "easy" items, whose size was either above the median for bigger items and below the median for smaller items, with, on the other hand, those "difficult" items the sizes of which fell in between the two extremes.

ANOVA, with VF and difficulty (easy/hard) as within subject measures, was calculated. There were no main effects for VF or for degree of difficulty. However, there was a significant interaction between difficulty and VF [$F_{1,19}$=4.16, p=0.05]. For easy items, RVF/LH vs LVF/RH processing speed (± S.E.) was 728.5 (33.3) msec vs 747.0 (38.4) msec [t=0.87, df=20; p=0.4]; while for difficult items, RVF/LH vs LVF/RH processing speed (± S.E.) was 756.8 (35.1) msec vs 720.7 (29.5) msec [t=2.29, df=20; p=0.03] (see Figure 2.3). In other words there was a distinct RH advantage for the more taxing size comparisons, these being processed more quickly in the RH than even the easy items.

Errors were too few to permit meaningful analyses.

Figure 2.3


Reaction Time (msec)
770
760
750
740
730
720
710
700
Left
Right
Hemisphere
NS
NS
NS
* p<0.05
'Easy' items
'Difficult' items

2.4 Discussion

The results show that despite the use of pictorial stimuli, an LH advantage can be elicited on a task requiring categorical or semantic judgements (see Seamon & Gazzaniga, 1973). An RH advantage on a task requiring judgements concerning the relative spatial dimensions of common entities proved more elusive. However, dividing the stimuli according to whether or not a correct response required a more fine-grained analysis did produce the predicted RH advantage. This is consistent with the dual route model implied by Kosslyn et al (1977), in which over-learned categorical information will override the more time-dependent calculation of spatial relationships and hence with easy size comparisons, the RH loses its advantage.

More generally, the results also show that the stimuli and apparatus are suitable for the needs of the experiment and that the two conditions are not substantially different in terms of overall difficulty. Furthermore, while the test is sensitive to stimulus variables it is reasonably free from such potential confounders as gender, age and IQ.

2.5 EXPERIMENT 2

This experiment, like the one above, consisted of i) a categorical-semantic task - (living/non-living) and ii) a spatial-imagery task - (bigger/smaller). Judgements were made on similar standardized pictorial stimuli, presented tachistoscopically to the right or left visual field, but with the "easy" items replaced by more difficult ones, i.e. those whose sizes were closer to that of the referent.

Materials and Methods

Subjects

Thirty new normal subjects drawn from academic and ancillary staff of the Institute of Psychiatry were tested. 17 were male; all were right-handers according to Annett's classification (1970). Mean age was 32.1 years (range 19-44).

IQ was estimated using the NART (Nelson & O'Connell, 1978): mean IQ=115, (range 90-125). Hence this group is younger and has a broader range of IQ than that of Expt 2.

Apparatus. As in Expt 1.

Stimuli

24 items from the Snodgrass and Vanderwart (1980) standardized line drawings as in Expt 1.

The same panel of 6 colleagues classed the 24 items, as bigger or smaller than a cat and living or non-living, with unanimous agreement. The "bigger" items were (in descending order of size): tree, sailing boat (NL), truck (NL), camel, cow, bed (NL), grand piano (NL), couch (NL), cooker (NL), zebra, lion, leg. The "smaller" items were (in descending order of size): kettle (NL), bunch of grapes, flower, bird, glass (NL), envelope (NL), spoon (NL), comb (NL), bulb (NL), ear, mouse, leaf.

The mean familiarity and visual complexity ratings (± S.D.) for these items, taken from the Snodgrass and Vanderwart norms on a 1 to 5 scale, were 3.72 (1.0) and 3.06 (0.9) respectively.

Each of the stimuli was presented to the left or right visual field, with the medial edge 3° lateral to a fixation cross. Pictures were between 2 cm and 6 cm across on the screen (approx 2° to 7°). Each stimulus was presented as in Expt 1. a total of 4 times, once to each visual field for each condition: bigger/smaller and living/non-living. Hence there were 96 presentations in all.

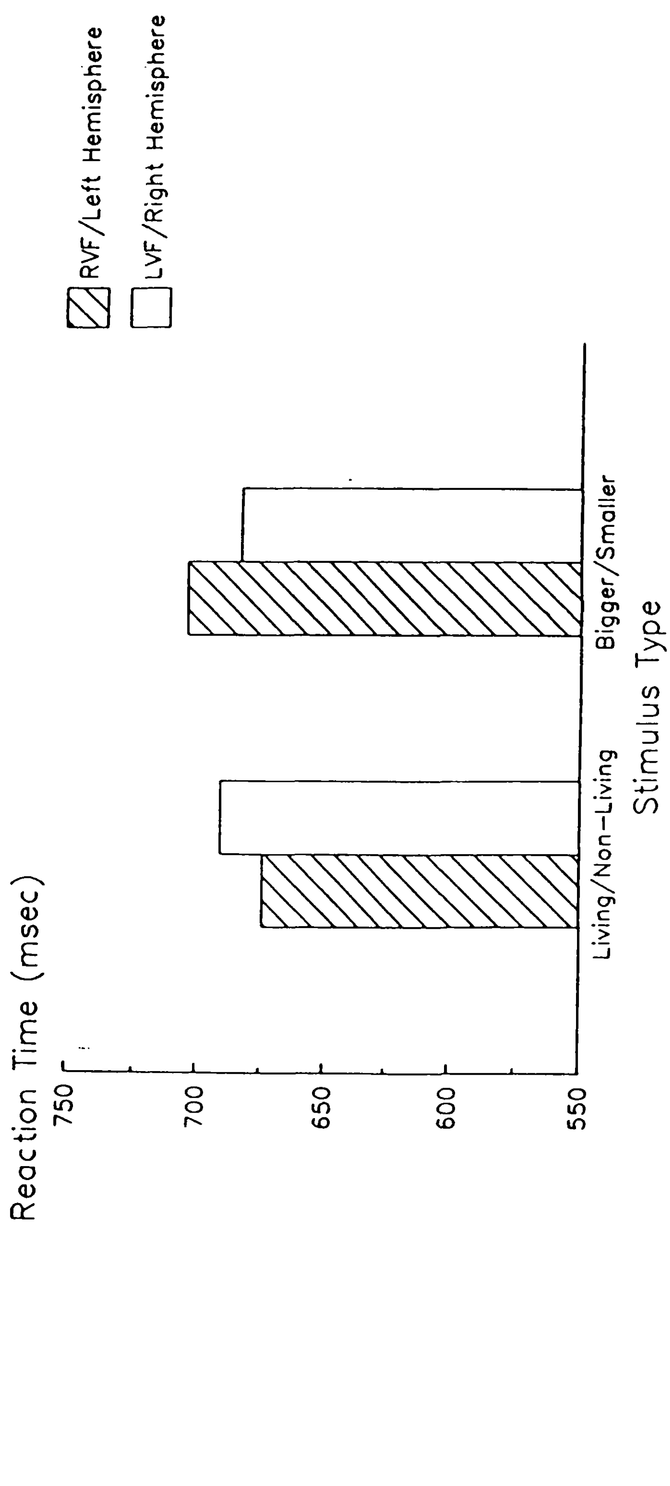
The 2 conditions were done in blocks, the order of which was balanced across subjects. 8 practice stimuli were shown prior to each block.

Procedure. As in Expt 1.

2.6 Results

Analysis of variance (ANOVA) was performed with reaction time (RT) as the dependent variable. The analysis was 3-way with condition (category or size) and visual field (VF) as the within-subject variables, and sex as a between-subject variable. There was no main effect for condition [$F_{1,28}$ =0.73; p=0.4]: the mean RT for the categorization or semantic task (living/non-living) for the 30 subjects was 682.4 msec, S.D. 112 msec; and for the dimensional or imagery task (bigger/smaller than a cat), 692.9 msec, S.D. 105 msec; though, unlike Expt 1, the dimensional task is marginally slower, suggesting that the attempt to improve the discriminating power of this condition by excluding easy size comparisons was successful. There were no main effects for visual field or sex. There was a significant interaction between field and condition [$F_{2,28}$ =10.86; p=0.003] (see Figure 2.4). Planned comparisons examining RTs in the RVF/LH vs LVF/RH for the living/non-living categorization task showed a significant LH advantage [(RT ± S.E.): 674 (19.8) msec vs 690 (21.3) msec; t=3.03; df=29, p=0.005]. Equivalent analysis for the bigger/smaller dimensional task revealed a RH advantage [703.0 (21.5) msec vs 682.4 (17.7) msec; t=2.16; df=29, p=0.04]. Furthermore, comparing the two tasks, the LH was clearly superior on the living/non-living versus the bigger/smaller task [t=2.38, p<0.05] while the RH advantage on the size versus category task did not reach significance. There were no interactions between sex and the other factors.

Figure 2.4


Reaction Time (msec)
750
700
650
600
550
Living/Non-Living
Bigger/Smaller
Stimulus Type
RVF/Left Hemisphere
LVF/Right Hemisphere

The correlation between the LH advantage on the category task and the RH advantage on the imagery task was weakly negative (Pearson's r=-0.12), suggesting at least the partial independence of the two processes. Correlations between the LH advantage on the categorization task and both age (r=0.13) and IQ (r=0.09) were negligible while those for the RH advantage on the imagery task were -0.06 and 0.29 for age and IQ respectively, suggesting that for this more demanding version, intelligence begins to exerts a slight positive influence.

Looking at accuracy revealed that the mean error rate by subject was 1.8/48 (3.75%) for the living/non-living versus 1.7/48 (3.54%) for bigger/smaller judgements; this difference was non-significant. 6 subjects were error-free on each condition. Again, overall error rates were considered too low to permit more detailed analyses.

Having established an RH advantage on the dimensional task in both experiments, provided judgements about relative size are at least minimally taxing, the next step is to confirm whether this is indeed a consequence of mental imagery. The criterion for this, as noted in the introduction, is traditionally taken as a significant correlation between RT and the spatial element, subject to manipulation by the imagery system, such as angle of rotation or, in this case, size (see Paivio, 1975).

Figure 2.5

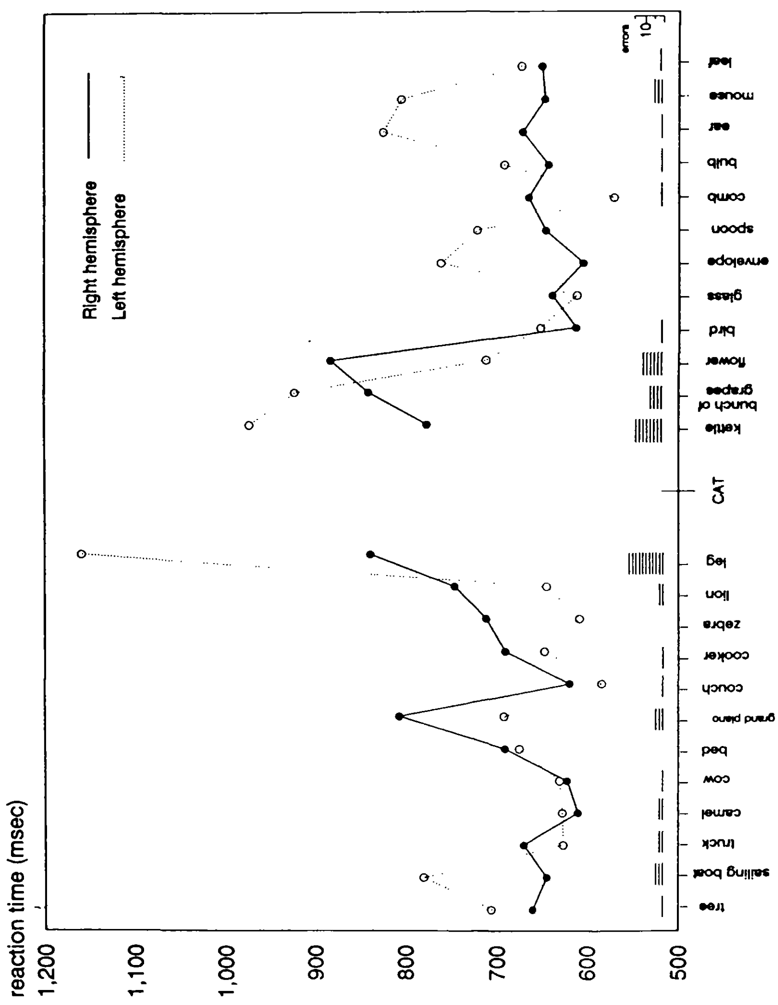

reaction time (msec)
1,200
1,100
1,000
900
800
700
600
500
Right hemisphere
Left hemisphere
errors
10
tree
sailing boat
truck
camel
cow
bed
grand piano
couch
cooker
zebra
lion
leg
CAT
kettle
bunch of grapes
flower
bird
glass
envelope
spoon
comb
bulb
ear
mouse
leaf

Figure 2.5 illustrates the relationship for each hemisphere, for the size difference between the probe item and the standard referent (a cat) along the x axis and RT along the y axis. Although the graph does not show a smooth correspondence, which is understandable given the small number of items and responses, there is a discernible relationship for LVF/RH presentations, between RT and the rank order of size of the items starting with the largest size difference, be it bigger or smaller, and ending with the item whose size was deemed nearest to that of a cat [RH: rank order correlation=0.48; p<0.05. LH: correlation=0.06; NS]. Figures 2.6 and 2.7 show the regression lines for RT by size difference for the right and left hemispheres, respectively. Similar analyses were carried out using a logarithmic transformation of RT (c.f. Moyer, 1973), which yielded an impressive correlation for RH presentations (0.61) but not for the LH (0.26). The effect of other stimulus parameters, namely familiarity and visual complexity, were also investigated. The results are shown in the table.

	SIZE (rank)	SIZE (log RT)	FAMILIAR	COMPLEX	SIZE living	:SIZE non-living
RH	0.48*	0.61***	0.01	0.28	0.61**	0.16
LH	0.06	0.26	0.02	-0.12	0.14	-0.09

Table 2.1: Correlations between Reaction Time and Stimulus Parameters for the Left and Right Hemisphere.

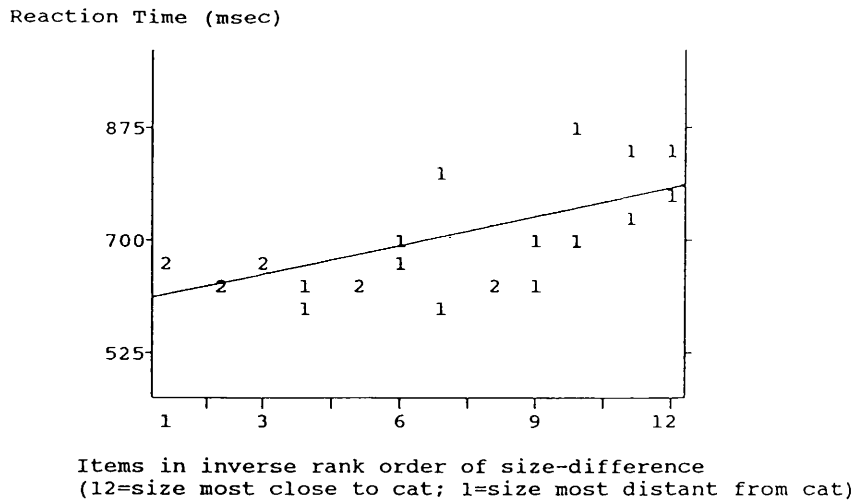
* p<0.05; ** p<0.01***; p<0.001 (1 tailed).

Note there were 24 stimuli for the size judgement task presented to each hemisphere. Of these 12 were living and 12 non-living; the significance of the correlation takes this into account.

The data show that familiarity and complexity do not influence RT, although the range of values was relatively restricted to avoid unfamiliar highly complex pictures. The effect of size was significant only for the RH but this was influenced by whether or not the item was 'living'.

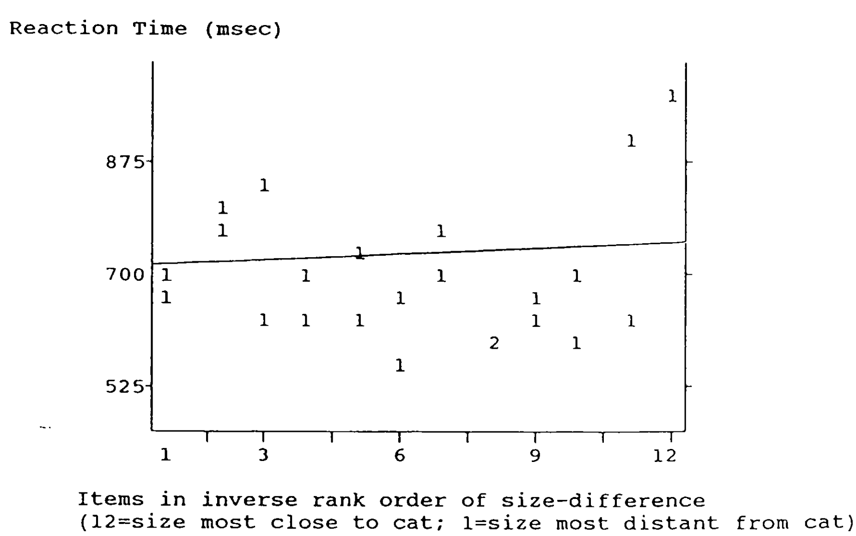
Figures 2.6 & Figure 2.7

FIGURE. 2.6 Reaction time by size for bigger and smaller items presented to the right hemisphere



Regression statistics:
Correlation 0.62: R Squared 0.38: p=0.0014
Intercept(S.E.) 599.4 (28.4) Slope(S.E.) 14.14 (3.9)

FIGURE. 2.7 Reaction time by size for bigger and smaller items presented to the left hemisphere



Regression statistics:
Correlation 0.12: R Squared 0.014: p=0.59
Intercept(S.E.) 679.3 (46.5) Slope(S.E.) 3 .59 (6.56)

2.7 Discussion

Experiment 2 confirmed on a second group of subjects that there is a reliable LH advantage on a test of semantic categorization, i.e. living or non-living. In addition, the RH advantage on the spatial test requiring the judgements of relative size was confirmed, provided stimuli are used which cannot obviously be classed as bigger or smaller than a standard, from semantic knowledge alone. The hypothesis that this latter task requires the use of visual imagery is supported by the inverse linear (and log-linear) relationship between the size difference and RT in the RH only, as shown by the correlation statistics. The fact that the majority of the variance is accounted for by the items within a single category (i.e."living things"), is consistent with Paivio's model (1975). Given that the standard referent used in the above experiment was a cat, direct comparison with another living thing, say a zebra (which shares membership of the same subordinate category, in this case 'four-legged animals') need not involve any intervening across-category processing. That it is the RH in particular which is most adept at within-category decisions is suggested by Cutting (1990), on the basis of patterns of impairment following unilateral brain damage noted in the neuropsychological literature.

Inspecting Figure 2.5 a number of features stand out. First, the item 'grand piano' appears to require more processing time than would be expected given its size in comparison to a cat. Perhaps one explanation for this is its high complexity score of 4.58 (according to normative data), the highest of any picture used. There is a suggestion that visual complexity does affect RT, though the correlation just failed to reach conventional levels of significance, as shown in the table. Secondly, the stimuli whose sizes were most close to that of a cat produce a massive increase in RT, particularly for the LH, which is mirrored by an increase in errors. This will be discussed further below.

2.8 GENERAL DISCUSSION

The results of the experiments described above, add support to the notion that a task requiring categorization of a picture stimulus according to semantic information, or knowledge about the item, is performed more efficiently by the left hemisphere. One explanation for this is that the LH has a richer semantic system than its counterpart, another would be more radical, namely that knowledge of class membership, including the classes living and non-living, simply does not exist in the RH and hence the problem information must be shunted to the LH for analysis, manifesting behaviourally in an increased RT. The usual factors which predict a LH superiority on tachistoscopic tasks, such as the use of linguistic stimuli and task difficulty, cannot be invoked as explanations, since pictorial stimuli were used and task difficulty, as assessed by RT and error rate, was matched in the corresponding task which produced a RH superiority.

The latter task made use of identical pictures and experimental procedures, but instead, required subjects to make a judgement about relative size. When the task used items in which this judgement could be reached by a variety of routes, no hemisphere difference emerged (Expt 1). However, when items which required more fine discrimination with regard to size were analysed separately, the RH advantage began to emerge. This was replicated in a separate experiment with a new and larger group of subjects. Furthermore, there appeared to be a direct relationship between RH processing speed and the size difference in the real world between the probe stimulus - a picture of a common object, plant or animal - and the stored representation of the reference item, in this case, a cat. Although the precise mental mechanisms underlying this task are hidden from direct observation, it is plausible that the stored representation of the cat was called up in the form of an internal visual image. This seems the most obvious way by which a subject could gain access to its relative dimensions. Subsequently, the probe stimulus, say a kettle, would be incorporated into the frame of the same internal display, directly from its picture without any abstract code-to-analogue stage being required (as would be necessary if the stimulus was the word KETTLE (Paivio, 1975)). Next the appropriate scaling would be carried out - calling upon visual memory. Finally the picture would be compared by "the mind's eye", or to use Kosslyn's term, the visual search controller, specialized in the analysis and calculation of spatial coordinates (Kosslyn, 1987). The last stage would be a simple two-choice motor command to press the correct button.

The observation that the stimuli depicting items whose size was most close to that of a cat produced marked increases in RT, particularly for the LH, leads to the following conjectures upon possible mechanisms. Semantic information is sufficient for the LH to perform size judgements in most instances, albeit slightly less efficiently than the RH. However with presentation to the RVF/LH of an item such as a human leg or a kettle, this knowledge is inadequate for the task. There are then a number of hypothetical courses of action open, given the time constraints imposed by the experimenter. The LH can guess on the basis of the information it has, with a correspondingly high risk of error, or it may use its own rudimentary image analyzer, or finally, it may transfer the information across the corpus callosum to the RH, at considerable cost in terms of speed and fidelity. Such a model, though speculative, appears to explain the pattern of the data obtained here. Unfortunately, the number of responses per subject was insufficient to allow further analyses of hand X field interactions which might have shed more light on this issue. It is also consistent with clinical reports of a division of "visual memory" from "verbal" or "semantic" memory across the 2 cerebral hemispheres (Milner, 1971; Wilkins & Moscovitch, 1978; Zaidel, 1987) and reports of another imagery function, visual rotation, being more disrupted by RH lesions (Ratcliff, 1979; Ditunno & Mann, 1990).

The lack of consensus as to hemisphere differences in imagery tasks in general (Sergent, 1990a; Ehrlichman & Barrett, 1983) may reflect hemispheric sensitivity to stimulus parameters (Voyer & Bryden, 1990). The use of non-linguistic yet meaningful stimuli in the studies reported here may have helped to reveal a RH superiority (Corballis & McLaren, 1984) on a task which, arguably requires a form of visual imagery. Further research using these non-rotational imagery tasks on brain damaged individuals would serve to validate or refute some of the claims with respect to cerebral organization made above. Single case studies, in which specific deficits in the functional sub-components of the processes described are evident, are necessary to illuminate further the nature of the cognitive activities currently subsumed under the label "visual imagery".

2.9 Summary

A divided visual field task was given to two groups of normal subjects to investigate hemisphere differences in the processing of standardised pictorial stimuli. There were two conditions: subjects were asked to decide whether an entity represented by a picture was living or non-living, a task involving a categorical judgement based on semantic information, or, in the second condition, whether these depictions represented entities which were bigger or smaller than a cat. This latter task, it is suggested, requires visual imagery to compare spatial dimensions. The first, categorical task produced an LH advantage in reaction time. The second, imagery task, produced an RH advantage provided the comparison involved items whose sizes were relatively close to that of a cat. Furthermore, the size difference was inversely related to reaction time, only when items were presented to the RH. The data obtained are consistent with the notion that there are at least two systems for processing visual information, one specializing in categorical and semantic distinctions related to LH functions, and the other, specialized in spatial coordinates, an aspect of visual imagery, related to the RH.

CHAPTER 3

PERCEPTUAL ASYMMETRY FOR HAPPY-SAD CHIMERIC FACES:

EFFECTS OF MOOD

3.1 INTRODUCTION

A number of recent studies have established the importance of right cerebral hemisphere (RH) specialization in the perception of faces (see, e.g. Ellis, 1983). This specialization includes recognition of faces *per se* (Hilliard, 1973; Rizzolati et al., 1971) and facial expression (Ley & Bryden, 1979; Strauss & Moscovitch, 1981). Studies on clinical populations with unilateral brain damage support the role of the RH in facial identity and affect recognition (Benton, 1980; Borod et al., 1986; Cicone et al., 1980; DeKosky et al., 1980).

Further evidence has come from studies using versions of the split-face technique devised by Wolff in 1933. Here facial composites or chimeras are made by placing together one or other side of the photograph of a face with its mirror image. Gilbert and Bakan (1973) required subjects to judge which of two composites most resembled a full face photograph. The authors found that the composite with two left halves (that is the side of the face to the viewer's left hereafter referred to as the Left Hemiface (LHF)) was judged to be more similar than the right-right composite. To test the extent to which the LHF Bias (LHFB) reflects a left visual field (LVF)/RH advantage for facial processing based on structural rather than attentional or arousal mechanisms, the authors manipulated certain test and subject variables. For instance, the same LHFB was found in Israeli subjects, accustomed to reading from right to left whereas left-handed subjects failed to show a lateral bias. Lawson (1978) using the same task confirmed these results with a larger sample but found no consistent differences between left-handers with different handwriting postures. Bennett et al., (1987) again replicated the LHF bias in perception and in addition found that the bias held when the comparison was made between the chimera and the stored representation of the whole face retrieved from memory. Also, instructions requiring different cognitive strategies including taking emotional expression into consideration, had no influence. Schwartz and Smith (1980) used chimeric faces consisting of two halves from different faces (similar to those used with split-brain patients (Levy et al., 1972)). The subjects performed a match to sample task of, chimeras presented tachistoscopically and whole face photographs in free vision. There was a strong LVF recognition accuracy superiority which was uninfluenced by auditory cues such as music, poetry and a tapping sound, suggesting that attentional mechanisms play a minimal role in the LVF/RH advantage.

Another variant of the split-face technique was introduced by Campbell (1978). She presented half-smiling half-neutral composites tachistoscopically, hence emotional expression was brought in as a new variable. Subjects had to judge which of two chimeras was the happier and they consistently chose combinations in which the smiling half was to their left. The effect was independent of the greater expressivity of the left half of the posers face. Levy and co-workers (1983a) have developed a similar task using chimeras combining open-mouthed smiles with neutral facial expressions (Heller & Levy, 1981). Dextrals perceived faces as happier when the smile was to their left and this applied regardless of whether the faces were viewed in free vision from a booklet or slides, or tachistoscopically. Sinistrals however, showed a much smaller bias with the free vision faces and no bias to either side with tachistoscopic presentation. Again, handwriting posture was not clearly related to the magnitude of perceptual bias. Levy's test has been applied extensively to normal subjects across the life span (Levine & Levy, 1986) and it appears that the LHFB persists through all ages.

The robustness and validity of the LHFB effect is supported by experiments in normal dextrals and in sinistral and clinical populations respectively. As already mentioned, several variations in stimulus materials and the manner in which they are administered have not altered the perceiver bias. Grega and colleagues (1988) systematically manipulated other test parameters in order to clarify this further. For example, they found that altering exposure duration, fixation control and by passing the image behind a central slit still did not minimise the bias, supporting the notion that it is not a visual field (VF) effect but, they conclude, though an image is scanned in both visual fields it is the internal representation of the image which is "weighted" asymmetrically. Levy and her group (1983b) proposed that the effect was due to an individual's stable pattern of hemispheric arousal and that leftward bias on the chimeric face task is related to reduced left hemisphere relative to right hemisphere arousal as reflected by a syllable-identification task.

The lack of or reduction in overall bias found repeatedly in left handers is in line with their diverse hemispheric specialization (Hécaen & Sauguet, 1971). The clinical populations studied with chimeric faces include commissurotomy patients (Levy et al., 1972) and those with focal resections (Kolb et al., 1983). Using dissimilar face chimeras, Levy et al (1972) found that the half-face available to only the disconnected RH was "chosen" in matching tasks irrespective of the responding hand. Kolb et al (1983), using the Gilbert and Bakan faces found that the usual LHFB was present in patients with left sided lesions regardless of site, but not right posterior lesions.

A combination of happy and sad faces has seldom been employed yet there are theoretical reasons why such stimuli may elicit clear cut lateral asymmetries. The dichotic listening paradigm, by providing competing inputs, seems to lead the specialized hemisphere to assert its dominance more fully. Using positive and negative emotions might also shed light on the proposed though disputed differing sensitivities of the two hemispheres for different emotions (Dimond & Farrington, 1976; Etcoff, 1984; Natale et al., 1983; Sackeim et al., 1982) [see, Campbell, 1982; Galin, 1974; Silberman & Weingertner, 1986; for reviews]. Reuter-Lorenz and Davidson (1981), by presenting two full faces simultaneously, one emotional (happy or sad) in one VF, and the other neutral in the opposite field, were able to demonstrate shorter reaction times (RT) for happy faces in the RVF and for sad faces in the LVF. This study has been replicated successfully (Reuter-Lorenz et al., 1983) but was not confirmed by a different group (Duda & Brown, 1984). In Natale et al's experiment III (1983) happy-sad chimeras were used and it was discovered that subjects rated them more positively when they appeared in the RVF but equally positive and negative in the LVF. Data are not given as to whether the half-face to the left exerted more influence on judgements than its counterpart to the right.

Another example of the use of a happy-sad combination is the schematic drawing of a face used by Jaynes (1976) (see also Roszkowski & Snelbecker, 1982). He claimed that when this drawing and its approximate mirror image are compared for degree of happiness, 80% of subjects choose the face whose smile is to their left.

The present study uses similar stimuli but differs in three important respects. First, several different faces are used which are less schematic and contain more detail so that judgements based on the presence of one feature, perhaps favouring a left hemisphere strategy (Patterson & Bradshaw, 1975) cannot be relied upon. Second, true mirror images are presented to control for asymmetries in the drawings (see Hellige, 1983). Thirdly, instead of comparing faces, subjects have to decide whether each face in turn is either happy or sad thus providing a means for examining the salience of these affects in the right and left visual spaces.

In addition, the possible interaction between the subject's mood and these judgements is examined in two ways. Initially by recording resting or "baseline" mood during testing and later by inducing depression and elation and comparing judgements in these two states. Techniques for inducing mood have been shown to influence cognition in subtle and measurable ways such as the speed of recall of pleasant and unpleasant memories (Teasdale & Fogarty, 1979). Mood induction in the laboratory has the advantage of being controlled and systematic and also allows the researcher to perform within-subject comparisons in different mood states (see Clark, 1983; for review). In one experiment, induced sadness appeared to interfere differentially with RT mediated by the RH (Ladavas et al., 1980). Neurophysiological evidence suggests that negative affect causes increased right frontal activation (Tucker et al., 1981) whereas positive affect increases activity in the left frontal cortex (Davidson et al., 1979); in both cases it is assumed that altered frontal activation modulates the arousal characteristics of the whole hemisphere (Tucker, 1988). It could therefore be hypothesized that these two mood states would exert opposite influences on the LHFB in viewing chimeric faces if the presence of the bias is related to arousal. Conversely, if it is assumed that the bias reflects structural properties of the RH, the parieto-occipital cortex in particular, a view supported by the literature, then altering mood should have no effect.

3.2 Method

Experiment 1

The purpose of the first and main experiment was to a) confirm the presence of a LHF perceptual bias with happy-sad chimeric faces; b) examine this effect in non-right handers; c) explore the influence of subjects' current mood.

Subjects

Sixty normal right handed subjects (30 male, 30 female, mean age 33.4±10.0) and eighteen non-right handers (10 male, 8 female, mean age 35.9±10.3) drawn from a wide range of hospital staff were tested. Handedness was classified according to the Annett questionnaire (1970). Subjects who used their right hands habitually for all of Annett's "primary" items (writing, throwing, striking a match; using a racket, hammer and toothbrush) were designated right-handers. None were converted left-handers. Non-right-handers included mixed- and left-handers and were so classified if they used their left hands for any of the primary items with or without "secondary" items. Subjects with a history of psychiatric or neurological disorder were excluded.

Materials

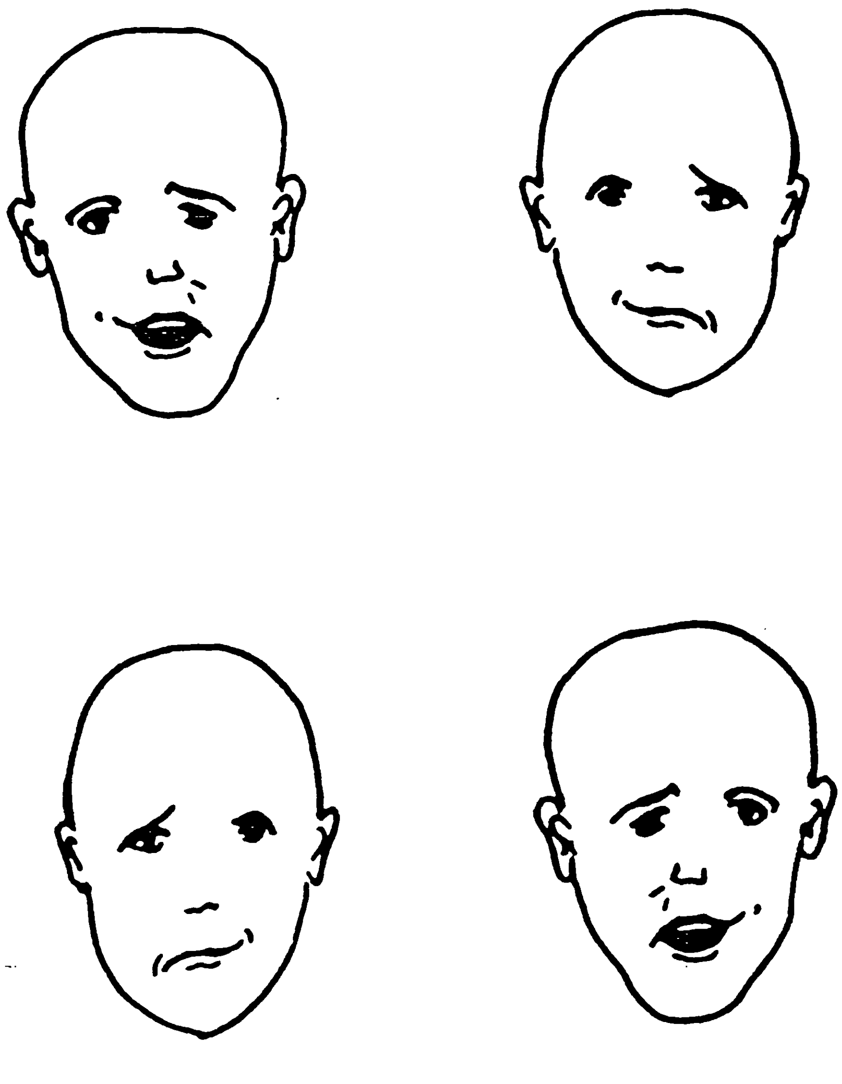
Twelve half-happy, half-sad line drawings of faces measuring approximately 5 X 4cm. were used. Faces differed in the amount of detail particularly around the mouth and eyes. Some had mouth-open, others mouth-closed expressions. Happy half-faces had an up-turned smile and a wide open eye while sad half-faces had down-turned mouths with a frown over the eye and brow (Figure 3.1). A precise mirror image was made of each.

Faces were presented in booklet form, with one face to a page. Each face was shown twice giving a total of 48 stimuli, and the order of presentation randomised.

Procedure

Subjects were told they would be looking at drawings of faces which would appear a little strange at first and were required to say whether they looked happy or sad. To answer "don't know" was not permitted in this "forced choice" design. Subjects were encouraged to report their first impression and not to spend too much time on each picture. Initially, many subjects were inclined to describe the faces as "anxious" or "quizzical" and so were directed to say whether the face was, for example "anxious in a positive or negative sense" and to respond accordingly. Rarely (less than 5% of subjects in each group), individuals felt they could not decide in which case they were instructed to close their eyes for a few seconds and on re-opening, respond immediately with whichever of the two emotions came into their mind. Testing took less than 10 minutes. Afterwards, subjects rated their mood at that moment, by marking their position on a 10 cm. visual analogue scale with "most depressed ever" at the extreme end to their left (scoring zero) and "most happy ever" to the right (scoring 100). The midpoint was not indicated on the scale.

Figure 3.1



3.3 RESULTS

Subject variables

The two groups were well matched for age and current mood (Table 3.1(a,b)).

(a) Variable	Right-handers mean (s.d) N=60	Non-right-handers mean (s.d.) N=18	*t*	
Age	33.37 (10.0)	35.94 (10.3)	1.17	NS
Mood	53.10 (14.7)	62.56 (12.7)	1.35	NS
(b)				
Left bias(%)*	20.42 (18.8)	3.25 (18.0)	3.34	P=0.001
Sad bias(%)#	17.35 (28.9)	14.58 (21.9)	0.38	NS

*(Number Left Correct N_l minus Number Right Correct N_r X 100)/48

#(Number Sad N_s minus Number Happy N_h X 100)/48

Table 3.1(a,b). Comparison between handedness groups. Mean values for right and non-right-handers. (Unpaired t-tests, 2-tailed)

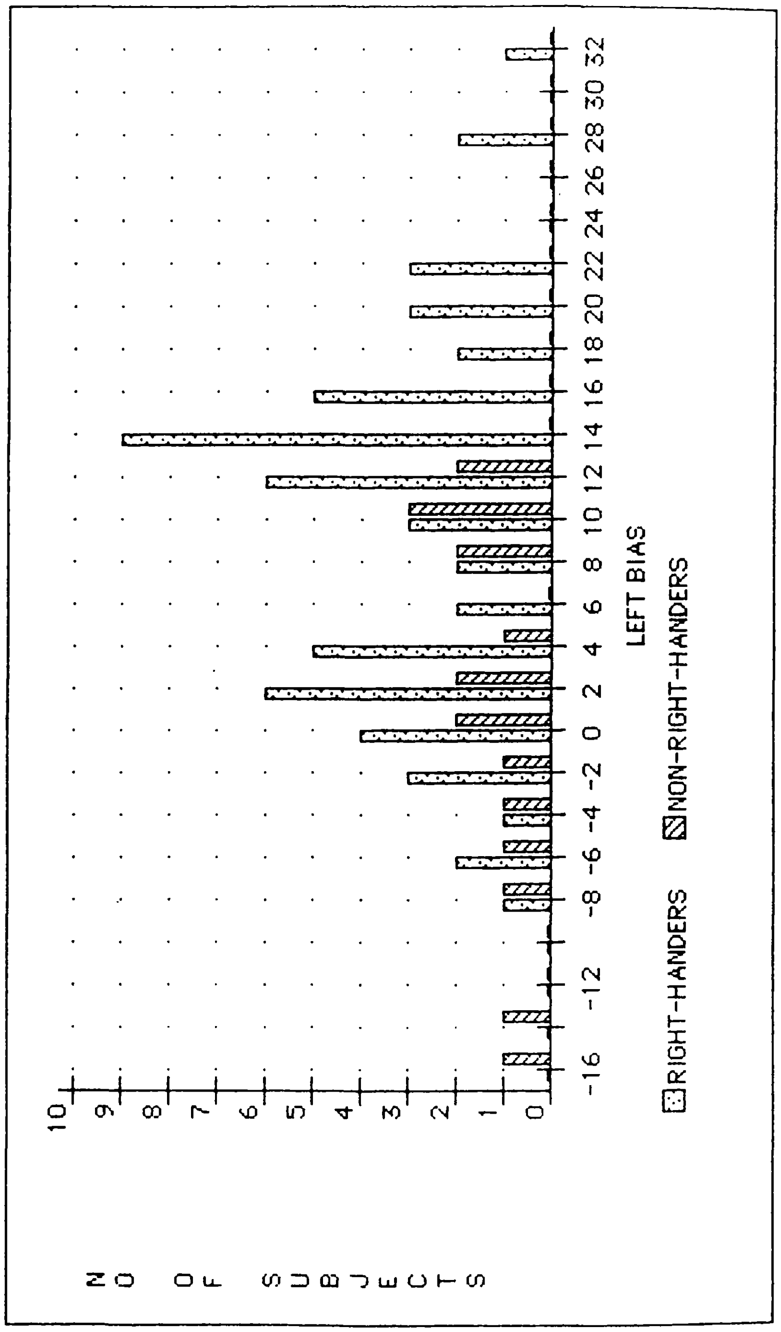
Perceiver bias

A bias towards judging emotion from the Left Hemiface can be expressed in slightly different ways. One way is score happy/sad choices as "left correct" if they coincide with the LHF of the stimulus (range 0-48, 24=no bias). Figure 3.2 shows the distribution of raw left bias scores for right and non-right handers. Another method is to subtract the total "right correct" (N_r) from "left correct" (N_l) (choices which coincide with the left Hemiface) for each subject, and divide by the number of stimuli [48]. This proportion (%) yields a "% left bias" score; 100% max left bias; -100% max right bias; 0=no bias). Results will be reported using the latter method as it conveys more simply the magnitude and direction of perceiver bias.

It soon became clear that subjects regarded the faces as sad more often than happy so this sad response bias was measured in a similar way. That is by simply recording the total number of sad" responses (0-48) or by calculating a "Sad Bias" by subtracting the number of happy (N_h) from the number of sad responses (N_s) and expressing this as a proportion.

The distribution of left bias scores for right handers is approximately normal (mean=9.80 (20.42%), S.D.=9.02 (18.79%); skewness=0.14). The mean for females was 11.60 (24.2%) and males 8.00 (16.7%) (NS). The mean from non-right handers was 1.56 (3.25%), S.D.=8.64 (18%). The difference between the observed bias and chance, i.e. zero bias, has been calculated in two ways: the binomial (sign) test (Table 3.2) which takes into account the presence, absence and direction of bias; and one sample t-test, which treats the bias as a continuous variable thus taking account of the size of the bias.

Figure 3.2



	Right-Handers	*Non-Right-Handers*
	Nº of Ss	Nº of Ss
Left Bias	NL > Nr = 49	NL > Nr = 9
Right Bias	NL < Nr = 7	NL < Nr = 7
No Bias	NL = Nr = 4	NL = Nr = 2
Total	*60*	*18*
	Z=5.48*, P<0.00001 (2-tailed)	P=0.80 (2-tailed)

*Sign test

Table 3.2. Binomial tests for Left Bias in right- and non-right-handers

The result of the one sample t-tests was for right-handers: $t(59)=8.41, P<0.0001$; non-right-handers: $t(17)=0.76$; $P\approx0.5$.

Comparisons between handedness groups

These are given in Table 3.1(b). The only significant between-group differences were in Left Bias, [$t(76)=3.34$, $P=0.001$]. Both groups exhibited an equal tendency to report sad more than happy. In each group, the Sad Bias was significantly greater than chance: right-handers, $t=4.64$, $P<0.001$; non-right-handers, $t=2.82$, $P<0.02$. An ANOVA with Left Bias as the dependent variable and Handedness and Sex as the independent variables revealed significant main effects for Handedness [$F(1,77)=11.66$, $P=0.001$] and for Sex, [$F(1,77)=5.45$, $P<0.05$], with females generally tending to show greater Left Bias. although male non-dextrals showed a mean right (negative) bias of -2.0 (-4.16%) S.D.=9.04 (18.8%), and female non-dextrals showed a small but positive bias of 6.0 (12.5%), S.D.=5.95 (12.4%), there was no significant Sex X Hand interaction overall ($P\approx0.3$). There were no other significant effects for sex nor any significant interactions with other variables.

Left-biased responses could be happy or sad. The proportion (%) of "happy correct (C_h)" i.e. the number of correct (leftward) happy responses / total happy responses, was compared with the proportion (%) "sad correct (C_s)" calculated similarly, for each handedness group separately (paired t-test, 2-tailed). right-handers, C_h (x=63.24% ±13.9); C_s (x=59.10% ±11.2) [t(59)=2.60, P<0.02)]: left handers, C_h (x=55.87% ±15.1); C_s (x=50.45% ±9.2) [t(17)=2.21, P<0.05]. This indicates that for both groups, happy choices, though less frequent than sad, were more often "correct" (left sided).

Since the basic observations have a binomial distribution (happy or sad, left or right), the variance will vary with the mean (Winer, 1971). In view of this, further comparisons were made between handedness groups, on the raw N_l (left correct) and also left Bias score following an arcsin transformation. The results in both cases remained significant at the P=0.001 level.

Correlations between age, current mood, sad and left biases were examined (Table 3.3). Age did not influence LHFB. As predicted, mood influenced subjects' choice of facial expression in obvious ways namely, the happier (greater) the mood, the greater the tendency to choose "happy" and *vice versa*. The hypothesis that resting mood would have no influence on bias towards the left side of space was upheld by the lack of correlation between Left bias and either self-rated mood or Sad Bias.

	Mood	*Left Bias*	*Sad bias*
Age	0.147	0.017	-.021
Mood	-	0.177	-.352*
Left bias	-	-	-.181

*P<0.01, 2-tailed.

Table 3.3. Correlation (Pearson's r) matrix of subject variables and test scores.

Reliability

The internal consistency and test-retest reliability of the chimeric faces test was measured amongst the dextrals in a number of ways. A fairly high correlation was found with Cronbach's $\alpha=0.60$ and the Guttman split-half coefficient $r'=0.68$. A single factor, repeated measures ANOVA was used to test the hypothesis that there was no change in the proportion of successful items over time. For dichotomous variables this generates a value for Cochran's $Q=726.97$, $P<0.0001$, supporting the hypothesis and confirming the internal consistency of the test (Winer, 1971).

Ten normal subjects, chosen at random were retested after one week. Left Bias scores were highly inter-correlated, $r=0.854$.

3.4 DISCUSSION

The results show that happy-sad chimeric face drawings elicit a strong and consistent LHFB in right-handed males and females, regardless of their current mood. Females tended to show a greater bias. This sex effect is consistent with a divided VF study by Ladavas et al., (1980) in which matching of expressive faces with a target emotion was found to be performed quicker and more accurately by females especially with LVF/RH presentations. This greater lateral asymmetry as compared to males, would be expected to give rise to a greater bias (i.e. the N_l - N_r difference). However, Safer (1981), while confirming the slight superiority of females over males especially with RVF/LH faces, found that females unlike males showed no asymmetry. Levy's group (Levy et al., 1983a) found a slightly greater left bias in females but this was not significant. These contradictory studies used different experimental designs and stimuli such that comparisons are extremely difficult. However, a tentative suggestion could be made, that the right hemisphere is more specialised for facial affect judgements in females than in males or that its "arousal" (Levy et al., 1983b) is set at a higher point.

Non-right handers as a group did not show a significant lateral bias though when analysed separately, males showed a slight right hemifacial bias (RHFB) and females a rather weak LHFB. This is compatible with data showing reduced or atypical asymmetries in left-handed males particularly (Piazza, 1980). It should be stressed that the Sex X Handedness interaction did not reach significance so that larger numbers of non-right handers would need to be studied to confirm or refute this possible sex effect. Furthermore, such a trend is not evident in LEVY's work (Heller & Levy, 1981; Levy et al., 1983a) despite the more conservative selection of pure left-handers.

There was a tendency for all subjects to make sad responses more often than happy. This trend, if taken to its extreme would be bound to reduce the LHFB score, i.e. if all responses were sad the left bias would equal zero. However, within the range of responses collected, there was only a weak, non-significant, negative correlation between the two measures. Low mood, though increasing the likelihood of a subject responding "sad" did not reduce the overriding bias towards the LHF to any appreciable degree. The effect of mood will be examined further in the next experiment.

3.5 Experiment 2

Subjects

Twelve normal right-handed volunteers (7 females, 5 males) mostly psychiatric nursing and medical staff were studied. It was anticipated that this group would respond readily to a mood induction procedure because of their empathic understanding of emotional disorders. The same exclusion criteria were applied as in the previous experiment. Mean age was 30.9 years, S.D.=10.5.

Materials

These were the same as in Experiment 1.

Procedure

This was the same as in Experiment 1 with the additional information given to subjects that they would be tested twice, in two different moods, depression and elation. The Velten mood induction procedure (Velten, 1967), the most widely used and validated technique (Clark, 1983), was then explained. Subjects were required to read silently, 20 cards containing self-referential statements for each mood such as, "I've doubted that I'm a worthwhile person" and "I'm discouraged and unhappy about myself" for depression, or "I feel cheerful and lively" and "Life is so much fun" for elation. They were encouraged to dwell on each card for 20-30 secs and to experience the emotion suggested. After each mood induction, the faces test was administered followed immediately by self-rating of mood on a visual analogue scale (as above). The measurement of the time taken to count to 10 was also noted as this has been found to correlate with both induced and endogenous depressed mood (Clark, 1983). A minimum difference of 20 points (out of 100) between the two mood states was taken as criterion for successful mood induction. Two male subjects failed to meet this and so their data were discarded. The order of moods induced was balanced across subjects.

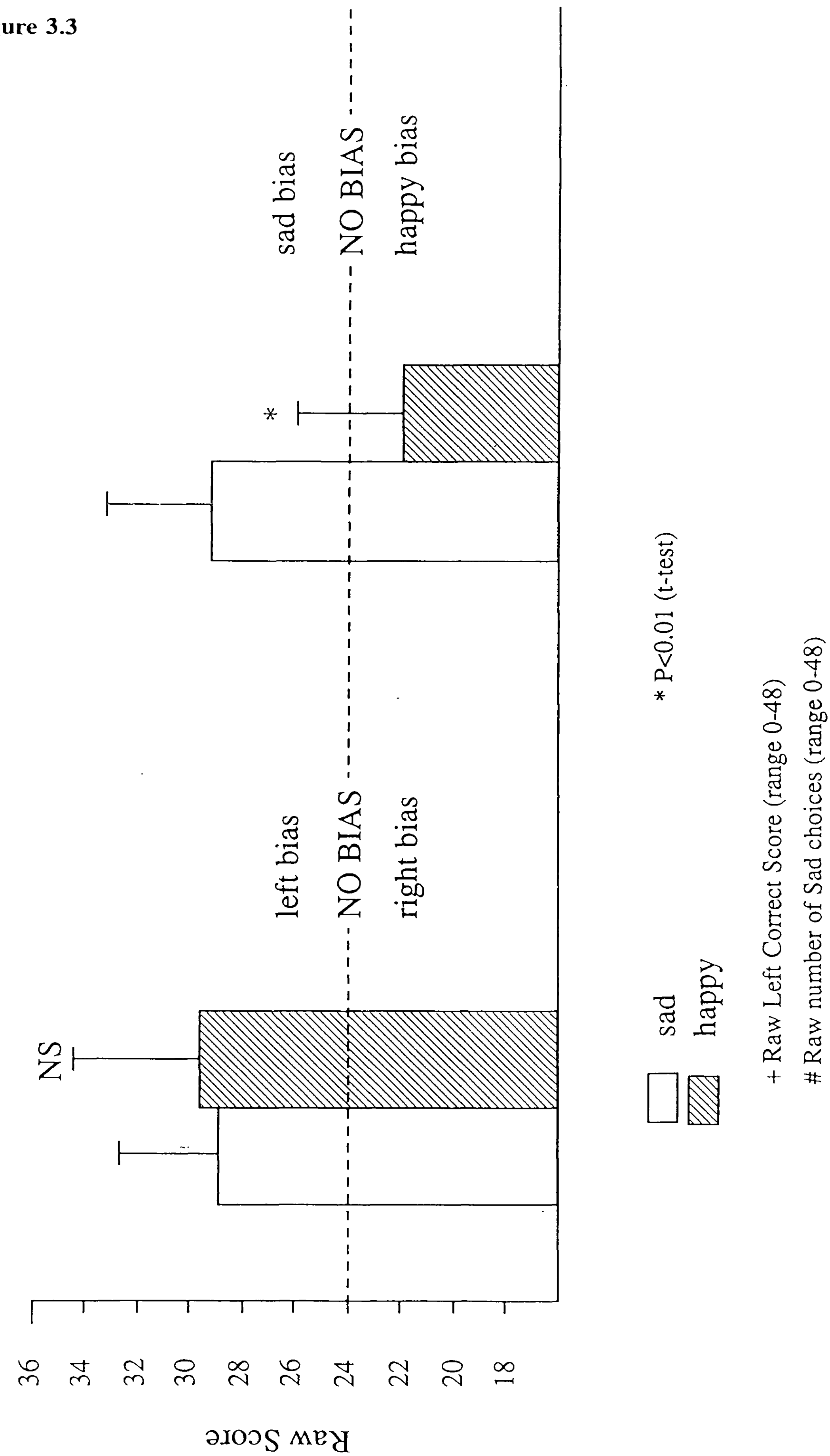
3.6 RESULTS

Self-rated mood differed on average by 26.8 points between the two conditions (mean (depressed)=44.6±12.6 vs mean (elated)=71.4±8.8, $P<0.0001$). If 50 is taken to denote neutral mood, the induced depression mood score of 44.6 just fails to differ significantly (one sample t-test: $P=0.1$). However, if the resting mood score actually obtained from the 60 right handers in experiment 1 is used (53.1) as a reference point then induced depression clearly differs from it ($t(9)=2.13$; $P<0.05$). Induced elation produced a markedly elevated mood score regardless of whether the 50 or 53.1 reference point was used ($P<0.001$). Counting time fell from mean (depressed) =6.47secs to mean (elated) =5.76, although the change was not significant ($P=0.4$).

Figure 3.3 illustrates the influence of the mood induction procedure on sad and left-correct (N_l) responses.

The procedure exerted a significant influence on sad responding with a mean (±S.D.) of 60.4±8.7(%), during depressed mood and 46.0±8.3(%), during elated mood [$t(18)=5.11$, $P<0.0001$, two-tailed]. However mean N_l was 28.9(%) ±3.8 and 29.6 (%) ±4.9, for the two moods respectively, [$t(18)=0.36$, $P=0.7$]. There were no significant changes in the proportions of sad and happy correct responses in the two mood states.

Figure 3.3


Raw Score
36
34
32
30
28
26
24
22
20
18
NS
*
left bias
NO BIAS
right bias
sad bias
NO BIAS
happy bias
sad
happy
* P<0.01 (t-test)
+ Raw Left Correct Score (range 0-48)
# Raw number of Sad choices (range 0-48)

3.7 Discussion

Experiment 2 shows that wide variations in mood induced in normal adults, especially elation, do not influence the LHFB, which remains remarkably stable. Mood did exert a major influence on the valency of affective judgement. It may be that the transparent nature of the mood induction procedure exaggerated this effect in compliant subjects but nevertheless self-rated mood and to a lesser extent counting time both support the validity of the method. No support was found for the claim that depressed mood differentially compromises RH function (Ladavas et al., 1980; Tucker, 1988). However, the induction procedure was less successful in lowering than elevating mood, so that the possibility remains that more pronounced depression would alter LHFB.

It could be contended that the verbal mood induction method by stimulating the LH, may have counteracted the activation of the RH produced by mood, though this does not seem to have been the case in other experiments (Ladavas et al., 1984; Tucker et al., 1981). It is also conceivable that a different induction procedure, such as listening to sad music, may have produced different effects. Unfortunately, music would be expected to stimulate RH processes independently of mood change (although see Schwartz & Smith, 1980) thereby introducing a confounder. Further studies using a variety of induction procedures are necessary in order to substantiate the interpretation of the results given here.

3.8 GENERAL DISCUSSION

The data presented confirm that happy-sad chimeric faces viewed in free vision, elicit a strong perceiver bias towards the LHF during judgements of facial affect by right-handers, regardless of subjects' mood. In comparison with Levy et al's research (1983b) using happy-neutral photograph chimeras the magnitude of the bias found in this study was somewhat smaller: 17% vs 29% for males and 24% vs 33% for females. Nevertheless, despite the use of the rather liberally defined non-right-handed group the difference between the two handedness groups in this study was equally striking. Levy's sinistrals, males and females, displayed LHFBs of 16% and 9.5% respectively, in contrast to the 6% for females and -2% for males (3% overall) shown in Experiment 1. It may be that sad-happy chimeras are more able to elicit atypical lateralization but such a conclusion must be tempered against the small number of non-right-handers in this study.

Current mood did not appear to alter LHFB though it did influence sad/happy choices, with lower mood increasing the Sad Bias. It could be argued that the Sad Bias tendency reflects the intrinsically lower mood of the right hemisphere (LeDoux et al., 1977; Sackeim et al., 1982) or its inclination to rate expressions more negatively (Natale et al, 1983; Reuter-Lorenz & Davidson, 1981). Although this may be so, it does not explain the unexpected finding that the proportion of happy responses which were "left correct" (C_h) that is, coincided with the expression of the LHF, was greater than the proportion of sad "left correct" responses (C_s). In other words, although happy responses were made less often, they were more often left biased. Perhaps the explanation is simply one of reliability given the "forced choice" design of the study. If a subject is unsure how to respond when confronted with a strange looking face, it appears he/she will usually answer "sad" so reducing the accuracy of those responses. In any event, it is clear that hemifaces, be they derived from photographs or drawings, elicit a perceiver bias to the left whether or not they are smiling. This finding, while not addressing directly the issue of right and left hemisphere contributions to affective valency, fails to support a specific association between the LH and positive affect.

The lack of effect on LHFB of lowered or raised mood, both spontaneous and induced, runs contrary to the study by Ladavas et al., (1984). However, it is possible that the effect is only manifest through slower RTs so would not have been detected. Measuring vocal RT and comparing left and right biased responses individually might clarify this discrepancy. Recently, Levy's test has been given to depressed patients in whom the LHFB though present appeared to be attenuated compared to normal controls (Jaeger et al., 1987). This was attributed to an alteration in RH arousal which has been demonstrated electroencephalographically in normals when their mood is negative and in clinically depressed populations (see Tucker, 1988). By way of contrast, the present study could be taken as supporting a distinction between normal and pathological mood states. Research with psychiatric patients using happy-sad chimeric faces has been undertaken to clarify this issue (see chapter 6).

3.9 Summary

Happy-sad chimeric face drawings were viewed in free vision by normal subjects. A significant and reliable perceiver bias toward the left hemiface when judging facial expression was found in right-handers whereas no consistent bias was found in non-right handers. This bias tended to be more pronounced in females. Subjects' current mood influenced their choice of facial affect but not their perceptual bias. In a further experiment, subjects were tested during induced elation and once more during induced depression. Again, though these moods increased the number of happy and sad choices respectively, the magnitude of the left hemifacial bias remained unchanged. The results are best explained by stable properties of the right hemisphere rather than arousal mechanisms. The implications of these findings are discussed in the light of the proposed hemispheric asymmetries in emotional perception and the possible lateralised effects of depressed mood on cognition.

CHAPTER 4

STROOP EFFECTS WITHIN AND BETWEEN THE CEREBRAL HEMISPHERES:

STUDIES IN NORMALS AND ACALLOSALS

4.1 INTRODUCTION

John Ridley Stroop's colour-word test has become one of the most widely used in experimental psychology, since it was invented in 1897 (Stroop, 1935; Jensen & Rohwer, 1966; MacLeod, 1991). Its use has reflected the preoccupations of the day such as the study of racial differences, intelligence, personality, and more recently, information processing, hemisphere asymmetries (Dyer, 1973a) and artificial intelligence (Cohen et al., 1990). The essence of the paradigm is the presentation of two stimuli in combination where the one to be reported - that is colour in the classical Stroop test - conflicts with the other - in this case, a colour word. The standard form of the test comprises of a colour word printed in a colour ink which is either congruent (e.g., the word RED written in red ink) or incongruent (e.g., the word RED in blue ink). Under these conditions, colour naming with the incongruent combination is consistently slower in comparison to the congruent combination. This "Stroop effect" is remarkably robust though subject to attenuation in the face of manipulations such as separating the two stimuli in time (Glaser & Glaser, 1982) and space (Kahneman & Chajczyk, 1983), and it generalises to other types of stimuli such as picture-word combinations (Glaser & Glaser, 1989).

Detailed examination of the Stroop effect has revealed at least two components: facilitation and inhibition. Facilitation refers to the speed advantage of colour naming in the congruent colour-word condition compared with a control condition such as a non-word - colour combination (Hintzman et al., 1972), a row of Xs (Dyer, 1973a) or a neutral word (Kahneman & Chajczyk, 1983). Similarly, inhibition refers to the speed disadvantage of colour naming in the incongruent, versus a neutral or control condition. The inhibition effect tends to be the slightly larger and more reliable of the two, accounting for around 60% of the combined Stroop effect (CSE) (e.g., Long & Lyman, 1987; Schmit & Davis, 1974).

The current study introduces a novel use of the Stroop effect in an effort to examine the transmission of information across the corpus callosum (see also Dyer, 1973b). In order to allow meaningful comparison, the CSE within each hemisphere and between the two hemispheres is contrasted. There has been work, using the divided visual field methodology to study the influence of hemisphere specialisation on the analysis of Stroop stimuli (Schmit & Davis, 1974). This showed that (manual) reaction time (RT) for colour naming of congruent colour-word stimuli was the same in both hemispheres whereas the incongruent stimuli produced the most slowing of RT when presented tachistoscopically to the left hemisphere (LH) (c.f. Dyer, 1973a). The analyses were complicated by a hand X field X congruence interaction (Guiard, 1981) but the overall results were interpreted as supporting the claim that the left hemisphere is pre-eminent in processing verbal information. Tsao et al., (1979) found an increase in errors to incongruent colour-word stimuli in the right visual field (RVF)/LH but not verbal RT. A series of careful studies by Hugdahl and colleagues (Hugdahl & Franzon, 1985; Franzon & Hugdahl, 1986; Franzon & Hugdahl, 1987) have taken these findings further. They have confirmed the increase in errors with RVF/LH incongruent colour-words, in male dextrals but not females or sinistrals. A corresponding increase in RT has proved more elusive and is influenced by speed-accuracy trade-offs (Franzon & Hugdahl, 1987). While the differences between male dextrals and sinistrals offers good support for the role of cerebral lateralisation in producing the LH error rates, a few inconsistencies remain. Firstly, other researchers have produced contradictory results which failed to show hemisphere asymmetries using comparable procedures (Warren & Marsh, 1978), although they found a trend for longer RTs for both congruent and incongruent colour-word combinations presented to the RH. Simon et al., (1985) found an overall LH advantage i.e., shorter RTs, for congruent *and* incongruent Stroop stimuli in both right- and left-handers, men and women. Hatta (1981) found Stroop interference for Japanese logographic characters in the RH but not for phonetic symbols in the LH. All three studies made use of manual RT as the dependent variable which may reduce the Stroop effect (Prichatt, 1968). This, in addition to other procedural differences, such as vertical versus horizontal presentation of words, and retinal eccentricity may limit direct comparison between studies. Secondly, the lack of an asymmetrical advantage favouring either hemisphere on the congruent condition has yet to be explained adequately given the fact that if a mechanism exists in one hemisphere, which renders it more susceptible to Stroop interference, the same mechanism would be expected to produce greater facilitation. So far, this has not been demonstrated (Franzon &

Hugdahl, 1986; Schmit & Davis, 1974; Simon et al., 1985). Therefore, there is still doubt as to whether apparent hemisphere differences, especially with regard to RT, have anything to do with the Stroop effect, as opposed to merely reflecting the speed of colour naming, under certain conditions, in the visual fields.

The use of Stroop interference/facilitation to examine interhemispheric transmission has received little attention apart from pioneering early work by Dyer (1973b). He described an experiment in which a colour stripe was separated from a colour word by 4 deg., straddling the mid-line. Incongruent colour words prolonged, and congruent colour words reduced vocal RT with respect to a control condition (a row of Xs). Mean interference and facilitation effects were +48 msec and -26 msec respectively. Dyer found that response times for the different visual fields were "almost identical" for both congruent and incongruent combinations giving "equivalent" combined Stroop effects (CSEs) regardless of the side on which the colour stripe was positioned. Further details are not given. Two other studies shed light on inter-hemispheric transfer. In one of a series of experiments manipulating stimulus onset asynchrony (SOA), Goolkasian (1981) presented colours at retinal eccentricities up to 7 deg., along with distracter colour words presented foveally. Facilitation effects persisted whereas interference diminished, suggesting a selective suppression of conflicting information during the processing of colour from either side. In an analogous group of experiments, Long and Lyman (1987) found a very different pattern of responses to SOA (though remarkably similar to a previous report by Glaser and Glaser, 1982), as well as to retinal eccentricity. They presented colour squares, 3 deg. lateral to the mid-line, along with a colour word at central fixation. The authors found that both inhibitory and facilitative effects persisted, on average +62 msec and -30 msec respectively, while both of these declined at SOAs outside a -100 to +100 msec window. While there was no overall hemisphere advantage, a lateral asymmetry emerged, namely, slower RTs to LVF/right hemisphere (RH) colours paired with incongruent words only. One interpretation of this finding is that the speed of RH colour naming reflects callosal transmission of the percept to the speaking LH (Geschwind & Fusillo, 1966; Levy & Trevarthen, 1981; Zihl & von Cramon, 1980), and hence is slower than LH naming (see also McKeever & Jackson,

1979) and that this difference is most manifest when there is an additional cognitive load.

Dyer's simpler methodology lends itself more readily to interpretations invoking callosal function. Additionally, the Stroop paradigm allows for the measurement of the transfer of both facilitative and inhibitory information across the callosum and whether the tract acts as a selective filter in any way. One means of examining this further, is to test subjects without a functioning corpus callosum. To my knowledge Stroop stimuli have not been used in commissurotomy cases in this way but given the obvious difficulty such patients have in matching items across the hemifields (e.g., Gazzaniga, 1970), and the evidence for hemispheric independence (Franco, 1977), the *a priori* assumption would be that Stroop effects do not occur under these circumstances. Studies of cross-integration have shown that affectively-laden (Sperry et al., 1979) and category information (Cronin-Golomb, 1990), as well crude sensory features including colour (Johnson, 1984; Sergent, 1986), are transferable from one hemisphere to the other through subcortical routes. There are also some tentative data on priming which suggest that some semantic information can be transferred between the hemispheres through nerve tracts other than the corpus callosum (Sidtis et al, 1981; Zaidel, 1983). More recent studies by Sergent (1986;1987;1990b) looking at the integration of numerical and facial identity information have extended the limit of sub-callosal transfer after commissurotomy to information that does *not* require translation into a specific verbal code. Returning to the Stroop test, clearly, it is the precise colour name which is necessary to bring about the effect so that interference/facilitation would not be expected across disconnected hemispheres.

Another approach to understanding the phenomenon of interhemispheric integration is to examine subjects with congenital absence of the corpus callosum. While such individuals do not as a rule exhibit the typical features of cerebral disconnection (Milner, 1983), and can match colours and forms presented bilaterally, they do so, somewhat less well than controls, in terms of accuracy and speed (Jeeves & Milner, 1987; Lassonde et al., 1988). This presumably reflects the limited efficiency of subcortical pathways and/or the isolated anterior commissure, present in many acallosals. One might therefore predict that while Stroop effects may be observed in such subjects with cross-field stimuli, they should be considerably less than in normal controls. Whether there is any selectivity in terms of interference versus facilitation within these pathways is not predictable on the basis of the available evidence.

The present study aimed to clarify some of these problems. First of all by comparing measures reflecting the combined Stroop effect (CSE) within the right and left visual fields of normal right-handed subjects, in an attempt to replicate the asymmetries observed by some authors. Second, to compare subjects' colour naming performance using lateralised and centrally presented Stroop stimuli, where in the latter, the two elements of the stimulus were separated across the fovea. Thirdly, the same procedures were used with 3 cases of agenesis of the corpus callosum in order the test the extent to which cross-field Stroop effects are carried by non-callosal fibres.

4.2 METHOD

Subjects

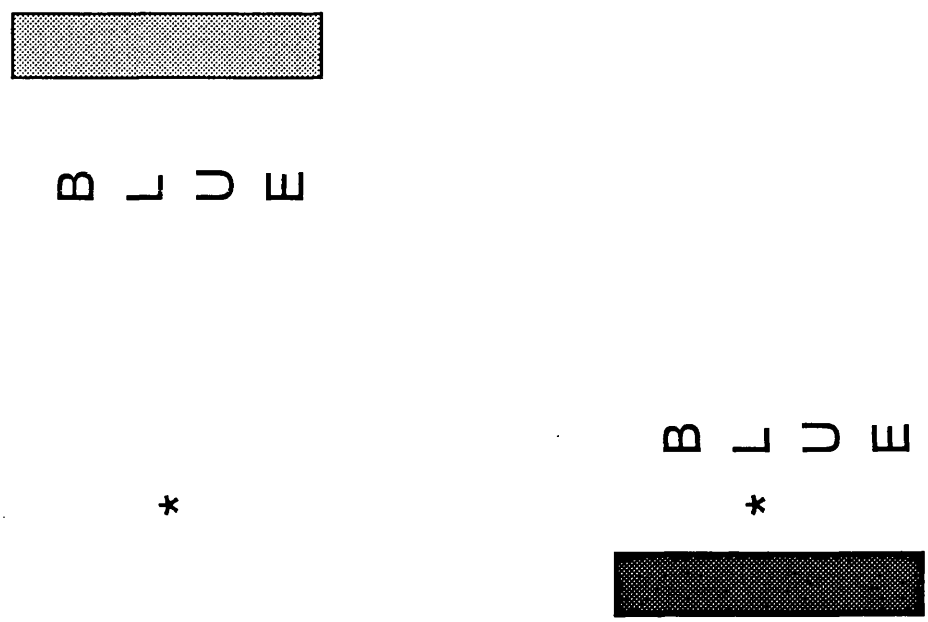
Forty-six normal subjects drawn from academic and ancillary staff of the Institute of Psychiatry were tested. 25 were male; all were right-handers according to Annett's classification (1970). Mean age was 33.2 years (S.D. 7; range 19-58). IQ was estimated using the National Adult Reading Test (NART) (Nelson & O'Connell, 1978): mean IQ=116, (S.D. 9; range 90-125). All subjects performed perfectly with the Ishihara colour blindness plates and had normal or corrected visual acuity. [16 of these were drawn from the 22 who participated in the first visual imagery experiment (no 1), chapter 2, and these were combined with the 30 subjects who participated in the second imagery experiment (chapter 2, experiment 2). 15 of the 30 subjects from experiment 2, chapter 2 also performed the tachistoscopic chimeric faces test (chapter 6). See appendix I].

Stimuli

Each of the stimuli was presented to the left or right visual field, with the medial edge 3 deg. lateral to a fixation cross, or centrally with the word on one side and the colour on the other. All stimuli consisted of a vertical colour strip approximately 1 deg. across and 3 deg. high, and a vertical colour-word in upper case letters in Helvetica Medium type, and with the same dimensions. In all stimuli, the word and colour strip were separated by 1.4 deg. In the central or "bilateral" condition, an X marked central fixation and was flanked by the word on one side and the colour on the other, separated by 1.4 deg. Three colours were used, red, blue and green; approximate Munsell numbers were 7.5R 4.5/16, 5PB 3/8 and 5G 5/10 respectively. Therefore each colour could be matched with a congruent word or one of 2 incongruent words. There were 72 stimuli in total, 24 left, 24 right and 24 central. Half were congruent and half incongruent. In each condition, 12 had the colour to the right of the word and 12 were the opposite way round. The number of stimuli was kept low so as not to introduce the confounding effects of practice and fatigue but also with a view to using the same tests on clinical populations. 8 practice stimuli were shown prior to each block. All subjects had to demonstrate their ability to read all the colour words and name all the colours, under test conditions, before proceeding to the test proper.

The stimuli were presented in the form of slides for use with a back-projection tachistoscope, at a rate of approximately 1 every 2.5 seconds, as determined by the experimenter.

Figure 4.1



Apparatus

Apparatus consisted of a Kodak S-AV 2050 projector with custom built shutter attachment, controlled by an Electronic Developments tachistoscope timer panel (as described in chapter 2, section 2). Slides were projected onto a perspex screen with a central fixation spot. Subjects were seated with their chins resting on a padded support, a fixed distance from the screen (50 cm). Responses were made by the subject's verbal report activating a voice key. Reaction time (RT) in milliseconds was recorded and entered directly into a personal computer for analysis. The maximum time allowed for a response was 2500 msec after which an error was recorded for that stimulus. The projector beam was passed though a polaroid filter to reduce glare. A constant background illumination was maintained throughout the testing sessions.

Procedure

Subjects were instructed to look at the central fixation spot at all times. A warning tone would sound over the subject's headphones, followed 500 msec later by the visual stimulus which would remain for 120 msec. Prior to testing, subjects were given a standard set of instructions, in which they were asked to name the colour as quickly and as accurately as possible.

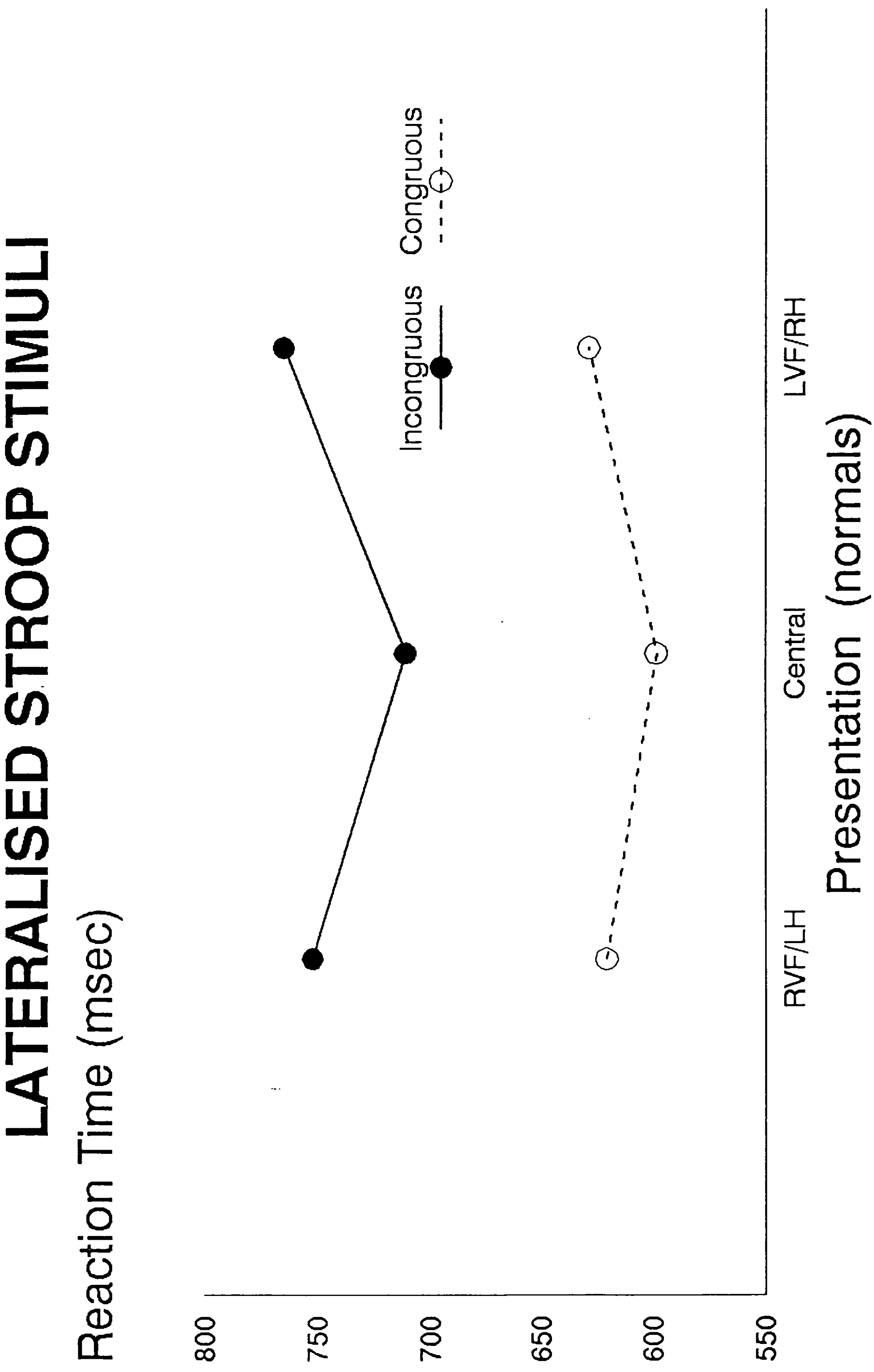
4.3 RESULTS

Results were analysed using subject-based analysis of variance (ANOVA) with RT as the dependent variable. The analyses were 3-way with congruity and visual field (right, left, central or "bilateral") as within-subject variables and sex as a between subject variable.

There were significant main effects for congruent versus incongruent colour-word combinations ($F(1,44)=349.2$, $P<0.0001$), and for visual field ($F(2,88)=43.9$, $P<0.0001$). The former is accounted for by the greater RT for incongruent stimuli (742 msec vs 616 msec) giving a combined Stroop effect (CSE) (incongruent minus congruent difference) of 126 msec; the latter, is to be anticipated in the light of studies showing a direct relationship between latency and retinal eccentricity (Eriksen &

Schultz, 1977). The field effect results from a combination of an advantage in the central condition versus the lateral conditions and a smaller RVF/LH advantage over LVF/RH presentations (see Figure 4.1). When central stimuli are excluded from the analyses, there is still of course a main effect of congruity ($P<0.0001$) as well as a main effect of field ($F(1,44)=5.28$, $P<0.05$) due to faster responses in the LH. However, a field X congruity interaction did not emerge, showing that conflicting and concurring Stroop stimuli are both responded to more quickly by the LH than the RH.

Figure 4.2


LATERALISED STROOP STIMULI
Reaction Time (msec)
800
750
700
650
600
550
Incongruous
Congruous
RVF/LH
Central
LVF/RH
Presentation (normals)

Of particular interest is the congruity X field interaction ($F(2,88)=3.96$, $P<0.02$) when all 3 positions are considered. This reflects the reduced CSE in the central versus lateral conditions and can be illustrated by comparing the CSEs in msec for left, right and central conditions, which are 135.5, 131.3 and 112.5 respectively. While left and right do not differ ($t(46)=0.42$, $P=0.7$), each side differs significantly from the central condition [left vs centre; ($t=2.8$, $P<0.01$), right vs centre: ($t=2.4$, $P<0.02$)]. Thirty of the 46 subjects had central CSEs less than or equal to their lateral CSEs ($P=0.055$, binomial test, 2-tailed). Since the central condition yields faster RTs, it is important to demonstrate that this, in itself, does not account for the reduced CSE. The Pearson correlation coefficient of mean RT with CSE was 0.16 (NS). Furthermore neither age nor IQ correlated significantly with CSE.

REACTION TIME (MSEC)

	Incongruent				*Congruent*				*All*
	LH	RH	BILAT	Total	LH	RH	BILAT	Total	
Females (N=21)	751	767	705	741	615	615	581	598	669
Males (N=25)	754	763	716	744	640	641	614	632	687
Total (N=46)	752	764	711	742	621	629	599	616	679

Table 4.1. Reaction times for colour naming of congruent and incongruent Stroop stimuli in the right and left visual fields and bilaterally/centrally, for males and females.

Sex

Results are summarised in Table 4.1. There was no main effect for sex but the sex X congruity interaction reached significance (F (1,44)=5.03, P<0.05) when all stimuli and when only lateral stimuli are analysed (F (1,44)= 5.24, P<0.05). This is explained by an overall larger Stroop effect in females. While females tended to make slightly faster responses, the mean CSE (msec) was 143 for females compared to 112 for males. Females had equivalent RTs (msec) for incongruent stimuli but appeared to benefit slightly more from congruent colour-word combinations than males. However, there were no significant sex X field (F=1.1, P=0.4) or sex X field X congruity interactions (F(2,88)=0.47, P=0.6).

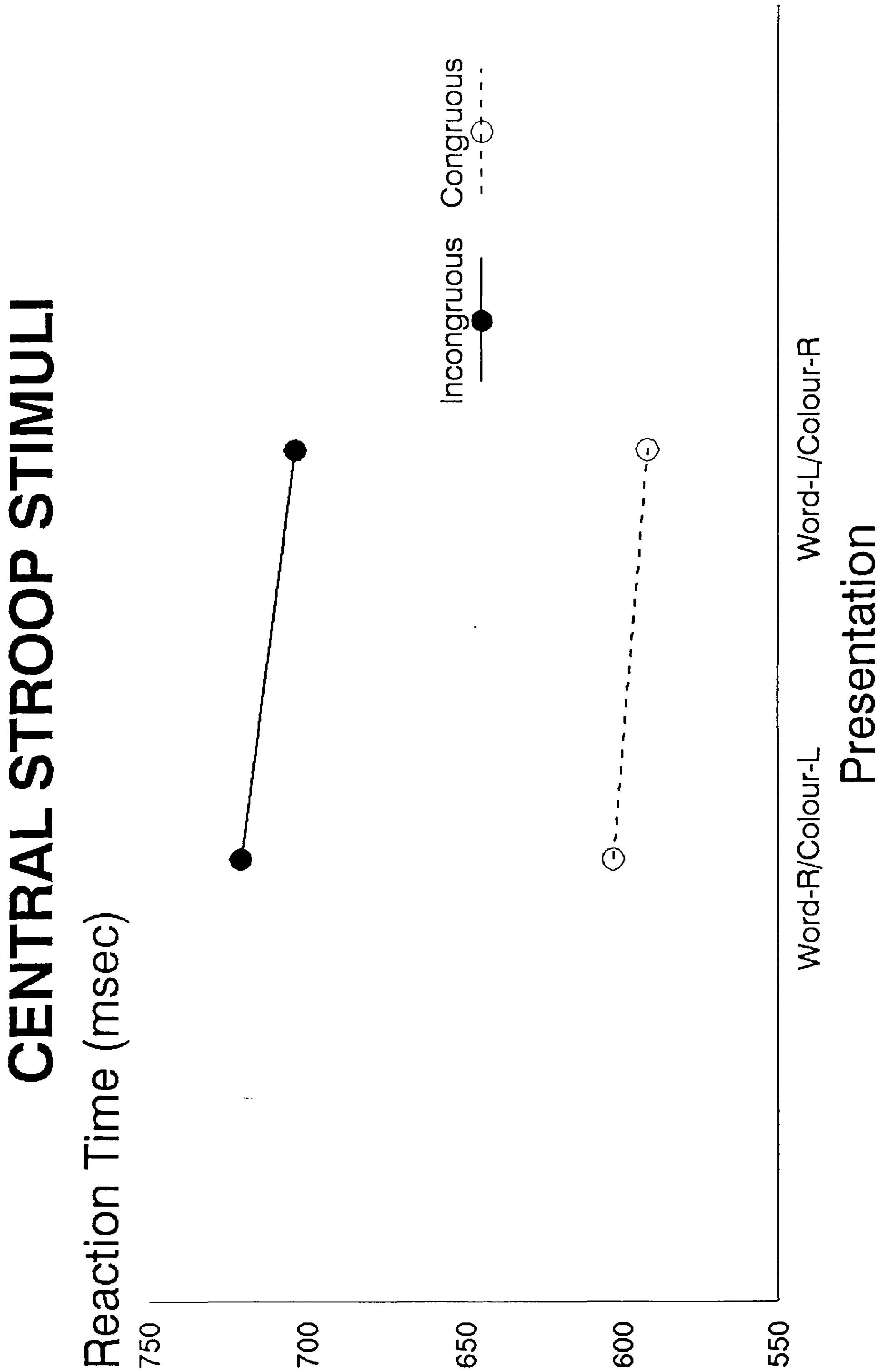
Central (Bilateral) presentations

Analyzing central presentations separately, revealed the expected main effect of congruity (F(1,44)=258.7, P<0.0001). There was also a significant effect for side, that is colour left *versus* colour right: (F(1,44)=5.0, P=0.03) with colours in the right hemifield (LH) being named more quickly (661 vs 649 msec, see Figure 4.3). There was no side by congruity interaction. Gender produced no significant effects or interactions.

Errors

Error rates were low: mean 1.8/72 (2.5%) S.D. 1.52, range 0-8%. The mean error rate on congruent trials was 0.87/36 (2.4%) compared to 1.17/36 (3.25%) on incongruent trials (P=0.07, Wilcoxon test, 2-tailed). Total error score did not correlate with RT for either congruent (r=-0.08) or incongruent (r=-0.02) stimuli, nor did it correlate with IQ or age. (IQ and RT were correlated significantly (r=0.39, P<0.01)).

Figure 4.3


CENTRAL STROOP STIMULI
Reaction Time (msec)
750
700
650
600
550
Incongruous
Congruous
Word-R/Colour-L
Word-L/Colour-R
Presentation

Test retest reliability

Five subjects were tested a second time after a 2 week interval. Correlation coefficients between RTs in the various conditions in terms of stimulus position and congruity ranged from 0.82 to 0.97. There was an overall improvement in RT of 89 msec, between the first and second test sessions.

4.4 DISCUSSION

There are 5 main conclusions to be drawn from this study: 1) Stroop effects can be reliably obtained from stimuli whose two dimensions are separated spatially. 2) There are no reliable hemisphere asymmetries in the manifestation of Stroop effects though there was a general LH advantage in this study. 3) Colour naming is faster when the target is in the RVF. This applies regardless of whether the colour is paired with a distracting or facilitating word in the same or opposite visual field. 4) Stroop effects carry over the mid-line when bilateral stimuli are used, colour to one side and colour-word to the other. 5) The size of the CSE is smaller in the central, compared with the lateral conditions. (See General Discussion 4.8).

4.5 Experiment 2 ACALLOSALS

METHOD

Subjects

Case 1. M.J. is a 14 year old boy. Pregnancy and delivery were normal and birth weight was 8lbs 5oz (3770 gms). As a baby his head circumference was noted to be abnormally large and a computerised tomography (CT) scan subsequently indicated agenesis of the corpus callosum. This has been confirmed by a recent magnetic resonance imaging (MRI) scan, which showed complete callosal agenesis with well developed longitudinally extending callosal bundles. The presence of the anterior commissure could not be confirmed. Other abnormalities included a minor degree of incomplete neuronal migration in the parietal white matter and deformity of the superior cerebellar vermis. EEG revealed no gross abnormalities and there is no history of epilepsy. Visual acuity is 6/9 in each eye.

M.J.'s intellectual level was assessed at age 11 on the Weschler Intelligence Scale for Children-Revised (WISC-R), and the following scores obtained.

Verbal Scale		Performance Scale	
Information	10	Picture Completion	6
Similarities	9	Picture Arrangement	8
Arithmetic	15	Block Design	5
Vocabulary	9	Object Assembly	1

(10 is an average subtest score; range 1-19; S.D.=0.3)

Verbal IQ	105	Performance IQ	68

Verbal intelligence is normal but there is impairment on non-verbal tasks with a constructional component. Reading and spelling were above age levels.

M.J.'s right hand (Rh) was preferred on all of Annett's primary items; writing was markedly superior with the Rh compared to the left hand (Lh). This is consistent with L hemisphere dominance for language. In tests of tactile naming he was correct with 3/7 common objects with his Lh and 4/7 with his right. Tactile cross-localisation was near perfect (22-24/24) for within-hand trials but he scored 19/24 correct on Rh to Lh trials and 14/24 on Lh to Rh trials, suggestive of some impairment of interhemispheric communication.

Case 2. S.B. is an 11:6 year old girl. Pregnancy and delivery were essentially normal, and birth weight was 7lbs 14oz (3575 gms). She has the hypermelanosis syndrome of Ito (features in her case include: horizonal and rotary nystagmus, bilateral optic nerve hypoplasia, linear hypermelanotic streaks of the forearm, facial naevus and complete agenesis of the corpus callosum, the latter confirmed by CT scan at age 9 which showed the typical appearances of callosal agenesis). Near vision is normal while distance vision is impaired. She has some problems with lateral ocular fixation.

S.B.'s intellectual level was assessed at age 9 on the WISC-R, and the following scores obtained.

Verbal Scale		Performance Scale	
Information	12	Picture Completion	11
Similarities	12	Picture Arrangement	9
Arithmetic	10	Block Design	11
Vocabulary	9	Object Assembly	11
Verbal IQ	105	Performance IQ	104

S.B.'s Rh was preferred on all of Annett's primary items. This is consistent with L hemisphere dominance for language. In tests of tactile naming she was correct with 2/8 common objects with her Lh and 3/7 with her right. Tactile cross-localisation was perfect (12/12) for within-hand trials but she scored 6/12 correct on Rh to Lh trials and 8/12 on Lh to Rh trials, suggestive of some impairment of interhemispheric communication.

Case 3. E.W. is a 31 year old woman. Pregnancy and delivery were complicated by hyperemesis. At age 3 she had a febrile convulsion and went on to have frequent seizures thereafter. She went to a school for the educationally subnormal and left without qualifications. She lives at home with her parents and younger brother and works part-time as a nursery nurse. There is no family history of note. The patient experiences seizures approximately twice yearly. These consist of premonitory dizziness followed by sudden twisting of her body to the left and loss of consciousness. On 2 or 3 occasions she has experienced left sided numbness after an attack, improving over a few days.

On examination she has slight facial asymmetry and shows slight left limb weakness. Tendon reflexes are brisker on the left and the plantar response equivocal on that side. Sensation is altered over the left side of her body. The visual fields are full to confrontation. No other physical anomalies are present. Current medication is phenytoin, 350 mg daily. Examination of the mental state is unremarkable. She is cheerful and cooperative, establishing a normal rapport though she becomes anxious when stressed by cognitive assessment. Her speech is normal in form and prosody. She spends her days working, looking after the family pets, listening to music on the radio and watching television. She does not complain of any specific difficulties with memory, orientation, recognising objects or faces or with language.

CT scan was first performed at age 29 to investigate the prolonged numbness following convulsions and this revealed agenesis of the corpus callosum and gross dysgenesis of the RH.

EEG showed intermittent 10 Hz alpha activity of modest amplitude over posterior regions. There were frequent, intermittent sharp and slow waves with a right frontal emphasis, sometimes occurring as brief trains of 12 Hz activity. This provided evidence of epileptiform activity arising form the right frontal region.

E.W.'s intellectual level was assessed on a shortened version of the Weschler Adult Intelligence Scale-Revised (WAIS-R), and the following scores obtained.

Verbal Scale		Performance Scale	
Digit Span	5	Picture Completion	4
Similarities	4	Picture Arrangement	6
Arithmetic	4	Block Design	5
Vocabulary	4		
Verbal IQ	69	Performance IQ	67

On the Warrington Recognition Memory Test, her performance was average for words (47/50) but poor for faces (23/50). On tests of recall, using the Wechsler Memory Scale, her performance was weak on the verbal part (5/24, 3/24: Logical Memory, Story A, immediate and delayed, respectively), and poor on the visual part (2/14, 0/14: Visual Reproduction, immediate and delayed, respectively. Her object naming and performance on a fragmented letters perception task were normal.

Intelligence is in the mental retardation range. Literacy skill were not selectively impaired (more detailed cognitive testing will be reported in a later publication).

E.W.'s right hand (Rh) was preferred on all of Annett's primary items; In tests of tactile naming she was correct with 4/5 common objects with her Lh and 5/5 with her right. Tactile cross-localisation was tested by asking her to retrieve objects with one hand after they had been felt by the opposite hand and her performance was good (6/6 correct) despite left hand sensory impairment. Tests of motor sequencing such as the fist-edge-palm task, were copied with great difficulty and could not be performed by the patient alone.

Tachistoscopic testing of each visual field showed that E.W. could read colour words (RVF 9/10; LVF 7/10) and name colours (RVF 8/8; LVF 7/8) relatively well but was on average around 400 msec slower with LVF items (see below).

METHOD

The same testing procedure was used for the 3 acallosals as with the normal subjects, with the exception that M.J. and S.B. were given the 72 stimuli twice and their responses averaged over 2 trials. As before, all three subjects were tested initially to confirm that they could reliably identify colours and read colour words presented tachistoscopically.

4.6 RESULTS

The results are summarised in Table 4.2. All subjects showed Stroop effects overall i.e., slower RT to incongruent stimuli (M.J. P=0.008; S.B. P=0.1; E.W. P=0.06). Error rates were low (range: 3-9%). M.J. showed little difference between his RT for congruent stimuli in the three test positions (ANOVA: P=0.9); while RT to incongruent stimuli was lowest in the central compared with the lateral positions, this interaction did not reach statistical significance (P=0.15). In other words, the trend was for CSE to be lowest with central (bilateral) presentations (Table 4.3). Although this pattern holds for all the acallosals it is complicated by lateral asymmetries. S.B. showed very little Stroop interference when colour-word combinations were presented in the RVF/LH suggesting that her LH is not competent for reading. Subject E.W.'s RH is clearly abnormal and this was reflected in impaired RH processing of simple colours and words as well as Stroop stimuli. Her data show no interference/facilitation whatsoever with RH colour-word pairs, moderate effects in the central condition while the effects in the LH were very large indeed.

REACTION TIME (MSEC)

	Incongruent				*Congruent*				*All*
	LH	RH	BILAT	Total	LH	RH	BILAT	Total	
M.J.	967	944	863	917	859	792	801	803	864
S.B.	1166	1192	1035	1120	1118	999	986	1044	1081
E.W.	1111	1308	961	1125	693	1418	766	950	1032
Total	1081	1148	953	1054	890	1070	851	932	992

Table 4.2. Reaction times for colour naming of congruent and incongruent Stroop stimuli in the right and left visual fields and bilaterally/centrally, for 3 acallosals.

	LH	RH	BILATERAL	"CALLOSAL INDEX"*
Normals (mean)	131	136	112	-21 (-34 to -8)
(n=46)				
Acallosals				
M.J.	108	152	62	-68
S.B.	48	193	49	-71.5
E.W.	418	-110	195	41

*"CALLOSAL INDEX" = CENTRAL STROOP-(LH STROOP+RH STROOP/2) with 95% confidence intervals.

Table 4.3. Combined Stroop effect (CSE) (incongruous minus congruous reaction times) for right, left and bilateral/central presentations, in normals and 3 acallosals. Also shown is the "Callosal Index", the difference between the CSE in the central position minus the mean of the CSE's in the 2 lateral positions.

Looking at the central/bilateral condition: CSEs did not significantly differ when the colour was left and the word was right for M.J. and S.B. Both showed a small (statistically insignificant) advantage of 21 msec and 20 msec respectively, when the colour was to the RVF/LH, similar to normals. E.W. showed a marked CSE for colour left - word right combinations in contrast to the opposite configuration (391 msec vs 15 msec; $t=4.65$; $P<0.01$). This can be interpreted as follows: when the colour goes to the malfunctioning RH and the word goes to the LH, E.W. makes her decision on the basis of the verbal information primarily. When the combination is congruent, it appears that verbally coded colour-word information can be transferred at speed interhemispherically, to confirm the response; when the stimuli are contradictory a more laborious process seems to take place which eventually produces the correct verbal response. Put another way, there was an advantage for "same" versus "different" responses in cross field matching. (N.B. Patient E.W. produced 5/72 errors in total all with incongruent stimuli, 3 central and 2 with RH presentation. With the central ones, she read the word rather than naming the colour).

4.7 DISCUSSION

The acallosals' performance requires cautious interpretation. M.J. gave the clearest results, in that the Stroop effects, which were of a similar order of magnitude as the normals, were approximately equal for both RH and LH trials. However, as predicted, the CSE was considerably reduced with central presentations implying that without the callosum (and in M.J.'s case, the anterior commissure), the transfer of the precise semantic information necessary for interference/facilitation of colour naming across the mid-line is impeded. The other cases' data are less easily explained since the within-hemisphere Stroop effects were unusual, in the LH for S.B. and the RH for E.W. The lack of word interference/facilitation in S.B.'s LH is not consistent with her cerebral dominance as inferred from her handedness, but may instead be related to difficulties in lateral gaze fixation. E.W. poor performance with RH stimuli is not surprising given her dysgenic RH as seen on the CT scan. If comparison is made between central and her more 'normal' RVF/LH performance, the reduced CSE when colour-word and colour strip are separated across the midline is impressive (195 vs 418; see Table 4.3).

4.8 GENERAL DISCUSSION

Normal subjects exhibited reliable Stroop effects with stimuli in which the two elements were separated in space (Kahneman & Chajczyk, 1983); indeed the size of effect (mean=126 msec) is very close to that of the previous authors (121 msec) for their central displays. It is however somewhat greater than the 74 msec found by Dyer (1973b) and presumably reflects the larger angle of separation in that study. The slightly larger effect found in females was not anticipated as it was not found in previous studies (Franzon & Hugdahl, 1987; Jensen & Rohwer, 1966; Simon et al., 1985) and will not be discussed further.

Overall RT in the present study is rather slow while error rates are low. It appears that the subjects may have concentrated on accuracy at the expense of speed. This may in part explain the second main conclusion, namely a lack of lateralised asymmetry for Stroop processing, since when Franzon and Hugdahl (1987) varied their task instructions to maximise accuracy, the asymmetry, which was clear for errors only, disappeared. However, the results can be taken as positive confirmation of two other studies (Simon et al., 1985; Warren & Marsh, 1978), neither of which showed asymmetry. Both congruent and incongruent colour-word pairs were named more quickly with LH presentations. This again is consistent with some studies (Simon et al., 1985; Warren & Marsh, 1978), but not others (Schmit & Davis, 1974; Franzon & Hugdahl, 1986; Hugdahl & Franzon, 1985). The finding is explained most parsimoniously with reference to studies on colour naming (Geschwind & Fusillo, 1966; Zihl & von Cramon, 1980; McKeever & Jackson, 1979), which suggest that the speed advantage is due to ready access to the LH naming system while colours presented to the RH require interhemispheric transfer, at some time cost, prior to naming.

The same line of reasoning explains the RT advantage with the central (bilateral) stimuli when colours are presented to the LH, and words to the RH. It might have been predicted that the CSE would be greater in the reverse condition, since the colour-word could have been anticipated to exert stronger effects (both facilitative and inhibitory) when directed to the LH while the RH attempted to deal with assigning a name to the colour strip. As can be seen most clearly by reference to Figure 4.3, there was no interaction of this sort: the incongruent and congruent 'lines' remain parallel as they pass from right to left. Interhemispheric transmission therefore appears to be bi-directional with respect to Stroop effects (essentially confirming Dyer's original observation; see also Nettleton & Bradshaw, 1983 for further discussion of this issue). This bidirectionality seems to be limited by both the capacity of the interhemispheric pathways and the normal functioning of the hemispheres. Case E.W. showed that the speed of colour naming in her abnormal RH was exquisitely sensitive to verbal information presented to the opposite hemisphere - presumably conveyed subcortically. On the other hand, the LH performed adequately, apparently oblivious to the word in the RH - presumably because it was only weakly represented. S.B. showed a degree of abnormal processing of RVF/LH Stroop stimuli but this did not disrupt performance in the central condition.

The distance between the lines in Figure 4.3, corresponds to the central CSE which, while substantial in normal subjects, is slightly less than the lateral CSEs derived from Figure 4.2 and given in Table 4.3. The difference between the lateral *versus* central CSE - the "Callosal Index" - implies that interhemispheric transmission, presumably via the corpus callosum, acts as a partial barrier to Stroop effects while intra-hemispheric interference/facilitation is relatively unconstrained and symmetrically distributed (see Friedman & Polson, 1981; Moscovitch & Klein, 1980) for related discussion). This picture is exaggerated in acallosal M.J. He is unable to benefit from the congruity between word and colour in the central/bilateral condition while he is less distracted by incongruity. Thus, the relevance of the callosum and possibly the anterior commissure, in this transmission, is supported. The other acallosals provide further support for this but their data are more equivocal given their asymmetrical processing speed with lateralised Stroops.

The question as to whether this barrier is selective in any way is less clear. Inspection of Figure 4.2 displays the sharp "V" of the upper, incongruent curve in comparison with the gentler concavity of the lower, congruent curve. This suggests that although interfering colour-word information is more successfully filtered than in the within-hemisphere condition, the same is true for congruent information. These differences cannot be resolved since the experiment reported here, unfortunately, did not included a neutral condition against which interference and facilitation could be quantified. The safest assumption (extrapolating from Dyer, 1973a) is that the cross-callosal Stroop effect, like its lateral counterpart, is a combination of both of these influences, in roughly the proportions 3:2 respectively.

One additional caveat must be inserted, concerning the effects of the position of visual presentation with respect to distance from the fovea, which were not entirely controlled. The selectivity of the "attentional spotlight" may differ according to visual angle (Downing & Pinker, 1985) and this could explain some of the lateral *versus* central effects noted. Further experiments which manipulate visual angle in the vertical plain are needed to clarify this. Nevertheless, an argument invoking differences in attention is not incompatible with and may even compliment the more neurologically based argument presented here.

In conclusion, the present study suggests that colour-words influence the speed of colour naming equally in both cerebral hemispheres. This influence is attenuated when the colour and its word partner are in separate visual hemifields, and is probably mediated by commissural tracts. Finally, the methodology described above appears suitable for testing the functional characteristics of interhemispheric transmission in acallosals, and may be useful in the study of other clinical conditions where abnormalities in this realm have been postulated (David, 1987; Nasrallah, 1985). This will be pursued in chapters 7 and 8.

4.9 Summary

Interference and facilitation of tachistoscopically presented colour stimuli by adjacent incongruent and congruent colour-words (the Stroop effect) was examined in the right and left visual fields, and centrally, in normal subjects and three acallosals. In the central condition, the word and colour were separated across the fovea. Normal subjects showed a small left hemisphere advantage for colour naming. The combined Stroop effect (CSE), that is the reaction time difference between incongruent and congruent pairs, was the same in both visual fields but reduced centrally. Furthermore, in the central condition, the CSE was the same regardless of the side on which the word or colour appeared. One of the acallosals, showed an exaggeration of this pattern, suggesting that the corpus callosum, by acting as a partial barrier, mediates the inter-hemispheric Stroop effects. The other acallosals while providing some tentative support for this, showed evidence of lateralised dysfunction so that their performance was less easily interpreted. The methodology described would appear to have applications in studying the functional characteristics of the corpus callosum in a variety of clinical groups.

PART II

CHAPTER 5

VISUAL IMAGERY AND VISUAL SEMANTICS IN THE CEREBRAL HEMISPHERES IN SCHIZOPHRENIA

5.1 INTRODUCTION

The deviation from the normal asymmetries in brain structure and function in schizophrenia has lead to a number of theories concerning brain development and physiology, and how these may become disordered (Flor-Henry and Gruzelier, 1983; Cutting, 1985; Crow, 1990). In the case of functional asymmetries, the failure to demonstrate the predicted psychological processing superiority of one or other hemisphere on a given task, is often used to explain the manifest phenomena of schizophrenia. For example the absence of the expected left hemisphere (LH) advantage may be linked to disorders of language production, while a right hemisphere (RH) deficit may be linked to affective or body image disturbance (Gruzelier, 1984; Cutting, 1990; see also Liddle, 1987).

Visual imagery is a psychological operation which has recently attracted considerable attention from neuropsychologists (Paivio and Te Linde, 1982; Ehrlichman and Barrett, 1983) particularly with respect to cerebral asymmetries (Kosslyn 1987; Kosslyn, et al., 1989). "Imagery" can be broken down into a series of component parts (Kosslyn 1987; Farah, 1984) which have been found to be distributed unequally in the cerebral cortex. There appear to be at least two systems for processing visual information, one specializing in categorical and semantic distinctions related to LH functions, and the other, specialized in spatial coordinates, more usually associated with the conventional notion of visual imagery, related to the RH. The present study employed tachistoscopic tests of visual processing, previously shown to produce reliable field and hence hemisphere superiorities in normals, in a group of schizophrenic and affective disorder patients. These processes underlying visual cognition (Humphreys and Bruce, 1989) were chosen since a disorder in this realm is a plausible basis for hallucinations (McGhie and Chapman, 1961; Seitz and Molholm, 1974; Slade and Bentall, 1988), a cardinal feature of schizophrenia, as well as other psychotic phenomena (see Cutting and Ryan, 1982). The study of imagery is therefore of obvious clinical relevance.

The tachistoscopic visual tests chosen were developed by the authors (David and Cutting, 1992; see chapter 2) with a view to their application on clinical subjects, and have a number of advantages in this regard. First, standardized picture stimuli were used which were familiar and easily identified even when presented tachistoscopically. Second, tasks which produce reliable RH advantages are hard to come by in experimental neuropsychology (Bradshaw and Nettleton, 1981; Davidoff, 1982). One visual imagery task, mental rotation, has been studied using divided visual techniques but the results with respect to hemisphere asymmetries have been contradictory (Fischer and Pellegrino, 1988; Ditunno and Mann, 1990; Sergent, 1990a). The tests employed in the current study have been shown to reveal lateralized differences, one producing a right and the other a left hemisphere advantage, on two independent samples (David and Cutting, 1992). The same stimuli were used for both tests, the only difference being the nature of the task requirements (c.f. Seamon and Gazzaniga, 1973). In one, subjects are asked whether or not the item depicted is a living thing - a visual semantic task, and in the other, whether it is bigger or smaller than a cat - a visual imagery task. Hence any observed hemisphere differences on the two tasks cannot be due to un-matched perceptual features of the stimuli, a problem when word and shape identification tasks are compared (Gur, 1978; Colbourn and Lishman, 1979; Eaton et al., 1979; see chapter 1 for discussion). Third, the use of non-linguistic stimuli reduces the confounding effects of education and literacy (Lezak, 1983) which may exaggerate any deficits found in schizophrenic patients in relation to controls (see chapter 1). Finally, the tasks were also designed to address the hypothesis proposed by Cutting (1990) that many of the features of schizophrenia can be reproduced by dysfunction of the right hemisphere.

Cutting (1990) argues that the primary function of the RH is to support the cognitive operations underlying judgements of individuality within a class of similar members, while that of the LH is to determine whether or not an entity belongs to a category or class. When the balance of activity between the hemispheres is disturbed, a range of perceptual disorders may ensue. The nature of these disorders will depend on which hemisphere is underactive relative to its partner. Cutting believes that much of the phenomenology of schizophrenia is best explained by relative RH underactivity.

The current study examined this hypothesis by measuring performance on visual cognitive tasks in a mixed group of patients with schizophrenia, suffering from a range of abnormal experiences. The relationship of hemisphere differences, to normal subjects' experiential vividness of visual imagery was also examined.

The purpose was two-fold: the first aim was simply to see whether the expected hemisphere asymmetries were maintained in schizophrenic patients and psychiatric controls. Of particular interest was whether advantages on visual semantic and visual imagery tasks would emerge in the schizophrenic group, for the LH and RH respectively, and if not, whether any deficit was specific to the disorder. The second aim was to explore the possible relationships between visual imagery, normal and disordered, and hemisphere functioning.

Hallucinations may be regarded as a consequence of disordered imagery a position from which at least two possible explanatory models may be proposed. The first is that hallucinations arise from internal images stored in semantic memory and which intrude into consciousness because of overactivation of certain elements or lack of supervisory control (see also Hoffman, 1986; Hemsley, 1987). In the second model, hallucinations may be seen to result from the direct manipulation of external images (as in visual illusions), as a consequence of an uncontrolled or malfunctioning visual imagery system.

5.2 METHOD

Subjects

Controls: Thirty normal subjects drawn from academic and ancillary staff of the Institute of Psychiatry were tested (details of their performance have been reported in chapter 2 and appendix I).

Patients: 46 schizophrenic patients from the Bethlem Royal and Maudsley Hospitals, London, who were mainly in-patients (n=29) though some out-patients were studied. Twenty-two affective disorder patients from the same hospital group were also recruited (These same patients participated in the experiments described in chapters 6, 7 and 8. See appendix I) Subjects with a history of brain disease, mental impairment or significant substance abuse, were excluded.

Patients were diagnosed according to DSM-III-R criteria (American Psychiatric Association, 1987) based on symptoms at interview - using the Present State Examination (PSE) (Wing, Cooper and Sartorius, 1974) - and those recorded in the case notes.

The schizophrenic patients were classified by their illness course, following DSM-III-R as: acute (8); sub-chronic with acute exacerbation (13); chronic (12); subchronic (7); and, in remission (6). Twenty one schizophrenics were on anticholinergics, 4 on antidepressants and 1 was on lithium.

The affective disorder patients comprised 12 with major depression and 10 with bipolar affective disorder. Ten patients were on lithium and 10 on antidepressant medication. All but 6 schizophrenics and 12 affectives were receiving neuroleptic drugs.

Tests of Visual Cognition

This experiment consisted of 2 tasks: in the first, subjects had to make a categorical judgement based on fundamental knowledge stored in semantic memory - namely whether an item depicted was living or non-living. Normals show quicker reaction time (RT) on this task when items are presented to the right visual field (RVF) compared with the left visual field (LVF) (Wilkins and Moscovitch, 1978). This distinction appears to have a strong neuropsychological basis in that focal brain lesions may produce dissociable impairments in naming and recognising living and non-living things (Warrington and Shallice, 1984). In this task, access to this knowledge store is via picture stimuli hence the term, visual semantics (Humphreys and Bruce, 1989; Farah et al., 1989).

The second task required the subject to make a relative size judgement. A picture of a common item was shown and the subject asked to state whether the item in real life was bigger or smaller than a domestic cat. Normals show quicker RT on this task when items are presented to the LVF/RH compared with the RVF/LH. Although it may be possible to make this judgement on the basis of visual semantics, close comparisons require the subject to form a visuo-spatial representation or "mental image", to scale, of the item sitting next to a cat, and then reach a decision. This calls upon RH specialisation. Support for this mechanism and its location comes from the finding that the closeness of the size difference is highly correlated with reaction time (RT) when items are shown in the LVF but not RVF (David and Cutting, 1992; see also Paivio, 1975; chapter 2).

Stimuli These consisted of 24 items from the Snodgrass and Vanderwart (1980) as described in chapter 2, experiment 2 (see Figure 2.1).

Apparatus and Procedure (as in chapter 2).
i) Visual semantic task: "You are going to see pictures of common things flashed up on either side of the screen. I would like you to decide as quickly and as accurately as possible whether the picture is of a living thing, such as an animal, plant, or part of the body or a non-living thing, such as a car, table etc."

ii) Visual imagery task: "You are going to see pictures of common things flashed up on either side of the screen. I would like you to decide, as quickly and as accurately as possible whether the thing in real life is bigger or smaller than a domestic cat. Imagine the thing next to a cat and decide whether it would be bigger or smaller."

Subjects were then instructed to press one of two buttons marked appropriately, with the middle or forefinger of one hand. Response hand was changed after every 24 stimuli, the order balanced across subjects.

Ratings
All subjects were administered the National Adult Reading Test (NART) (Nelson and O'Connell, 1978) to give an estimate of IQ and their years of education recorded. All were right-handers according to Annett's classification (1970).
Normal subjects completed a questionnaire for hallucinatory predisposition (Launay

and Slade, 1981), which consists of a 12-item scale measuring vividness of auditory and visual imagery (e.g., "On occasions I have seen a person's face in front of me when no-one was in fact there").

Overall psychopathology was rated on the modified Brief Psychiatric Rating Scale (BPRS) (Bech, Kastrup and Rafaelson, 1986); range 0-36. The number of hospital admissions was also recorded. Depressives were given the Beck Depression Inventory (BDI) (Beck et al., 1961).

5.3 RESULTS

Means and standard deviations for age, IQ, years of education and BPRS scores are given in Table 5.1 for the 3 groups.

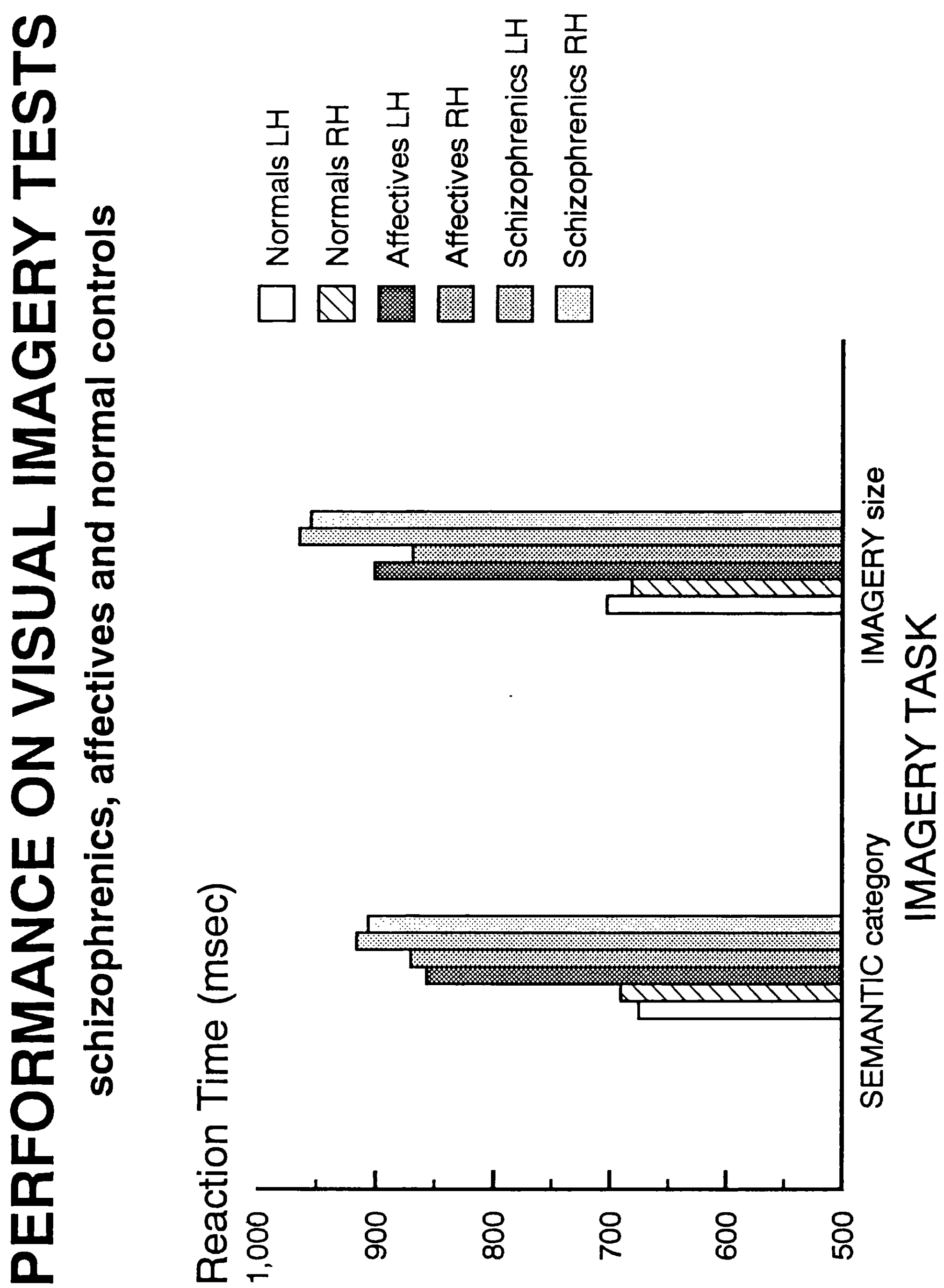
	Normals	Affectives	Schizophrenics
Sex, M/F	17/13	8/14	30/16
Age, yrs	33.1 ± 6.1	37.4 ± 13.7*	30.9 ± 7.6
IQ (NART)	115.5 ± 8.5	113.1 ± 9.2	107.2 ± 11.7#
Education	16.6 ± 3.2	14.3 ± 3.5	12.4 ± 2.9#
BPRS	-	15.9 ± 4.7	17.0 ± 6.9
Hospital admissions	-	2.9 ± 2.6	3.7 ± 2.9

Table 5.1. Comparison of normal controls, patients with affective disorder and schizophrenia for background characteristics: Means±SD.

Comparison of groups using ANOVA and the Least Significant Difference procedure: *Affectives differ from both normals and schizophrenics at $P<0.05$. #Schizophrenics differ from affectives and normals at $P<0.05$. Patient groups not significantly different on BPRS ($P=0.5$) or number of hospital admissions ($P=0.3$).

Statistical analyses were carried out using SPSS/PC software. Subject-based analysis of variance (ANOVA) was performed with reaction time (RT) as the dependent variable. The analysis was 2X2X2X3, with condition (category or size), and visual field as the within-subject variables and sex and diagnosis as between-subject variables. There was no main effect for gender ($F=.80$, df 2,92; $P=0.4$). The main effect of visual field approached significance ($F=3.03$, $P=0.08$). Diagnosis produced a highly significant effect ($F=19.47$, $P<.001$). There was also a significant main effect of condition ($F=4.39$, $P=0.04$). The only significant interactions were condition X field ($F=7.18$, $P<0.01$) and of most interest, the interaction, diagnosis X condition X field ($F=3.51$, $P=.03$) see Figure 5.1).

Figure 5.1


PERFORMANCE ON VISUAL IMAGERY TESTS
schizophrenics, affectives and normal controls
Reaction Time (msec)
1,000
900
800
700
600
500
SEMANTIC category
IMAGERY size
IMAGERY TASK
Normals LH
Normals RH
Affectives LH
Affectives RH
Schizophrenics LH
Schizophrenics RH

From Figure 5.1 it is evident that both patient groups show slowed RT with the schizophrenics slowest of all. This was presumably a consequence of non-specific illness related factors. Neuroleptic medication did not produce any systematic effects. The main effect of condition was due to the generally longer RTs for the imagery task. The diagnosis X condition X field interaction was due to the schizophrenics' loss of the expected LH advantage for the visual semantic task; in fact the data point to a RH advantage. However, the expected RH advantage for the imagery task was maintained.

Having established an RH advantage on the size task, the next step was to examine the relationship between size difference and RT for each hemisphere (Paivio, 1975; David and Cutting, 1992; chapter 2). There was a clear relationship for RH presentations, between RT and the rank order of size of the items starting with the largest size difference, be it bigger or smaller, and ending with the item whose size was deemed nearest to that of a cat (RH: rank order correlation=0.43; P=.04. LH: correlation=0.0; NS). Similar analyses were carried out using a logarithmic transformation of RT (Moyer, 1973), which yielded a stronger correlation for RH presentations (r=.48, P=.02) but no correlation for the LH.

Error rates were uniformly low (<10%). ANOVA performed with errors as the dependent variable revealed no main effects or interactions with diagnosis. Error rate correlated with RT (r=.37, P<.01) excluding speed-accuracy trade-off.

Among the normals alone, IQ and age exerted little effect on the performance of either the imagery or visual-semantic task (all Pearson's r<.29).

Taking the subjects as a whole, overall RT correlated with IQ (-.32, P<01), age (.12) and (patients only) BPRS scores (.58, P<.001) and number of admissions (.34, P<.01).

Since the groups were not matched for some of these variables it was decided to derive simple indices for hemisphere advantage for the 2 tasks and use these as the dependent variables rather than raw RT. The LH advantage for the visual semantic task (living/non-living) was calculated by subtracting the RVF RT from the LVF RT. The RH advantage for the visual imagery task (bigger/smaller than a cat) was calculated by subtracting the LVF RT from the RVF RT. The index of LH advantage on the categorical-semantic task did not correlate significantly with RT on any of the subject variables including age and education, within the normal or psychiatric groups. The index of RH advantage on the spatial-imagery task showed a negative correlation with IQ (r=-.28) and error rates (r=-.3) but none of the other variables. BPRS and BDI did not correlate with any of these new measures.

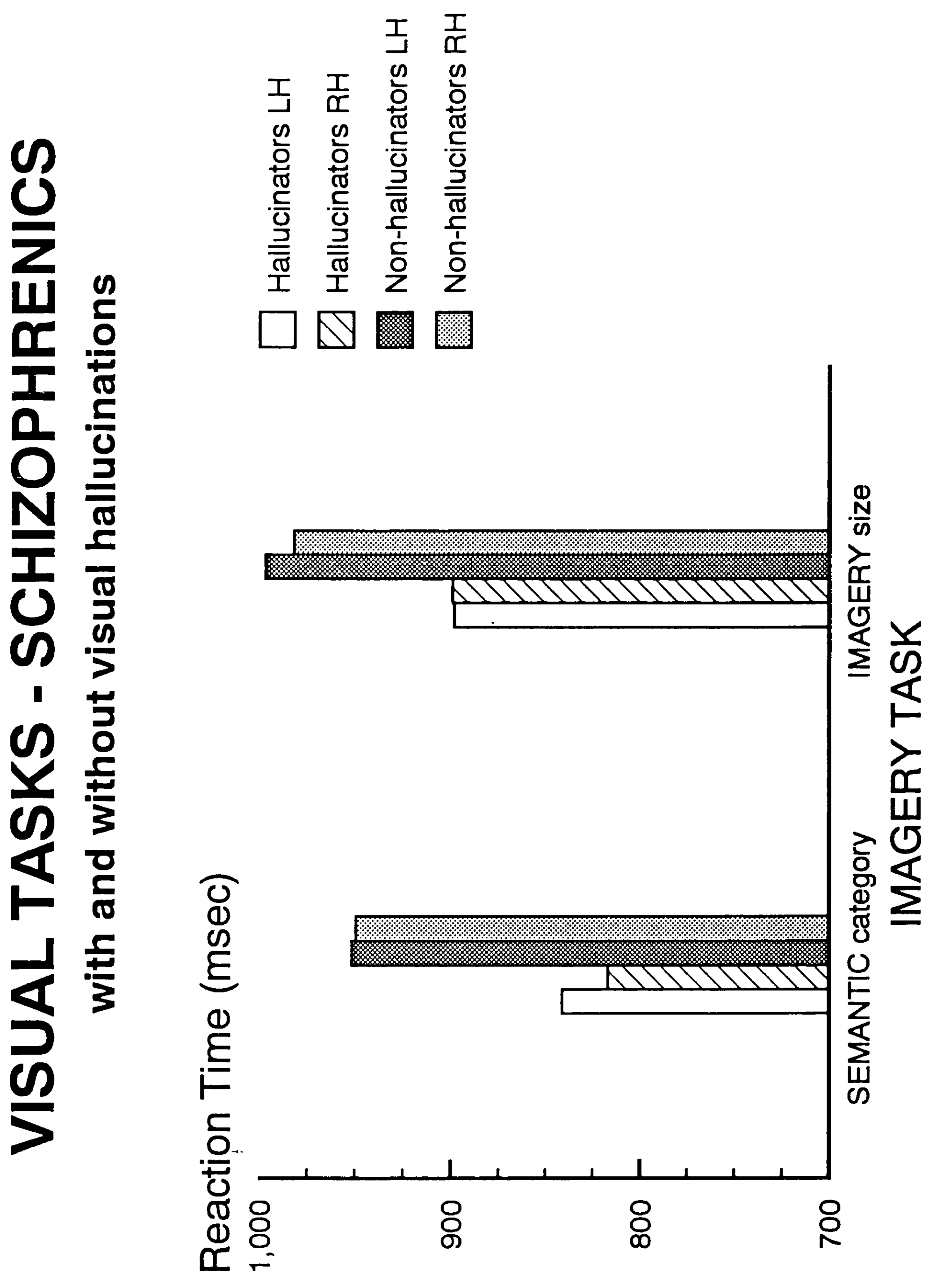
When comparing the 3 diagnostic groups on these variables, there was no difference for the RH advantage (imagery task); ANOVA, F=1.25, P=.3; while the LH advantage (semantic task) approached significance; ANOVA, F=2.8, P=.06. Planned comparisons using the least significant difference test showed that the schizophrenics differed significantly from controls (P<.05).

5.4 Hallucinatory Predisposition and Hallucinations

Normal subjects' scores on the Launay-Slade hallucinatory predisposition scale did not correlate significantly with RT for the imagery task for either hemisphere but showed a modest but significant negative correlation with LH semantic RT (r=-.25, P<.05, 2-tailed) but not LVF/RH semantic RT (r=-.19, NS). This points to LH activity being relevant to hallucinations rather than RH activity.

In the schizophrenics, the presence of auditory hallucinations or first rank symptoms, as classified by the PSE (Wing et al, 1974), did not influence RT on any of the tasks, for either hemisphere. Fifteen patients had experienced visual hallucinations in the previous month. ANOVA with condition, and field as within-subject factors and hallucination status as the between-subject factor, showed significant or near significant main effects for all three factors (Figure 5.2). While the hallucination X condition X field interaction failed to reach significance (F=1.4, P=.2) post-hoc t-tests revealed that visual hallucinators had faster RT than non-hallucinators on the semantic task (t-test, P=.06) but not on the imagery task (P=.2) (they were generally faster responders). This was more pronounced for RH (p=.04) vs LH (P=.2) presentations (see Figure 5.2).

Figure 5.2


VISUAL TASKS - SCHIZOPHRENICS
with and without visual hallucinations
Reaction Time (msec)
1,000
900
800
700
SEMANTIC category
IMAGERY size
IMAGERY TASK
Hallucinators LH
Hallucinators RH
Non-hallucinators LH
Non-hallucinators RH

CT Scanning

Brain CT scans were performed on 31 schizophrenics. The scanned patients did not differ from the remaining 15 on mean IQ, age, years of education or BPRS score, (all P>0.5 by t-test, 2 tailed). The size of the lateral ventricles and intracranial space was determined by manual planimetry from the slice showing the largest lateral ventricular area by a colleague (Dr Peter Jones) blind to the psychological test results. Ventricle:brain ratio (VBR) was then calculated (Synek et al, 1976). VBR showed weak negative correlations with RT on both visual tasks r=-.18 for the living/non-living task and r=-.25 for the size judgment task. VBR was not related to hemisphere differences.

5.5 DISCUSSION

It was possible to carry out tachistoscopic testing of visual cognition in a relatively large group of operationally defined schizophrenic and affective disorder patients. While schizophrenics showed the poorest performance as determined by RT, they were not in general more impaired in comparison to psychiatric controls many of whom shared the same medication, and who as a group, had similar levels of psychopathology and number of hospital admissions. The study showed that a RH advantage on a task requiring visual imagery in order to make a judgement of relative size, though small, was confirmed. The assumption that this task requires the use of visual imagery is supported by the inverse linear (and log-linear) relationship between the size difference and RT in the RH only, as shown by the correlation statistics. This finding is entirely consistent with the situation seen in the normal sample, reported in detail in chapter 2.

Surprisingly, the expected LH advantage for categorical judgements using semantic memory was not seen in the schizophrenic patients. This asymmetry was present in psychiatric controls and is a robust effect in normals (David and Cutting, 1992). This differential deficit seen in the schizophrenics is unlikely to be due to task difficulty in that semantic categorisation was, if anything, the less taxing of the two tasks, as reflected in faster RTs (see chapter 1). Similarly, the lack of relationship to cerebral atrophy as measured from CT scans also suggests that the finding is not a consequence of global neuropsychological impairment (Owens et al., 1985) seen in some schizophrenic patients. Whether this lack of functional asymmetry is related to lateralised structural abnormalities must await investigation in which details of brain morphology such as those obtained from magnetic resonance imaging are coupled with data from divided visual field and similar techniques.

The lack of asymmetry on the visual semantic task suggests some impediment to gaining access to the LH semantic system from an external visual image in schizophrenia. The fact that error rates were generally low and did not differ between the three groups, points to a problem of access rather than degradation of the store of information in schizophrenia (see Shallice, 1988, for more on this distinction). This accords with recent reports of memory functioning in chronic schizophrenia (Tamlyn et al., 1992).

Level of psychopathology did not strongly affect the pattern of results obtained in either clinical group although it caused a diffuse slowing of RT. In the depressives, higher Beck depression scores were not related to attenuated function of either hemisphere as has been suggested using attentional paradigms (David and Cutting, 1990; see chapters 3 and 6). The exception to this overall impression was hallucinations. The pattern of data hint that the LH may be responsible for vivid visual imagery in normals but that an imbalance between the hemispheres, with the RH relatively overactive, underlies visual hallucinations in schizophrenics. The results from both normals and schizophrenics point to the visual semantic system as seat of "hallucinations" in both cases rather than the system which underlies visuo-spatial imagery. However, further inspection of Figure 5.2 points to the loss of the expected RH advantage on the imagery (size) task amongst hallucinators. It may therefore be the combination of a poor imagery system and an overactive RH semantic system which leads to the visual hallucinations. It must be acknowledged that these speculations based upon presumed imbalances allow for more degrees of freedom in comparison to hypotheses based on absolute deficiencies. They must therefore be regarded for the moment as avenues for further research rather than definitive findings.

In conclusion, the study reported shows a specific deficit in a task requiring access to the LH semantic system from pictorial stimuli in schizophrenia. The RH visual imagery system appears to be intact. Such an imbalance may be implicated in the production of certain abnormal phenomena such as visual hallucinations.

5.6 Summary

Divided visual field tasks were given to normal subjects, and patients with schizophrenia and affective disorder, to investigate hemisphere differences in the visual processing of standardised pictorial stimuli. There were two conditions: in the first, subjects were asked to decide whether a common entity represented by a picture was living or non-living, a task involving a categorical judgement based on semantic information; a left hemisphere task. In the second condition, subjects judged whether these depictions represented entities which were bigger or smaller than a cat; a right hemisphere task requiring visual imagery to compare spatial dimensions. It was found that the patient groups, while showing slower reaction time (RT) overall, both displayed a right hemisphere (RH) advantage on the imagery task. Furthermore, the schizophrenics' RHs showed the normal relationship between closeness of size comparison and RT, additional evidence that the visual imagery mechanism is intact. However, these patients failed to show the expected left hemisphere advantage on the visual-semantic task. Performance on the semantic task was related to the experience of vivid imagery in normals and visual hallucinations in the schizophrenics. The possible contribution of hemispheric imbalance in the production of visual hallucinations from a disordered semantic system is discussed.

CHAPTER 6

SPATIAL AND SELECTIVE ATTENTION IN THE CEREBRAL HEMISPHERES IN DEPRESSION, MANIA AND SCHIZOPHRENIA

6.1 INTRODUCTION

Neuropsychological research in psychiatry is concerned with the physiological basis and cerebral localisation of disordered psychological *processes*, for example, attention, and *states* such as depression and psychosis. Work to date has uncovered different contributions by the two cerebral hemispheres to affective disorder and schizophrenia (Cutting, 1985; Flor-Henry, 1986). Some research points to a link between disordered affect in general and the right hemisphere (RH) (Taylor & Abrams, 1987) while other work looking at the effects of brain lesions suggests that mania and depression are the result of left and right hemisphere dysfunction respectively (Sackeim et al., 1982; Silberman & Weingertner, 1986) (c.f. Robinson et al., 1988). Most authors favour the LH as the site of disturbance in schizophrenia (Flor-Henry, 1986; Crow, 1990) although others recognise the likelihood that both hemispheres may be involved (Gruzelier, 1984), perhaps because of corpus callosum dysfunction (David, 1987), some emphasising RH disturbance (Cutting, 1990). EEG Studies of mood and arousal show a similar lack of consensus (Tucker et al., 1981; Davidson et al., 1985; Ahern & Schwartz, 1985).

The techniques of experimental neuropsychology such as divided visual field studies, have shown an RH advantage in perceiving sad facial expressions and an LH advantage for happy expressions, (Reuter-Lorenz et al., 1983) while other studies have shown an RH advantage regardless of the valence of the affect in both normal (Ley & Bryden, 1979; Strauss & Moscovitch, 1981) and brain damaged populations (Borod et al., 1986). Facial perception, facial affect recognition in particular, has been found to be impaired in schizophrenic and depressed patients (Morrison et al., 1988; Zuroff & Colussy, 1986). There is doubt as to the specificity of this deficit, particularly in schizophrenia. Some have argued that it is due to global cognitive impairment across a range of tasks, regardless of which hemisphere is being probed (Novic et al., 1984), while others propose that poor facial processing is secondary to psychological deficits localised to the RH (Magaro & Chamrad, 1983; Cutting, 1990).

In order to clarify some of these issues, particularly the contribution of lateralised hemisphere dysfunction leading to abnormal attention, arousal and affect, in psychiatric disorders, a chimeric faces test was employed (Campbell, 1978; Levy et al., 1983a; David, 1989c). When right-handers are required to judge whether a chimeric face is happy or sad, a consistent bias towards the composite whose half-face falls to their left, a "left hemi-facial bias (LHFB)" is observed. The effect of mood was studied by David (1989c) using schematic happy-sad chimeric face drawings. Induced depression and elation in normal volunteers resulted in substantial effects on sad and happy choices respectively but did not affect the LHFB (see chapter 3). Jaeger et al., (1987) gave depressed patients photo chimeras with one half neutral and the other smiling (Levy et al., 1983a) and found that the normal LHFB, though present was attenuated, supporting RH dysfunction. David and Cutting (1990) confirmed the reduced LHFB in clinically depressed patients, and in addition, hypomanic and manic patients were shown to have an increased bias. A schizophrenic group showed no significant bias in either direction.

What is the LHFB due to? There is evidence that this attentional bias is due to RH "dominance" in spatial organisation (Grega et al., 1988) which is evoked only by faces (Rhodes et al., 1990) and is a stable property of that hemisphere (Schwartz & Smith, 1980; Bennett et al., 1987; Hoptman & Levy, 1988; Luh et al., 1991). Evidence supporting the RH's role in this phenomenon includes the observation that non-right handers do not show a consistent bias to either side of space (Levy et al., 1983a; David, 1989c; Lawson, 1978; see chapter 3), and studies on patients with focal brain resections (Kolb et al., 1983) have revealed that only right posterior lesions alter the bias. Thus the work by David and Cutting (1990; plus see chapter 3) may be interpreted as showing RH hypofunction in depression and schizophrenia, and RH hyperfunction in mania. Given the RH's role in the overall control and distribution of attention (Heilman & Van Den Abell, 1979; Weintraub & Mesulam, 1987), this may shed light on the disturbances of perceptual processing seen in psychiatric patients (McGhie & Chapman, 1961).

Recent research in normal subject has explored the relationships between LHFB and performance on other tests of hemisphere function in several sensory modalities. The results show an association with other indices of RH arousal, usually limited to the visual modality, in some studies (Levy et al., 1983b; Luh et al., 1991; Hellige et al., 1988) though not all (Kim & Levine, 1992). Wirsen et al., (1990) found that subjects with reduced LHFB were slower on an independent measure of RT, pointing towards the RH's role in cerebral activation and arousal.

The present study used a tachistoscopic version of the happy-sad chimeric faces test on a new group of patients and controls since the test, though simple, appears to be a powerful method for showing lateralised disturbances. As well as attempting to replicate David and Cutting's results using a different means of stimulus presentation, the aim was to study the pattern of correlations between this and another test of visual attention, the Stroop test (see MacLeod, 1991 for review), in the same group of patients. A novel version of the Stroop paradigm was used (David, 1992; chapters 5,7 & 8)) whereby a colour, and a colour word which may be congruent or incongruent, were separated by a fixed visual angle. Both elements were presented in one of three positions: both to the RVF, both to the LVF and bilaterally, with the word going to one visual field and the colour going to the other. Differences were found for schizophrenics in the bilateral condition which produced larger Stroop effects (described in detail in chapter 7). Since the same patients also performed both this and the faces test it is possible to examine the relationship between Stroop interference and spatial attentional bias, in normals and psychiatric patients.

The purpose of the current study was therefore to combine the psychological approaches to psychiatric phenomena which posit disorders of attention, with neuropsychological approaches, which attempt to localise such dysfunction in the brain.

6.2 METHOD

Subjects

Patients were diagnosed according to DSM-III-R criteria (American Psychiatric Association, 1987) based on symptoms at interview - using the Present State Examination (PSE) (Wing, Cooper and Sartorius, 1974) - and those recorded in the case notes.

Forty-five schizophrenic patients from the Bethlem Royal and Maudsley Hospitals, London, were studied. (These were the same as those described in chapter 5 with the exception of one case who failed to complete the chimeric faces test).

Twenty-two affective disorder in-patients and day patients from the same hospital group were also recruited. Ten were suffering from hypomania or mania, (8 of whom were on Lithium) and 12 from major depression (10 of whom were on antidepressant medication). All but 6 schizophrenics and 12 affectives were receiving neuroleptic drugs. Exclusion criteria are described in chapter 5.

Twenty-three normal right-handed subjects drawn from hospital staff served as controls (these were drawn from the normal subjects described in chapter 2, experiments 1 and 2. 15 also performed on both the faces and Stroop tasks. See below and appendix I).

Ratings: All subjects were administered the National Adult Reading Test (NART) (Nelson & O'Connell, 1978) to give an estimate of IQ and their years of education recorded. All were pure right-handers according to Annett's classification (1970).

Overall psychopathology was rated on the modified Brief Psychiatric Rating Scale (BPRS) (Bech, Kastrup & Rafaelson, 1986); range 0-36. The number of hospital admissions was also recorded. Depressives were given the Beck Depression Inventory (BDI) (Beck et al., 1961).

Stimuli

Chimeric faces test

Twenty-four happy-sad chimeric face drawings (12 in standard orientation and 12 reversed) were presented in turn, centrally, so that each hemiface occupied a hemifield (see chapter 3.2 and figure 3.1). Pictures were approximately 6 cm by 10 cm across on the screen (approx 7° to 12°). Four practice stimuli were shown prior to testing.

Lateralised Stroop test

(see chapter 4, Figure 4.1 and section 2 for full description of stimuli and testing conditions). Each of the stimuli was presented to the left or right visual field, with the medial edge 3° lateral to a fixation cross, or centrally with the word on one side and the colour on the other. There were 72 stimuli in total, 24 left, 24 right and 24 central. Half were congruent and half incongruent.

Apparatus

This consisted of a Kodak S-AV 2050 projector with custom built shutter attachment, controlled by an Electronic Developments tachistoscope timer panel. Slides were projected onto a perspex screen with a central fixation spot (see chapter 2 section 2 and chapter 4 section 4 for details of apparatus).

Procedure

(See chapter 2 section 2, and chapter 4 section 4 for details). A warning tone would sound over the subject's headphones, followed 500 msec later by the visual stimulus which would remain for 120 msec. Stimuli were presented at a rate of approximately 1 every 2.5 seconds, as in the previous experiments.

For the chimeric faces, subjects had to state whether the face was happy or sad. Left Bias was scored by subtracting the number of responses which coincided with the half-face to the (viewer's) right (min=0, max=12) from those which corresponded to the half-face to the left (min=0, max=12). The possible range for Left Bias scores was therefore +12 to -12. For Stroop stimuli, subjects responded by saying the colour of the strip. The Stroop Effect was calculated by subtracting the RT for congruent stimuli from incongruent. This was done for all presentations combined and also for the both lateral positions. Testing took approximately 3/4 hour.

6.3 RESULTS

Table 6.1 shows the age, IQ, and clinical information on patients and controls plus scores on the chimeric faces test including mean Left Bias scores. Normals and manics showed a clearly significant Left Bias when calculated in either of two ways: binomial test and one sample t-test. Depressives showed a weaker bias which failed to reach significance. Schizophrenics showed no significant bias in either direction regardless of statistical method.

Chimeric faces

Analysis of variance (ANOVA) showed that there were main effects by diagnosis for Left Bias: (df=3,86, F=12.5; P<0.0001); RT for left-hemiface responses: (F=2.76; P<.05); and age: (F=4.3; P<0.01); and IQ: (F=3.3; P=0.02). There were no main effects or interactions with gender. Although the groups were not perfectly matched for age and IQ, re-analysis with these factors as covariates did not alter the results appreciably.

	Normals (n=23)	Depressives (n=12)	Manics (n=10)	Schizophrenics (n=45)	F	Sig
Age (SD)	33.9 (6.3)	41.3 (12.9)	32.8 (13.8)	30.9 (7.6)	4.3	.01¶
Sex	12F 9M	8F 4M	6F 4M	15F 30M		
IQ	115.3 (10.3)	113 (8.4)	113 (10.6)	107 (11.6)	3.3	.02§
BPRS	-	14.6 (3.9)	17.4 (5.4)	17.0 ± 6.9	.76	.5
Hospital Admissions	-	2.8	3.0	3.7	.54	.6
*Left Bias	7.91 (4.4)	2.08 (6.5)	8.8 (5.5)	0.0 (6.4)	12.5	.000
No of cases						
>0:	22	7	10	22		
<0:	1	3	0	17		
=0:	0	2	0	6		
Binomial Test:	P<.0001	P=.3	P=.002	P=0.5		
One Sample t-test :	P<.001	NS	P<.01	NS		
Left RT	1065 (231)	1384 (486)	1132 (351)	1277 (383)	2.76	.05≈
Right RT	1182 (299)	1442 (530)	1135 (376)	1279 (336)	1.81	.15
R-L Diff	P=.01	NS	NS	NS		
#Sad Bias	2.61 (4.6)	3.25 (7.0)	1.9 (7.8)	2.13 (5.9)	.14	.9

*Left Bias equals the number of responses which correspond to the Left hemiface minus the number which respond to the right hemiface (the mean for each group is shown). Normals differ significantly from depressives and schizophrenics; manics differ significantly from depressives and schizophrenics (all P<.05, Least Significant Difference procedure).
#Sad Bias equals the number of sad responses minus the number of happy responses.
¶ Depressives differ from other 3 groups (P<.05)
§ Normals and schizophrenics differ (P<.05)
≈ Normals differ from depressives and schizophrenics (P<.05)

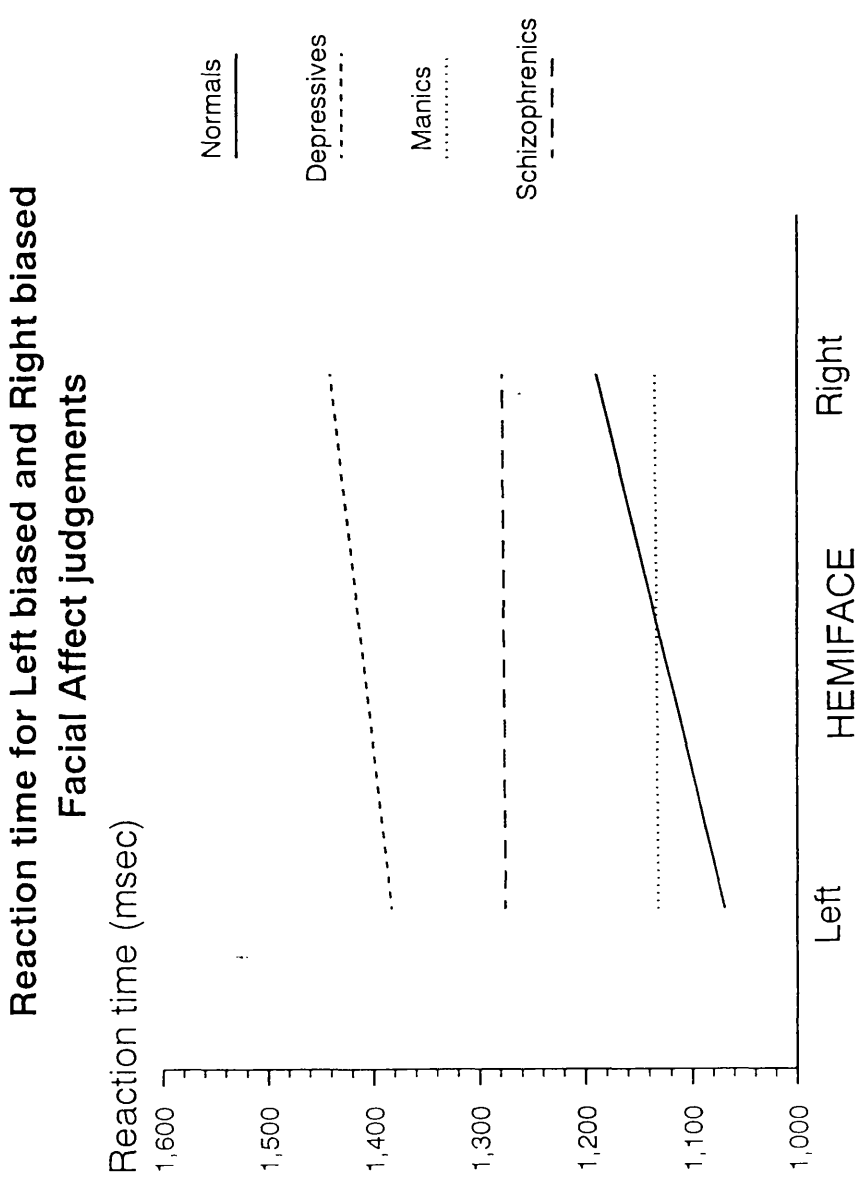
Table 6.1. Comparison of psychiatric patients with normal controls. Demographic and Chimeric Faces test variables.

Regarding Left Bias, the Least Significant Difference procedure showed that normals differed significantly from depressives and schizophrenics as did the manics. Schizophrenics therefore did not differ significantly from depressives and the manics did not differ from normal controls. Looking at RT, left sided responses were slower for depressives and schizophrenics versus normals while right sided responses did not differ significantly between the groups (see Figure 6.1). Although ANOVA showed a non-significant trend for a diagnosis X side interaction, within the normal group, left biased responses were significantly faster than right (paired t-test, $P<.01$). A similar trend was noted for the depressives while the remaining patients groups clearly did not show a right/left RT difference.

Age, IQ and years of education did not correlate with Left Bias or any of the RT measures for individual groups although there was a weak positive correlation between IQ and left bias ($r=.25$. $P<.05$) for the sample as a whole. Amongst the patients, BPRS did not correlate significantly with any of the measures although there were trends towards decreased bias and slower RT with higher scores in the schizophrenics and depressives but increased bias and faster RT in the manics. Subdividing the schizophrenic group on the basis of course did not reveal significant differences.

All groups on average displayed a positive Sad Bias (a tendency to say sad more often than happy), the magnitude of which did not differ significantly between them, although the extent of the Sad Bias was greatest in the depressives and lowest in the manic patients. In the depressed group there was no correlation between Sad Bias and BDI (Pearson's $r=-0.13$; mean 14.0, SD 6.0) although RT increased with increasing depression (both left--and right-face RT: $r=.42$; $P=.02$) and Left Bias showed a non-significant tendency to be reduced ($r=-.28$).

Figure 6.1


Reaction time for Left biased and Right biased
Facial Affect judgements
Reaction time (msec)
1,600
1,500
1,400
1,300
1,200
1,100
1,000
Left
HEMIFACE
Right
Normals
Depressives
Manics
Schizophrenics

Stroop tests

ANOVA of the Stroop effect - the incongruent-congruent difference - revealed no main effects for diagnosis or visual field (right and left) or significant interactions, when either RT or error rate was the dependent variable (Table 6.2), although RT was slowest in the schizophrenic group. Correlations between the chimeric faces test and Stroop effects for each visual field were not different from combined Stroop effect so only the latter are presented (Table 6.3). The association between Left Bias, left response RT and the Stroop effect are shown for each diagnostic group (see discussion).

STROOP	Normals* (n=15) (SD)	Depressives (n=12)	Manics (n=10)	Schizophrenics (n=45)	F	Sig
#Reaction time (msec):						
Incongruent	781.7 (91.4)	855.7 (185.5)	810.1 (186.7)	927.8 (196.8)	3.1	.03§
Congruent	656.2 (98.0)	729.7 (164.9)	684.9 (129.2)	795.1 (176.3)	5.6	.02~
Stroop effect (msec):						
Overall	125.5 (46.9)	126.1 (74.6)	125.2 (78.0)	132.7 (71.8)	.07	.9
L hemisphere minus R hemisphere RT difference (msec):						
	7.8 (34.1)	0.7 (46.0)	13.1 (13.8)	-0.8 (56.1)	.30	.8
Errors (%)	2.7 (2.8)	2.9 (2.9)	2.4 (2.2)	5.1 (5.1)	2.4	.07

§ Normals and schizophrenics differ (P<.05)

~ Schizophrenics differ from manics and normals (P<.05)

*15 Normals did both Stroop and face tests

#Correct responses only

Table 6.2. Comparison of psychiatric patients with normal controls. Stroop test variables.

	RIGHT HEMISPHERE		LEFT HEMISPHERE
	L Bias	Left face-RT	Right face-RT
Normals (n=15)			
STROOP#	.33	-.44*	-.10
Left RT	-.36	-	.75***
Depressives (n=12)			
STROOP	-.32	.21	-.03
Left RT	-.50*	-	.75***
Manics (n=10)			
STROOP	.03	.51*	.60*
Left RT	-.11	-	.79***
Schizophrenics (n=45)			
STROOP	.11	.10	.07
Left RT	-.16	-	.88***

#STROOP: Stroop effects (incongruent minus congruent RT)

*P<.05

***P<.005

Table 6.3. Correlations (Pearson's r) between Stroop effects, and perceptual bias and vocal reaction time to each half-face on the chimeric faces test.

6.4 DISCUSSION

Tachistoscopic presentation of happy-sad chimeric face drawings provoked the anticipated LHFB in normal, right-handed subjects (Heller and Levy, 1981). The data also confirm prior reports of reduced LHFB in clinically depressed patients (Jaeger et al., 1987; David and Cutting, 1990) and point to RH hypofunction in depression. In addition, hypomanic and manic patients showed a strong LHFB consistent with RH hyperfunction, although the small number of manics and normals may have precluded the emergence of a significant difference between them. The schizophrenic group showed no significant bias, pointing to RH hypofunction (Cutting, 1985; Magaro & Chamrad, 1983) and indicating that schizophrenia is quite unlike mania in this respect. These results are entirely in keeping with a previous report using the same stimuli viewed in free vision (David and Cutting, 1990) and are supported by cerebral blood flow studies (Uytdenhoef et al., 1983; Gur et al., 1985).

The present study was able to measure RT to each stimulus. In normals, left biased judgements correlated with faster RT (see also Wirsen et al., 1990). A similar pattern was seen in the depressives but with the lateral RT asymmetry reduced. Surprisingly, the manic and hypomanic patients, while showing a strong Left Bias did not differ in their RT according to whether they were responding to the left or to the right hemiface. The schizophrenics showed little perceptual bias and no lateral asymmetry of RT. In other words, results from the chimeric faces showed that neither RT nor Left Bias alone can be regarded as a measure of hemisphere "activation", since they may be dissociated in pathological states.

The Stroop results add further complexity to this picture. For the normals (and the larger group reported elsewhere of which this is a sub-set (David, 1992; chapter 4)), there was no significant difference between the combined effects of congruent and incongruent colour-words on colour naming for each group of subjects, or between right and left hemisphere presentations. This version of the Stroop paradigm permits a measure of selective attention. Specifically, if a subject is able to ignore the colour-word, a zero Stroop effect will be achieved. The ability to do this, or to use a common metaphor, to focus the spotlight of attention, seems to be equal in both hemispheres (c.f. Palmer & Tzeng, 1990) and in a variety of psychiatric groups. This contradicts some studies in normals using traditional Stroop stimuli and vocal RT (Franzon & Hugdahl, 1987) but confirms others (Warren & Marsh, 1978; Simon et al., 1985). A divided visual field study of negative priming using successive Stroop stimuli also showed no main effects of visual field, yet interactions were found with gender and measures of schizotypy (Claridge et al., 1992). The ability to deal with valid and invalid cues occurring in different spatial locations has been extensively investigated by Posner and his colleagues (Posner et al., 1984). One such study on schizophrenic patients revealed deficits in ignoring invalid cues, especially with the LH (Posner et al., 1988), although the data can be interpreted as showing a loss of the advantage for valid cues in the RH (Coppola & Gold, 1990; chapter 1, section 6). Normal subjects showed no main effects for visual field. Taken together, these reports render the lack of cerebral asymmetries in the current study of Stroop effects unsurprising.

Of interest, was the relationship between the two tests of hemisphere function in which attention plays significant but distinct roles. The pattern of correlations suggests that in normals and depressives, these two attentional systems remain coupled. However, with more severe psychological disturbances, namely mania and schizophrenia, performance on the two tasks and, indeed the direction of perceptual bias and time to respond on the faces task, become dissociated. In mania, the perceptual bias remains strong suggesting RH hyper-arousal. Faster RT for *both* sides is *inversely* related to this bias, and leads to a "widening of the attentional spotlight" (increased Stroop effect), perhaps the result of bilateral hemisphere activity. In schizophrenia, no relationship between RT and Left Bias is seen (the Left Bias itself is much reduced) and between these and the Stroop results. This suggests a more extensive disruption of attentional processes in the disorder.

Although the overall picture can be accommodated with a range of complicated hypotheses involving hemisphere hyper- or hypo-function, singly or in tandem, the most parsimonious explanatory framework implicates the RH alone since clinical and experimental data point to its preeminence in the control of attention (Heilman and Van Den Abell, 1979; Weintraub & Mesulam, 1987). Schizophrenics appear to have the most dysfunction in this regard.

What might this dysfunction be due to? It is well known that dopamine has a profound influence on attentional systems in the human brain (Clark et al., 1989). Developmental disorders may result in asymmetric dopamine depletion with subsequent hemisphere differences of visual attention (Craft et al., 1992). Asymmetric dopamine imbalance remains a powerful theoretical impetus for schizophrenia researchers (Early et al., 1989) and has been implicated in affective disorders (Flor-Henry, 1986; Keshavan et al., 1986). This background would provide a rationale for neuroimaging using dopamine ligands (Sedvall, 1990) in conjunction with the neuropsychological testing described above, as well as psychopharmacological manipulations. The current study is not able to shed light on this issue since many of the schizophrenic patients were receiving dopamine antagonist drugs. Although it should be noted that medication did not appear to influence results across subjects. Alternatively, high resolution structural neuroimaging may reveal lesions which relate to these cognitive deficits.

In conclusion, avenues for further research into cognitive processes underlying psychopathology may employ usefully the psychological tests described, in conjunction with other physiological investigations.

6.5 Summary

Two tachistoscopic tests examining distinct aspects of attention were administered to normal subjects and patients with depression, mania and schizophrenia. The first examined spatial attentional bias using happy-sad chimeric faces, known to elicit a perceptual bias to the left side of space in normal right-handers provided the right cerebral hemisphere is intact. The second used a lateralised version of the Stroop task, a traditional test of selective attention. Normals showed the expected leftward perceptual bias but showed equivalent susceptibility to the Stroop effect in both visual fields. As previously demonstrated with chimeric faces viewed in free vision, depression and mania were associated with weak and strong biases respectively with schizophrenics showing no bias to either side of space. The relationship between perceptual bias, as assessed by reaction time and absolute performance, and the Stroop effect, showed differences according to diagnosis. This points to the dissociability of attentional processes as well as lateralised differences in the pattern of cerebral activation in affective disorders and schizophrenia. The independence of performance variables on these tests in the schizophrenic group is interpreted as evidence for severe neuropsychological dysfunction.

CHAPTER 7

CALLOSAL TRANSFER IN SCHIZOPHRENIA:

TOO MUCH OR TOO LITTLE?

7.1 INTRODUCTION

The corpus callosum has been implicated in the pathophysiology of insanity ever since Wigan's observations in 1844 (see Clarke, 1987). These speculations received a considerable boost following a post-mortem study showing thickened corpus callosa in chronic schizophrenic patients (Rosenthal & Bigelow, 1972). This was followed by numerous behavioural, physiological and anatomical studies - particularly magnetic resonance imaging (MRI) - examining callosal function and size in psychiatric groups (for reviews see Cutting, 1985; David, 1989a; Doty, 1989; Coger & Serafetinides, 1990; and chapter 1).

Raine and colleagues (Raine et al., 1990) reviewed 10 MRI studies and presented data on a new sample. In all, 6 out of 11 showed abnormal callosal dimensions in schizophrenics versus controls and of these, 4 had thicker or longer callosa, in at least a subgroup. As for functional measures, most researchers have looked specifically for evidence of disconnection. The reasons for this are, firstly, split-brain patients have occasionally been observed to exhibit "quasi-psychotic" behaviour - albeit fleetingly (Galin, 1974; David, 1989b) and second, a vast body of experimental research has been performed with these individuals providing a reliable data-base of the effects of cerebral disconnection (Gazzaniga, 1970; Benson & Zaidel, 1985). While a few studies have suggested some limited disconnection as inferred from reduced transfer of visual and tactile information in schizophrenic patients (Beaumont & Dimond, 1973; Green, 1978; Carr, 1980; David, 1987), other authors have not found this (Merriam & Gardner, 1987; Raine et al., 1989).

There is at least one major limitation to the approach of looking only for signs of disconnection. The studies do not address the qualitative changes in interhemispheric transfer in schizophrenia postulated by some authors, such as misconnection (Randall, 1983), partial disconnection (Nasrallah, 1985), defective integration (Green, Hallet & Hunter, 1986), and increased transmission of emotionally laden material (Oepen et al., 1987). Indeed the notion of hyperconnection taken at face value, fits more readily with the relative increase in callosal size found at post-mortem and using MRI. Furthermore, interest in neurodevelopment provides a mechanism whereby unnecessary or even aberrant connections may form and persist due to a failure in pruning (Goodman, 1989; Jones & Murray, 1991). It is therefore possible that the apparent disconnection effects noted may reflect inefficient or excessively "noisy" transfer. Finally, the notion of hyperconnectivity would appear to accord with models from information processing which have long put forward the view that schizophrenia is caused by difficulties in filtering and selecting relevant information (McGhie & Chapman, 1961; Braff & Geyer, 1989), with the adaptation that the filtering occurs during the flow of information from one part of the brain to another.

The current study entails the application of a novel, tachistoscopic, divided visual field technique for examining callosal connectivity. It employs a version of the Stroop test in which a colour patch is paired with a colour word which may be either congruent (the word RED with a red patch) or incongruent (the word BLUE with a red patch). The slowing of reaction time (RT) or interference in identifying the colour patch when accompanied by an incongruent word is known as the Stroop effect and has been extensively studied over decades (see MacLeod, 1991; for review). Similarly though less robust, is a speeding-up or facilitation of RT when the colour and colour-word match. The author has adapted the Stroop test by separating the colour and the colour-word across the mid-line, in order to measure interhemispheric transfer, since some transfer of information must take place for interference or facilitation to occur (Dyer, 1973; David, 1992; see chapter 4). To control for intra-hemisphere effects, the same Stroop stimuli can be presented to a single visual field. Research in normal subjects (chapter 4) has shown that the combined Stroop effect (CSE), that is the difference between RT for incongruent and congruent Stroop stimuli, is approximately equal in the left visual field (LVF) and the right visual field (RVF) but is reduced in the central or "bilateral" condition in which the colour and word are separated so that one element (e.g., the colour patch) goes one visual field and the other element (e.g., the colour word) goes to the opposite field. This was interpreted as indicating relative interhemispheric disconnection, and was supported by data from at least 2 out of 3 subjects with callosal agenesis (chapter 4). A pattern of results where the CSE is greater centrally than laterally, could be taken as evidence for relative hyperconnection.

This paper chapter the results of the application of this version of the Stroop test to a mixed group of schizophrenic patients. The results are compared with those from both normal subjects and psychiatric controls with affective disorder. The relationship between an index of callosal connectivity and clinical characteristics of both the patients and normals is also studied.

7.2 METHOD

Subjects

One hundred and fourteen subjects were tested. These included 46 schizophrenic patients from the Bethlem Royal and Maudsley Hospitals, London, who were mainly in-patients (n=29) though some out-patients and day patients were also studied. Also included were 22 in-patients and day patients with affective disorder from the same hospital group, and 46 normal controls drawn from the academic and ancillary staff of the Institute of Psychiatry, London. These subjects and rating scales used in their assessment, have been described in chapters 2 (normals) and 5 (patients). See appendix I

Patients were diagnosed according to DSM-III-R criteria (American Psychiatric Association, 1987) based on symptoms at interview - using the Present State Examination (PSE) (Wing, Cooper & Sartorius, 1974) - and those recorded in the case notes. The schizophrenic patients were classified by their illness course, following DSM-III-R as: acute or sub-chronic with acute exacerbation (21); chronic and subchronic (19); and, in remission (6). The affective disorder patients comprised 12 with major depression and 10 with bipolar affective disorder. Prescribed medication is described in chapter 5.

Overall psychopathology was rated on the modified Brief Psychiatric Rating Scale (BPRS) (Bech, Kastrup & Rafaelson, 1986); range 0-36.

Family history of psychiatric disorder was determined from patient interview and case note review. A positive family history was defined as hospitalization for probable psychosis or suicide in a first degree relative.

Normal subjects completed a questionnaire for hallucinatory predisposition (Launay & Slade, 1981), which consists of a 12-item scale measuring susceptibility to auditory and visual hallucinations. All subjects were administered the National Adult Reading Test (NART) (Nelson & O'Connell, 1978) to give an estimate of IQ and their years of education recorded.

Means and standard deviations for age, IQ, years of education and BPRS scores are given in chapter 5, Table 5.1 for the 3 groups.

Tachistoscopic Stroop Tests

Stimuli and Apparatus

Details of stimuli and apparatus are given in chapter 4, Figure 4.1 and section 4.2.

There were 72 stimuli in total, 24 left, 24 right and 24 central. Half were congruent and half incongruent. In each condition, 12 had the colour to the right of the word and 12 were the opposite way round. All subjects had to demonstrate their ability to read all the colour words and name all the colours, under test conditions, before proceeding to the test proper.

Apparatus consisted of a custom built back-projection tachistoscope (as in chapters 2,4,5 and 6). As before, responses were made by the subject's verbal report activating a voice key. Reaction time in msecs was recorded and entered directly into a personal computer for analysis.

Procedure

This was identical to that described in chapter 4, section 2. Presentation was brief enough (120msec) to prevent voluntary saccades (Young, 1982). Occulographic methods of monitoring fixation are too intrusive for many acutely psychotic patients and techniques requiring identification of a digit or letter at fixation contribute an additional cognitive load (see chapter 1). Hence, perfect fixation could not be guaranteed. Prior to testing, subjects were given a standard set of instructions, in which they were asked to name the colour as quickly and as accurately as possible.

7.3 RESULTS

Results were analysed using subject-based analysis of variance (ANOVA) with RT as the dependent variable. The analyses were 4-way with congruity and visual field (right, left, central) as within-subject variables and sex and diagnosis as between subject variables. Sex was included because of gender-related differences in callosal size noted in some published reports (Raine et al., 1990). Preliminary analyses examining the effects of neuroleptic treatment were also performed.

There were no main effects or interactions for sex nor for medication. The main effect of neuroleptics was F=.07, P=.8. These variables will no longer be considered in the analyses. There were significant main effects for congruent versus incongruent colour-word combinations (F(1,108)=407.8, P<0.0001), and for visual field (F(2,216)=54.2, P<0.0001). The former is accounted for by the greater RT for incongruent stimuli; the latter, is the result of the advantage in the central condition versus the lateral condition. Diagnosis also produced a significant main effect (F(2,108)=19.0, P<0.0001) with schizophrenic patients slower than affectives who in turn were slower than normals (see Table 7.1). The diagnosis X congruity interaction was not significant (F(2,108)=0.85, P=0.4), that is the different groups did not differ in their susceptibility to the Stroop effect in general. However, the diagnosis X congruity X field interaction was significant (F(4,216)=4.6, P=0.001). This is explained by the greater CSE for central/bilateral stimuli in the schizophrenic group as compared with controls. The effect of neuroleptic medication on the diagnosis X congruity X field interaction was examined within the patient group and found to be non-significant (F=1.8, P=.2). Subtracting congruent from incongruent RT, affords a control for the predictable general slowing in the patient groups. As can be seen illustrated in Figure 7.1, the CSE does not differ between the groups in the 2 lateral positions (left CSE: F(2,111)=0.28, P=0.7: right CSE F(2,111)=0.30, P=0.7) but does so centrally (central CSE F(2,111)=5.1, P=0.0075: all statistics by one-way ANOVA).

That is the schizophrenics differ in terms of the difference in RT between congruent and incongruent Stroops only when the facilitation and interference involve interhemispheric transfer. Within the normal group, the bilateral CSE is significantly smaller than the left and right field CSEs (paired t-test: $t=2.82$, $P<.01$ and $t=2.35$, $P<.05$, respectively), while in the schizophrenic group, the bilateral CSE is larger than the left and right CSEs ($t=-2.45$, $P<.02$ and $t=-2.18$, $P<.05$, respectively). The pattern of results for the affectives is similar to normals but the results are not statistically significant (see Figure 7.1).

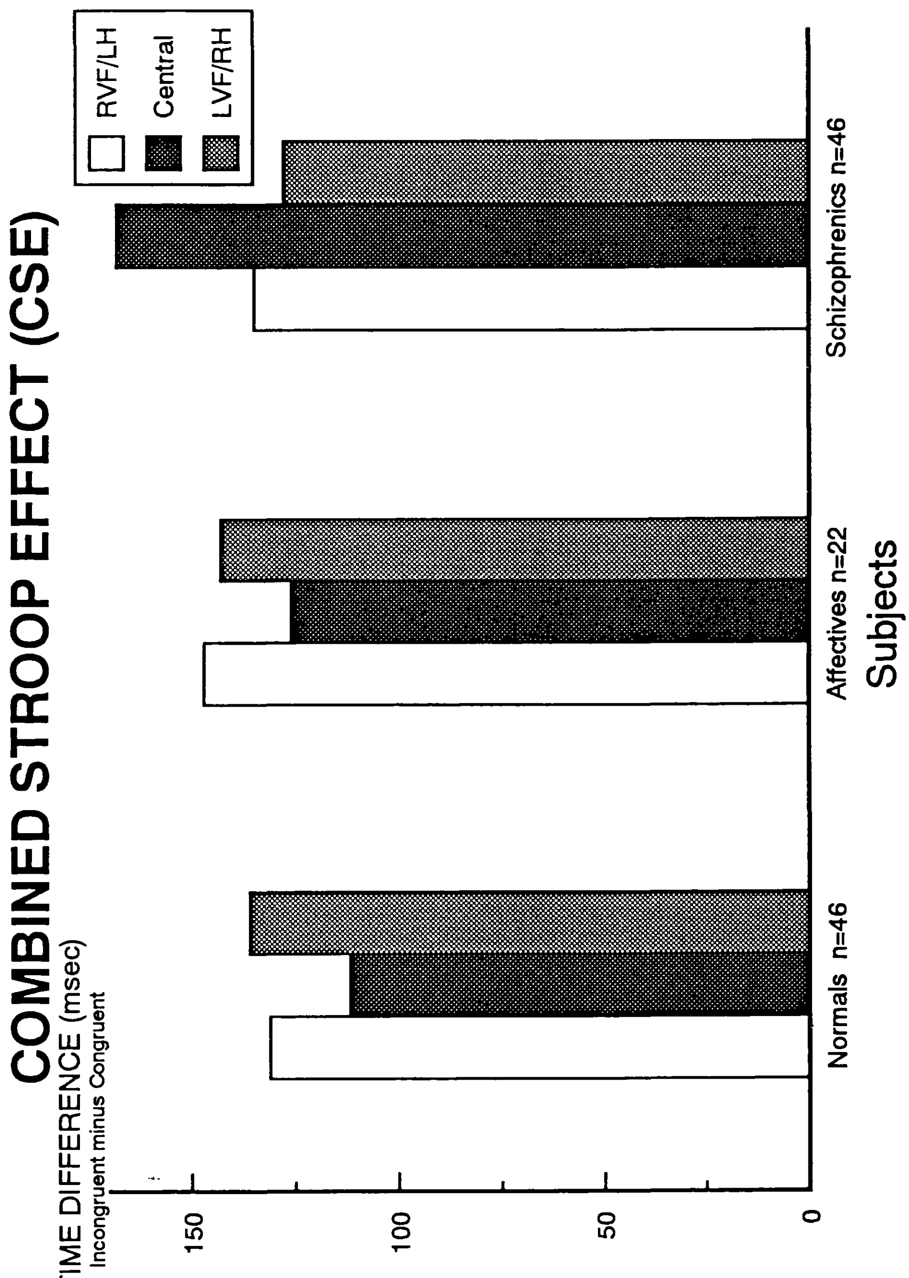
In order to ensure that the CSEs were not simply related to "baseline" performance, Pearson correlation coefficients were calculated for congruent RT and right, left and bilateral CSEs. These were all non-significant: $r = -0.05$, 0.22, and 0.13, respectively.

An index of this increased callosal transfer, the "callosal index", can be derived from subtracting the mean of the 2 lateral CSEs from central CSE. The values for this for normals, affectives and schizophrenics are given in Table 7.1. Schizophrenic patients differ significantly from both control groups, (ANOVA: $F(2,111)=9.3$, $P=0.0002$). The magnitude of the callosal index was not related to congruent RT ($r=0.08$).

Errors

Error rates were low (see Table 7.1), attesting to adequate fixation, and the ANOVA did not reveal an overall group difference ($P=0.4$). There was a trend for incongruent trials to induce more errors ($P=0.16$) and the interaction between diagnosis and congruity reached significance ($P<0.05$). This is accounted for by the higher error rate in the schizophrenics in the incongruent condition.

Figure 7.1


COMBINED STROOP EFFECT (CSE)
TIME DIFFERENCE (msec)
Incongruent minus Congruent
0
50
100
150
RVF/LH
Central
LVF/RH
Normals n=46
Affectives n=22
Schizophrenics n=46
Subjects

	Normals	*Affectives*	*Schizophrenics*
Reaction time (msec)	679 ± 84	772 ± 162	863 ± 182*
CONGRUENT RT	621 ± 84	709 ± 148	797 ± 175*
Right visual field	621 ± 83	710 ± 160	806 ± 186*
Left visual field	629 ± 84	718 ± 147	812 ± 175*
Bilateral	599 ± 85	682 ± 142	758 ± 170*
INCONGRUENT RT	737 ± 90	835 ± 183	930 ± 195*
Right visual field	752 ± 86	857 ± 195	941 ± 193*
Left visual field	764 ± 107	862 ± 188	940 ± 205*
Bilateral	711 ± 93	805 ± 181	926 ± 206*
Combined Stroop effect	116 ± 46	126 ± 74	133 ± 71
Errors (%)	1.8 ± 2.5	1.9 ± 4.7	3.7 ± 5.1#
¶Callosal index	-20.9 ± 42.9	-22.6 ± 54.3	36.8 ± 95.1#

Comparison of groups using ANOVA and the Least Significant Difference procedure: *Schizophrenics differ from normals and affectives at P<0.05; affectives also differ from normals at P<0.05. #Schizophrenics differ from affectives and normals at P<0.05. Subject groups not significantly different on combined Stroop effect (P=0.4).

¶Callosal index = Cen CSE - (L CSE + R CSE)/2.
RT = Reaction time

Table 7.1. Comparison of normal controls, patients with affective disorder and schizophrenia on reaction time and percent errors with congruent and incongruent tachistoscopic Stroop stimuli: Means±SD.

7.4 Relationship between test performance and clinical characteristics

Given that the groups were not matched for IQ, age, education, it is important to determine the influence of these factors on the dependant variables of interest. Pearson correlation coefficients for these 4 variables with test performance for stimuli in the 3 positions of presentation and also the callosal index were calculated on the subjects as a whole and within groups. These were all non-significant ranging from 0.19 to -0.14. ANOVAs calculated on the CSEs and callosal index were essentially unaltered by covarying for IQ, age, education and BPRS, despite the wide range in the patients' clinical state. Error rate was correlated with IQ, education and BPRS at -0.37, -0.35 and 0.30 respectively, but not age. There were significant correlations with overall mean RT at -0.20 and -0.24 for IQ and education, and 0.47 for BPRS, respectively.

Only 16/46 (34.7%) normal subjects and 8/22 (36.4%) of affectives had central CSEs greater than their lateral CSEs while 26/46 (56.5%) schizophrenics showed this distribution of scores (df 2, χ^2=5.04, P=0.06). These 16 normals did not differ from the remainder on any of the background variables.

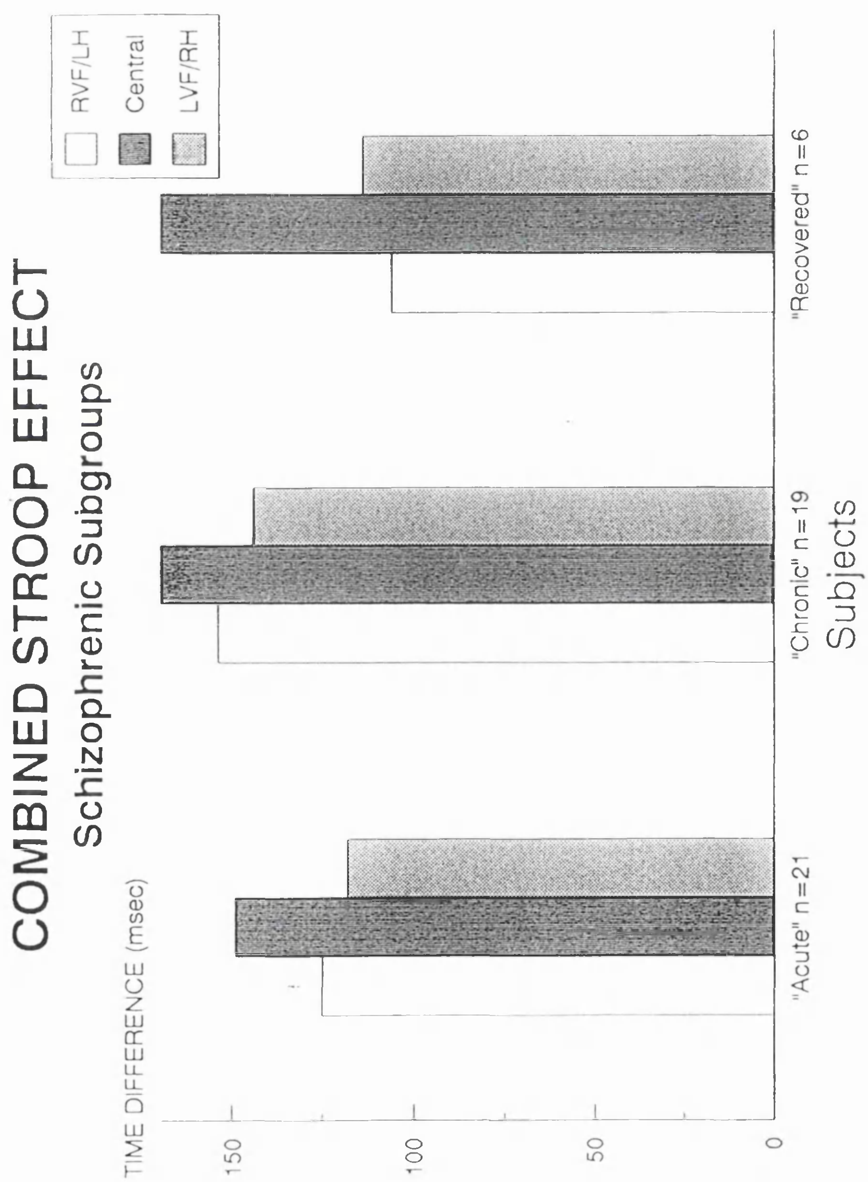
Hallucinatory predisposition (normal subjects)

Scores on the Launay and Slade scale (1981) ranged from 0 to 7 (mean 1.2±1.7). There was no significant association between this measure and RT or the CSEs. Thirteen subjects scored >1. When these were contrasted with the remaining 33 subjects on the callosal index the scores were: -17.1±42.5 versus -30.6±44.1; [t(44)=0.34, P=0.3]. Left and right CSEs were not significantly affected by hallucinatory disposition.

7.5 Schizophrenic subgroups

There were no systematic differences between any of the schizophrenic subgroups on the tachistoscopic tests. Of some interest is the non-significant trend towards a greater callosal index in the recovered group (n=6) of 71.0 compared with 31.6 for the others (see Figure 7.2).

Figure 7.2


COMBINED STROOP EFFECT
Schizophrenic Subgroups
TIME DIFFERENCE (msec)
150
100
50
0
"Acute" n=21
"Chronic" n=19
"Recovered" n=6
Subjects
RVF/LH
Central
LVF/RH

Other clinical variables were examined for their influence on the callosal index including the presence of auditory hallucinations (n=29), first rank symptoms (as defined in the PSE (Wing et al., 1974); n=20) and a positive family history (n=15). None of these had significant effects. Similarly, those schizophrenic patients whose callosal index was >0 did not differ from the rest.

7.6 DISCUSSION

The results showed that for normal subjects and psychiatric controls, both interference and facilitation are reduced in the central condition suggesting a partial filtering of colour or word information interhemispherically, or relative disconnection. The schizophrenic patients showed the opposite pattern, suggesting a specific failure to regulate interhemispheric transmission or functional "hyperconnection". This double dissociation cannot be explained by non-specific effects such as hospitalization and level of symptoms since the affective disorder group, who had equivalent levels of psychopathology to the schizophrenics, resembled normals. Also, the central condition was "easier" then the two lateral conditions, as reflected in the shorter RTs, so that the difference between schizophrenics and the other groups is unlikely to be a consequence of task difficulty. Further support for this is the larger effect in recovered schizophrenic patients. Background characteristics such as age and IQ did not influence test results on the measures of callosal function in the sample as a whole or in the schizophrenic group in particular. Neuroleptic medication has been postulated to reduce callosal transfer (Myslobodsky, Mintz & Tomer, 1983) although no support for this was found. The lack of difference between patients on and off neuroleptics, both schizophrenics and non-schizophrenics, implies that the difference between groups is unlikely to be due to medication. Disturbance within one or other hemisphere is also unlikely to account for the data since the CSE did not differ between the LVF and RVF. Finally, a difficulty with processing Stroop stimuli per se (see Liddle & Morris, 1991) is excluded since the CSE, which takes into account non-specific slowing of RT, did not differ between the groups (Everett, Laplante & Thomas, 1988).

These results can be seen as supporting previous work by the author employing tachistoscopic colour perception tests, only insofar as abnormal callosal function is implicated in both. The former study (David, 1987) measured only error rates, which were relatively high because of the brief duration of stimuli (30 msec), rather than RT, so may have been less sensitive. Also the design, which involved cross field colour-matching, was not capable of revealing hyperconnection only a global callosal deficit.

The earlier study did show a relationship between callosal transfer and symptom profile, namely the presence of first rank symptoms, consistent with Nasrallah's partial disconnection model (Nasrallah, 1985), while the current study showed no relationship to these or other variables. In fact the trend pointed towards more callosal connectivity in relatively symptom free patients. In addition, the pattern of results in normal subjects who are prone to hallucination-like experiences was not in the direction of the schizophrenic patients. Can these findings be reconciled? It is important to consider the dynamic role of the corpus callosum in regulating hemisphere functioning (Cook, 1986; Zaidel, Clarke & Suyenobu, 1990). While the tract clearly has a major role in conveying information from one hemisphere to the other, it also appears to have a role in inhibiting hemisphere activity. It is therefore possible that while the data presented here show an increased flow of information across the callosum, this could reflect some compensatory strategy designed to obviate a primary disturbance within the hemispheres. Hence the lack of association with current hallucinatory symptoms in both psychotics and normals, and the suggestion of an association with recovery. However, this hypothesis would predict that the callosal index should be positively correlated with the lateral CSE. In fact the correlation is not significant (-0.14 for Stroop stimuli in the LVF and -0.06 for those in the RVF).

Alternatively, since the majority of the schizophrenic group showed the abnormality, it could be argued that excess callosal transfer is a vulnerability marker (Green et al, 1986), perhaps non-familial in this case, rather than being directly related to the production of psychotic symptoms. Further research which tests patients at different stages of their illness and non-affected relatives is necessary to clarify this. Another question that remains is whether the functional measures reported have a structural basis (Günther et al., 1991), and if so, what region of the callosum is implicated. It might be predicted that the splenium would be involved given its role in colour transfer (David, 1987). On the other hand, since precise semantic information, in the form of a colour name, is also involved, the anterior portion would probably be site of transfer (Zaidel, Clarke & Suyenobu, 1990). A study using MRI on a sub-sample of the schizophrenic patients which addressed this issue will be described in the following chapter (chapter 8).

In conclusion, the evidence that the functioning of the corpus callosum may be abnormal in schizophrenia, and that this abnormality is one of hyperconnection, is gradually accumulating. Although some of the evidence is contradictory, it comes from diverse sources including neuroimaging (Raine et al., 1990), neuropsychology (Green et al., 1986; Doty 1989), cerebral blood flow (Günther et al, 1991), EEG coherence (Merrin, Floyd & Fein, 1989), somato-sensory evoked potentials (Gulmann, Wildschivødtz & Ørbæk, 1982), and neurochemistry (Deakin, Slater & Simpson, 1989). What remains to be determined is its precise role in the pathogenesis of schizophrenia.

7.7 Summary

Evidence from diverse sources has pointed to an abnormality in callosal transfer in schizophrenia. To examine this further, a test was devised which measures Stroop interference and facilitation within and between the cerebral hemispheres. 46 heterogeneous schizophrenic patients were tested and it was found that lateralised Stroop effects were equivalent in the left and right hemispheres and did not differ from normal or psychiatric controls with affective disorder. In controls, Stroop effects which required inter-hemispheric transfer of coded information, were reduced relative to those requiring intra-hemispheric transfer, while the schizophrenic group showed greater Stroop effects in the inter-hemispheric condition, presumably reflecting increased callosal connectivity. An index of callosal transfer did not correlate with gender, age or IQ in any of the groups, nor did it relate to clinical characteristics in the schizophrenic patients. The results support a specific functional abnormality of excessive callosal transfer in schizophrenia though its role in pathogenesis remains unspecified.

CHAPTER 8

STRUCTURE AND FUNCTION OF THE CORPUS CALLOSUM IN SCHIZOPHRENIA: WHAT'S THE CONNECTION?

8.1 INTRODUCTION

The corpus callosum (CC) has been the target of much structural brain research, ever since the post-mortem study showing thickening in chronic schizophrenic patients (Rosenthal and Bigelow, 1972; see also Bigelow et al., 1983), and functional neuropsychological research, since the divided visual field study showing impaired interhemispheric transfer (Beaumont and Dimond, 1973; see Doty, 1989; Coger and Serafetinides, 1990; for reviews; see chapter 1). Both approaches have tended to progress in parallel with few studies combining functional and structural measures, on the same group of subjects.

One such study (Raine et al., 1990) using magnetic resonance imaging (MRI), replicated previous work in showing increased anterior callosal thickness in female psychotic patients (see also Nasrallah et al., 1986; and Uematsu and Kaiya, 1988). Unfortunately, dichotic listening and tactile tests of intra- and inter-hemispheric function did not relate to callosal dimensions. Another recent report related increased callosal thickness with positive symptoms (Günther et al., 1991), but did not report neuropsychological tests of callosal function. Woodruff et al., (in press) reported a reduction in the mid-callosal area in schizophrenics versus normal controls, which they believe may relate to reduced temporal lobe volume which, in turn is related to auditory hallucinations (Barta et al., 1991). They also found an inverse correlation between mid-sagittal callosal and cerebral areas, and delusions.

While several studies have shown a relationship between global cognitive impairment in schizophrenia and cerebral atrophy (e.g. Johnstone et al., 1976), consistent brain-behaviour relationships between more specific, localizable cognitive tests and particular brain areas have proved more elusive (DeLisi et al., 1991). This pattern applies even more strongly to the corpus callosum. While it has an undoubted role in conveying information between, and modulating the activity within the cerebral hemispheres (Benson and Zaidel, 1985), it is a structure with considerable variation in size and shape (Demeter et al., 1988; Casanova et al., 1990). Hence, attempts to correlate reliably morphology with function in normal individuals, have proved difficult (Zaidel et al., 1990) even when relatively gross differences such as handedness were investigated (see Habib, et al., 1991).

Previous work using a tachistoscopic test of colour naming and matching designed to tap callosal function in schizophrenia showed evidence of impaired interhemispheric connectivity. Further investigation suggested that this impairment was associated with first rank symptoms (Schneider, 1959) and inversely correlated with cerebral atrophy as estimated from CT scan ventricle-brain ratio (VBR) (David, 1987). A theoretical relationship between certain symptoms such as disturbances of the possession of thought and auditory hallucinations etc., with callosal dysfunction, has been proposed by a number of authors (Randall, 1983; Nasrallah, 1985).

The present study employed a novel version of the Stroop test to measure interhemispheric function (see chapters 4 & 7). The classical Stroop paradigm consists of a colour patch paired with a colour word which may be either congruent or incongruent. The slowing of reaction time (RT) or interference in naming the colour patch when accompanied by an incongruent word is known as the Stroop effect (see MacLeod, 1991; for review). Similarly there is often a speeding-up or facilitation of RT when the colour and colour-word, match. The Stroop test has been adapted by separating the colour and the colour-word across the mid-line, in order to measure interhemispheric transfer, since some transfer of information must take place for interference or facilitation to occur (Dyer, 1973b; David, 1992; chapters 4 & 7). Research in normal subjects (David, 1992) has shown that the combined Stroop effect (CSE), that is the difference between RT for incongruent and congruent Stroop stimuli, is approximately equal in the left visual field (LVF) and the right visual field (RVF) but is reduced in the "bilateral" condition in which the colour and word are separated so that one element (e.g., the colour patch) goes one visual field and the other element (e.g., the colour word) goes to the opposite field. This was interpreted as indicating relative interhemispheric disconnection in normals. The technique has been applied to a large group of schizophrenic patients and psychiatric controls and it was found that unlike normals and controls, the schizophrenics showed a greater mean CSE in the bilateral compared to the unilateral condition, which may be taken as evidence for relative callosal hyperconnection. This pattern of results, is consistent with theories which emphasise defective integration and misconnection (Green et al., 1986; Randall, 1983; Nasrallah, 1985; Oepen et al., 1987; chapter 7) rather than dis-connection as the underlying callosal abnormality in schizophrenia (Beaumont and Dimond, 1973).

It has been possible to obtain CT and MRI scans on a sub-sample of these patients. The CT scans have been used to calculate VBRs and the mid-sagittal MRI scans, to acquire data on the dimensions of the CC. The measures from the structural imaging techniques were used to determine whether the functional abnormalities revealed by the interhemispheric Stroop test and inferred from symptoms profiles, had a structural basis.

8.2 METHOD

Subjects

31 subjects had CT scans (20 males, 11 females) of whom 20 had MRI scans (14 males, 6 females). They represent an unselected subgroup of the 46 schizophrenic patients from the Bethlem Royal and Maudsley Hospitals, London, who participated in the earlier neuropsychological study (see appendix I and Chapters 5,6 & 7 for details).

The MRI group were part of an independent study of consecutive schizophrenic admissions, reported in detail elsewhere (Harvey et al., 1991).

Patients were diagnosed and assessed as described in chapter 5. The schizophrenic patients were classified by their illness course, following DSM-III-R. In this sub-sample, 2 were acute, 5 in remission and the remainder were chronic or subchronic. All but 2 were receiving neuroleptic drugs. Overall psychopathology was rated on the modified Brief Psychiatric Rating Scale (BPRS) (Bech et al., 1986); range 0-36, and IQ on the NART. Family history of psychiatric disorder was determined from patient interview and case note review. A positive family history was defined as in chapter 7, section 2.

Stimuli and Apparatus

The lateralised and bilateral Stroop stimuli were presented as described in chapter 7 section 2. Apparatus and procedure were as before.

The measures of interest are: The magnitude of the Combined Stroop Effect (CSE) (incongruous RT minus congruous RT) in the LVF/right hemisphere, the *"Left Stroop"*; and the RVF/left hemisphere, the *"Right Stroop"*. These give a measure for the Stroop effects within each hemisphere and so provide a comparison for the "between hemispheres" condition. Of most interest is the between-hemispheres or bilateral condition where the colour-word is in one visual field and the colour patch is in the other: the *"Bilateral Stroop"*. From these can be derived indices of callosal function namely the *"Callosal Index"* which is the difference between the Bilateral Stroop and the mean of the two unilateral Stroop presentations [i.e. Callosal Index=Bilateral Stroop - (Left Stroop+Right Stroop)÷2]. The magnitude of this index is independent of RT (chapter 7 section 3).

In addition, the Bilateral Stroop can be broken down to 2 presentations corresponding to whether the colour is to the left or the right visual field. Studies in normals have shown that the colour-right position results in a small RT advantage presumably because the colour can be named directly by the left hemisphere (McKeever and Jackson, 1979) while the colour-left position requires an addition callosal transfer of the colour information from the right hemisphere to the left hemisphere. Hence a large difference in RT between the *"colour-left minus colour-right"* conditions would also reflect reduced callosal transfer and a small or negative value would reflect increased transfer (see chapter 4, Figure 4.3).

8.3 IMAGING

MRI

A single mid-sagittal image was obtained over three minutes using a T_1 weighted sequence ($SE_{200/300}$) on a 0.5 Tesla Picker scanner at the National Hospital, Queen Square, London. This was accurately positioned in the mid-sagittal plane through the use of two orthogonal pilot scans (McManus et al., 1989). Slice thickness was 10mm, with a matrix size of 256 x 256 pixels, and a 30 cm field of view (i.e. each pixel is 1.37 mm^2), and two excitations used. Geometric distortion on this scanner is 1% in each plane.

Images were transferred on magnetic tape to an image display system (Sun Microsystems Inc., California) and identified by number alone to retain blindness during measurements. Image analysis was performed with the software package "Analyze" (Robb and Barillot, 1989). The CC was outlined using a semi-automated "region-growing" program, which could be altered interactively until it coincided visually with the callosal boundary; the area was then calculated automatically. All ratings were made by one person (Dr Ian Harvey,National Hospital, Queen Square), with satisfactory test-retest reliability (intra-class correlation coefficient of 0.76)

Given the variation in size and shape of the callosum (Demeter et al., 1988; Casanova et al., 1990) and the possibility of producing a type I error from the over-zealous selection of areas of interest for correlation with the behavioural data, it was decided to measure only the anterior portion as well as total area. This seemed logical given the fact that the interhemispheric Stroop effect depends on the transfer of precise semantic information (i.e a colour name) which is thought to rely on anterior callosal fibres (Zaidel et al., 1990). Also, the bulk of data from callosal studies in schizophrenia point to differences in the anterior portion (Bigelow et al., 1983; Nasrallah et al., 1986; Uematsu and Kaiya, 1988; Raine et al., 1990).

The anterior area portion was calculated using a radial rather than linear method (see Clarke et al., 1989), modified for the "Analyze" program. A line was drawn through the CC at its greatest anterior-posterior length and then a radius placed at 12° so that it intersected the CC approximately between the genu and body. The anterior callosal area was the area of the rostrum and genu enclosed by this line as indicated using the region-growing technique. Results from this method were compared to those from a linear method, namely measuring regions 1 and 2 as described by Witelson (1989), and found to be highly correlated (r=0.88). The radial method was adopted as it seemed to take better account of the curved callosal anatomy.

In order to minimise the confounding effects of gender, ethnicity and height (Harvey et al., in press), the callosal areas in cm^2 were adjusted for intracranial volume (see also Nasrallah et al., 1986; DeLisi et al., 1991) by calculating a ratio of callosal area to intracranial volume. The latter measure was derived from an interleaved set of 24 transverse 5 mm slices, covering the entire supratentorial volume and taken at the same time as the mid-sagittal slice. These structural measurements were then analysed with respect to the clinical, demographic and psychometric data.

CT

Brain CT scans were obtained on a Siemens CT9800 scanner. The intracranial and lateral ventricular areas were determined by semi-automated planimetry at the scanner console, soft tissue and fluid density being markedly lower (0-99 Hu) than surrounding bone (>1000 Hu). The slice showing the largest ventricular area, and all pixels with Hounsfield units of 0-25, equivalent to cerebrospinal fluid (Harvey et al., 1989), was used to calculate the Ventricle:brain ratio (VBR). Two raters (Dr Peter Jones and Dr Carine Minne, Institute of Psychiatry and Maudsley Hospital) rated the scans and intraclass correlation coefficient for intracranial and lateral ventricle area were 0.98 and 0.89 respectively.

8.4 RESULTS

The 31 CT scanned patients did not differ from the remaining 15 of the original sample on mean IQ (108.3), age (30.7), years of education (12.4) or BPRS score (16.6), (all P>0.5 by t-test, 2 tailed) or any of the RT measures reflecting callosal function (all P>0.3). However, they tended to have a slower RT (±SD) overall [944 (236) vs 824 (136); P=0.08]. Similarly, the MRI scanned patients were no different from those not scanned in terms of IQ, age or BPRS (all P >0.1) although they had more admissions to hospital [4.8 vs 2.8; P=0.02] and had spent more years in education [13.3 vs 11.6; P=0.05]. RT overall and on measures reflecting callosal function was comparable for the two groups (all P>0.3).

8.5 Relationship between test performance, clinical characteristics and neuroimaging

As previously shown, there was no significant association between IQ, age, education, number of admissions and BPRS and any of the callosal Stroop measures. As in the larger study (chapter 7), the sub-samples reported here both showed that the Bilateral Stroop condition gave the largest Stroop effect compared with the two unilateral positions which, in turn, did not differ significantly from each other (see Table 8.1). This yields positive Callosal Indices.

	Stroop-L	Stroop-R	Bilateral	Callosal Index	Position X Cong F	P
VBR Patients (n=31)	106.9 (76.5)	126.7 (80.1)	157.2 (116.0)	40.4 (91.5)	4.69	0.001
MRI Patients (n=20)	113.0 (84.2)	136.6 (90.7)	178.9 (139.1)	54.1 (115.6)	3.22	0.05

*ANOVA performed with RT as the dependent variable and position of stimuli presentation (left, right, bilateral) and congruity (congruent, incongruent) as the independent variables. There was the expected significant main effect for congruity, P<0.001 (i.e. the Stroop effect). There is a significant interaction between position and congruity accounted for by the greater Stroop effect in the bilateral condition.

Table 8.1. Stroop RT (±SD) in msec. with left and right visual field presentation, bilateral presentation, "Callosal Index" and results of ANOVA*.

CT Scanning

VBR did not correlate significantly with any clinical variable including IQ (r=-.04), age (0.16) and BPRS (r=-.06). There was a weak negative correlation with overall RT (r=-.14) and no significant correlation with the Stroop tests of callosal function including the Callosal Index (r=-.09) and "colour-L minus colour-R" (r=-.18).

MRI Scanning

Mean total CC cross-sectional area (cm^2) was 4.57 (0.72); anterior area was 1.02 (24.2). Mean intracranial volume (cm^3) was 1221 (118); mean total CC area adjusted for volume, 0.0377 (0.0067), and anterior area adjusted for volume, 0.0084 (0.0018). The results for Pearson correlation coefficients between morphometry, Stroop tests and demographic/clinical variables are given in Table 8.2. The Callosal Index correlated with adjusted anterior area at r=0.39. The "colour-L minus colour-R" measure correlated inversely with anterior callosal area when taken as a ratio of the whole CC (r=-0.44). That is, as would be predicted, the larger the anterior callosum relative to the whole CC, the smaller the RVF/left hemisphere advantage for colour naming. VBR did not correlate with callosal measures or intracranial volume.

	Age	IQ	BPRS	L-Stroop	R-Stroop	Bilat	Callosal Index	Colour-L minus Colour-R
Callosal Area								
Total :	-.19	-.13	.07	.25	.03	.18	.12	.15
Anterior :	-.48*	.05	.06	-.07	-.27	.14	.29	-.26
Ant:total[1] :	-.41	.18	.01	-.29	-.29	-.01	.20	-.44*
Anterior - adjusted[2]:	-.44*	-.05	.17	-.12	-.19	.21	.39#	.24

[1] Anterior callosal area to total callosal area ratio.

[2] Anterior callosal area adjusted for intracranial volume.

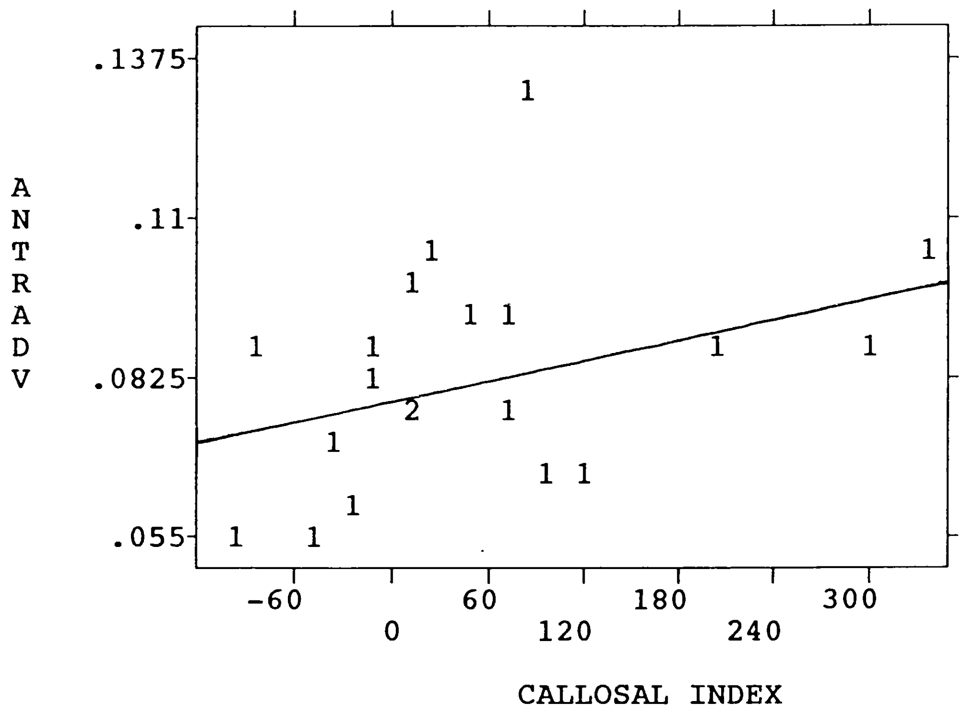
*Significant, P≤0.05

#trend, P=0.08

Table 8.2. Correlations (Pearson's r) between MRI measures of the corpus callosum and demographic, neuropsychological and clinical variables.

Figure 8.1 PLOT OF ANTERIOR CROSS-SECTIONAL AREA WITH INTERHEMISPHERIC STROOP EFFECT "CALLOSAL INDEX"

(Radial method - adjusted for intra-cranial volume)



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20 cases plotted. Regression statistics:
Correlation = 0.382

R Squared .14565 Sig. .0968

Hallucinations

MRI patients with auditory hallucinations (n=10) had smaller anterior callosal areas than the rest and this difference was more pronounced when adjusted for intra-cranial volume (t=2.18; P=0.04) (see Table 8.3). Those with first rank symptoms did not differ from the other patients on any MRI brain measure. VBR was not related to these symptom complexes.

	VBR (n=31)	Callosal Index	Colour-L minus Colour-R	CC area (Total)	Ant Area	Ant Area (adjusted)
Non-hallucinators (n=10)	5.64 (2.6)	84.6(135)	6.5 (96)	4.70 (.72)	1.12 (.27)#	.92(.02)*
Hallucinators (n=10)	6.48 (3.2)	23.5(88)	11.1 (48)	4.45 (.73)	.93 (.21)	.75 (.01)

#Trend, P=0.07

*Significant, P=0.04

Table 8.3. Comparison of hallucinating and non-hallucinating schizophrenic patients on functional and structural measures of the corpus callosum.

Family History and Sex Differences

MRI patients with a positive family history (n=7) tended to have slightly smaller callosa than the others [4.68 (0.75) vs 4.38 (0.65)] but this difference was not significant. The CT scanned group with a positive family history (n=12; 9 male, 3 female) also tended to have smaller VBRs (i.e. less atrophy) than non-familial cases [5.08 (2.6) vs 6.83 (3.1); P=0.1]. This trend was accentuated when males only were analysed with respect to family history [5.26 (2.4) vs 8.00 (2.1); t=2.72; P<0.02].

Males tended to have larger VBRs (i.e. greater atrophy) [6.77 (2.6) vs 5.05 (3.5)] and larger corpra callosa [4.61 (0.63) vs 4.49 (0.95)] than females, even when adjusted for intracranial volume. However, these differences were not statistically significant.

8.6 DISCUSSION

Two salient findings arose from this study. First, there was a near significant positive correlation of 0.39 between the key measure of callosal function the "Callosal Index", previously shown to be increased in schizophrenia, and the adjusted anterior callosal area. This was in line with prediction. The magnitude of the correlation is of the same order as that found in normal (Zaidel et al., 1990) and epileptic (O'Kusky et al., 1988) subjects when attempts are made to map laterality indices on to CC dimensions. Second, a significant difference was found between hallucinating and non-hallucinating patients with the former having smaller anterior callosal areas, while a global rating of psychopathology, the BPRS, was not significantly associated with callosal size. The hallucinators also tended to show less functional connectivity as reflected in the smaller Callosal Index. This pattern was unexpected and difficult to interpret. However, it is consistent with preliminary work by Woodruff et al., (in press), who argue that callosal area reduction may be secondary to temporal lobe dysgenesis. It does not accord with the simple notion of Randall (1983) that hallucinations are the result of unwanted "cross-talk" between the hemispheres due to an excess of callosal fibres.

Similarly, the significant inverse correlation between the "colour-L minus colour-R" measure, obtained from presentations of the bilateral Stroop stimuli, and anterior callosal area, though consistent with increased callosal connectivity, is not straightforward. This measure, unlike the Callosal Index, did not reveal differences between schizophrenic patients and controls in a previous study (chapter 7). It cannot therefore be assumed that a simple relationship exists between anterior callosal size, interhemispheric Stroop transfer and the clinical manifestations of schizophrenia. One possible explanation is that the increased callosal connectivity predisposes to schizophrenia but that once this has occurred, a relative reduction in anterior fibres dis-inhibits (Cook, 1986; Zaidel et al., 1990) those brain areas, perhaps in the right hemisphere, which produce hallucinations.

No significant findings emerged with respect to callosal area as a whole, or VBR. In particular neither VBR nor first rank symptoms related to tests of interhemispheric function (cf. David, 1987). This suggests that abnormalities on tests of callosal function are not the consequence of a generalised, perhaps acquired, brain disorder. Some interesting trends did arise out of comparisons between those with and without a positive family history of major psychiatric disorder. For instance, those with a family history appeared to have smaller callosa while they (especially males) had less cerebral atrophy as inferred from the VBR. This is consistent with the report of reduced cerebral volume in familial patients, in the absence of ventricular enlargement (Schwarzkopf et al., 1991). However the small size of the sample precludes firm conclusions on this score and results must be regarded as tentative. Further research which examines the genetic and environmental influences on CC development will be of value in generating hypotheses of relevance to schizophrenia (David et al, 1992).

No major sex differences were noted either on functional or structural measures. This is in contrast to previous work showing increase anterior callosal size in female schizophrenics (Raine et al., 1990; Nasrallah et al., 1986). Again, the few female cases in the present study prevents any secure judgement on this matter. There were some age effects namely the inverse correlation between age and anterior callosal size which must be borne in mind in future studies where subjects' ages fall into a wide range.

In conclusion, the current study represents an initial attempt to correlate structural and functional aspects of the corpus callosum in schizophrenia. The small numbers make the findings somewhat preliminary. Nevertheless, there does appear to be a relationship between an index of callosal connectivity using a novel application of the Stroop paradigm, and anterior callosal size in schizophrenic patients. This may also relate to important clinical phenomena such as auditory hallucinations. However the precise nature of the links between these different measures will require further study.

Summary 8.7

Tests of both structure and function of the corpus callosum have revealed abnormalities in schizophrenic patients. One such functional test employed lateralised Stroop stimuli presented tachistoscopically, to measure the transfer of interference and facilitation between the cerebral hemispheres. An attempt was made to relate indices of callosal transfer to clinical and demographic variables including family history, as well as to indices of brain morphology. The latter included ventricle:brain ratio (VBR) measured by CT scanning on 31 DSM-III schizophrenics, and the cross-sectional area of the corpus callosum from MRI, obtained from 20 of these patients. VBR did not relate to functional measures. However, anterior callosal area correlated with indices of callosal connectivity. Patients with auditory hallucinations had smaller anterior callosal areas and tended to show less connectivity. The results point to links between functional and structural measures of the corpus callosum but their precise nature remains unclear.

CHAPTER 9

CONCLUSIONS

9.1 CONCLUSIONS

This thesis began with a review of divided visual field studies in schizophrenia from which it was inferred that any statement locating the origin of schizophrenic disturbance to a particular brain region on the basis of neuropsychological tests, would be premature. Indeed, all brain regions examined, defined broadly as the left hemisphere (LH), the right hemisphere (RH) and the corpus callosum (CC), in at least some studies, had been shown to be dysfunctional in schizophrenics in comparison with controls. Many of these studies were open to criticism on the grounds of patient selection and diagnosis as well as inadequacies in experimental design.

One of the problems was that the individual tests may not have done what they purported to do. That is, there was doubt as to whether slow reaction time (RT) on say, the recognition of shapes presented to the left visual field, was a secure test of right hemisphere integrity. In chapters 2 to 4, the problem was attacked "from scratch" with the design and implementation of new tests, each of which had clear a rationale in terms of lateralised psychological processes or corpus callosum function, and which in themselves were anticipated to have relevance to the eventual understanding of psychotic disorders. Thus in chapter 2, visual imagery was tackled from the computational perspective advanced by Kosslyn (1987) and a test devised which separated left and right hemisphere contributions to the production and classification of visual images. When the test was applied to schizophrenic patients and psychiatric controls, it was found that, while generally lacking in "efficiency" in terms of processing speed, the schizophrenic group showed the normal RH advantage on the task requiring judgements on the relative size of mental images, and the normal relationship between the difficulty of size comparison and RT time in that hemisphere. However, the schizophrenic patients appeared to have lost the expected LH advantage in determining categorical relationships (chapter 5). This was especially so for those patients who had experienced visual hallucinations. The finding appeared to be linked with the experience of vivid visual imagery in normal subjects. Relating psychiatric disturbances to normal phenomena as well as to an anatomical substrate is arguably, the ultimate aim of neuropsychological research in psychiatry. However, the asymmetry of processing advantage elicited by the two visual cognitive tasks was not as robust as had been hoped and the range of performance or variance in the patient groups was large so that other important though subtle differences may have been obscured.

The next test to be developed involved the perception of facial affect from chimeric face drawings in which half of the chimera was sad and the other half, happy (chapter 3). Variations on this paradigm had been exploited in the study of cerebral laterality most notably, by Jerre Levy and colleagues (e.g. Levy et al, 1983a). The happy-sad version proved a reliable and sensitive measure of RH function. In addition it allowed the study of dynamic changes in hemisphere arousal in different mood states, which had been suggested by previous work. Although peripheral to the main thrust of the thesis, the distinction between hypomanics/manics and depressives, in the affective disorder group, allowed a more precise test of the specificity of the abnormalities uncovered in the schizophrenic patients. (The affective group was not sub-divided in the other experiments described in chapters 5, 7 & 8 since this would have detracted from the main purpose of the research on schizophrenia. However, post-hoc analysis of manics *versus* depressives on Stroop test performance and the tests of visual cognition did not reveal any significant differences.) The chimeric faces test evokes a perceptual bias which results in an increased salience to the half face to the viewers left - the left hemifacial bias (LHFB). This was not seen consistently in non-right handers, as predicted. Normal and induced variations in mood did not affect perceptual bias but abnormal variations in mood amounting to clinical disorder, did exert an effect (chapter 6). Manics tended to have increased LHFB, depressives, reduced bias, and schizophrenics, little or no bias. This tachistoscopic study replicated one using the same stimuli presented in free vision, to a different population of patients (David & Cutting, 1990).

The mechanism of the perceptual bias shown in these and other studies, and its relationship to other measures of hemisphere functioning, is a topic of debate in the neuropsychology literature. In chapter 6, it was regarded simply and parsimoniously, as an index of directed visual attention. The use of this paradigm was an attempt to go beyond the application of tests merely because of some supposed allegiance to a single hemisphere, or to some unitary psychological construct such as "attention". Rather the aim was to address both psychological and anatomical concerns together. Just as chapters 2 and 5 were concerned with the LH's visual semantic system, so chapters 3 and 6 focused on the RH's visual attentional system. A further preliminary step was taken in chapter 6 which included analyses making use of data gathered using a divided visual field version of the Stroop test (see below). This was an effort to further refine the study of hemisphere-specific attentional processes by looking at Stroop performance - regarded as a test of selective (within a location), as opposed to directive (towards as location), attention. Such an approach is in its infancy, and the results reported are tentative, yet this is a direction for future study. In brief, selective attention as deduced from Stroop performance was not disturbed in either hemisphere in schizophrenia but the relationships between performance on this and the chimeric faces test appeared to have broken down, consistent with the view that there is a general disruption of the coordination of processing sub-components in schizophrenia. Less equivocally, the results from the chimeric faces confirm RH dysfunction in schizophrenia, in addition to the LH deficit demonstrated using visual semantic/imagery tasks (chapter 5).

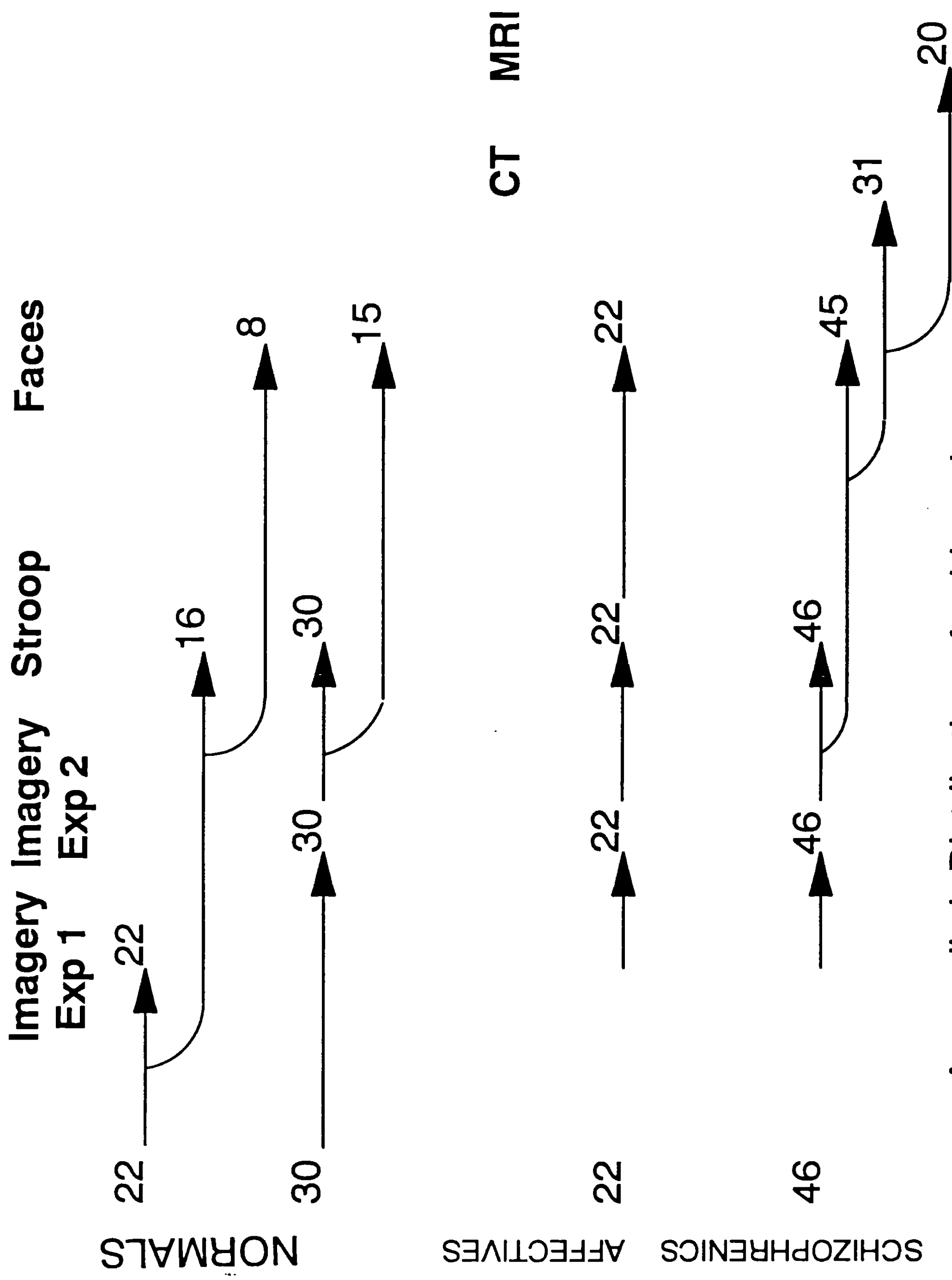
Chapters 4, 7 and 8 dealt with the use of an adaptation of the Stroop test. In the traditional test, two conflicting (or concurring) elements, such as a colour strip and a colour-word, are combined into a single composite stimulus (see MacLeod, 1991). By separating the two elements so that the word and colour can be each presented to a different visual field/hemisphere, yet the word still exerts an influence on the retrieval of the colour's name, it is possible to gain information on the flow of information between the hemispheres. Only precise, semantic information (that is the meaning of words in this case) is capable of producing Stroop interference/facilitation. Hence, it may be predicted that such high-level information requires the corpus callosum as its conduit (see Zaidel et al, 1990). Some empirical support for this was provided in chapter 4 on the basis of experiments in patients with callosal agenesis, who showed reduced interhemispheric Stroop effects. The design of the study allowed ready controls or comparisons at several levels. First, identical stimuli were presented "unilaterally" as were presented "bilaterally". A discrepancy between the two hemispheres' individual performance would have rendered conclusions based on the interhemispheric condition, "unsafe". Fortunately, this did not occur. Secondly, a measure of the combined Stroop effect (CSE) can be derived by subtracting the invariably shorter RT for congruent stimuli from that of incongruent stimuli. This allowed the influence of response speed (significantly slowed in the patient groups) to be "partialled out". The results given in chapter 7 show that the schizophrenics exhibited a greater Stroop effect in the bilateral condition compared with the controls, while the within-hemisphere Stroop effect was very similar between all the subject groups. Is this then, a true differential deficit according to Chapman and Chapman's criteria (Chapman and Chapman, 1973)? In one sense, the answer is "Yes", in that the schizophrenics were matched against psychiatric and normal controls with respect to Stroop performance when this was intra-hemispheric. However, it would not be strictly accurate to describe the increased Stroop effect as a deficit since it combines increased facilitation with inhibition. The contribution of each component could not be ascertained, given the design of the study, since there was no "neutral" condition (neither congruent nor incongruent) against which this could have been measured. This is clearly an avenue for further research.

Having found a performance index which appeared to distinguish schizophrenics from controls, there were two obvious directions in which to extend the finding. One was to look for clinical-performance correlations. For example, it was hypothesised that abnormally increased corpus callosal function would related to psychotic phenomena such as auditory hallucinations. This was not shown to be the case, indeed a trend in the opposite direction was noted. Similarly, an association with a positive family history of psychiatric disorder was sought but later excluded. Another direction was to look for correlations between performance and phenomenological variables, with structural measures of the corpus callosum (chapter 8). The increased trans-callosal "traffic" implied by the greater bilateral Stroop effect in the schizophrenic patients, correlated with the anterior width of the corpus callosum, after corrections were made for intracranial volume, in a sub-group of 20 schizophrenics. Ventricle:brain ratio was not related to performance, as had been suggested by an earlier study (David, 1987). Patients with auditory hallucinations scored low on functional and structural measures of "callosal connectivity", thus providing a complete chain of association between symptoms, neuropsychological performance and brain structure. However, the integrity of each link in the chain is not sufficient to support too much weight at present. The strength of association, represented statistically as a correlation coefficient, at each point in the chain accounted for only a modest, albeit significant proportion of the variance. Other additional factors must therefore be exerting an influence.

Future directions

The experimental work outlined above showed deficits in relatively well-defined psychological processes in the RH, the LH and the corpus callosum. It seems therefore that the continued search for a solitary dysfunctional process in a single cerebral site would be unproductive. Indeed the range and variety of manifestations seen in the schizophrenic disorders makes such an endeavour unpromising from the outset. That is not to say that schizophrenia is a diffuse cerebral malfunction which compromises all functions in all locations to the same degree. While the disorder can be viewed as the end result of many different aetiologies and pathogeneses, from genetically programmed maldevelopment to an acquired insult to the brain, it maintains a coherence as a syndrome (Wing et al., 1974). The approach taken in this thesis was to isolate different kinds of deficits allied to different cerebral locations and to attempt to relate these to the phenomena of the disorder. It may be that starting with the phenomena (e.g. auditory hallucinations), as seen in a pure form in rare cases - the cognitive neuropsychological approach - may be a useful way to proceed having established a general relationship between the phenomena and the psychological process in a heterogeneous group as a first stage. The localisation of the underpinnings to such disturbances in the brain will be progressively easier with the growing sophistication of neuroimaging techniques, both structural and functional. The ultimate understanding of the schizophrenic disorders will nevertheless depend on advances in knowledge relating to normal cognitive processes and their physical substrates, against which abnormal process can be gauged. This in turn will rely more on the ingenuity of the psychological investigator and the sophistication of his or her ideas than on the technical wizardry of the physicist.

Appendix I.



Appendix I: Distribution of subjects by test

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