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Attentional Capacity in Patients with Systemic Lupus Erythematosus

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ABSTRACT

The presence of cognitive deficits may represent a marker of Central Nervous System (CNS) disease in Systemic Lupus Erythematosus (SLE; Carbotte et al. 1986; Hanly et al. 1992). This finding points to the importance of identifying the early onset of, and the nature of cognitive deficits in patients with SLE. Based on the findings of previous research and on patients subjective complaints, it was postulated that CNS involvement in SLE disproportionaly reduces attentional capacity.

The attentional capacity of 35 women meeting the American College of Rheumatology criteria for having SLE and who had had a recent medical examination was measured using the Attentional Capacity Test (ACT; Weber, 1986), and the Gordon Diagnostic System (GDS; Gordon, 1991). Neuropsychiatric involvement was determined based on the major criteria used by two major research groups (e.g. Carbotte et al. 1986; Hanly et al. 1991). The performance of the SLE subjects (19 neuropsychiatric and 16 non-neuropsychiatric SLE subjects) was compared to 23 females with Rheumatoid Arthritis (RA) and 42 healthy females using multivariate and univariate procedures.

The major findings were that: 1) neuropsychiatric SLE subjects were more impaired on effortful auditory attention than healthy controls (ACT Total $p<.01$; ACT Highest Level Achieved $p<.05$; ACT Levels Missed $p<.01$); and 2) neuropsychiatric SLE subjects (excluding depressives) were more impaired on effortful visual attention than healthy controls (GDS Total Score $p<.001$; GDS Commission Errors $p<.05$). Automatic attention was preserved. Thus, as the demands on attentional capacity increased, the ability of neuropsychiatric SLE subjects became impaired.

No significant differences were found between neuropsychiatric SLE and non-neuropsychiatric SLE subjects

or between neuropsychiatric SLE and RA subjects. The effects of depression, age, medications, and disease severity and duration on capacity measures were not significant; therefore, they did not explain the lack of differences. However, a significant correlation between disease activity and ACT measures suggests that disease activity may account for reduced auditory attentional capacity in some patients. Disease activity alone did not explain the extent of deficits observed in Neuropsychiatric SLE subjects. Attentional capacity deficits appear to be primarily related to CNS abnormalities.

Limitations of the study and directions for future research are outlined.

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DEDICATION

Dedicated to my parents,
Henry Campbell Kerr, Q.C. and Eleanor Nellis (Blake) Kerr,
with my deepest love and gratitude.

Their faith in my ability and their heartening support
provided me with the inspiration and the tenacity
to strive for my potential.

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CHAPTER ONE

INTRODUCTION

Over the past decade there has been an increasing interest in the cognitive deficits associated with Systemic Lupus Erythematosus (SLE), a chronic systemic autoimmune disease. It has been estimated that up to 70% of all patients with SLE experience Central Nervous System (CNS) complications (Abel, Gladman, & Urowitz, 1980; Bluestein, 1987; Hughes, 1980). When the CNS is implicated in a disease, psychiatric manifestations, particulary depression (Cassem, 1990) and organic mental disorders (American Psychiatric Association, 1987), are common. Hence, the potential for cognitive impairments is a legitimate concern. Interestingly, the cognitive deficits documented in patients with SLE are not limited to those individuals with overt CNS manifestations. Cognitive deficits have been reported in up to 88% of *all* patients with SLE, suggesting the presence of either residual (Carbotte, Denburg, & Denburg, 1986; Denburg, S., Carbotte, & Denburg, 1987; Fisk, Eastwood, Sherwood, & Hanly, 1993), or subclinical CNS involvement in some patients (Carbotte et al.; Denburg, S. et al. 1987; Koffler, 1987). This finding points to the importance of identifying and understanding the early onset, and nature of cognitive deficits in patients with SLE. To date, however, the specific pattern of cognitive deficits associated with this disease remains ill-defined (Denburg et al. 1987; Hanly et al., 1992; Kutner, Busch, Racis, & Krey, 1988; Wekking, Nossent, van Dam, & Swaak, 1991). A general objective of the present study is to examine one of the fundamental cognitive

deficits reported in patients with SLE, attention.

Rationale for the Study

SLE is a chronic, relapsing-remitting autoimmune disease characterized by multiple system tissue disruption (Hall, Popkin, Stickney, & Gardner, 1979). Disruption to the CNS has been estimated to occur in 50% to 70% of all cases of SLE at some time during the disease (Abel et al., 1980; Bluestein, 1987; Hughes, 1980), but it is one of the most poorly understood manifestations (Hanly et al., 1992).

The presence of cognitive abnormalities is considered to be an important descriptor of CNS involvement in patients with SLE (Singer, Denburg, & the Ad Hoc Neuropsychiatric Workshop Group, 1990). Neuropsychological studies have revealed that the prevalence of objective cognitive deficits in patients with SLE is as high as 88% (Carbotte et al., 1986; Koffler, 1987). The majority of these patients has either an active or past history of CNS involvement. However, cognitive deficits have also been documented in a large portion of patients with SLE who have never experienced CNS involvement (Carbotte et al., 1986; Hanly et al., 1992; Hay et al., 1992; Koffler, 1987; Kutner et al., 1988). It has been suggested (Carbotte et al., 1986; Hanly et al., 1992; Hay et al., 1992; Koffler, 1987; Kutner et al., 1988) that the presence of cognitive deficits in patients with NON-CNS SLE provides evidence for the presence of subtle subclinical CNS dysfunction in some patients.

Although the use of psychometric tests appears to be useful in detecting clinical and subclinical CNS disease, at the present time, no solid evidence exists to confirm a

specific pattern of cognitive deficit associated with SLE (Denburg S. et al., 1987; Hanly et al., 1992; Kutner et al., 1988; Wekking et al., 1991). The deficits which have been documented (e.g. reasoning, complex problem solving, verbal and visual fluency, visuospatial skill and visual and verbal memory) are not unitary processes. A more precise description of the functions which are impaired is needed. One means of accomplishing this is to assess the specific cognitive processes which are common to and underlie the documented cognitive deficits (Wolkowitz & Weingartner, 1988).

Attention is an elementary process which is fundamental to all cognitive functioning. As a result, impairments in attention have the potential to adversely affect all areas of cognition (Naglieri & Das, 1990). Without an adequate evaluation and understanding of attention, speculation about higher cortical functioning is difficult (Berg, 1990).

Attention may be defined as "the aspect of consciousness that relates to the amount of effort exerted in focusing on certain aspects of an experience, activity, or task" (Kaplan & Sadock, 1991, p.20). Tasks requiring attention can be considered in terms of automatic and effortful attention. Automatic attentional processes tend to occur quickly and without much conscious awareness. They do not interfere with ongoing mental activity and require little of an individual's limited attentional capacity (Posner, 1978; Tariot & Weingartner, 1986). In contrast, effortful attentional processes place greater demands on one's limited processing capacity. They require

intentional, sustained attention (Posner & Presti, 1987; Tariot & Weingartner, 1986; Wolkowitz & Weingartner, 1988).

Automatic attentional processes such as attention span and rote learning have been found to be intact in patients with SLE (Denburg S. et al., 1987; Wekking et al., 1991), these tasks do not overload attentional capacity (Crossen & Weins, 1988). The nature of effortful attentional processing or attentional capacity has not been specifically addressed in previous studies of cognitive functioning in patients with SLE. However, the cognitive deficits documented in previous research (to be reviewed in Chapter 2) and the subjective complaints of patients with SLE, suggest that as the demands on attentional capacity increase, the performance of patients with SLE, particulary those with CNS involvement becomes impaired.

Objectives of the Study

The overall objective of the present study is to examine the nature of attentional processing in patients with SLE. This study is designed to assess auditory attentional capacity and the effects of distraction on sustained visual attention. Auditory and visual attention were assessed under increasingly demanding conditions in order to understand the nature of attentional processing and effort on a limited capacity system. It is postulated that patients with SLE, particulary those with CNS involvement, will show significant impairments on tasks demanding high degrees of effort. Specific objectives are:

1) to assess auditory attentional capacity;
2) to assess sustained visual attention with and without distraction;

3) to examine the extent to which CNS involvement (past or active history) in SLE affects performance of tasks requiring attention;
4) to examine whether disease activity and disease chronicity contribute to performance on tasks requiring attention; and
5) to determine whether attention difficulties in SLE are specific to SLE.

Scope of the Study

The present study focuses on female patients with SLE who met the American College of Rheumatology (ACR) criteria (formerly called the American Rheumatism Association; ARA) for having the disease, and who had had a recent medical examination. Thirty five subjects with SLE were volunteers recruited from the SLE clinic at the University of Calgary Medical Clinic.

While CNS involvement may be a major etiology of cognitive impairment in patients with SLE and other chronic illnesses, it is not the only one. Additional etiological theories suggest that cognitive deficits in chronic illnesses may be: (a) secondary to complications of the disease; (b) side effects of medication; or (c) secondary to other psychological disturbances associated with the disease. Variations in cognitive functioning among patients with SLE due to non-organic factors require comparison to other groups.

Twenty three female patients with Rheumatoid Arthritis (RA), recruited from the Arthritis Clinic at the University of Calgary Medical Clinic, and 42 healthy female control subjects, recruited from the community, were

assessed to determine whether deficits reported in subjects with SLE are specific to having SLE or more generally to other complications associated with a chronic autoimmune disease.

CHAPTER TWO

REVIEW OF THE LITERATURE

SLE: An Overview

Systemic Lupus Erythematosus (SLE) is a chronic, relapsing-remitting, autoimmune disorder characterized by multiple organ tissue damage (Hall & Stickney, 1984; Roberts & Hughes, 1989). SLE was once thought to be rare. However, the development of better diagnostic procedures, treatment, and increased awareness and interest in the disease has resulted in higher prevalence rates (Giang, 1991; Roubenoff & Hochberg, 1991). Estimates of community prevalence rates range from 30 (Bauman, Barnes, Schrieber, Dunsmore & Brooks, 1989) to 50 cases per 100,000 (Giang, 1991; Roubenoff & Hochberg, 1991). The disease afflicts females approximately 9 times more frequently than males (Hall et al., 1979; Lishman, 1988). While all age groups are affected by the disease (Hall & Stickney, 1984; Reeves & Lahita, 1987), SLE primarily affects women of child bearing years (Lishman, 1988; Rothfield, 1985).

Little is known about the etiology of SLE (Dubois, Wierchowiecki, Cox, & Weiner, 1974; Hall & Stickney, 1984). Viral, genetic, environmental and hormonal factors are believed to be involved (Zvaifler & Woods, 1985). The disease "is characterised by the presence of multiple autoantibodies which participate in immunologically mediated tissue damage" (Rothfield, 1985, p. 911). An abnormal production of antibodies is believed to result from an imbalance of the immune system. In turn, these antibodies damage healthy tissue (Denburg, S. et al., 1987; Rothfield, 1985). Tissue damage may be limited to one

system or organ. Alternatively, many systems may be involved. Moreover, the involvement of organs may vary over time. As a result, the manifestations of SLE are extremely diverse (Lishman, 1988; Roberts & Hughes, 1989; Rothfield, 1989).

Antinuclear antibodies are present in up to 95% of patients with SLE. High titers correlate with disease activity. Antinuclear antibodies cause damage by forming immune complexes which can be deposited in tissues thereby causing damage to organs. Most patients with SLE have multiple antinuclear antibodies present. Antinuclear antibodies can be considered in four main groups: 1) those directed against double stranded DNA; 2) those directed against single stranded DNA; 3) those directed against histones; and 4) those directed against nucleic acid-protein complexes including SM antigen, RNP, SS-A/Ro and SS-B/La (Tan, 1985).

The combination of antinuclear antibodies, double stranded DNA, and a low complement count has increased diagnostic specificity to virtually 100%. Edworthy, Zatarin, McShane, and Bloch (1988) used recursive partitioning and found that the presence of anti-DNA antibodies was the best overall indicator of SLE. Anti-DNA antibodies are rarely seen in other diseases and in SLE is linked with more severe disease. The absence of anti-DNA antibodies throughout the patient's clinical course is associated with increased prognosis (Zvaifler and Woods, 1985). Anti-SM antigen is another antibody believed to be specific to SLE; 75-95% of patients with anti-SM have SLE. It is believed to be associated with photosensitive skin

rash, mild nonprogressive arthritis, and mild CNS and renal disease (Zvaifler and Woods, 1983).

Antiphospholipid antibodies, antibodies which react to a type of fat molecule on the cell membrane, are another class of antibodies associated with more severe SLE. These antibodies interfere with the normal function of the blood vessels by causing clots in the vessels or by causing narrowing of the vessel walls, both of which can lead to stroke, heart attack and miscarriage (Zvaifler and Woods, 1985).

The onset of SLE may be acute. However, an insidious onset is more common (Rothfield, 1989). Arthritic complaints and fever are the most frequent presenting features (Grigor, Edmonds, Lewkonia, Bresnihan, & Hughes, 1978). Other symptoms include weight loss, muscle weakness, lethargy, pleurisy, changes in the skin, poor circulation in the extremities, and swollen lymph nodes (Grigor et al., 1978; Roberts & Hughes, 1989). Organ involvement may include the skin, renal system, liver and spleen, musculoskeletal system, gastrointestinal system and the nervous system (Hall & Stickney, 1984). A chronic and progressive course characterised by periods of symptom flare up and remission is common. Nonetheless, disease states in which a mild illness reoccurs after prolonged periods of inactivity are also described (Lishman, 1988).

Clinical diagnosis of SLE relies on an *a priori* suspicion based on the patient's history, the clinical presentation of the patient, and serological tests (Edworthy et al., 1988). For research purposes, classification is dependent on a set of standard

criteria (Edworthy et al., 1988; Tan et al., 1982). A classification system used in numerous studies (e.g., Carbotte et al., 1986; Denburg, S. et al., 1987; Hall, Stickney, & Gardner, 1981; Rimon, Kronqvist, & Helve, 1988; Wekking et al., 1991) is one which was proposed by the American Rheumatological Association (ARA; now called the American College of Rheumatology; ACR) in 1971 and revised in 1982 (Tan et al., 1982). According to this classification system, an individual is considered to have SLE if any 4 of 11 criteria are serially or simultaneously present: 1) malar rash (a facial rash across the bridge of the nose extending onto the cheeks); 2) discoid rash (raised scaly patches on the skin); 3) photosensitivity; 4) oral ulcers; 5) arthritis (swelling or tenderness of two or more peripheral joints); 6) pleurisy (chest pain on deep breathing caused by inflammation of the lining of the lung) or pericarditis (pain due to an inflammation of the sac around the heart); 7) renal disorder (identified by protein or cellular casts in the urine); 8) neurologic disorder (characterized by psychosis or seizures); 9) haematologic disorder; 10) immunologic disorder; and 11) antinuclear antibody (i.e. the presence antibodies directed to cell nuclei).

Any combination of clinical symptoms may present at any given time. As a result, the diagnosis of SLE is difficult, often taking several months to several years to make (Reeves & Lahita, 1987).

CNS Involvement in SLE

Involvement of the Central Nervous System (CNS) is one of the most poorly understood manifestations of SLE (Hanly

et al., 1992). There is considerable inconsistency within the literature in defining CNS manifestations. The ACR criteria limit the definition of neurological involvement in SLE to psychosis and seizures (McCune, MacGuire, Aisen, & Gebarski, 1988; Singer et al., 1990; Tan et al., 1982). It has been suggested (Singer et al., 1990) that this definition is insufficient because it neglects important clinical symptoms. A diverse range of neurological and psychiatric (neuropsychiatric) manifestations are believed to exist (Bresnihan, 1982; Carbotte et al., 1986; Giang, 1991; Kassen & Lockshin, 1979; Yancey, Doughty, & Arthreya, 1981). When a broad range of neuropsychiatric symptoms is considered, CNS involvement is estimated to occur in 50% (Bluestein, 1978; Bresnihan, 1982; Harris & Hughes, 1985; Hughes, 1980) to 70% of all cases at some stage of the disease (Abel et al., 1980; Bluestein, 1987; Giang, 1991; Hughes, 1980). Patients with more subtle signs may go unrecognized, therefore, these estimates may be low (Hughes, 1980). The neuropsychological studies, reviewed in the next section, support this notion.

In response to the restrictive criteria outlined by the ACR, several attempts have been made to classify neurological abnormalities (e.g. Bresnihan, 1982; Carbotte et al., 1986; Harris & Hughes, 1985; Kassen & Lockshin, 1979; Yancey et al., 1981). The classification system proposed by Carbotte and colleagues (Carbotte et al., 1986; Denburg, S. et al., 1987; Denburg, J., Carbotte, & Denburg, S. 1987; Denburg, Carbotte, Long, & Denburg, 1988), a research group investigating cognitive functioning in patients with SLE, is one example. Within their

classification system, any one major event (i.e. cerebrovascular event, neuropathy, movement disorder, transverse myelitis, seizure, organic brain syndrome, meningitis, affective disorder, or schizophreniform disorder) attributed to the disease process meets the criteria for the diagnosis of neuropsychiatric SLE. Any one minor event (i.e. subjective numbness, headache, cognitive disorder, mood swings, or adjustment disorder) when occurring in combination with an abnormal electroencephalogram (EEG), brain scan, cerebral spinal fluid (CSF) or cerebral angiogram also meets the criteria for the diagnosis of neuropsychiatric involvement (Carbotte et al., 1986).

The minor neuropsychiatric signs have not been accepted by all research groups. For example, Hanly et al. (1992), another research group investigating cognitive functioning in patients with SLE, opted to rely heavily on clinical assessment believing that this approach is typically used by physicians in their clinical practice. In contrast to Carbotte et al. (1986), this group did not include minor signs. Hanly (personal communication, 1992) felt that the minor signs occurring in isolation (i.e. without being substantiated by laboratory tests and imaging studies) did not justify the diagnosis of CNS SLE. As a result, the Hanly group relied only on the presence of any one major event (i.e. stroke, transient ischemia, cranial neuropathy, peripheral neuropathy, transverse myelitis, seizure, organic brain syndrome, psychosis, or depression requiring medical intervention) to classify patients as having neuropsychiatric involvement.

In response to the inconsistencies of defining CNS manifestations, a meeting of investigators, held in 1989 (Singer et al., 1990), attempted to standardise a definition of, and classification system for, CNS disease in SLE. It was agreed that organic brain syndrome, one of the most frequently reported CNS disturbances in patients with SLE (Baker, 1973; Bresnihan, 1982; Feinglass et al., 1976; Hall et al., 1981), was too broad a descriptor (Singer et al., 1990). The American Psychiatric Association (1987) defines organic brain syndrome as psychological or behavioral abnormalities "associated with transient or permanent dysfunction of the brain" (p.98). The consensus of the 1989 meeting was to break the term into more precise descriptors including, dementia, objective limited cognitive dysfunction, delirium, and subjective limited cognitive dysfunction. It was further agreed that generalized seizures, psychosis (brief reactive or atypical), transverse myelitis, global cognitive dysfunction (dementia), and focal seizures are the five most important descriptors of neuropsychiatric SLE. Limited cognitive dysfunction, objectively assessed, and attentional cognitive dysfunction were rated, respectively, as the 9th and 15th descriptors out of 33 descriptors (Singer et al., 1990).

Unfortunately, to date no one classification system has been universally accepted. The lack of consensus regarding definitions and descriptors makes the comparability of research and the accumulation of knowledge difficult (Singer et al., 1990). Given the unanimity of the significance of the presence of cognitive impairments

in identifying CNS involvement in patients with SLE, an understanding of the nature of cognitive deficits associated with SLE is important.

Cognitive Dysfunction in SLE

Subjective Cognitive Deficits

Subjective cognitive impairment is considered to be an important descriptor of organic brain syndrome (Singer et al., 1990), one of the most frequently reported CNS disturbances in patients with SLE (Baker, 1973; Bresnihan, 1982; Feinglass et al., 1976; Hall et al., 1981). Subjective neuropsychiatric symptoms have been used in conjunction with laboratory and imaging tests to classify CNS involvement in SLE (e.g. Carbotte et al., 1986).

Kinash (1982) conducted a descriptive study to document the needs and experiences of patients with SLE. 85% of the patients interviewed reported mood swings involving anger, frustration or depression. Episodes occurred at least once a week, and lasted from a few hours to several days. Of this 85%, 68% also reported impairments in cognitive functioning. The majority of these patients experienced memory deficits of varying natures. Episodes of mental confusion were reported less frequently (18%), and were highly individualized.

Similar results have been reported by Baker (1973) who conducted interviews with patients with SLE. Slowed thinking and difficulties in concentration were frequent complaints, particulary in patients with diagnosed psychiatric syndromes. Other subjective complaints of cognitive functioning from patients with SLE include difficulties in immediate attention, concentration, rote

learning, cognitive flexibility (Denburg, S. et al., 1987), listening to a conversation while other conversations are going on, doing two or more things simultaneously, word finding (Personal Patient Contact), and short term memory (Denburg, S. et al., 1987; Lim et al., 1988). It is important to note that, in general, subjective memory complaints, when objectively assessed, often turn out to be impairments in attention, concentration, or conceptual tracking (Spreen & Strauss, 1991).

Objective Cognitive Deficits

Despite the agreement of the importance of cognitive abnormalities in defining organic brain syndrome as well as in classifying involvement of the CNS in SLE (Singer et al., 1990), very few studies have systematically assessed cognitive functioning in patients with SLE (Carbotte et al., 1986; Koffler, 1987; Wekking et al., 1991). One means of conducting a thorough evaluation is to use neuropsycholgical procedures.

The primary purpose of clinical neuropsychological assessment is to examine the functional status of an individual's brain (Rourke, Bakker, Fisk, & Strang, 1983). Although imagining techniques identify structural abnormalities and changes, such changes may not be of clinical or behavioral significance. Imaging techniques are not always conclusive. Neuropsychological assessment has proven to be valuable in detecting cerebral abnormalities in conditions where there is no evidence of structural change (Benton, 1992). The procedures objectively assess changes in higher cognitive functioning (Papero, Bluestein, White, & Lipnick, 1990) and are

believed to assist in differentiating between functional and organic symptoms (Koffler, 1987).

A research group from Hamilton, Ontario (Carbotte et al., 1986; Denburg, S. et al., 1987; Denburg, J. et al., 1987; Denburg et al., 1988) recently conducted a series of comprehensive studies investigating cognitive functioning in patients with SLE using neuropsychological procedures. These studies employed a large battery of neuropsychological tests in order to gain a comprehensive assessment of a wide range of functions (Denburg, S. et al., 1987). Patients were classified according to whether neuropsychiatric involvement (defined on pg. 12) had ever been present, and if present, whether involvement was active or inactive at the time of the assessment. A high prevalence of cognitive dysfunction was documented. Cognitive deficits were found in 66% of the patients with neuropsychiatric SLE regardless of whether the neuropsychiatric involvement was active or inactive. 42% of patients who had *never* experienced neuropsychiatric involvement also showed signs of cognitive impairment. The overall incidence of impaired cognitive functioning in *all* patients with SLE was 88% compared to 17% of a selected group of patients with Rheumatoid Arthritis (RA) and 14% of healthy control subjects (Carbotte et al., 1986).

In contrast to the Carbotte et al. (1986) study, Hanly et al. (1992) found that a much lower proportion (21%) of their patients experienced cognitive impairment. The difference in the prevalence rates was explained (Hanly et al., 1992), in part, by the fact that in the Carbotte et al. (1986) study there was a greater proportion of patients

with active and inactive neuropsychiatric involvement. Ascertaining what factors may have played a role in the difference is difficult, however, because the studies used different inclusion criteria for their neuropsychiatric groups. Regardless, in both studies, impairment was documented in those patients with active neuropsychiatric involvement and in those patients with inactive neuropsychiatric involvement, suggesting residual CNS involvement in the latter group (Carbotte et al. 1986; Denburg, S. et al. 1987; Fisk et al. 1993). Moreover, in both studies, cognitive deficits were documented in those who had never experienced neuropsychiatric involvement.

Additional studies (Hay et al., 1992; Koffler, 1987; Kutner et al., 1988) substantiate the finding of neuropsychological dysfunction in patients with SLE in the absence of documented neuropsychiatric disease. The results have been interpreted (Carbotte et al., 1986; Hanly et al., 1992; Hay et al., 1992; Koffler, 1987; Kutner et al., 1988) as providing evidence for the presence of subtle subclinical CNS dysfunction in some patients with SLE.

An array of cognitive deficits have been reported in patients with SLE. Denburg S. et al. (1987) report that there are no significant differences in type or extent of impairment between patients with active and inactive neuropsychiatric involvement. However, compared to patients with SLE who had never experienced neuropsychiatric involvement, those with an active or past history of neuropsychiatric involvement were significantly more impaired on tests of delayed memory, nonverbal

productivity, and verbal speed/fluency. Compared to healthy control subjects, patients with either active or past histories of neuropsychiatric involvement, as a group, were also significantly impaired on tests of delayed verbal and visual memory, visual-spatial and verbal reasoning, and nonverbal productivity (Denburg S. et al., 1987).

Additional studies substantiate the findings of the existence of cognitive impairment in patients with neuropsychiatric SLE. In a large study focusing primarily on general intellectual functioning and memory, Fisk et al. (1993) found that patients with neuropsychiatric SLE (active or inactive involvement) were significantly more impaired than patients with non-neuropsychiatric SLE on a measure of verbal recognition memory. These researchers interpreted this finding as being indicative of a deficit in the initial storage of information into memory. Additional studies and smaller scale studies have documented deficits in concentration (van Dam, Wekking, & Oomen, 1991; Wekking et al., 1991), complex attention (Ginsburg et al., 1992), speed and flexibility in information processing (Wekking et al., 1991), higher reasoning (Kutner et al., 1988), complex problem solving (Papero & Lipnick, 1988; Papero et al., 1990), memory (van Dam et al., 1991), arithmetic, visual processing (Koffler, 1987), and perceptual speed (Kutner et al., 1988) in patients with neuropsychiatric SLE.

Cognitive impairments have also been documented in a significant proportion of patients who had never experienced neuropsychiatric involvement (Carbotte et al., 1986). Although patients with non-neuropsychiatric SLE are

not as impaired on cognitive tests as patients with documented neuropsychiatric involvement, they have been found to be significantly more impaired on a test of visuospatial-motor speed compared to healthy control subjects. Furthermore, a significant number of individuals with non-neuropsychiatric SLE demonstrated impairments in visuospatial memory, verbal productivity and fund of general information (Denburg S. et al., 1987).

All of the studies reviewed above employed a large battery of neuropsychological tests in order to assess a broad range of functions. One of the problems which arises when the ratio of subjects to dependent variables is low is that statistical power is lost resulting in an increase in the chance error rate (Kerlinger, 1986). Therefore, the results of many of the studies, particulary the smaller scale studies, should be considered as being exploratory in nature.

Although the use of psychometric tests with patients with SLE appears to be useful in detecting the presence of clinical, residual, and subclinical CNS disease (Carbotte et al. 1986; Denburg, S. et al., 1987; Fisk et al. 1993; Koffler, 1987) at the present time, no solid evidence exists to confirm a specific pattern of cognitive deficit associated with CNS involvement in SLE (Denburg, S. et al., 1987; Kutner et al., 1988; Wekking et al., 1991). As Denburg, S. et al. (1987) indicate, the heterogeneity of neuropsychological test results is commensurate with the heterogeneity of manifestations present in SLE. Furthermore, the presence of specific areas of cognitive impairments in some individuals in the absence of group

differences emphasizes the problems in defining the nature of cognitive impairment in patients with SLE (Denburg S. et al., 1987).

Cognitive Processes

It has been suggested (Hanly et al., 1992) that because of the time and cost involved, routine neuropsychological assessments of all patients with SLE cannot be justified. Early identification of cognitive impairment, however, may facilitate early treatment thereby forestalling major cognitive impairment (McCune & Golbus, 1988). If neuropsychological assessments are reserved only for those patients with overt CNS manifestations then a considerable proportion of patients with cognitive deficits (i.e. patients with residual or subclinical CNS involvement) may not be recognized. Ideally, a screening instrument tapping a fundamental deficit could be used to identify cases in need of more thorough neuropsychological evaluations, monitor the course of CNS disease, and help in understanding the onset and nature of CNS involvement in patients with SLE.

The cognitive impairments discussed in the previous section are not unitary processes. For example, while deficits in memory are commonly reported by patients with SLE (Baker, 1973; Denburg, S. et al., 1987; Kinash, 1982) and substantiated on psychometric tests (Denburg, S. et al., 1987; van Dam et al., 1991), impaired performance may not be directly due to memory. Impairments in sensory processing, perceptual strategies, attentional functions, encoding processes, retrieval functions, and response functions may underlie deficits. Wolkowitz and colleagues

(e.g. Wolkowitz, Tinklenberg, & Weingartner, 1985; Wolkowitz & Weingartner, 1988) stress the importance of assessing the specific processes which underlie cognitive ability in order to provide a more precise description of functions which are impaired.

Attention, defined as "the aspect of consciousness that relates to the amount of effort exerted in focusing on certain aspects of an experience, activity, or task" (Kaplan & Sadock, 1991, p. 20), is fundamental to cognitive functioning (Cooley & Morris, 1990; Naglieri & Das, 1990; Weber, 1990; Wolkowitz et al., 1985; Wolkowitz & Weingartner, 1988). As a result, deficits in attentional processing have the potential to adversely affect all areas of behaviour (Naglieri & Das, 1990). Disruptions of attentional processes may result from very minor insults to the CNS (Sohlberg & Mateer, 1987). They are among the most common mental deficits associated with brain injury (Lezak, 1983; Moscovitch, 1979; Van Zomerern, Brouwer, & Delman, 1984) and tend to be present to some degree regardless of locus of brain damage (Goodglass, 1986). Moreover, impairments in attention tend to persist long after individuals have apparently recovered from insult to the brain (Lezak, 1983; Stuss et al., 1985).

Attention and SLE

Clinical evaluation of attention often relies on tests such as digit span and digit symbol substitution (described below). Unfortunately, there is a lack of consensus as to what these tests measure (Shum, McFarland, & Bain, 1990). Shum et al. (1990) examined the construct validity of common tests of attention, several of which have been used

in studies investigating cognitive functioning in patients with SLE. Three factors labelled, visual/auditory attention span, visuomotor scanning, and sustained-selective attention were identified in university students, community adults and closed head-injured adults. These factors will be used as a framework for describing the performance of patients with SLE on attention tests.

The first factor identified by Shum et al. (1990) was labelled visual/auditory attention span. The tests which loaded on this factor (digit span forward, digit span backward, and Knox cubes) all require the individual to register stimuli presented in a brief sequence (auditory or visual) and immediately repeat the sequence. In the case of digit span backward, repetition must be in a reverse order to that presented. Lezak (1983) refers to these abilities as simple mental tracking. Digit span forward and backward have consistently been shown to be intact in patients with SLE (Denburg, S. et al., 1987; Wekking et al., 1991). Visual span as measured by Corsi blocks (a task similar to Knox cubes described above) has also been found to be intact (Denburg, S. et al., 1987). Therefore, it appears that visual/auditory span or simple mental tracking is unaffected by SLE.

The second factor reported by Shum et al. (1990) received loading from tests involving visuomotor scanning abilities (e.g. Trail Making and Digit Symbol Substitution). Sustained[1] focused concentration, visual

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[1] **Sustained attention** refers to "the ability to maintain a consistent behavioral response during continuous or repetitive activity" (Sohlberg & Mateer, 1987, p. 119).

shifting and complex scanning or tracking are common elements of these tests (Lezak, 1983). Reports of performance on Trail Making by patients with SLE have been inconsistent. On Trail Making, the individual is required to join numbers in serial order as quickly as possible (Trail A) and to join letters interspersed with numbers in serial order respectively as quickly as possible (Trail B). The test is considered to be highly sensitive to brain injury (Lezak, 1983). Denburg, S. et al. (1987) found that patients with neuropsychiatric SLE are significantly impaired on Trail Making part A and part B compared to healthy control subjects but not compared to patients with non-neuropsychiatric SLE. The researchers suggested that the latter finding may be due to the presence of subtle subclinical CNS disease in the non-neuropsychiatric SLE group. However, the difference between the non-neuropsychiatric SLE group and healthy control subjects was not significant.

While these results provide preliminary support for deficits in visuomotor scanning or visual conceptual tracking, interpretation must be made with caution. Denburg, S. et al. (1987) performed ANOVAs on 37 raw scores, including performance on Trail A and Trail B. When ANOVAS are repeatedly utilized or as the number of dependent variables increases, the number of variables which may become significant by chance alone also increases. As a result, significance on the Trail Making may have occurred due to chance alone.

Neither Wekking et al. (1991) nor Kutner et al. (1988) found significant results on the Trail Making test. In

both instances, failure to find significant results was explained in part by the small sample size used. Kutner et al. (1988) suggested that the non significant results may have been due either to increased variance or increased time taken to complete the task by the SLE group compared to an illness control group. Wekking et al. (1991) suggested that using a chronic illness group for a control group may have resulted in the non significant results. The latter observation raises questions related to the origin of impairment. Specifically, it raises doubts as to whether deficits are specific to CNS involvement or more generally to having a chronic illness.

Performance on Digit Symbol, a second attention measure loading onto the visuospatial scanning factor identified by Shum et al. (1990), was found to be significantly impaired in the neuropsychiatric SLE and non-neuropsychiatric SLE groups compared to healthy control subjects in the Denburg, S. et al. (1987) study. Digit symbol is a psychomotor performance test which requires motor speed, persistence, visual-motor coordination, and sustained attention (Peck, Stephens, & Martelli, 1987). This test has been proven to be highly sensitive to brain dysfunction (Denburg, S. et al., 1987; Lezak, 1983; Peck et al., 1987). Denburg, S. et al. (1987) interpreted the significant finding as an impairment in Psychomotor Speed/Fluency. Denburg, S. et al. (1987) also documented a significant impairment in *Verbal* Speed/Fluency in neuropsychiatric SLE compared to non-neuropsychiatric SLE subjects and healthy control subjects. Verbal Speed/Fluency was a summary variable based on performance

on the Mental Control subtest of the Wechsler Memory Scale which assesses automatisms and simple mental tracking (Lezak, 1983), Trail Making A, and reading speed on the Stroop Colour Word test (described below).

Finally, sustained-selective[2] attention, the third factor identified by Shum et al. (1990) was comprised of serial 7's, serial 13's (counting backward from 100 by 7's and 13's respectively), and the interference score of the Stroop Colour Word Test. Sustained attention, selective extraction, and processing of information are believed to be common features of these tests (Shum et al., 1990). The Stroop test "is primarily a measure of rapid automatized naming and demands a minimal degree of effort" (August & Garfinkel, 1990). However, the interference subtest of the Stroop test has been considered to be a measure of divided attention (Kenny & Meltzer, 1991). In this subtest, the individual is required to name the colour of ink in which a word is written. The word to be read is a colour name (e.g., the word "red" written in blue ink). When performance is impaired, automatic processing overrides effortful processing and the individual responds by reading the actual word rather then naming the colour of ink (Weber, 1986). Patients with neuropsychiatric SLE have been found to be impaired on the Stroop test compared to normal control subjects (Denburg, S. et al., 1987), chronic

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[2] **Selective attention** refers to the ability to focus and maintain concentration on an assigned task while ignoring irrelevant stimuli. It "requires activation and inhibition of responses dependent upon discrimination of stimuli" (Sohlberg & Matter, 1987, p. 119).

illnesses control subjects (Wekking et al., 1991), and patients with non-neuropsychiatric SLE (Denburg, S. et al., 1987; Wekking et al., 1991). Further support for an impairment in sustained selective attention, comes from Ginsburg et al. (1992) who found that SLE patients successfully performed a simple choice reaction time test (described in the next section) but their performance on a more complex choice reaction time task was significantly worse than Rheumatoid Arthritis control subjects[3].

The attention tests reviewed above require the individual to exert different amounts of effort in order to perform well. It was found that simple mental tracking is intact in patients with SLE. However, the degree of effort required by the measures used to assess attention span or simple tracking is low (Crossen & Wiens, 1988). Effortful processing is associated with tests which measure rapid speed of mental operations (Crossen & Weins, 1988), performance under time pressures (Kahneman, 1973), or sustained attention.

The equivocal results of patients with SLE on Trail Making, as well as impaired performance on Digit Symbol Substitution and fluency tests raise the speculation that the performance of patients with SLE may become impaired when effortful processing is required. Further support for the speculation that cognitive deficits in SLE may reflect impairment in the ability to allocate cognitive effort comes from impaired performance by patients with

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[3] Although SLE subjects performed significantly lower than Rheumatoid Arthritis subjects, the mean of SLE subjects was 96% correct responses compared to 99% for Rheumatoid Arthritis patients.

neuropsychiatric SLE on a test tapping sustained-selective attention.

It appears that as the demands for exerting effort increase, the ability of patients with SLE, particulary those with CNS involvement, becomes impaired. It is hypothesized that the impairment is related to a disproportional reduction in attentional capacity.

Attentional Capacity

Researchers investigating attention often assume that there is a limited amount of attentional resources which can be allocated across tasks. This concept is generally referred to as attentional capacity (Kahneman, 1973; Weber, 1988). Deficits in attentional capacity present as difficulties in concentration, memory, comprehension, and computation. An individual with an acquired deficit in attentional capacity may still be able to carry out the same tasks as she or he previously could but those tasks seem to require more effort or are stressful (Weber, 1990). Additionally, performance in a structured situation or with a well known routine may be relatively normal, however, deficits may be evident in situations such as a busy office (Stuss et al., 1985). Attentional capacity has been found to be impaired in individuals with head injuries (Weber, 1988), attention deficit disorder (Borcherding et al., 1988), dementia (Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986; Weber, 1988; Weingartner, 1988), and schizophrenia (Cornblatt, Lenzenweger, & Erlenmeyer-Kimling, 1989; Earle-Boyer, Serper, Davidson, & Harvey, 1991). The present study hypothesizes that attentional capacity is also impaired in patients with SLE.

Attentional capacity is associated with what Kahneman (1973) considered a primary functional component of attention - effort. Much mental activity can occur without having to exert substantial effort (Kahneman, 1973). As the familiarity with the type of stimulus being attended to decreases or as the number of stimuli to be attended to within a given time increases, the sense of effort experienced by the individual increases (Weber, 1990). The amount of attentional energy required to complete activities is believed to fall along a continuum between 1) automatic activation (Hasher & Zacks, 1977; Posner & Synder, 1975; Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977) and, 2) conscious (Posner & Snyder, 1975), controlled (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977) or effortful processing (Hasher & Zacks, 1979; Roy-Bryne, Weingartner, Bierer, Thompson, & Post, 1986; Tariot & Weingartner, 1986; Wolkowitz et al., 1985; Wolkowitz & Weingartner, 1988). In this review, the latter will be referred to as effortful processing.

Automatic processes are rapid mental operations which are not under an individual's control (Fisk & Scerbo, 1987) and are not limited by the individual's attentional capacity (Cooley & Morris, 1990; Fisk & Scerbo, 1987; Hasher & Zacks, 1979; Posner, 1978; Tariot & Weingartner, 1986; Wolkowitz et al., 1985; Wolkowitz & Weingartner, 1988). They may occur without intention (Hasher & Zacks, 1979; Posner, 1978) or without conscious awareness (Cooley & Morris, 1990; Posner, 1978; Tariot & Weingartner, 1986). Automatic processes do not interfere with other ongoing mental activity. As a result, an individual can perform

more than one automatic activity at a time (Posner, 1978).

In contrast to automatic processing, effortful processing is dependent on and highly demanding of the individual's limited attentional capacity (Posner & Presti, 1987; Shiffrin & Schneider, 1977; Tariot & Weingartner, 1986). It requires intentional, sustained attention (Tariot & Weingartner, 1986). Effortful processing occurs slowly (Cooley & Morris, 1990; Fisk & Scerbo, 1987; Hasher & Zacks, 1977), serially (Cooley & Morris, 1990; Fisk & Scerbo, 1987; Hasher & Zacks, 1977; Posner & Presti, 1987), and is regulated by the individual (Cooley & Morris, 1990; Fisk & Scerbo, 1987).

Task difficulty alone does not appear to account for the amount of exertion required. Complex activities can occur automatically if they are, or become habitual (Posner, 1978), for example tying a shoe lace or driving a car. On the other hand, tasks which usually are considered to be simple (e.g. subvocal rehearsal, the choice and execution of free responses, and tests of recall of familiar material) actually require considerable concentration. Effortful processing tends to occur when active rehearsal is required, when there are time pressures, when tasks place considerable demands on attentional capacity (Kahneman, 1973), or when several attributes need to be considered (Posner & Presti, 1987). Because of the demands placed on attentional capacity, the number of effortful operations which can be performed at one time is limited. The overload on the individual's attentional capacity, due to the competition between tasks for attentional resources, is assumed to result in reduced

or impaired performance (Posner & Synder, 1975; Tariot & Weingartner, 1986; Wolkowitz & Weingartner, 1988).

Measures of Attentional Capacity

Choice reaction-time tasks, continuous performance tasks, and divided attention tasks have been found to be sensitive to detecting deficits in attentional capacity in a variety of head-injured populations (Weber, 1986).

Choice reaction-time tasks are frequently used in research to assess selective attention. The individual must assess what stimulus has occurred and respond as quickly as possible when a pre-specified stimulus is detected. Performance is based on the number of stimuli correctly identified and the speed of response (Sano, 1988). Schneider and Shiffrin (1977) indicate that a deficit in selective attention implies an attentional capacity limitation.

Continuous performance tasks have been developed (e.g. Rosvold, Mirsky, Sarson, Bransome & Beck, 1956) to assess sustained attention or vigilance. The format is similar to reaction-time tasks in that the individual is required to respond each time a specified stimulus or target occurs in a sequence of stimuli. The individual must also inhibit responding to extraneous targets (Cooley & Morris, 1990). While all continuous performance tasks are believed to measure vigilance, there is disagreement as to whether they measure automatic or effortful processing (Borcherding et al., 1988; Earle-Boyer et al., 1991). Borcherding et al. (1988) suggests that the ambiguity may be due to the fact that continuous performance tasks assess simple recognition and response which may seem automatic in nature. However,

the length of the test makes it effortful. Another explanation for the ambiguity may be that the processing requirements (i.e. the demands on the individual's limited attentional capacity) vary in relation to the nature of the stimuli presented. For example, familiar target stimuli such as letters or numbers are believed to require less effort than unfamiliar targets. The amount of effort required may also be influenced by the length of the target sequence (e.g., two stimuli rather than one), event rate (i.e., fast or slow) or with the presence of distraction stimuli (Earle-Boyer et al., 1991).

Attentional capacity has also been examined in research through the use of divided attention tasks. Divided attention tasks require the individual to perform two unrelated tasks simultaneously. If the tasks selected require automatic processing, an individual should be able to perform each task successfully. However, if each of the tasks require effort there will be a competition between the tasks for the individual's limited attentional capacity and the individual's overall performance will be impaired (Posner & Synder, 1975; Tariot & Weingartner, 1986; Wolkowitz & Weingartner, 1988).

While choice-reaction time tasks, continuous performance tasks, and divided attention tasks have been used to assess attentional capacity, they restrict the range of attentional capacity that can be measured. In addition, they are research tools which are not adequately normed for use with clinical populations (Weber, 1986; 1988; Weber & Segalowitz, 1990). The Paced Auditory Serial Addition test (PASAT; Gronwall & Sampson, 1974), a complex

conceptual tracking task, was designed as a *clinical* measure to assess the rate of information processing[4] and attention. The demands on attention capacity are increased by increasing the speed of the stimuli presentation while maintaining a constant level of task complexity (Spreen & Strauss, 1991). While the PASAT has been found to be sensitive to detecting deficits in attentional capacity in patients with brain injuries, the range of attentional capacity assessed by this measure is restricted. Furthermore, there is the added requirement of speed and accuracy of addition skill (Weber, 1986; 1988; Weber & Segalowitz, 1990).

Weber (1986) developed the Attentional Capacity Test (ACT) as a measure of auditory attentional capacity in order to overcome the limitations of the research measures described above and of the PASAT. The task requires controlled, focused attention to sequentially presented numbers. While mentally tracking numbers, the individual is required to select out and mentally count targets. Thus, the individual must divide attention between stimulus selection and counting. Because task complexity is increased over a number of sequential levels, the approach is appropriate to assess the amount of processing a individual can manage (Weber, 1986). Weber (1986) indicates poor performance on the ACT may result from

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[4] Weber (1986, 1988) suggests that the term information processing is synonymous with attentional capacity because "...the amount of information that can be attended to within a given time is the same as the amount that can be processed" (Weber & Segalowitz, 1990, p. 14).

either a limited or slowed capacity to process information, and from a loss of ability to use one's existing capacity in a goal-directed manner.

In a validation study (Weber, 1986), the ACT was found to be significantly correlated to the PASAT. Weber (1986) interpreted this finding as validating the ACT as a measure of attentional capacity. However, in contrast to the PASAT, which was highly correlated to a serial addition measure (r=.70), the ACT was only mildly correlated to serial addition (r=.13). The difference between the PASAT and ACT correlations was significant at the .001 level, suggesting that the ACT is a "purer" clinical measure of attentional capacity (Weber, 1986, 1988). The content validity of the ACT was assessed through clinical trials. Staff working with brain-injured patients rated the attentional capacity, defined as "the ability to focus and sustain attention in situations requiring selective and or divided attention" (Weber, 1988, p. 65), of their patients on a five point scale. Staff ratings were significantly correlated with ACT scores ($r = .73$, $p < 0.001$; Weber, 1988). Weber (1986, 1988) interpreted the results as confirming the clinical validity of the ACT.

The Gordon Diagnostic System (GDS; Gordon, 1991) is a clinical continuous performance test, designed to assess sustained visual attention with and without distraction. Accurate differentiation between hyperactive and non-hyperactive children has been made based on GDS test performance (Gordon & Mettelman, 1987). Moreover, it has been shown (Houtz, 1990) that the GDS was able to detect attention deficits in the early stages of Alzheimer's

disease. Specifically, the GDS was able to discriminate healthy control subjects from individuals with mild Alzheimer's disease as well as individuals with mild Alzheimer's disease from those with moderate Alzheimer's disease (Houtz, 1990). In addition, compared to control subjects, decreased performance on the distraction task has been documented in adult psychiatric patients, sleep apnea patients, closed head injured patients (Burg et al., 1992), and multiple sclerosis patients (Burg et al., 1992; Rasile, Burg, Rumsey, Burright & Donovick, 1993). A ceiling effect was observed for all but the closed head injured group on the task *without* distraction. Burg et al. (1992) concluded that the GDS is useful for assessing attention deficits in adult psychiatric and neurologic populations.

Limitations in attentional capacity have not been specifically addressed or assessed in previous studies of cognitive functioning of patients with SLE. The present study, designed to examine the nature of auditory and visual attentional capacity in patients with SLE, employs two clinical measures discussed above: The ACT (Weber, 1986), and the GDS (Gordon, 1991).

Confounding Clinical Variables

The literature review has been concerned with describing cognitive impairments in patients with SLE. The findings have been interpreted as being related to, or providing evidence of the involvement of the CNS. Some doubt as to whether involvement of the CNS is the primary or only cause of cognitive impairment was raised. Based on the findings of their study examining the prevalence of cognitive impairments in patients with SLE compared to

patients with Rheumatoid Arthritis (RA), Wekking et al. (1991) concluded that the occurrence of cognitive impairment is not unique to SLE patients.

When the CNS is involved in an illness, organic mental disorders (American Psychiatric Association, 1987) and depression (Cassem, 1990) are common. While CNS involvement may be a major etiology of cognitive impairment in patients with SLE, and in patients with other chronic illnesses, it is certainly not the only one. Numerous confounding clinical variables exist. Other etiological theories have proposed that cognitive deficits in chronic illnesses may be secondary to biological, pharmacological, or psychological complications. These three confounding variables will be reviewed below.

Biological Factors

Cognitive deficits in SLE may be secondary to complications of the disease (Carbotte et al., 1986; Hanly et al, 1992; Harris and Hughes, 1985; Huapaya & Ananth, 1980; McCune & Golbus, 1988). Biological factors such as hormonal, nutritional, electrolyte, or endocrine abnormalities have been found to be related to psychological difficulties in chronic illnesses (Hall & Beresford, 1985). In SLE, psychological disturbances associated with hypertension, renal failure (Hanly et al., 1992; Harris & Hughes, 1985; McCune & Golbus, 1988), and infarction (Harris & Hughes, 1985) have been reported. In some studies (e.g. Carbotte et al., 1986; Hanly et al., 1992) the diagnosis of neuropsychiatric involvement was made only if other causes for metabolic changes could not be detected.

The effects of disease activity on cognitive test performance remains unclear. Fisk et al. (1993) reported that increased SLE disease activity (SLE disease activity index; SLEDAI) was significantly associated with impairments in immediate memory and attention, suggesting possible transient, diffuse CNS involvement. However, Ginsburg et al. (1992), using the System Lupus activity measure (SLAM), failed to find such an association. Denburg, Carbotte and Denburg (1993) report that cognitive impairment in patients with SLE has not been found to be related to the presence of active disease or to the involvement of any organ system other than the CNS. They concluded, therefore, that the presence of cognitive impairment in patients is not a function of having a systemic illness, but rather, is due to the disease's attack on the brain.

Pharmacological Factors

Neuropsychiatric symptomatology observed in patients with SLE may result from treatment with medications (Fava & Molar, 1987; Huapaya & Ananth, 1980). In SLE, this association is particulary true for treatment with corticosteroids (Bresnihan, 1982; Harris & Hughes, 1985; McCune & Golbus, 1988). Corticosteroids are used in response to acute active phases of the disease (Sutton, Navarro & Stevens, 1984) to control the disease, alleviate the symptoms, and reduce morbidity (Bluestein, 1987). High doses and/or chronic use of steroids may put an individual at risk for developing adverse reactions, including impairments in mental and cognitive functioning, personality changes, and the appearance of depression

(Carpenter & Gruen, 1982), particulary when the dose is greater than 40 mg of prednisone per day (Boston Collaborative Drug Surveillance, 1972; Hall et al., 1979; Lewis & Smith, 1983; Ling, Perry, & Tsuang, 1981; Wolkowitz et al., 1990a). The incidence of psychological side effects of prednisone ranges from 1.8% to 57% (Wolkowitz et al., 1990a).

A classic presentation of steroid induced psychological problems does not exist (Kershner & Wang-Cheng, 1989). Changes in affect (Ling et al., 1981), particulary euphoria, depression and psychosis (Kershner & Wang-Cheng, 1989; Lewis & Smith, 1983; Ling et al., 1981) have been observed. Corticosteroids also cause difficulties in attention and memory (Wolkowitz et al., 1990b). For example, Varney, Alexander and MacIndoe (1984) described six patients who developed significant disturbances in attention, concentration, retention and mental speed while on steroids. These changes resolved or improved substantially when the steroids were discontinued. According to the authors, none of the patients had underlying disease states which could explain the mental changes. Impairments in memory secondary to treatment with corticosteroids have been substantiated in other studies, including those involving patients with SLE (Hall et al., 1979) and healthy adults (Wolkowitz et al., 1990b).

There does not appear to be any obvious underlying condition (e.g. premorbid personality, history of a previous psychiatric disorder or a previous psychosis) which predisposes an individual to adverse reactions (Hall et al., 1979), although being female (Lewis & Smith, 1983;

Ling et al., 1981), having SLE and receiving high doses of steroids (Lewis & Smith, 1983) are risk factors. Carpenter and Gruen (1982) suggest that an interaction of steroid dose, environmental stress and pre-existing vulnerability may predispose an individual to the development of psychological changes.

Although the use of steroids can result in neuropsychiatric symptoms, it is often difficult to determine whether the manifestations are caused by the use of steroids or are manifestations of a disease process involving the CNS. Furthermore, whether cognitive deficits observed in patients on corticosteroids are directly related to steroids or are secondary to psychiatric disturbances (primary, reactive or steroid induced) is difficult to ascertain (Mitchell & Collins, 1984; Wolkowitz et al., 1990a). Impairments in attention and memory are often seen in depressed individuals.

Several studies (Carbotte et al., 1986; Denburg, S. et al., 1987; Ginsburg et al., 1992) have found that the cognitive deficits documented in patients with SLE are not related to psychological stress or to corticosteroid dose. Klippel and Zvaifler (1975) stated that impairments in orientation, judgement, memory and perception are highly unusual side effects of corticosteroids. The authors asserted that the presence of such abnormalities should be attributed to the disease process.

Psychological Factors

Cognitive deficits in chronic illnesses may be secondary to organic, secondary or reactive psychological difficulties. One example which is particulary relevant to

the current study is the effect of depression on cognitive functioning. Depression and other psychiatric manifestations may be: (a) a primary feature of SLE; (b) secondary to other complications of the disease such as uraemia, hypertension or infarction (Harris & Hughes, 1985); (c) secondary to treatment with corticosteroids (Bresnihan, 1982; Harris & Hughes, 1985); or (d) a reaction to having a chronic illness (Bresnihan, 1982; Guze, 1967; Harris & Hughes, 1985; Lim et al., 1988). Prior to reviewing the association between cognitive deficits and depression, the psychiatric manifestations of SLE will be reviewed.

Psychiatric manifestations of SLE. There is considerable variability in the presentation of psychiatric symptoms in patients with SLE. Anxiety, lability of mood, personality change, depression, hallucinations, paranoia and psychosis have all been reported (Hall et al., 1981) either as isolated symptoms or as florid illnesses causing marked functional impairment (Baker, 1973; Guze, 1967). Depression is reported to be one of the most frequently occurring psychiatric disturbances in SLE (Magner, 1991; Wekking, 1993). It is estimated that approximately 50% of all patients with SLE display depressive symptomatology (Magner, 1991).

The distinction between organic and non-organic disturbances is not always clear. Both types of features may be present. Depression may also mask organic features (Klippel & Zvaifler, 1975). While psychological disturbances in SLE may be primarily related to the disease, secondary to complications of the disease or a

side effect of medication, psychiatric or psychological disturbances in SLE (Bresnihan, 1982; Guze, 1967; Harris & Hughes, 1985; Lim et al., 1988) and other chronic diseases (Huapaya & Ananth, 1980) may also result as a reaction to having a chronic illness or to its related complications. In this case, the origin of difficulties is considered to be due to psychosocial factors rather than to organic involvement (Magner, 1991). Denial, anger, anxiety and depression are among the psychological reactions invariably reported (Pakaslahti & Achte, 1982; Westbrook & Viney, 1982).

A considerable body of research regarding adaptation or maladaptation to chronic disease has accumulated. While a complete review of related research is beyond the scope of the present study, a few findings are noteworthy.

The results of several studies (e.g. Cassileth et al., 1984; Felton & Revenson, 1987) point to the understanding that symptom experience is not directly related to depression. In spite of the fact that chronic illnesses vary a great deal, the results of these studies suggest that, in general, the demands placed on individuals with different diseases are universal (Cassileth et al., 1984; Felton, Revenson, & Hinrichsen, 1984) and evoke a common set of reactions (Cassileth et al., 1984; Felton & Revenson, 1987). For example, Cassileth et al., (1984) assessed psychological adjustment in 758 patients with chronic illnesses suffering from one of six diseases (i.e major depressive disorder and five physical diseases, one of which was SLE). Patients in the five physical disease groups did not differ from one another or from the general

public but were significantly better adjusted than patients being seen for depression. The researchers concluded that psychological adjustment in patients with chronic illnesses is independent of diagnosis. Mediators, including disease activity and severity (Newman, Fitzpatrick, Lamb, & Shipley, 1990; Smith, Dobbins, & Wallston, 1991), functional ability (Smith et al., 1991) and illness intrusiveness (Devins, 1989) are believed to intervene between disease and adjustment. Poor adjustment or depression, in turn, can have a significant impact upon cognitive functioning.

Depression and Cognitive Functioning. In a major review of depression literature, Miller (1975) documented the impact of depression upon cognitive functioning. Despite the awareness of this potential influence, current knowledge of the association remains limited (Sweet, Newman, & Bell, 1992). Following a review of literature on neurological disease and depression, Sweet et al. (1992) concluded that depression has the definite potential of having a negative effect on cognitive functioning. Decreased performance on simple and complex attention tasks and verbal and visual memory have been documented (e.g. Cohen, Weingartner, Smallberg, & Pickar, 1982; Golinkoff & Sweeney, 1989; Roy-Bryne et al., 1986; Weingartner, Cohen, Murphy, Martello, & Gerdt, 1981).

Following a review of literature on cognitive functioning in depression, Willner (1984) concluded that the learning and memory deficits documented in depressed individuals stem from decreased ability to concentrate or to sustain effort. Depression is believed (Hasher & Zacks,

1979) to reduce attentional capacity. Impairments in tasks which require effortful recall, recognition or processing are considered to be the greatest deficits seen in depressed individuals. Tasks which tap automatic processing are usually spared (Cohen et al 1982; Golinkoff & Sweeny, 1989; Roy-Bryne et al., 1986; Tancer et al., 1990; Weingartner et al., 1981; Wolkowitz & Weingartner, 1988).

Implications

Ascertaining the contributing causes of cognitive impairments documented in patients with SLE can be difficult. The possibility that the etiology of neuropsychiatric disturbances is a primary or a secondary manifestation of the disease is particulary high in neoplastic, infectious, endocrine, systemic, autoimmune (Lipkin, 1989), and neurological disorders (Cassem, 1990; Lipkin, 1989). Moreover, the possibility that neuropsychiatric manifestations, are secondary to side-effects of corticosteroids, or depression is a legitimate concern. Variations in cognitive functioning within a sample of patients with SLE due to non-organic factors, require comparison to other groups. In studies investigating cognitive functioning in patients with SLE, a chronic illness control group and a healthy control group are vital for determining the factors which contribute to cognitive deficits and for understanding the impairments which are specific to CNS involvement in SLE.

In the present study, patients with Rheumatoid Arthritis (RA) were chosen to serve as control subjects because many features of the disease are similar to SLE.

Like SLE, RA is a chronic autoimmune disease with periods of remittance and flare ups, is treated with similar medications (Giang, 1991), and afflicts more women than men. However, in contrast to SLE, RA primarily involves inflammation of the joints (Anderson, Bradley, Young, McDaniel, & Wise, 1985) and spares the CNS (Giang, 1991; Magner, 1991).

Problem Statement

A consensus holds that the presence of cognitive impairment is an important descriptor in diagnosing CNS involvement in SLE (Singer et al., 1990). Over the past decade there has been an increasing interest in understanding the cognitive deficits which present in patients with SLE during the course of the disease. Cognitive deficits have been documented in patients who have active neuropsychiatric involvement and inactive neuropsychiatric involvement, as well as those who have never experienced neuropsychiatric involvement. Accordingly, it has been suggested (Carbotte et al., 1986; Hanly et al., 1992; Koffler, 1987; Kutner et al., 1988) that the presence of cognitive deficits may be a marker of subclinical CNS disease.

This study is an attempt to extend previous studies of cognitive functioning in patients with SLE by examining the nature of attentional processing in this group. Although previous studies (e.g. Denburg, S. et al., 1987; Hanly et al., 1992; Koffler, 1987; Kutner et al., 1988; Wekking et al., 1991) have documented cognitive impairment, a consistent pattern of deficit has not been reported (Denburg, S. et al., 1987; Kutner et al., 1988; Wekking et

al., 1991). Impairments in attentional capacity may be a fundamental cognitive deficit in patients with SLE. Support for this conjecture and the relevance of studying attention in patients with SLE are summarized below.

First, an analysis of deficits documented in patients with SLE raises the speculation that the ability to perform tasks which place demands on an individual's attentional capacity may be significantly more impaired in patients with SLE than in control subjects.

Second, impairments in attentional processes do not have unique behavioral outcomes (Lezak, 1983). They may adversely affect all areas of functioning (Naglieri & Das, 1990). The multitude of cognitive impairments which may result from deficits in attention may partially explain the inconsistent pattern of cognitive deficits in patients with SLE.

Third, deficits in attention (Goodglass, 1986) and attentional capacity (Weber, 1990) are not selectively associated with a specific brain lesion; they tend to be present to some degree regardless of locus of brain injury. The lack of specificity of locus of damage is consistent with the diffuse pathology of CNS involvement in SLE.

Fourth, impairments in attentional activities are among the most common mental deficits associated with brain injury (Lezak, 1983; Moscovitch, 1979; Van Zomerern et al., 1984). They may persist long after individuals have apparently recovered from brain disease or trauma (Lezak, 1983; Stuss et al., 1985). The persistence of attention problems may explain why patients with SLE with a past history of neuropsychiatric involvement and those with

active neuropsychiatric involvement are equally impaired on tests of cognitive functioning.

Finally, disruptions of attentional processes may result from very minor insults to the CNS (Sohlberg & Mateer, 1987). Therefore, attention deficits may be observed in patients with SLE who have subtle subclinical CNS involvement.

The past research suggests that impairments in attention capacity may be a fundamental cognitive deficit in patients with SLE with overt CNS involvement, those with inactive CNS involvement, and those suspected of having subtle subclinical CNS involvement. To date, no study has specifically examined attentional capacity in patients with SLE.

An understanding of the nature of attention deficit in patients with SLE compared to control subjects, may be helpful in establishing attentional markers of the CNS involvement. In turn, the finding of attention deficits through screening could identify patients in need of more thorough neuropsychological assessments.

The purpose of this study is to examine auditory and visual attention under increasingly demanding conditions in order to understand the nature of attentional processing and effort on a limited capacity system. It is postulated that patients with SLE, particulary those with CNS involvement, will show significant impairments on tasks demanding high degrees of effort.

Research Hypotheses

The findings of previous studies as well as an analysis of the types of cognitive deficits documented in

patients with SLE led to the hypotheses tested in this study.

Hypothesis 1: Performance on a test of auditory attentional capacity will significantly discriminate patients with SLE from medical and healthy control subjects.

Hypothesis 2: Performance on a visual sustained attention task will significantly discriminate patients with SLE from medical and healthy control subjects.

Hypothesis 3: Patients with SLE with previously diagnosed neuropsychiatric involvement will be more impaired on attention tasks than patients without a previous diagnosis of neuropsychiatric involvement.

Hypothesis 4: Patients with SLE without a previous diagnosis of neuropsychiatric involvement will be more impaired on attention tasks than medical or healthy control subjects.

Hypothesis 5: Patients with SLE without a previous diagnosis of neuropsychiatric involvement who subsequently received a diagnosis of neuropsychiatric involvement will be more impaired on attention tasks after the onset of neuropsychiatric involvement.

Hypotheses 6: Performance on attention tasks by patients with SLE with either active or inactive neuropsychiatric involvement at the time of the initial assessment will be unchanged subsequent to a change in their neuropsychiatric activity status.

CHAPTER THREE

METHODOLOGY

The overall objective of the present study was to examine the nature of attentional capacity specific to patients with SLE.

Ethical Considerations

The present study was reviewed and approved by the Department of Educational Psychology Ethics Review Committee, the Conjoint Medical Ethics Committee, and the Education Joint Research Ethics Committee at the University of Calgary.

Recruitment of Subjects

Systemic Lupus Erythematosus (SLE) Subjects

Female SLE patients meeting the American College of Rheumatology (ACR) 1982 revised criteria for having SLE were recruited through the University of Calgary Lupus Medical clinic. Potential SLE subjects were identified by their rheumatologist or the clinic coordinator. In the latter case, the coordinator contacted the rheumatologist involved in the patient's care to see if she could approach the patient about the study. The coordinator verified that each subject had a definite diagnosis of SLE and then contacted potential subjects to ask whether they would be willing to talk with the researcher to discuss participation in this study. If the individual was interested, and with her permission, her name was passed to the researcher. Alternatively, the researcher's name and phone number were given to the patient. Once contact had been made between the researcher and the individual, the researcher provided a brief description of the study

including what the individual's participation would entail. If the patient was still interested in participating, an appointment time was scheduled to complete the consent form, screening, and the assessment.

Assessment appointments were made as close to the subject's medical appointment as possible so that the relationship between attention performance and current disease activity and severity could be investigated. For patients with SLE who were receiving corticosteroids, the research appointment was scheduled to coordinate with their corticosteroid schedule. In order to control for possible effects of corticosteroids on attention performance, patients were seen in the morning prior to taking their medication, thereby ensuring that the medication was out of their system for at least 24 hours.

Rheumatoid Arthritis (RA) Subjects

Female RA patients who had a definite diagnosis for having the disease were recruited to serve as medical control subjects. Recruitment occurred through two processes: 1) through research personnel dealing with RA patients from the University of Calgary RA Medical Clinic; and 2) through letters sent to RA patients homes.

In the former process, an individual already doing research with patients with RA telephoned potential subjects and asked whether they would be willing to talk with the researcher to discuss participation in the present study. In the latter process, a letter (see appendix A) was sent to 26 clinic patients who had been identified by their rheumatologist. Follow-up telephone calls were made to RA individuals who did not reply to the mail-out in

order to ask whether they would be willing to have the researcher contact them.

If the individual was interested, and with her permission, her name was passed to the researcher. The researcher then telephoned potential subjects and provided a brief description of the study including what the individual's participation would entail. If the subject was willing to participate, an initial screening was conducted to rule out a history of neurological or mental illness. Individuals who reported the presence of the above conditions were thanked for their interest in the study and were provided with an explanation as to why their participation would not be required. If the individual did not report any of the exclusion criteria, the researcher arranged an appointment to complete a consent form, further screening, and the assessment.

Healthy Subjects

Healthy female control subjects were recruited through two advertising sources: the Neighbours section of the Calgary Herald newspaper; and bulletin board postings at the University of Calgary. The advertisements (see appendix A) solicited healthy female volunteers without a history of chronic illness to serve as control subjects in a research study examining attention in chronically ill women.

Interested persons contacted the researcher by telephone. The researcher then provided a brief description of the study including what the callers participation would entail. If the caller was still interested in participating, an initial screening was

conducted to rule out the presence of a history of a chronic, neurological, or mental illness, uncorrected vision or hearing problems, and treatment for a current medical illness. Callers who reported the presence of any of the above conditions were thanked for their interest in the study and provided with an explanation as to why their participation would not be required. If the caller did not report any of the exclusion criteria, the researcher arranged a mutually agreeable appointment to complete a consent form, further screening, and the assessment.

Screening Instruments

Participation in this study required one 50 to 60 minute session during which all screening and test instruments were administered. All subjects read and completed the following screening instruments:

1. a letter of informed consent;
2. a personal questionnaire; and
3. a depression measure.

In addition, healthy control subjects read and completed an attention deficit screening questionnaire.

Letter of Informed Consent

A letter of informed consent (see appendix B) was provided to each individual prior to commencing other screening or test instruments. The researcher informed individuals of the following: "This letter of informed consent outlines the nature of the study as well as what your participation in the study entails. If you have any questions please do not hesitate to ask."

Personal Questionnaire

The personal questionnaire (see appendix C) included questions to illicit demographic data and subjective reports of mood and cognitive functioning. Specifically, it looked at fluctuations in mood, anger, happiness, depression, frustration, concentration, and memory on day of testing compared to most days, and during period of disease activity compared to periods of disease inactivity. The questionnaire for SLE and RA subjects were the same except that the term "RA" was substituted for "SLE". The questionnaire for healthy controls included every third question, thereby excluding those items related to periods of remission or exacerbation.

Depression Measure

The Centre for Epidemiological Studies in Depression Scale (CES-D; Radloff, 1977) was used to screen for level of depression.

The CES-D contains 20 self-report items designed to assess the severity and number of depressive symptomatology over the past week. The individual has the choice of one of four responses to each item which are scored as follows: "rarely or none of the time (< 1 day) = 0, " "some or a little of the time (1-2 days) = 1, " "occasionally or a moderate amount of time (3-4 days) = 2," or "most or all of the time (5-7 days) = 3." Scoring for items 4, 8, 12, and 16 are reversed. The total score represents the depression score. High scores represent high levels of depression (Orme, Reis, & Herz, 1986).

The CES-D shows good internal consistency reliability and good short-term test-retest reliability (Orme et al.,

1986). Alpha reliability coefficients for internal consistency ranged from .84 to .90 in field trial data collected on community volunteers. Test-retest reliability coefficients for two week, four week, six week and eight week intervals ranged from .51 to .67 (Radloff, 1977). Devins et al. (1988) reported a test-retest reliability of .63 after a 3 month interval.

Radloff (1977) demonstrated convergent validity with the Hamilton Rating Scale. Coefficients range from .50 to .80.

The CES-D appears to be suitable for screening depression or general distress in individuals with whom there may be confounding results due to an overlap of symptoms related to having a chronic disease and symptoms related to depression. In a large study (Devins et al., 1988), the psychometric properties of the CES-D were shown to be constant across various healthy and ill populations. The CES-D has been widely used in research with patients with chronic diseases, including patients with RA (Callahan, Kaplan, & Pincus, 1991), progressive renal disease, end stage renal disease, and cancer (Devins et al., 1988).

Attention Deficit Screening

It was felt that an advertisement for healthy control subjects might attract individuals who believed they had attention difficulties. Therefore, a screening measure was given to healthy control subjects to screen for adult attention deficit disorder. This questionnaire (see appendix D) was a written version of a checklist used in an assessment interview developed by Weiss (1992) which she

adapted from the Diagnostic and Statistical Manual of Mental Disorders (DSM-111; American Psychiatric Association, 1980). The questionnaire contained all 27 items assessed in interview form by Weiss. Weiss indicates that 'Yes' responses by adults to 40 percent of the items when accompanied by a history of the same behaviours in childhood is indicative of attention deficit disorder in adults. The present study used an a priori cut off score of ten 'Yes' responses to indicate possible attention deficits. The attentional capacity performance of healthy control subjects obtaining a score of ten or more were to be compared to healthy control subjects obtaining a score of less than ten. If there were no significant differences in performance, the two groups would be combined to form one group. However, if there were significant differences, the healthy control subjects would form two control groups; those with suspected attention deficit disorder and those without.

Measures of Disease in SLE Subjects

Disease Activity

Disease activity in patients with SLE was determined by the ratings on two measures routinely used by University of Calgary Medical Lupus Clinic. These are: (1) the SLE Disease Activity Index (SLEDAI; Bombardier et al., 1992); and (2) the revised Systemic Lupus Activity Measure (SLAM; Liang, Socher, Larson, & Schur, 1989; revised in 1991). Ratings on these scales are derived from clinical manifestations and laboratory results. Both measures have been found to have good inter-visit and inter-rater reliability (Liang et al., 1989).

The SLEDAI includes weighting on 19 manifestations across six organs: 1) CNS (i.e. seizure, psychosis, organic brain syndrome, visual abnormalities, cranial nerve disorder, SLE headache, and cerebrovascular accident); 2) Vascular (i.e. vasculitis); 3) Renal; 4) Musculoskeletal 5) Skin; and 6) Serositis. Each manifestation is rated as being absent or present. However, weightings for variables vary across specific organs, with those manifestations involving the CNS and Vascular systems receiving the highest weightings and those involving the Skin or Serositis receiving the lowest weightings. Ratings are made if the manifestation is present in the 10 days prior to and including the medical. The maximum score is 49. A modified version of the SLEDAI (SLEDAI-M) was included in the present study. In addition to the six organ systems listed above, the modification included ratings on immunologic laboratory results, haematologic studies, and constitutional symptoms. The maximum score for the modified SLEDAI is 54.

The SLAM-R, which covers 24 clinical manifestations and 8 laboratory results, rates symptoms over the month prior to its use. Ten organ systems are rated; 1) Constitutional; 2) Integument (i.e. oral ulcers, alopecia, erythematous or discoid rash, and vasculitis); 3) Eye; 4) Reticuloendothelial[5] (i.e. disease of the lymph

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[5] Reticuloendothelial system refers to "a network of cells and tissues found ... in the blood, general connective tissue, spleen, liver, lungs, bone marrow, and lymph nodes." (Miller & Keane, 1987, p. 1081).

nodes, and enlargement of the liver or spleen); 6) Pulmonary; 7) Cardiovascular; 8) Gastrointestinal; 9) Neuromotor (i.e. stroke syndrome, seizure, cortical dysfunction, headache, and myositis); 10) Joint; and 11) Laboratory results including blood work and serum creatinine level. Each of the 24 clinical manifestations and 8 laboratory results is rated as present or active. The scale is also graded so that the overall scores also reflects disease severity.
The maximum score is 79.

In as many cases as possible, the ratings on the three scales were made from the medical and laboratory examinations closest to the date of the attention assessment and within two months of that assessment. In some cases laboratory tests were not ordered due to lack of clinical evidence of disease activity. In the case of any missing data, information was obtained from the closest examination in which this information was complete.

Disease Severity

Global disease severity was determined by the patient's rheumatologist during routine medical examination. Level of severity is a percentage rating based on the type and number of organs involved in the disease.

Neuropsychiatric Involvement

The clinic medical charts of all SLE subjects were reviewed by the researcher, under the supervision of a Rheumatologist. The subject's present or past history for neuropsychiatric involvement as determined by a Rheumatologist, and in most cases confirmed by a

neurologist, during routine medical examinations was determined. The presence of neuropsychiatric involvement was based on a predetermined set of criteria (Table 1) which combined all but one[6] of the "solid" neuropsychiatric features used by the two major North American research groups (e.g. Carbotte et al., 1986; Hanly et al., 1992) investigating cognitive functioning in patients with SLE.

Table 1

Criteria for Neuropsychiatric Involvement

Cerebrovascular event (stroke, TIA)	Meningitis
Cranial neuropathy	Seizure
Peripheral neuropathy	Organic brain syndrome
Movement disorder	Affective disorder[7]
Transverse myelitis	Psychosis

Definitions for the psychological disorders included in Table 1 may be found in the Dictionary of Rheumatic Diseases, Volume I: Signs and Symptoms (ARA Glossary Committee, 1982) and are based on the definitions in DSM-111 (American Psychological Association, 1980). If the

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[6] Schizophreniform disorder was not included in the neuropsychiatric criteria of the present study because a definition of this disorder is not found in the Dictionary of Rheumatic Diseases. Accordingly, it was felt that this term would not have been used by a Rheumatologist during routine medical assessment. Rather, manifestations of the disorder likely would have been subsumed under Psychosis.

[7] Depression was included only if it required medical intervention.

Rheumatologist or Neurologist felt that neuropsychiatric manifestations were secondary to medications, then a diagnosis of neuropsychiatric involvement was not made. In addition, if the serum creatinine was greater than 200, then it was assumed that neuropsychiatric manifestations were secondary to other complications of the disease and a diagnosis of neuropsychiatric involvement was not made.

Attention Measures

Two attention measures were administered:

1. The Attentional Capacity Test (ACT; Weber, 1986; 1988); and
2. The Gordon Diagnostic System Model III-R (GDS; Gordon, 1991).

The Attentional Capacity Test (ACT)

The 24-item version of the ACT (Weber, 1986; 1988) was used in the present study to assess auditory attentional capacity. The ACT assesses the individual's ability to attend to and process auditory input. The demands on attentional capacity are increased by increasing the content demands over eight levels (see Table 2). As, a result, the ACT is suitable for assessing a wide range of ability (Weber, 1986). Level 1 is suitable for patients just out of a coma, while level 8 is challenging for university students (Weber, 1986, 1988). Furthermore, as Weber (1986, 1988) indicates, the ACT is suitable for monitoring progress or deterioration in a patient's attentional capacity regardless of his or her level of performance.

Each level is preceded by practice stimuli given by

the tester. Test stimuli are presented from a pre-recorded tape. The recording was produced by a computerized procedure to ensure that each number is consistently pronounced in the same way and to ensure that all stimuli are presented at the same level of loudness. The speed of stimulus, one per second, is also controlled (Weber, 1986; 1988).

Table 2

Task Requirements of Each Level of the ACT[8]

Level	*Requirements*
1	Repeat single number.
2	Count number of "ee" sounds in a sequence of ee's.
3	Count number of 8s in a sequence of 8s.
4	Count number of 8s in a sequence of mixed numbers (i.e., the numbers 1 through 10 in random order)
5	Count number of 8s and 5s in a sequence of mixed numbers (one total).
6	Count number of 8s, 5s, 4s, and 7s in a sequence of mixed numbers (one total).
7	Count number of sequential pairs, 4-7 and 5-8, in a sequence of mixed numbers (one total).
8	Count numbers of sequences 5-number-8 in a sequence of mixed numbers. The number in the middle can be any number from 1 to 10 and it is possible to have overlaps between two such sequences if 5-5-8-8 occurs.

The prerequisites for this test are the ability to hear and to count from 1 to 10. The task of processing targets is not affected by response speed because responses are given upon completion of each trail. Responses may be given orally, in writing, by pointing to a number card, or by blinking. Discontinuation criteria are provided for low scorers (Weber, 1986; 1988). Performance has not been found to be related to the age or sex of the individual

[8] Reproduced with permission from the Author (see appendix E).

(Weber, 1988).

A 60-item version (Weber, 1986; 1988) and the shorter 24-item version (Weber, 1988) were validated on normal adult subjects and brain injured subjects.

The Gordon Diagnostic System (GDS)

The GDS Model III-R (Gordon, 1991) was used to assess sustained visual attention with and without distraction. The GDS is a clinical test which was specifically designed to assess attention deficits (Gordon, 1991). The individual is required to respond to visually presented stimuli displayed on a portable electronic device (Gordon & Mettelman, 1988).

There are two adult subtests; a vigilance task and a distractibility task. Both subtests assess the extent to which an adult can maintain concentration under situations demanding sustained attention. These subtests are based upon the Continuous Performance tasks described in Chapter Two. The individual is required to respond only when a pre-specified combination of numbers is presented (Gordon, 1991).

The Vigilance subtest, which in the present study was administered as a baseline measure for the Distractibility subtest, assesses the individual's ability to focus and maintain attention on a task over time. The individual is required to press a button each and every time the number 9 has been preceded by the number 1. The number 1 serves as an altering stimulus to cue the individual that the number 9 may follow. The number 9 is the stimulus to which the individual is required to respond if cued by the number 1 (Gordon, McClure, & Post, 1986).

The Distractibility subtest measures level of distractibility while sustaining attention. The task is the same as the Vigilance task in that the individual is required to press a button each and every time the number 9 has been preceded by the number 1. However, there is the addition of distraction stimulus. Numbers flash at random in columns on either side of the task stimulus. These numbers are not part of the task. Rather, they serve as distractions to the task. The individual is informed that she should only respond to the "1/9" number combination when it appears in the middle column (Gordon & Mettelman, 1988).

In the adult version of the GDS Vigilance and Distractibility subtests, digits in the middle column appear on a screen for 200 msec at a rate of one digit per second over a 6 minute task (Gordon, 1991).

In the present study, two simplified versions of the Vigilance task were programmed into the GDS by the researcher and were administered as baseline measures in case the expected ceiling effects were not reached on the Vigilance subtest. In the first of these baseline measures, the numbers 0 through 9 appeared at random in the middle column at a rate of one stimulus per second for 30 seconds. The subject was told to press the button each and every time she saw a number flash on the screen. In the second of these baseline measures, the numbers 0 through 9 appeared at random intervals in the middle column. This time the subject was told to respond each time the number "0" appeared. The rate of stimulus was one per second and the task duration lasted one minute.

Standardization data for the Vigilance and Distractibility subtests for children[9] ages 6-16 (similar tasks to those described above but each lasting 9 minutes) was collected on over 1250 non-hyperactive school children over a four year period (Gordon & Mettelman, 1988). The variables within each subtest (i.e. correct responses and commission errors) were highly correlated. However, variables between the two subtests were not closely related. Gordon and Mettelman (1988) interpreted these findings as providing support for the fact that the two subtests measure different aspects of functioning. Correlational analysis (Rasile et al., 1993) between the Vigilance and Distractibility subtests with healthy adults (n=44) and patients with multiple sclerosis (n=56) support Gordon and Mettelman's (1988) finding.

The test-retest reliability coefficients of ninety children randomly selected from the standardization sample ranged from .67/.72 (total correct on Distractibility task and Vigilance tasks respectively) to .85/.84 (total commissions on the Distractibility and Vigilance tasks respectively; Gordon & Mettelman, 1988).

Procedures

Participation in this study required one 50 to 60 minute session. All assessments were completed in a

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[9] Preliminary normative data for adults (n=60; ages 19-74) is available in the manual (Gordon, 1991). Additional normative data has been collected (Burg et al., 1992) for college students (n=136), healthy adults (n=44), adult psychiatric patients (n=87), multiple sclerosis patients (n=51), sleep apnea patients (n=27), and closed head injured patients (n=10).

medical examination room with bare essentials in furnishings in order to ensure a minimum of external distractions. Attention tasks and screening instruments were administered to all subjects by the researcher in the following order:

1. Letter of Informed Consent;
2. The GDS (baseline measures, followed by the Vigilance subtest, and then the Distractibility subtest);
3. Personal Questionnaire, the CES-D, and in the case of healthy control subjects, the Attention Questionnaire; and
4. The ACT.

No subjects withdrew at any point during the assessment. Subjects requesting information about their attention functioning were provided with written feedback by the researcher. Subjects requesting information regarding the results of the study were mailed a summary of the research following the defense of the study.

The medical charts of RA and SLE subjects were reviewed after all subjects had completed the attention assessment. As a result, information abut disease activity, or neuropsychiatric involvement was not known at the time of the assessment. The charts of SLE subjects were initially reviewed by the researcher to determine disease duration[10], ACR criteria, disease activity rating, the presence of a history of seropositivity and

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[10] Disease duration was defined as the length of time from diagnosis until attention assessment date.

neuropsychiatric manifestations, medications, and co-morbid illnesses. Each SLE case was subsequently reviewed by a rheumatologist to document disease activity and severity.

The charts of RA subjects were reviewed by the researcher to document medications, disease duration, co-morbid illnesses, and a history of seropositivity as demonstrated by abnormal amounts of serum rheumatoid factor[11] or a positive antinuclear antibody test.

Statistical Analyses

Six dependent measures of attentional processing were included in this study as measured by the ACT and the GDS:

1. Total score on the ACT;
2. Highest level achieved on the ACT;
3. Number of levels missed on the ACT;
4. Total number correct on the GDS distractibility subtest;
5. Total commission errors on the GDS distractibility subtest; and
6. Mean latency on the GDS distractibility subtest.

Ideally, a quasi experimental 4 x 3 x 3 (i.e. diagnostic group, by disease activity, by disease severity)[12] factorial design would have been used to

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[11] Rheumatoid factor is a specific antibody frequently found in the serum of patients with RA and is considered to have diagnostic value (Vaughan, 1993).

[12] The variables expand as follows: Groups = SLE subjects with neuropsychiatric involvement, SLE subjects without neuropsychiatric involvement, RA subjects, and healthy controls. Activity = inactive, mildly active, and active. Severity = no severity, mildly severe, and severe.

investigate the nature of attentional capacity with depression used as a covariate. Unfortunately, this design would have required a minimum of 360 subjects. At the outset of this study, it was decided that it was unlikely that a sufficient number of volunteers from the patient groups, or community could be recruited to meet this requirement. Therefore, a less powerful design was employed.

The six dependent variables were analyzed in the primary analyses. Two separate MANCOVAs across diagnostic groups (i.e. SLE, RA, and healthy control) were computed. The first MANCOVA was computed on the 3 dependent variables for auditory attention. A separate MANCOVA was computed on the 3 dependent variables for visual attention. In order to separate out the effects of neuropsychiatric involvement, the SLE group was broken into two groups: those with a history of neuropsychiatric involvement[13] and those without a history of neuropsychiatric involvement (non-neuropsychiatric). The above MANCOVAs were re-computed across the four diagnostic groups (i.e. neuropsychiatric SLE, non-neuropsychiatric SLE, RA, and healthy controls).

Univariate procedures (ANCOVAs) were subsequently employed with those MANCOVA's demonstrating significance in order to test for the significance of the individual

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[13] Previous research (Carbotte et al., 1986; Hanly et al., 1992) has failed to reveal significant differences between those patients with active neuropsychiatric involvement and those with past histories of neuropsychiatric involvement, therefore, these individuals formed one group-neuropsychiatric SLE.

dependent measures. Level of depression (i.e. the CES-D score) was used as the one covariate in each of the above analyses. Post hoc comparisons using the Scheffé test were computed on any of the dependent variables demonstrating significance.

Based on the significance of descriptive statistics, the above procedures were re-computed with age as a covariate, and with education as a covariate.

In secondary analyses, multivariate analysis using Hotelling's T^2 was computed between the two SLE groups with the three measures of disease activity serving as the dependent measures. A t-test was computed between the two SLE groups with disease severity serving as the dependent measure. In addition, Pearson Product-Moment correlations were computed to explore the significance of the relationship between (a) each of the dependent measures demonstrating significance in primary analyses and (b) disease activity and severity measures, and medications.

Descriptive analyses were computed on all dependent and independent variables.

An alpha of .05 was set for all analyses. The Statistical Package for Social Sciences (SPSS) was employed for all analyses.

The assumption of random sampling, normal distribution of the data, homogeneity of variance, and independence are stipulations for the types of analyses used in this study. While not all of these assumptions were met, MANCOVA is considered to be robust to breaking the assumption so long as independence of samples is maintained.

CHAPTER FOUR

RESULTS

The present study collected data from three diagnostic groups: the experimental group (patients with Systemic Lupus Erythematosus; SLE), and two control groups (patients with Rheumatoid Arthritis; RA, and healthy adults). Descriptive statistics on each of the diagnostic groups, on mood and cognition, and on test instruments will be described first, followed by the results of hypotheses testing, and of testing for potentially confounding clinical variables.

Descriptive Statistics

Description of Subjects

Systemic Lupus Erythematosus (SLE) subjects. Over a ten month period, the data of 35 subjects with SLE, primarily from the Calgary area, was obtained. The researcher was provided with the names and telephone numbers of 40 patients with SLE. All but 5 agreed to participate upon hearing about the study.

SLE subjects ranged in age from 20 to 59 years, with a mean of 39.34 years (SD = 10.02). Seventeen percent (n=6) had secondary schooling, 63% (n= 22) had 1 to 5 years of college or university training, and 20% (n=7) had 6 or more years of college or university training.

Disease duration ranged from 1 to 49 years, with a mean of 10 years (SD = 9.53). Cumulative disease manifestations for the SLE sample are summarized in Table 3. Disease activity based on the SLAM-R ranged from 0 (no activity) to 14, with a mean of 3.46 (SD = 2.68). On the

SLEDAI, disease activity ranged from 0 to 18, with a mean of 6.57 (SD = 4.64). On the modified SLEDAI (SLEDAI-M), disease activity ranged from 0 to 20, with a mean of 8.57 (SD = 5.282). Data on disease severity was available on 17 subjects and ranged from 0% to 50%, with a mean of 18.82% (SD = 17.37). The incidence of co-morbid illnesses is summarized in Table 4. The incidence of medication is summarized in Table 5.

Table 3

Cumulative SLE Disease Manifestations

Manifestation	SLE n=35	NP* SLE n=19 (54.3%)	NON-NP SLE n=16 (45.7%)
Malar Rash	n=25 (71.4%)	n=13 (68.4%)	n=11 (68.8%)
Discoid Rash	n=12 (34.3%)	n=8 (42.1%)	n=4 (25%)
Photosensitivity	n=14 (40%)	n=10 (52.6%)	n=4 (25%)
Oral Ulcers	n=14 (40%)	n=10 (52.6%)	n=4 (25%)
Arthritis	n=18 (51.4%)	n=9 (47.4%)	n=9 (56.3%)
Serositis	n=16 (45.7%)	n=6 (31.6%)	n=10 (62.5%)
Renal Disorder	n=25 (71.4%)	n=11 (57.9%)	n=14 (87.5%)
Haematologic Disorder	n=16 (45.7%)	n=9 (47.4%)	n=7 (43.8%)
Immunologic Disorder	n=25 (71.4%)	n=14 (73.7%)	n=11 (68.8%)
Seropositivity**:			
Antinuclear Antibody	n=34 (97.1%)	n=18 (94.7%)	n=16 (100%)
Anti-DNA	n=18 (51.4%)	n=9 (47.4%)	n=9 (56.3%)
Anti-Smith	n=4 (11.4%)	n=3 (15.8%)	n=1 (6.3%)
Anti-RNP	n=8 (22.8%)	n=5 (26.3%)	n=3 (18.8%)
Anti SS. A/RO	n=9 (25.7%)	n=3 (15.8%)	n=6 (37.5%)
Anti SS. B/LA	n=6 (17.1%)	n=2 (10.5%)	n=4 (25%)
Anti-cardiolipin	n=7 (20%)	n=4 (21.1%)	n=3 (18.8%)

* NP = Neuropsychiatric involvement.

** DNA = deoxyribonucleic acid; RNP = ribonucleoprotein; SS =Sjögren's Syndrome.

Table 4

Incidence of Co-morbid Illnesses by Disease

Illness	SLE	RA
Hypothyroid or Hashimoto's thyroiditis	n=8 (22.9%)	n=3 (13%)
Fibromyalgia	n=11 (40%)	n=3 (13%)
Breast Cancer	n=1 (2.9%)	---
Asthma	n=5 (14.3%)	n=1 (4.3%)
Sarcoidosis	n=1 (2.9%)	---
Hypertension	n=1 (2.9%)	---
Sjögren's Syndrome	n=3 (8.6%)	n=2 (8.7%)
Peptic Ulcer Disease	n=1 (2.9%)	---
Rheumatoid Arthritis	n=1 (2.9%)	---
Mitral valve prolapse or Rheumatic heart disease	n=1 (2.9%)	n=1 (4.3%)
Obstructive Pulmonary Disease	---	n=1 (4.3%)

Table 5

Medications by Disease Classification

Medication[14]	NP SLE (n=19) #* Dosage**	NON-NP SLE (n=16) # Dosage	RA (n=23) # Dosage
Prednisone	9 (47.4%) 2.5-1000	10 (62.5%) 1.3-20	3 (25%) 5-7.5
Plaquenil	4 (21.1%) 200-400	5 (31.3%) 200	1 (4.3%) 200
Methotrexate	---	---	9 (39.1%)
Aralen	1 (5.3%) 250	2 (12.5%) 250	---
NSAIDS***	5 (26.3%)	4 (25%)	14 (60.9%)

* Number of subjects (percent of subjects).
** The range of dosage in milligrams per day is given.
*** NSAIDS = non-steroidal anti inflammatory drugs.

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[14] **Prednisone** is used as an antiinflammatory and immunosuppressive.
Plaquenil and **Aralen** are used in treatment of skin lesions and in controlling arthritis.
Methotrexate is used as an antiinflammatory or immunosuppressive when an individual does not respond well to steroids.
NSAIDS (e.g. aspirin, ibuprofen) are used to decrease inflammation (Carr, 1986).

A history of neuropsychiatric involvement was documented in 54% (n=19) of the SLE subjects. Manifestations of neuropsychiatric involvement included cerebrovascular disease (n=2), cranial neuropathy (n=5), peripheral neuropathy (n=4), transverse myelitis (n=2), seizure disorder (n=5), psychosis (n=1), and affective disorder (n=10)[15]. Cumulative disease manifestations for the neuropsychiatric and non-neuropsychiatric samples are summarized in Table 3.

Rheumatoid Arthritis (RA) subjects. Over a ten month period, the researcher assessed 23 female control subjects, primarily from the Calgary area. The names of 22 patients with RA were given to the researcher; all but 3 agreed to participate upon hearing about the study. Five RA patients responded to an advertisement which was mailed to the homes of 26 patients. One of these five withdrew from the study before attending the appointment. Two individuals agreed to participate upon a follow-up telephone call. Two individuals were excluded due to histories of neurological complications.

RA subjects ranged in age from 28 to 74 years, with a mean of 54.91 years (SD = 12.90). Sixty-one percent (n=14) had secondary schooling, while 39% (n=9) had 1 to 5 years of college or university training. Disease duration ranged from 2 years to 35 years, with a mean of 14.96 years (SD = 11.18). Data on testing for serum rheumatoid factor activity was available on 21 of the 23 RA subjects; 19 of

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[15] Affective disorder was characterized in all cases as depression requiring medical intervention (i.e. n=10).

these subjects tested positive (90.5%) at sometime in their history. Data on antinuclear antibody testing was available on 19 RA subjects; 68.42 % (n=13) subjects tested positive for this antibody at sometime during their history. The incidence of co-morbid illnesses is summarized in Table 4. The incidence of medications is summarized Table 5.

Healthy subjects. Over a ten month period, there were 61 inquires from individuals in the community about the attention study. Forty-five inquires were responses from the newspaper advertisement. Sixteen responses were from the posters. All but two agreed to participate upon hearing about the study. Three individuals were excluded from the study at the phone call stage because they self reported one of the exclusion criteria, eight failed to keep their appointments, and six were excluded at the appointment stage because of their current or past medical histories. Therefore, the data of 42 healthy community female volunteers from the Calgary area was obtained.

Healthy control subjects ranged in age from 18 to 72 years, with a mean of 37.10 years (SD = 12.55). Fourteen percent (n= 6) had secondary schooling, 69% (n= 29) had 1 to 5 years of college or university training, while 17% (n=7) had 6 or more years of college or university training. Scores on the attention deficit screening questionnaire ranged from 0 to 8, with a mean of 2.81 (SD=2.31). An a priori cut off score of ten YES responses was used to indicate possible attention deficits. The highest score was 8, therefore all healthy control subjects formed one group.

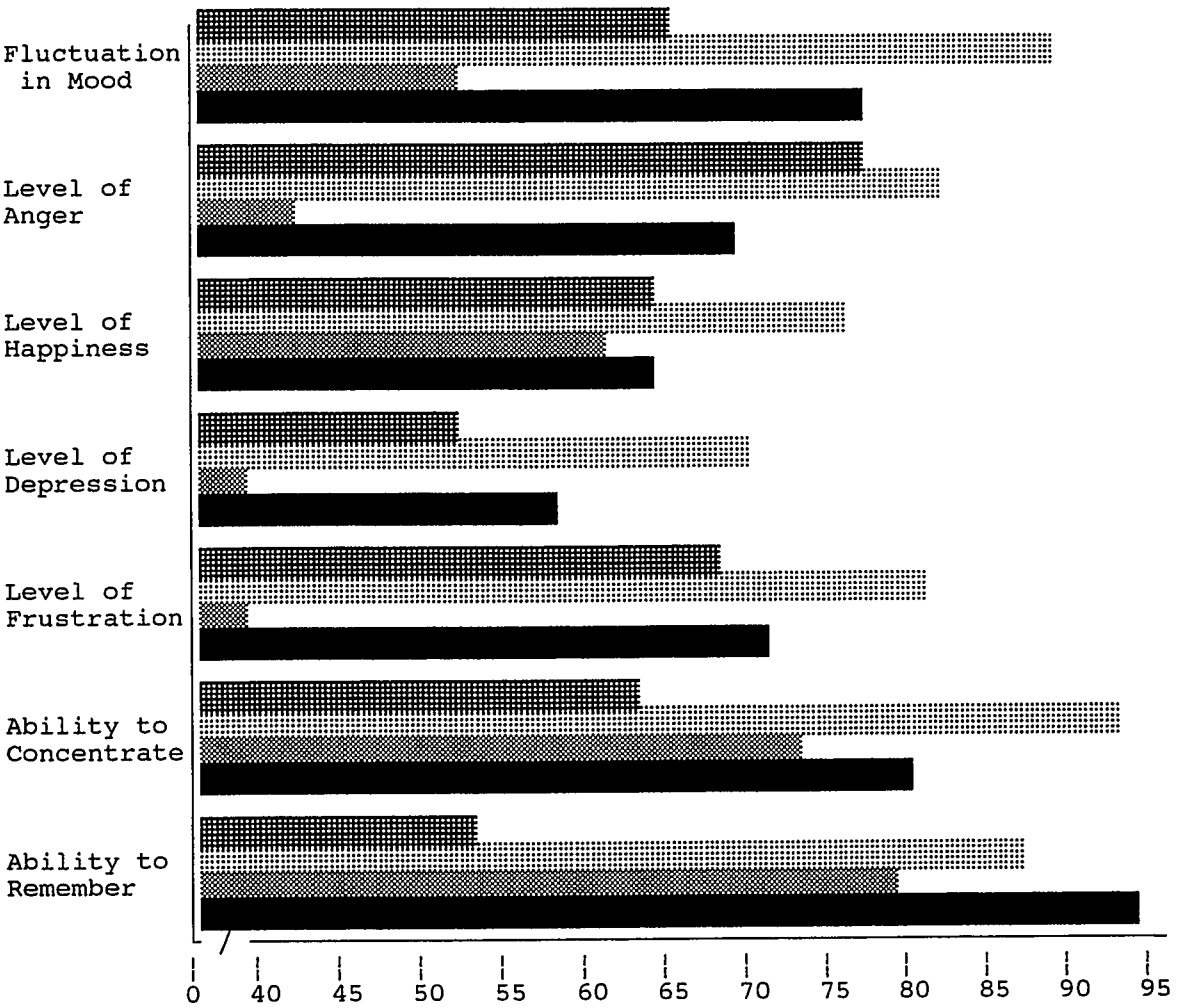
Homogeneity of subjects. An ANOVA computed on age across the three diagnostic groups (i.e. SLE, RA, and healthy control subjects) was significant ($F(2,97) = 18.25$, $p<.001$). Scheffé tests revealed a significant difference in age between SLE subjects and RA subjects ($F(2,97) = 16.39$, $p<.001$), and between RA and healthy control subjects ($F(2,97) = 16.97$, $p<.001$), with the RA subjects being significantly older. There was no significant difference between the ages of the SLE subjects and the healthy control subjects. A Chi Square test of significance computed on education across the three main diagnostic groups was significant ($p < .001$), with the RA subjects appearing to have achieved a lower level of education. A t-test for independent samples between the disease duration of SLE and RA subjects was not significant, nor was a t-test between the disease duration of neuropsychiatric SLE and RA subjects.

Reports on Mood and Cognition

Subjective ratings on mood and cognition were obtained from all subjects (see Figure 1). During the week prior to the attention assessment, the majority of subjects (i.e. combined diagnostic groups) reported that fluctuations in their mood (73%), level of anger (66%), level of happiness (65%), level of depression (54%), level of frustration (65%), ability to concentrate (77%), and ability to remember (82%) were about the same as in most weeks.

Figure 1

Percentage* of Subjects, by Group, Rating Mood and Cognition to be "about the same" on Assessment Day Compared to Most Days



An inspection of Figure 1 reveals, that the percentage of RA subjects reporting that their level of anger, depression and frustration was "about the same as on most days" appears to be considerably lower than the other groups. In respect to levels of anger, and frustration the

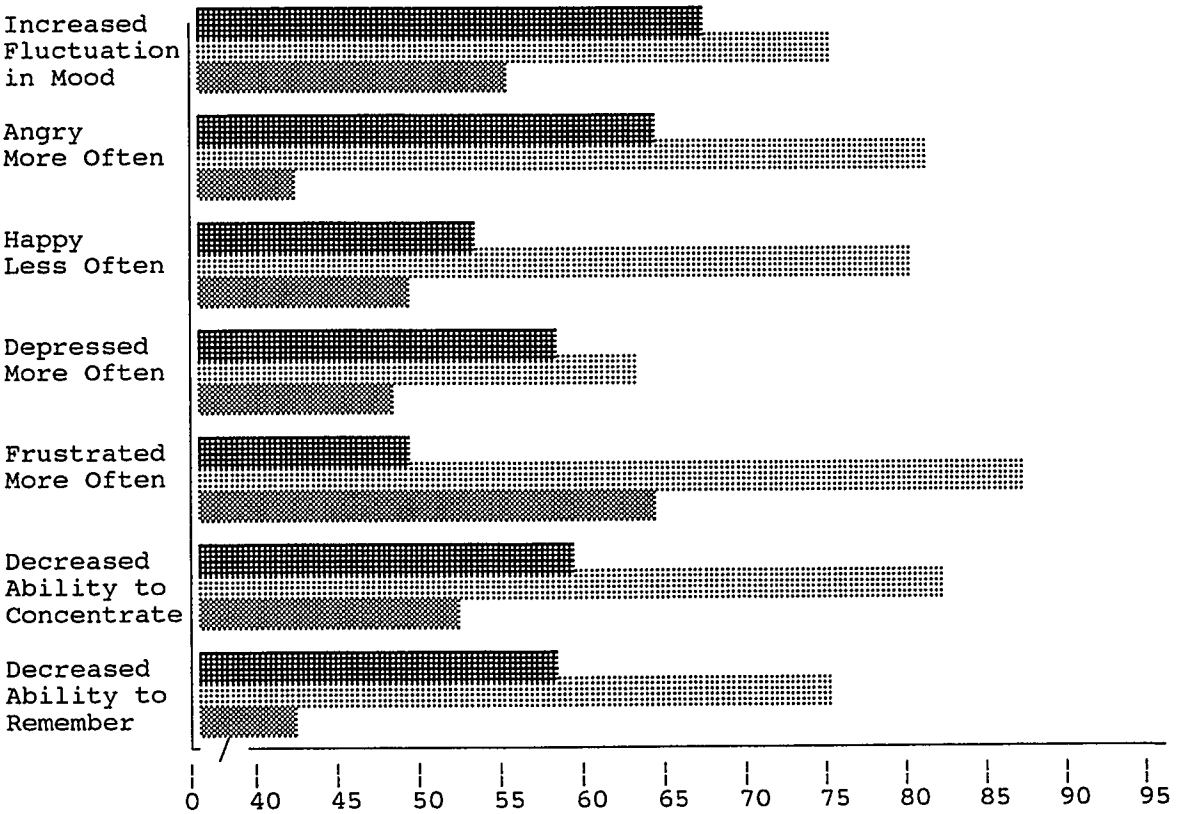
highest proportion of RA subjects reported that these levels were about the same. A smaller proportion reported that they were angry less frequently or more frequently (26.1 % respectively), and less and more frustrated (21.7% and 34.8% respectively). In respect to level of depression, a highest proportion of RA subjects reported that they were less depressed than on most days (43.5%).

Overall, the ratings suggest that the majority of individuals within a diagnostic group rated their mood and cognitive functioning as being "about the same as on most days", suggesting that performance on attention measures may be considered representative of an individuals usual state and not a "good" or "bad" day.

Figure 2 depicts the percentage of subjects, by group reporting fluctuations in their mood and cognitive functioning during periods of disease activity compared to periods of inactivity. Compared to periods of disease inactivity, during periods of disease activity or symptom flare-up, 71.4% of the SLE subjects reported an increase frequency in fluctuations in their mood, 71.4% reported being angry more often, 65.7% reported being happy less frequently, 60% reported feeling depressed more often, 65.7% reported feeling frustrated more often, 68.6% reported that their ability to concentrate was not as good, and 65.7% reported that their ability to remember was not as good. Non-neuropsychiatric SLE subjects were more inclined than neuropsychiatric SLE subjects to report that their ability to concentrate (85.3% compared to 57%) and remember (75% compared to 57%) were not as good during periods of disease activity.

Figure 2

Percentage of Subjects, by Group, Rating Mood and Cognition During Periods of Disease Activity Compared to Inactivity



* Percentages represented in figure are estimates

In comparison to SLE subjects, during periods of disease activity or symptom flare-up, 56.5% of the RA subjects reported an increased frequency in fluctuations in their mood, 43.7% reported being angry more often, 47.8% reported being happy less frequently, 47.8% reported feeling depressed more often, 65.2% reported feeling frustrated more often, 52.2% reported that their ability to concentrate was not as good, and 43.5% reported that their ability to remember was not as good (see Figure 2).

Assessment Measures

The means and standard deviations of assessment measures for all subjects, by group, are documented in Table 6.

Table 6

Means and Standard Deviations Obtained on Assessment Measures by Group

Measure	NP SLE Mean SD (Range)*	NON-NP SLE Mean SD (Range)	RA Mean SD (Range)	Healthy C. Mean SD (Range)
Depression Level (CES-D)	20.11 8.7	16.13 11.21	12.61 10.51	8.00 6.71
ACT: Total	17.05 2.44	18.19 2.01	17.78 1.57	19.07 1.76
Highest Level	6.84 1.54 (3-8)	7.31 .87 (5-8)	7.48 .67 (6-8)	7.67 .57 (6-8)
Levels Missed	1.37 1.50	.94 .34	.78 .60	.48 .59
GDS Vigilance: Total	27.74 6.67 (1-30)	29.75 .58 (28-30)	29.57 1.04 (26-30)	29.57 1.09 (25-30)
Commissions	1.84 3.50	.13 .34	.35 .93	.38 .66
Latency	47.84 11.83	45.81 9.42	45.53 7.94	45.60 9.89
GDS Distraction: Total	23.32 7.12 (4-30)	26.31 3.24 (19-30)	25.62 4.73 (14-30)	27.81 2.33 (21-30)
Commissions	3.37 5.81	.94 1.29	1.91 3.72	1.10 1.39
Latency	47.42 9.56	47.19 9.62	48.30 8.25	45.17 11.02

* Numbers in brackets indicate the range of scores.
Commissions = the number of commission errors made.
Latency is in milliseconds.

An inspection of the means and standard deviations of error in Table 6 reveals a trend for an increasing level of depression across the four groups, with the healthy controls appearing least depressed and the neuropsychiatric SLE subjects appearing most depressed. Level of depression was used as a covariate in the quantitative analysis used to test the research hypotheses. The means and standard deviations of error on the GDS vigilance task (a baseline

measure) suggest, as expected, that the four groups do not appear to differ. The one possible exception is the performance by the neuropsychiatric SLE group, whose total appears to be slightly less than the other three groups, and who made slightly more commission errors, and took slightly longer to respond.

The means and standard deviations of errors produced on the ACT and GDS distractibility task (the dependent measures) by neuropsychiatric SLE subjects and healthy control subjects suggest, as expected, that the neuropsychiatric SLE group is more impaired. The means and standard deviations produced by the non-neuropsychiatric SLE group and the RA subjects on the ACT and the GDS distraction task were unexpected; they do not appear to differ. The significance of the above findings and possible explanations are tested in the quantitative analysis reported below.

Hypotheses Testing

Hypothesis 1

Hypothesis 1 predicated that the SLE subjects would be significantly more impaired on tests for auditory attentional capacity than the RA and healthy control subjects. A MANCOVA by group, with depression covaried, was computed on the three dependent measures for auditory attentional capacity (i.e. ACT Total, ACT Highest Level Achieved, and ACT Number of Levels Missed).

The effect of depression across the three groups on the three dependent measures was not significant. A significant interaction was evident on the MANCOVA between the three groups and the auditory attention performance

measures (F (6,188) = 2.88, p <.01). Univariate analyses indicated all measures of auditory attentional capacity to have significant effects (see Table 7). Scheffé tests were conducted on each of these significant univariate analyses to identify all significant comparisons between pairs of mean scores between diagnostic groups.

Compared to the combined means of the two control groups, the SLE subjects scored significantly lower on the ACT Total score (F (2,97) = 3.28, p<.05), the ACT Highest Level Achieved (F (2,97) = 4.06, p<.05), and scored significantly higher on the ACT Number of Levels Missed (F (2,97) = 5.01, P<.01). Therefore, the results of the Scheffé tests support the hypothesis that overall, the SLE subjects are significantly more impaired on auditory attention measures than the combined group of control subjects. However, when the control groups were looked at separately, the results were not as supportive.

Compared to healthy control subjects, SLE subjects scored significantly lower on the ACT Total score (F (2,97) = 5.63, p<.01), the ACT Highest Level Achieved (F (2,97) = 4.27, p<.05), and scored significantly higher on the ACT Number of Levels Missed (F (2,97) = 6, p<.01). There were no significant differences between the RA control group and the SLE group on the three auditory measures. An unexpected finding was that the RA control subjects scored significantly lower than healthy control subjects on the ACT Total score (F (2,97) = 3.32, p<.05); Their scores on the ACT Highest Level Achieved, and the ACT Number of Levels Missed were not significantly different.

Table 7

Results of Univariate Analyses for MANCOVAs Demonstrating Significance

Dependent Measure	Covariate	# of Groups	DF	F Value	P
ACT Total ACT Highest Level ACT Levels Missed	CES-D	3	(2,96)	5.87 3.81 6.08	P <.01 P <.05 P <.01
ACT Total ACT Highest Level ACT Levels Missed	CES-D	4	(3,95)	5.09 3.41 4.96	p <.01 p <.05 p <.01
Distractibility Total	Education	4	(3,95)	5.23	p <.01

Three groups refers to SLE, RA, and healthy control subjects.
Four groups refers to neuropsychiatric SLE, non-neuropsychiatric SLE, RA, and healthy control subjects.

Because age and eduction were found to significantly differ across groups, with the RA subjects being older and having less education than the SLE and healthy control subjects, two separate MANCOVAs with age, and than education were computed in secondary analyses. Neither age, nor education had a significant effect across the three groups on the three dependent measures for auditory attentional capacity.

Hypothesis 2

Hypothesis 2 predicated that the SLE subjects would be significantly more impaired on the tests for visual attentional processing than the RA and healthy control subjects. A MANCOVA by group, with depression covaried, was computed on the three dependent measures for visual attention (i.e. GDS Distractibility Total score, number of commission errors, and mean latency).

The effect of depression across the three groups on the three dependent measures was not significant. The

interaction between the three groups and the visual attention measures observed on MANCOVA was not significant.

Because age and eduction were found to significantly differ across groups, in secondary analyses, two separate MANCOVAs with age, and then education were computed in secondary analyses.

The effect of age across the three groups on the three dependent visual measures was significant ($F(3,94) = 3.29$, $p<.05$). Univariate analyses revealed a significant effect of age on the Total score ($F(1,96) = 9.67$, $p<.01$), and on the number of commission errors ($F(1,96) = 6.91$, $p<.01$). However, the results of the MANCOVA indicated that the interaction between the three groups on the visual attention measures was not significant[16]. The effect of education across the three groups on the three dependent measures was not significant[17].

Hypotheses 3 and 4

Hypotheses 3 and 4 predicated that (a) SLE subjects with previously diagnosed neuropsychiatric involvement would be significantly more impaired on attention tasks than SLE subjects without a previous diagnosis of neuropsychiatric involvement; and (b) SLE subjects without a previous diagnosis of neuropsychiatric involvement would be more impaired on attention tasks than medical or healthy

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[16] ($F(6, 188) = 1.96$, $p<.10$). Univariate analyses revealed a significant difference between groups on the Total score ($F(2,96) = 5.02$, $p<.01$).

[17] The effect of education across the groups on the visual attention measures was significant at $p<.10$. The interaction between the groups and the dependant measures was significant at the $p<.10$.

control subjects. Two MANCOVAs were computed to determine (a) significant differences in measures of auditory attention performance across the four groups (i.e. neuropsychiatric SLE, non-neuropsychiatric SLE, RA, and Healthy control subjects); and (b) significant differences in measures of visual attention performance across the four groups. Level of depression was used as the covariate in both sets of analyses. The results on the auditory measures will be presented first, followed by the results on the visual measures.

Auditory attentional capacity. The effects of depression across the three groups on the dependent measures for auditory attention were not significant. A significant interaction was evident on MANCOVA between the four groups and the auditory attention measures ($F(9,266) = 2.33$, $p<.05$). Univariate analyses indicated all measures of auditory attention capacity to have significant effects (see Table 7).

To test Hypothesis 3, Scheffé tests were computed on each of the dependent variables to identify all significant comparisons between pairs of mean scores between the neuropsychiatric and non-neuropsychiatric SLE subjects. The results failed to reveal any significant differences between the two groups. Therefore, Hypothesis 3 was not supported for the auditory measures.

To test Hypothesis 4, Scheffé tests were computed on each of the dependent auditory measures to identify all significant comparisons between pairs of mean scores between the non-neuropsychiatric SLE subjects and the combined group of control subjects. The results failed to

reach significance. Scheffé tests were then computed between the non-neuropsychiatric SLE group and each of the control groups. The results failed to reach significance. Therefore, Hypothesis 4 was not supported for the auditory measures.

The observed significance on univariate analyses was explained by significant differences between the neuropsychiatric SLE sample and the healthy controls on the ACT Total score ($F(3,96) = 4.87$, $p<.01$), the ACT Highest Level Achieved ($F(3,96) = 3.68$, $p<.05$), and the ACT Number of Levels Missed ($F(3,9) = 5.03$, $P<.01$), with the SLE sample being more impaired.

The difference in mean scores on the three dependent measures between the neuropsychiatric SLE sample and the RA control group were not significant. It is noteworthy that no significant differences were found between the scores of RA control subjects and healthy control subjects on the auditory attention measures. This result is inconsistent with the significant difference demonstrated on the ACT Total score between these two groups on the analyses across three groups (see Hypothesis 1). The inconsistency in significance likely represents a Type 1 error in the analyses across three groups in which all SLE subjects were considered as one group. Statistical power was increased by considering neuropsychiatric SLE subjects, and non-neuropsychiatric SLE subjects as separate groups and thereby reducing unexplained variance. The result of the more powerful analyses was that RA subjects and healthy control subjects did not differ significantly on the ACT Total score.

Because age and eduction were found to significantly differ across groups, with the RA subjects being significantly older and having less education than the SLE and healthy control subjects, two separate MANCOVAs with age, and then education were computed in secondary analyses. There was no significant effect of age or education across the four groups on each of the three dependent auditory attention measures.

Visual attentional processing. The effects of depression across the three groups on the dependent measures for visual attention were not significant. The interaction on MANCOVA between the four groups and the visual measures was not significant. Therefore, Hypothesis 3 and 4 were not supported by performance on the dependent measures for visual attention.

Because age and eduction were found to significantly differ across groups, two separate MANCOVAs with age, and then education were computed in secondary analyses. The effect of age across the four groups on the visual measures was not significant[18]. The effect of education across the four groups on the visual measures was not significant. However, the interaction observed on MANCOVA with education covaried (9, 226) = 1.92, $p<.05$), was barely significant. Given the number of independent MANCOVAs computed on the same dependent measures it is possible that this significant finding occurred due to chance alone.

Subsequent univariate analyses indicated one measure, Distractibility Total, to have significant effects (see

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[18] (F (3, 93) = 2.65, $p<.10$).

Table 7). Scheffé tests were computed on the Distractibility Total score measure to identify all significant comparisons between pairs of mean scores among the four groups and to test Hypotheses 3 and 4. The only significant finding was a significant difference between the neuropsychiatric SLE subjects and the healthy control subjects ($F(3, 96) = 4.84$, $p<.01$); the neuropsychiatric group receiving a significantly lower score.

Hypotheses 5 and 6

Hypotheses 5, and 6 predicted that (a) SLE subjects without a previous diagnosis of neuropsychiatric involvement who subsequently received a diagnosis of neuropsychiatric involvement would be more impaired on attention tasks after the onset of neuropsychiatric involvement; and (b) performance on attention tasks by patients with SLE with either active or inactive neuropsychiatric involvement at the time of the initial assessment would be unchanged subsequent to a change in their neuropsychiatric activity status.

No subjects met the above conditions, therefore, these hypotheses could not tested.

Possible Confounding Clinical Variables

Disease Activity

A Hotellings T^2 was computed to determine whether three measures of disease activity (i.e. the SLAM-R, the SLEDAI, and the modified SLEDAI) differed significantly between the neuropsychiatric and non-neuropsychiatric SLE subjects. No significant interactions were found. Pearson Product-Moment correlations were then computed to examine whether significant relationships existed between each of

the three measures of disease activity and any dependent measures demonstrating significance in the primary analyses (see Table 8).

An inspection of Table 8 shows a significant linear association between one of the disease activity rating scales and performance on two of the auditory attention measures: ACT Highest Level Achieved ($r = -.6150$, $p<.001$), indicating that as the SLAM-R rating increased, level reached on the ACT decreased; and ACT Number of Levels Missed ($r = .5664$, $p<.05$), indicating that as the SLAM-R rating increased, the number of levels missed on the ACT also increased. The association between the SLAM-R rating and the Total score on the ACT was not significant.

Table 8

Correlational Analyses Between Disease Measures and Dependent Variables

Measure	N=	ACT Total	ACT HLA	ACT MISS	GDS Total
Duration	58	.0136	.0500	-.0211	.0163
Activity					
ANA titre	35	-.0173	-.2467	.1886	.2570*
Creatinine	30	-.0119	.0515	-.0696	-.1020
Severity	17	-.3056	-.1580	.2448	-.1280
SLAM-R	35	-.2734*	-.6150***	.5664***	.0529
SLEDAI	35	.1592	-.0007	.0572	.0865
SLEDAI-M	35	-.0010	-.1222	-.0488	.0990
Medication					
Prednisone	22	.1649	-.0101	-.0445	-.0700
Plaquenil	10	-.5177*	-.6215**	.6872**	-.3015

HLA = Highest Level Achieved; MISS = Number of Levels Missed; GDS Total = Total score on the Distractibility subtest; Duration = Disease Duration; ANA = antinuclear antibody.
* = p <.10 1-tailed significance
** = p <.05 1-tailed significance
*** = p <.001 1-tailed significance

Disease Severity

A t-test was computed to determine whether disease

severity differed significantly between the neuropsychiatric and non-neuropsychiatric SLE samples. It was not significant. Pearson Product-Moment correlations were then computed to examine whether a significant relationship existed between the disease severity and any dependent measures demonstrating significance in the primary analyses (see Table 8). An inspection of Table 8 does not reveal a significant correlation between disease severity and attention measures.

Medications

Pearson Product-Moment correlations were performed to examine whether specific medications were significantly related to dependent measures demonstrating significance in primary analyses (see Table 8). Given that the use of Prednisone was controlled for in the internal design of the study, a significant linear association was not expected between this medication and attention performance. An inspection of Table 8 does show a significant linear association between Plaquenil dose and performance on two of the auditory attention measures: ACT Highest Level Achieved ($r = -.6215$, $p<.05$), indicating that higher doses of plaquenil were related to decreased scores on the highest ACT Level achieved; and increased scores on ACT Number of Levels Missed ($r = .6872$, $p<.05$). The relationship between Plaquenil dose and total score on the ACT was not significant.

Nine RA subjects were taking Methotrexate, a medication which was not currently being used by any of the SLE subjects. In order to examine the effects of Methotrexate on attention capacity performance, the performance of RA subjects taking Methotrexate were

compared to RA subjects not taking Methotrexate in two multivariate analyses. A Hotelling's T^2 computed across the auditory dependent variables was not significant. A Hotelling's T^2 with age covaried, computed across the visual dependent variables was not significant. Therefore, it does not seem likely methotrexate affected test performance.

Neuropsychiatric Classification

Depression requiring medical intervention was a manifestation used to classify subjects as having neuropsychiatric SLE. Because depression may have been due to reasons other the CNS involvement and because depression did not have an effect on attentional capacity, it was assumed that including depressed subjects in the neuropsychiatric SLE group may have contributed to the lack of significant findings documented in this study. Therefore, a modified neuropsychiatric SLE sample was studied in exploratory analyses. SLE subjects whose only neuropsychiatric manifestation was depression requiring medical intervention (n=5) were excluded from the neuropsychiatric group and included in the non-neuropsychiatric group. Hypotheses 3 and 4 were re-tested using the modified SLE groups. Two MANCOVAs, with age and education covaried, were computed. The results of the MANCOVA testing the interaction between the four groups (i.e. modified neuropsychiatric SLE, modified non-neuropsychiatric SLE, RA, and healthy control subjects) and the auditory measures will be presented first, followed by the results for the visual measures.

Auditory attentional capacity. As expected, the effects of age and education across groups on the three

auditory measures was not significant.

The results of MANCOVA were significant ($F(9, 224) = 2.50$), $p < .01$). Univariate analyses indicated all measures of auditory attention capacity to have significant effects (see Table 9).

To re-test Hypothesis 3, Scheffé tests were computed between the neuropsychiatric SLE sample and the non-neuropsychiatric SLE sample on all three auditory measures. The results were not significant. Therefore, Hypothesis 3 was not supported for the auditory attention measures.

To re-test Hypothesis 4, Scheffé tests were computed between the non-neuropsychiatric SLE sample and the combined group of control subjects on all three auditory measures. The results were not significant. When the control groups were considered individually, the results were also not significant. Therefore, Hypothesis 4 was not supported for the auditory attention measures.

Table 9

Results of Univariate Analyses for MANCOVAs Demonstrating Significance in Exploratory Analyses*

Dependent Measure	Covariates	DF	F Value	P
ACT Total	Age & Education	(3,94)	5.10	$p < .01$
ACT Highest Level			5.67	$p < .001$
ACT Levels Missed			5.99	$p < .001$
Distractibility: Total	Age & Education	(3,94)	5.68	$p < .001$
Commission Errors			3.78	$p < .05$
Mean Latency**			.61	NS

* Exploratory analyses were computed across four groups: a modified neuropsychiatric SLE sample; a modified non-neuropsychiatric SLE sample; RA control subjects; and healthy control subjects.

** Mean Latency is in milliseconds.

Scheffé tests revealed that the significance observed on the univariate analyses could be explained by significant differences between the neuropsychiatric SLE subjects and the healthy control subjects on the ACT Total score ($F(3,96) = 10.36$, $p<.001$), and the ACT Number of Levels Missed ($F(3, 96) = 5.67$), $p<.01$), with the neuropsychiatric SLE subjects being more impaired. No other significant difference between pairs of mean scores and the four groups were observed.

Visual Attentional Processing

The effect of age and education across groups on the three visual measures was significant ($F(6, 184) = 2.40$, $p<.05$). Univariate analyses revealed that the effect was significant on the Distractibility Total score ($F(2,94) = 4.86$, $p <.01$), and on the Mean Latency ($F(2,94) = 3.86$), $p<.05$).

The results of MANCOVA were significant ($F(9, 224) = 2.50$), $p <.01$). Univariate analyses indicated two measures of visual attention to have significant effects (see Table 9).

To re-test Hypothesis 3, Scheffé tests were computed between the neuropsychiatric SLE sample and the non-neuropsychiatric SLE sample on the two visual measures demonstrating significance in univariate analyses. The difference between the two groups on the Distractibility total score was not significant, however the difference between the mean scores on the number of commission errors made was significant ($F(3, 96) = 3.53$, $p<.05$). Therefore, Hypothesis 3 was partially supported for the visual measures with the modified neuropsychiatric SLE sample making significantly more commission errors than the non-

neuropsychiatric SLE subjects.

To re-test Hypothesis 4, Scheffé tests were computed between the non-neuropsychiatric SLE sample and the combined group of control subjects. The results were not significant. When the control groups were considered individually, the results were also not significant. Therefore, Hypothesis 4 was not supported for the visual measures.

Scheffé tests revealed that the significance observed on the univariate tests were partially explained by significant differences between the neuropsychiatric SLE subjects and the healthy control subjects on the Distractibility Total score ($F(3,96) = 6.04$, $p<.001$), and on the number of commission errors made ($F(3,96) = 3.86$, $p<.05$), with the neuropsychiatric SLE subjects being more impaired. No other significant differences between pairs of mean scores and the four groups were observed.

Because significance was demonstrated on the Distractibility measures for the GDS, a MANCOVA, with age and education covaried, was computed on the Vigilance measures. The effect of age and education across the four groups on the three Vigilance measures was not significant. The interaction observed on MANCOVA was not significant.

Summary of Results

Data was collected on 35 SLE subjects, 23 RA subjects, and 42 healthy subjects. Age and education were found to differ significantly between groups, with RA subjects being significantly older and having less education. In primary analyses, level of depression was covaried and was found to have no effect on the six dependent measures examined in this study. Age was covaried in secondary analyses and

found to have no significant effect on the auditory measures, but to have a significant effect across groups on the visual measures. Educational level was also covaried in secondary analyses and found to have no effect on the dependent measures.

Four MANCOVAs were computed in the primary analyses to test the research hypotheses: two were computed on the auditory measures, and two were computed on the visual measures. For Hypotheses 1 and 2, analyses were computed across the three main groups of subjects. For Hypothesis 3 and 4, analyses were computed across four groups of subjects (i.e. neuropsychiatric SLE, non-neuropsychiatric SLE, RA, and healthy control subjects). Significant interactions were revealed for MANCOVAs examining auditory measures. Univariate analyses were computed for any MANCOVAs demonstrating significant interactions. Scheffé tests were then computed on any dependent measures demonstrating significance.

Hypothesis 1 predicted that SLE subjects would perform significantly worse on auditory attentional capacity measures than control subjects. Results of the Scheffé tests partially supported the research hypothesis. SLE subjects (composite of neuropsychiatric SLE and non-neuropsychiatric SLE subjects) were found to significantly differ from the control subjects (composite of RA and Healthy control subjects) on all three auditory attentional capacity measures. However, when the control groups were considered individually, significant differences were found only between the SLE subjects and the healthy control subjects. Moreover, the RA subjects differed significantly from the healthy controls on one auditory measure (ACT

Total) based on the MANCOVA between three main groups. When a MANCOVA was computed between four groups (i.e. the neuropsychiatric SLE, non-neuropsychiatric SLE, RA, and healthy control groups) the difference between the RA subjects and the healthy controls was not significant. It was argued that the former result likely represents a Type 1 error.

Hypothesis 2 predicted that SLE subjects would perform significantly worse on visual attentional processing measures than control subjects. The interaction between groups on the three dependent measures was not significant. Therefore, Hypothesis 2 was not supported.

Hypothesis 3 predicted that neuropsychiatric SLE subjects would perform significantly worse on attention measures than non-neuropsychiatric SLE patients. This hypothesis was not supported for either the auditory attention measures or the visual measures.

Hypothesis 4 predicted that non-neuropsychiatric SLE subjects would perform significantly worse on attention measures than control subjects. This hypothesis was not supported for the auditory measures or the visual measures.

The significance observed on the MANCOVA for auditory measures across the four groups was between the neuropsychiatric SLE subjects and healthy control subjects, with the neuropsychiatric SLE subjects being more impaired.

A re-classification of the neuropsychiatric SLE groups (i.e. excluding those subjects whose only manifestation was depression) resulted in a significant MANCOVA on visual measures, with the neuropsychiatric SLE subjects scoring significantly lower on the distractibility total score, and making significantly more commission errors than the

healthy control group.

Hypotheses 5 and 6 could not be tested due to a lack of change in any SLE subject's neuropsychiatric status during the course of this research.

Potentially confounding influences of depression, medications, and disease activity, severity, and duration, were examined.

CHAPTER FIVE

DISCUSSION

Based on the subjective complaints of patients with Systemic Lupus Erythematosus (SLE) and on the findings of previous research, it was postulated that Central Nervous System (CNS) involvement in SLE disproportionaly reduces attentional capacity. Therefore, it was hypothesized that patients with SLE who have histories of neuropsychiatric manifestations would be impaired on tasks measuring attentional capacity. Since subtle subclinical CNS involvement has been documented in patients with SLE who have never experienced overt CNS manifestations, it was further hypothesesed that these patients would show impairments in attentional capacity but not to the extent of those with documented neuropsychiatric involvement.

This study used two clinical measures, the Attentional Capacity Test (ACT; Weber, 1986) and the Gordon Diagnostic System (GDS; Gordon, 1991), to examine attentional capacity and the effects of effort on a limited capacity system. Performance on these dependent measures, along with data collected from medical charts, and screening instruments were examined through qualitative and quantitative analysis. The results are discussed below in relation to attentional capacity, potentially confounding variables, and CNS involvement. The chapter concludes with a description of the limitations, and the importance and implications of the study.

Attentional Capacity

In this study, attentional capacity was conceptualized as a limited mental resource which can be allocated across tasks. Attentional capacity was considered along a

continuum from automatic processing to effortful processing. Essentially, as the number of stimuli to be attended to increases, or as the extent of familiarity of the stimuli to be attended to decreases, the sense of effort experienced by the individual increases (Weber, 1990).

As expected, a ceiling effect was observed for all diagnostic groups[19] on the Vigilance subtest of the GDS, a continuous performance measure which requires the individual to sustain attention while simply responding to recognition of target stimuli in a sequence of stimuli. Furthermore, the performance of SLE subjects on the early levels of the ACT in which the demands on attentional capacity are low was intact. All subjects were able to repeat a single number, count the number of "ee" sounds in a sequence of "ee" sounds, and count the number of "8s" in a sequence of "8s" (i.e. levels 1, 2, and 3). Therefore, the results of this study appear to support an a priori assumption that automatic processes or tasks which place few demands on the individual's limited capacity are intact in patients with SLE[20]. As the demands on attentional capacity increased, the performance of SLE subjects in general, and those with neuropsychiatric manifestations in particular, demonstrated impairment.

On the ACT, the demands on attentional capacity are

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[19] For a minority of subjects in the neuropsychiatric SLE group, performance appeared to be quite impaired.

[20] It is possible that the tasks which were considered to tap automatic attentional processes were effortful for some individuals.

increased by increasing the content demands over eight levels (Weber, 1986). Compared to the composite of control subjects, SLE subjects were significantly impaired on the ACT Total Score, ACT Highest Level Achieved, and the Number of ACT Levels Missed. These results provide preliminary support for the conjecture that patients with SLE show significant impairments on tasks demanding high degrees of effort. When the SLE subjects were subdivided into those with neuropsychiatric and those with non-neuropsychiatric SLE, only those individuals with neuropsychiatric involvement were significantly impaired compared to the composite of control subjects. These findings suggest neuropsychiatric manifestations disproportionaly reduce attentional capacity. The implication is that impaired performance is associated with CNS involvement in SLE. The results on the Distractibility subtest of the GDS, while not as conclusive, also provide some support for these inferences.

Although the composite of SLE subjects was not significantly impaired on the Distractibility subtest of the GDS compared to the composite of control subjects, SLE subjects with neuropsychiatric manifestations (excluding those whose only manifestation was depression requiring medical intervention) were significantly more impaired compared to healthy control subjects. The neuropsychiatric SLE subjects made significantly more commission errors and received a significantly lower total score. This exploratory finding suggests that the deficits in attentional capacity associated with neuropsychiatric SLE are not task specific.

The lack of further significant findings on the

Distractibility task is likely due to a trend towards a ceiling effect (a perfect score was achieved by some subjects within each of the diagnostic groups). It is possible that the task did not sufficiently tap effortful processing. With an increase in the length of the task (Borcherding et al., 1988; Weber, 1990), the event rate (Earle-Boyer et al., 1991; Weber, 1990), or the length or complexity of the target sequence, or with the addition of distraction stimuli (Earle-Boyer et al., 1991) attentional capacity becomes increasingly important in performance. The Vigilance subtest of the GDS and the Distractibility subtest of the GDS differ only in respect to distraction stimuli; the length of the task, the length of the target sequence, and the event rate remain constant. Most subjects from all diagnostic groups commented that the Distractibility task was difficult, and appeared to focus more while completing that task then when completing the baseline tasks. These observations suggest that the increased demands of the Distractibility task over the Vigilance task did increase the demands on attentional capacity to some extent; however, the results indicate that the range assessed was restricted. As a result, the GDS may not have been sufficiently sensitive for assessing impairments in attentional capacity in the present study.

Potentially Confounding Variables

An attempt to control for potentially confounding variables was made through the internal design of the study and through statistical techniques. A chronic illness and a healthy control group were considered vital for determining the factors which contribute to performance on attentional capacity measures and for understanding whether

impairments could be attributed to SLE. The finding that the Rheumatoid Arthritis (RA) control group (a chronic illness which is thought to spares the CNS) did not differ significantly from the neuropsychiatric SLE group suggests that the influences on attentional capacity performance may not be limited to SLE. Major research studies (Carbotte et al. 1986; Hanly et al. 1992) investigating cognitive functioning in patients with SLE have documented the prevalence of cognitive deficits in SLE subjects compared to RA subjects but have not compared the test performance of these groups. Carbotte et al. (1986) documented a significant difference in prevalence rates of cognitive impairment between neuropsychiatric SLE patients and RA patients but not between non-neuropsychiatric SLE patients and RA patients. Smaller scale studies (e.g. Kutner et al., 1988; Wekking et al., 1991), however, have reported the lack of significant differences between SLE subjects and chronic illness control subjects on cognitive tasks. Possible explanations for the lack of difference between these groups include the influence of medications, disease activity, disease duration, mood and motivation, and co-morbid illnesses. These variables are discussed, in turn, below.

Medications

Use of Prednisone was controlled for in the internal design of the study. Therefore, it was not believed to have had an influence on test performance of either the SLE subjects or the RA subjects. The lack of significant results of the correlational analyses between last Prednisone dose and measures of attentional capacity provide support for this belief. While Plaquenil dose was

significantly negatively correlated to performance on the ACT, the finding is not sufficient to explain the lack of significant differences between the RA and neuropsychiatric SLE groups; only one individual with RA was taking Plaquenil at the time of the assessment. In contrast, nine RA subjects were on Methotrexate, a medication which was not currently being used by any of the SLE subjects. In order to see whether Methotrexate compromised performance on measures of attentional capacity, the performance of RA subjects taking Methotrexate was compared to RA subjects not taking Methotrexate. The results were not significant. The effect of NSAIDS was not examined and may have had influence of attention performance.

It was assumed that medication use did not account for the lack of significant differences in attentional capacity between the neuropsychiatric SLE and RA groups.

Disease Duration, Activity, and Severity

There were no significant differences between the disease duration of neuropsychiatric SLE subjects and RA subjects. Moreover, disease duration was not significantly correlated with measures of attentional capacity. Therefore, it is unlikely that disease duration could account for the lack of significant differences between the two groups on the attention measures.

Cognitive deficits in chronic illnesses may be secondary to complications of the disease. Biological factors such as hormonal, nutritional, electrolyte, or endocrine abnormalities have been implicated (Hall & Beresford, 1985). A diagnosis of neuropsychiatric SLE was made only if other causes for metabolic changes associated with disease activity could not be detected.

Unfortunately, data was not collected on the current disease activity and severity of RA subjects due to recruitment difficulties. One measure of disease activity (SLAM-R) used with SLE subjects was found to be significantly correlated with measures of auditory attentional capacity. It is possible that a similar association existed for RA subjects. Responses by RA subjects to the questionnaire on mood and cognitive functioning indicated that a high percentage of individuals reported that their ability to concentrate and remember was not as good during periods of disease activity. Although previous research (Ginsburg et al., 1992) did not find a significant correlation between disease activity and cognitive test performance of either SLE or RA subjects, it is possible that the extent of disease activity (e.g. mild, moderate, or severe) may be an explanation as to why RA and neuropsychiatric SLE subjects did not significantly differ on test performance. Moreover, previous research has found that in chronic illnesses, disease activity and severity (Newman et al., 1990; Smith et al., 1991), functional ability (Smith et al., 1991), and illness intrusiveness (Devins, 1989) intervene between disease and adjustment. Poor adjustment, or depression, in turn, may have had a significant impact upon attentional capacity.

Mood and Motivation

Although level of depression appeared to differ between groups, it was not found to have a significant effect on attentional capacity performance. This finding is consistent with previous studies (Carbotte et al., 1986; Denburg, S. et al., 1987; Ginsburg et al., 1992) which also failed to document an association between emotional

distress and cognitive impairment. It appears that cognitive impairment in patients with SLE is independent of emotional distress.

Motivation may be a key to the amount of effort that an individual used in performing the task and in persisting on difficult items. Some difficulty was experienced in recruiting RA subjects possibly because the focus of the study was on understanding attentional capacity in patients with SLE. It is conceivable that the RA subjects who did volunteer were not as motivated as SLE subjects to do the best they could on the attention tasks, particulary as the task difficulty increased.

Co-Morbid Illnesses

The association between the incidence of co-morbid illnesses and performance on the measures of attentional capacity is not known and remains a confounding variable. It is important to note, however, that: 1) SLE subjects experienced more co-morbid illnesses than RA Subjects; 2) all but one illness (i.e. obstructive pulmonary disease) experienced by RA subjects were also experienced by SLE subjects; and 3) the percentage of subjects experiencing any one co-morbid illness was low. Accordingly, it is unlikely that the presence of co-morbid illnesses could account for the lack of significant differences on measures of attentional capacity between SLE and RA subjects.

Summary

The lack of significant differences on the measures of attentional capacity between the RA subjects and neuropsychiatric SLE subjects indicates that the CNS involvement may not be the only influence on attentional capacity ability. The extent to which disease activity,

motivation, or their interaction, affected the attentional capacity performance of RA subjects is difficult to ascertain.

Central Nervous System (CNS) Involvement

In order to examine the involvement of the CNS, SLE subjects were divided into two groups based on a history of neuropsychiatric manifestations (i.e. neuropsychiatric SLE and non-neuropsychiatric SLE subjects). Because previous research (Carbotte et al., 1986; Denburg, S. et al., 1987; Hanly et al., 1992) failed to reveal significant differences between patients with *active* neuropsychiatric involvement and those with *inactive* neuropsychiatric involvement, these individuals were combined to form one group; the neuropsychiatric SLE group. In order to examine whether the results of the above studies could be generalized to individuals, the present study proposed to re-assess patients with either active or inactive neuropsychiatric involvement subsequent to a change in their neuropsychiatric activity status. Unfortunately, a change in neuropsychiatric status was not reported in any of the SLE subjects, therefore, no re-assessments took place.

Previous studies (e.g. Carbotte et al., 1986; Denburg, S. et al., 1987; Hanly et al., 1992) have documented cognitive deficits in SLE subjects in the absence of documented neuropsychiatric involvement and have interpreted this finding as providing evidence for the presence of subtle or subclinical CNS involvement in some of these patients. The present study failed to reveal any significant differences between the attentional capacity performance of neuropsychiatric SLE subjects and the non-

neuropsychiatric SLE subjects. Similar results have been reported by Denburg S. et al. (1987), Hanly et al. (1992), and Fisk et al. (1993). Denburg S. et al. (1987) found that patients with neuropsychiatric SLE were significantly impaired on visuomotor scanning compared to healthy control subjects but not compared to non-neuropsychiatric SLE subjects. In the study by Hanly et al. (1992), the prevalence of cognitive impairment did not differ between neuropsychiatric SLE subjects and non-neuropsychiatric SLE subjects. In a follow up study, Fisk et al. (1993) failed to document significant differences between the two groups on the majority of memory tests administered. Denburg S. et al. (1987) and Fisk et al. (1993) suggested that the lack of differences between the neuropsychiatric SLE and non-neuropsychiatric SLE groups may be due to the presence of subtle subclinical CNS disease in the non-neuropsychiatric group. This explanation may also account for the lack of significant differences documented in the present study.

Another explanation for the lack of significant differences between the neuropsychiatric and non-neuropsychiatric SLE subjects is that a relationship may exist between disease activity and attentional capacity performance. A large proportion of SLE subjects reported that their ability to concentrate (68.6%) and remember (65.7%) was not as good during periods of disease activity. Non-neuropsychiatric SLE subjects were more inclined than neuropsychiatric SLE subjects to report that their ability to concentrate (85.3% compared to 57%) and remember (75% compared to 57%) were not as good during periods of disease activity. Despite the apparent association between

subjective changes in cognitive functioning and increased disease activity, the relationship between ratings on disease activity and attentional capacity performance, objectively assessed, were not conclusive.

In the present study, the correlations between the SLEDAI, and the SLEDAI-M (two measures of disease activity) and measures of attention were not significant. However, significant correlations were documented between disease activity, as measured by the SLAM-R, and auditory attentional capacity measures. Given the time allowance between medical appointments and attention assessments, it is possible that the SLAM-R score was a more accurate representation of disease activity. In contrast to the SLAM-R which rates symptoms over the *month* prior to it's administration, the SLEDAI and SLEDAI-M are based on the presentation of symptoms *10 days* prior to it's administration. Furthermore, in most cases, the SLAM-R was completed at the time of the medical and within 2 months of the attention assessment, whereas the SLEDAI and SLEDAI-M were completed in retrospect based on reports in the medical chart. In some cases, the retrospective reports dated back as far as two years.

A second explanation for the equivocal findings on the association between disease activity and attentional capacity performance is that the overall score on the SLAM-R also represents a measure of disease severity. Although the Rheumatologists' subjective ratings of disease severity were not significantly correlated with measures of attentional capacity, it is possible that the co-occurrence of disease activity and severity (using the SLAM-R) accounted for the significant correlation.

Denburg et al. (1993) reported that cognitive impairment in patients with SLE has not been found to be related to the presence of active disease or to the involvement of any organ system other than the CNS. However, the results of the present study along with the results of a study by Fisk et al. (1993) provide support for the notion that disease activity affects attention. As in the present study, Fisk et al. (1993) documented significant correlations between disease activity (as measured by the SLEDAI) and performance on tests of immediate memory and attention.

The results of the present study indicate that, on average, disease activity across all SLE subjects would be considered mildly active (SLAM-R=3.46), ranging from no activity (SLAM-R=0) to moderate activity (SLAM-R=14). There were no significant differences between the neuropsychiatric SLE subjects and non-neuropsychiatric SLE subjects on any of the measures of disease activity or on the rheumatologists' ratings of disease severity. While disease activity may partially explain the lack of difference in attentional capacity performance between the SLE groups, it is not sufficient to explain the extent of impairment documented in the neuropsychiatric SLE subjects. Fisk et al. (1993) suggested that the association between cognitive impairments and disease activity may represent transient and diffuse CNS abnormalities in patients, while the cognitive deficits observed in neuropsychiatric SLE subjects may represent a fixed neurological deficit.

An additional explanation for the lack of significant differences between the neuropsychiatric and non-neuropsychiatric SLE groups is that concurrent medications

affect attentional capacity. As discussed earlier, the use of Prednisone was controlled for in the internal design of the study. Furthermore, the last dose (which ranged from 2.5-1,000 milligrams with 1,000 milligrams representing pulse of solumedrol) was not found to be significantly correlated to measures of attentional capacity. Several previous studies (Carbotte et al., 1986; Ginsburg et al., 1992) have also failed to document significant correlations between steroid use and cognitive test performance of SLE subjects. In the present study, level of Plaquenil dose (given once a week) was significantly associated with measures of auditory attentional capacity. While it is possible that the effect of Plaquenil accounts for the lack of difference between the neuropsychiatric SLE subjects and the non-neuropsychiatric SLE subjects, only a minority of subjects were currently being prescribed Plaquenil. It is possible that the use of Plaquenil is associated with increased disease activity, and that one, the other, or the combination of both may compromise attentional capacity and account for the lack of significant differences between groups. Finally, the effects of NSAIDS on cognitive functioning was not examined and remains unclear.

Although disease activity and medication use may be associated with attentional capacity ability, they do not account for all of the observed abnormalities. The neuropsychiatric SLE subjects, but not the non-neuropsychiatric SLE subjects were significantly more impaired on measures of attentional capacity relative to healthy control subjects. Having considered potentially confounding variables, it seems likely that the documented impairments are related to the involvement of the CNS.

Anatomically, impairments in attention capacity are associated with diffuse damage to the CNS (Weber, 1990).

Limitations of the Study

Several methodological problems must be considered in the interpretation of this study.

First, SLE is not a unitary disorder. Disease presentation is unique to each individual. The diverse manifestations of neuropsychiatric involvement documented in this study illustrate this point. Therefore, the SLE subjects are not a homogeneous group. Attentional capacity deficits were observed in individual cases in absence of group differences. Likewise, some individuals with neuropsychiatric SLE did not demonstrate impairments in attentional capacity, despite the groups differences. The results of this study suggest that cognitive deficits in patients with SLE may be associated with subjective changes in abilities over time, in association with symptom flare up, and/or with medications. The best way to look at these influences would be to assess individuals longitudinally from the onset of SLE.

Second, while this research attempted to see each medical subject as close to their scheduled medical appointment as possible, this was not always feasible. Moreover, laboratory tests necessary for completing disease activity ratings for patients with SLE were not always ordered at the medical appointment due to lack of clinical evidence of disease activity. As a result, the understanding of the effects of disease activity and severity on test performance was compromised in some subjects. Ideally, full laboratory work, a rheumatologist appointment, a neurologist appointment, and the attention

assessment would have been completed on the same day, or within a few days of one another.

Third, the selection process of subjects limits the study. The medical groups were selected samples. In the case of SLE, a nursing coordinator identified potential subjects, followed by the approval of the patient's rheumatologist. In some cases, the rheumatologist did not feel it was in the patient's best interest to be approached. This selection process may have resulted in the selection of subjects with milder disease activity. In addition, SLE subjects suspected of having CNS involvement, or who complained of difficulties with their memory may have been favoured for referral to the study. In the case of RA subjects, most were already involved in research projects, a small number were selected by a rheumatologist. To compensate for this selection process, it would be possible to examine the profiles of patients not selected to see if they differ from those who were. In order to overcome selective sampling, all patients attending medical clinics should be approached to participate in the study or a randomization study should be conducted.

Fourth, the study was limited to a volunteer sample. Community volunteers may differ from those who did not volunteer. An a priori suspicion was that individuals who believed they had attention problems might be more inclined to inquire about the study. An attempt to screen for adult attention deficit disorder was therefore part of the screening process.

Fifth, while the sample size was adequate for the design of the study, external validity was reduced by the lack of random sampling procedures discussed above.

Finally, the issue of cognitive abilities fluctuating with "good" and "bad" days was raised by many of the SLE subjects. It is possible that day-to-day fluctuations could influence the test results, not only for the SLE subjects but also for the control groups. Associated with subjective fluctuations in cognitive ability, is the individual's mood and motivation on the day of testing. It was hoped that the questionnaire on mood and cognition, and the use of a depression inventory would objectify "good" or "bad" days. However, an individual's motivation is difficult to control. The majority of subjects across groups reported that their mood and cognitive abilities on the day of the attention assessment were about the same as on most days. It might be more informative to follow individuals over time to determine whether test performance is related to subjective reports of "good" or "bad" days.

Importance and Implications of Research Findings

The results of this study provide a number of findings which may lead to advancements in the understanding of cognitive deficits in patients with SLE. First, the results support the postulate that automatic attentional processing is preserved in patients with SLE. Second, the results support the postulation that as the demands on attentional capacity increase, the performance of patients with CNS involvement becomes impaired. Third, the results provide some support for a conclusion drawn by Fisk et al. (1993), that impairments are not only associated with CNS dysfunction but are also associated with disease activity. Fourth, the issue of medications on cognitive functioning remains unclear. In the past, much focus has been placed on the effect of corticosteroid medication on cognitive

functioning. The results of the present study raise speculations about the effects of other medications, particulary the use of Plaquenil, on cognitive functioning. The use of NSAIDS should also be assessed. Finally, while medications and disease activity appear to be related to reduced attentional capacity, these variables alone did not account for the presence of cognitive impairment in the neuropsychiatric SLE group. It was concluded that impairments in attentional capacity are related to neuropsychiatric involvement in SLE.

These findings have important implications for the study and understanding of cognitive deficits in patients with SLE, as well as for the development of screening measures for clinical practice. Deficits in attentional capacity may underlie some of the cognitive disturbances evident in CNS SLE. Measuring attentional capacity has relevance to clinical practice in identifying individual's in need of more thorough neuropsychological assessments, and in monitoring CNS disease, disease activity, and effects of medications.

Continued research using the ACT is desirable. It appears to be a promising clinical measure which is easy to administer. Weber (1986) indicates that the ACT is sensitive to measuring changes in an individual's performance whether he or she has very good attention or has poor attention. The measurement of visual attentional processing used in this study needs further refinement if it is to be used to assess changes in attentional capacity. Inherent in the GDS is the ability to adjust the event rate. Such an alteration, along with the distraction stimuli may be a useful third level for assessing effortful

attentional processing.

The irregular pattern of SLE complicates the understanding of documented impairments in attentional capacity and cognition. The association between episodic exacerbations and remissions of the disease and cognitive functioning has not been examined. Therefore, future research should include a longitudinal design. It would be interesting to follow subjects over time in order to assess attentional capacity during times of disease inactivity, and mild, moderate and severe activity, and to assess the effects of different medication trials. The results of such studies would help in determining the association between disease course and attentional capacity ability. In order to fully understand whether attentional capacity performance can contribute to a differential diagnosis of CNS involvement in SLE, or is more appropriate for monitoring it's course following diagnosis, research assessing a wide range of subjects across varying disease states is needed.

Finally, an examination with a functional measure of behaviour may help reveal the impact of attentional capacity dysfunction on the individual's daily living.

CHAPTER SIX

SUMMARY

The purpose of this study was to examine a fundamental cognitive deficit, attention, in patients with Systemic Lupus Erythematosus (SLE). The presence of cognitive abnormalities is considered to be an important descriptor of CNS involvement in SLE (Singer et al., 1990). However, the nature of cognitive deficits observed in patients with SLE remains nonspecific. One means of providing a more precise description of the functions which are impaired is to assess the specific cognitive processes which are common to and underlie documented impairments (Wolkowitz et al., 1988).

The cognitive deficits documented in previous research and patients' subjective complaints, suggest that as the demands for exerting effort increase, the performance of patients with SLE, particulary those with CNS involvement becomes impaired. Limitations in attentional capacity had not been specifically addressed or assessed in previous studies of cognitive functioning of patients with SLE. Therefore, the present study was designed to assess the nature of auditory and visual attention under increasingly demanding conditions in order to examine effortful attention on a limited capacity system. It was postulated that CNS involvement in SLE disproportionaly reduces attentional capacity.

The attentional capacity of 35 women meeting the American College of Rheumatology criteria for having SLE and who had a recent medical was measured using the Attentional Capacity Test (ACT; Weber, 1986), and the Gordon Diagnostic System (GDS; Gordon, 1991).

Neuropsychiatric involvement was determined based on the major criteria used by two major North American Research groups examining cognitive functioning in patients with SLE (e.g. Carbotte et al., 1986; Hanly et al., 1991). A chronic illness control group and a healthy control group were considered vital for determining the factors (i.e. biological, pharmacological, and psychological) which potentially contribute to attention deficits and for understanding the impairments which are specific to CNS involvement in SLE. The performance of the SLE subjects (19 neuropsychiatric SLE and 16 non-neuropsychiatric SLE subjects) was compared to 23 women with Rheumatoid Arthritis (RA) and 42 healthy women, using multivariate and univariate analyses.

The major findings were that: 1) neuropsychiatric SLE subjects were significantly more impaired on effortful auditory attention than healthy control subjects; 2) neuropsychiatric SLE subjects (excluding those whose only neuropsychiatric manifestation was depression requiring medical intervention) were more impaired on effortful visual attention than healthy control subjects; and 3) the performance of neuropsychiatric SLE subjects did not differ significantly from non-neuropsychiatric SLE subjects or from RA subjects.

When the above results were examined within a framework of automatic versus effortful attention, they provided support for the a priori assumption that automatic attention is intact in SLE subjects. Moreover, as the demands on attentional capacity increased, the ability of neuropsychiatric SLE subjects became impaired. The implication is that impaired performance is associated with

CNS involvement in SLE. The fact that the RA and non-neuropsychiatric SLE groups did not differ significantly from the neuropsychiatric SLE group, however, raised the speculation that the documented reduction in attentional capacity may not be limited to CNS involvement in SLE.

The potentially confounding influences of depression, age, medication, disease activity, severity and duration, co-morbid illness, and mood and motivation were considered. The effects of depression, age, medication, disease severity and duration, and co-morbid illnesses on attention capacity were not sufficient to explain the extent of deficit observed in the neuropsychiatric SLE group. Disease activity, however, was significantly correlated to auditory attentional capacity measures and may have accounted for reduced auditory performance in some patients. In these cases, reduced performance may have been related to diffuse and transient CNS disturbance (Fisk et al., 1993) or may have been secondary to other complications of the disease. Despite the apparent association, disease activity, alone, did not explain the extent of deficits observed in the neuropsychiatric SLE group. Reductions in attentional capacity in the neuropsychiatric SLE subjects appeared to be primarily related to CNS abnormalities.

The selection process, lack of coordination of medical and assessment appointments, and failure to observe patients over time were the main limitations of the present study. These limitations could be overcome by carrying out a randomized, longitudinal study in which medical appointments, laboratory work and cognitive assessments are completed within a few days of one another.

Despite the limitations, the findings of the present study do contribute evidence that assessment of cognitive functioning is useful for identifying those individuals with CNS involvement. The extent to which exacerbation of disease activity affects cognition confounds interpretation of the results. Nonetheless, it was proposed that the findings of a disproportional reduction in attentional capacity in patients with neuropsychiatric SLE may lead to a means of screening for cognitive deficits and CNS involvement in SLE. In turn, the use of a screening instrument may lead to advancements in the understanding of the early onset and nature of CNS involvement and cognitive impairments in patients with SLE.

REFERENCES

Abel, T., Gladman, D.D., & Urowitz, M.B. (1980). Neuropsychiatric Lupus. The Journal of Rheumatology, 7, 325-333.

American Psychiatric Association (1980). Diagnostic and statistical manual of mental disorders, DSM-III, Washington D.C.

American Psychiatric Association (1987). Diagnostic and statistical manual of mental disorders, DSM-III-R, Washington D.C.

Anderson, K.O., Bradley, L.A., Young, L.D., McDaniel, L.K., & Wise, C.M. (1985). Rheumatoid arthritis: Review of psychological factors related to etiology, effects, and treatment. Psychological Bulletin, 2, 358-387.

ARA Glossary Committee (1982). Dictionary of the rheumatic diseases. Volume 1: Signs and symptoms. New York: Contract Associates International Ltd.

August, G.J., & Garfinkel, B.D. (1990). Comorbidity of ADHD and reading disability among clinic-referred children. Journal of Abnormal Child Psychology, 18, 29-45.

Baddeley, A., Logie, R., Bressi, S., Della Sala, S., & Spinnler, H. (1986). Dementia and working memory. The Quarterly Journal of Experimental Psychology, 38A, 603-618.

Baker, M. (1973). Psychopathology in systemic lupus erythematosus. Seminars in Arthritis and Rheumatism, 3, 95-110.

Bauman, A., Barnes, C., Schrieber, L., Dunsmore, J., & Brooks, P. (1989). The unmet needs of patients with systemic lupus erythematosus: Planning for patient education. Patient Education and Counseling, 14, 235-242.

Benton, H. (1992). Clinical Neuropsychology: 1960-1990. Journal of Clinical and Experimental Neuropsychology, 14, 407-417.

Berg, R.A. (1990). Screening for brain damage over the life-span. In A.M. Horton Jr. (Ed.), Neuropsychology across the life-span. New York: Springer Publishing Company.

Bluestein, H.G. (1987). Neuropsychiatric disorders in systemic lupus erythematosus. In R.G. Lahita, (Ed.), Systemic Lupus Erythematosus. New York: John Wiley & Sons.

Bombardier, C., Gladman, D.F., Urowitz, M.B., Caron, D., Chang, C.H., & the committee on prognosis studies in SLE. (1992). Derivation of the SLEDAI. A disease activity index for Lupus patients. Arthritis and Rheumatism, 35, 630-640.

Borcherding, B., Thompson, K., Kruesi, M., Bartko, J., Rapoport, J.L., & Weingartner, H. (1988). Automatic and effortful processing in attention deficit/hyperactivity disorder. Journal of Abnormal Child Psychology, 16(3), 333-345.

Boston Collaborative Drug Surveillance Program. (1972). Acute adverse reactions to prednisone in relation to dosage. Clinical Pharmacological Therapy, 13, 694-698.

Bresnihan, B. (1982). CNS lupus. Clinics in Rheumatic Diseases, 8, 183-195.

Burg, J.S., Rasile, D.A., Davino, S.M., Major, L.F., Burright, R.G., & Donovick, P.J. (1992). Normative data on the Gordon Diagnostic System in Psychiatric and Neurological Populations. ADHD/Hyperactivity Newsletter, 18, 2.

Callahan, L.F., Kaplan, M.R., & Pincus, T. (1991). The Beck Depression Inventory, Center for Epidemiological Studies Depression Scale (CES-D), and General Well Being Schedule Depression Subscale in Rheumatoid Arthritis. Arthritis Care and Research, 4, 3-11.

Carbotte, R.M., Denburg, S.D., & Denburg, J.A. (1986). Prevalence of cognitive impairment in systemic lupus erythematosus. The Journal of Nervous and Mental Disease, 174, 357-364.

Carpenter, W.T., & Gruen, P.H. (1982). Cortisol's effect on human mental functioning. Journal of Clinical Psychopharmacology, 2, 91-101.

Carr, R.I. (1986). Lupus erythematosus. A handbook for physicians, patients and their families. Lupus Foundation of America, Inc.

Cassem, E.H. (1990). Depression and anxiety secondary to medical illness. Psychiatric Clinics of North America, 13, 597-613.

Cassileth, B.R., Lusk, E.J., Strouse, T.B., Miller, D.S., Brown, L.L., Cross, P.A., & Tenaglia, A.N. (1984). Psychological status in chronic illness. New England Journal of Medicine, 311, 506-511.

Cohen, R.M., Weingartner, H., Smallberg, S.A., Pickar, D., & Murphy, D.L. (1982). Effort and cognition in depression. Archives of General Psychiatry, 39, 593-597.

Cooley, E.L., & Morris, R.D. (1990). Attention in children: A neuropsychologically based model for assessment. Developmental Neuropsychology, 6, 239-274.

Cornblatt, B.A., Lenzenweger, M.F., & Erlenmeyer-Kimling, L. (1989). The continuous performance test-identical pairs version:II. Contrasting attentional profiles in schizophrenic and depressed patients. Psychiatry Research, 29, 65-85.

Crossen, J.R., & Wiens, A.N. (1988). Residual neuropsychological deficits following head-injury ion the Wechsler Memory Scale-Revised. The Clinical Neuropsychologist, 2, 393-399.

Denburg, J.A., Carbotte, R.M., & Denburg, S.D. (1987). Neuronal antibodies and cognitive function in systemic lupus erythematosus. Neurology, 37, 464-467.

Denburg, J.A., Carbotte, R.M., & Denburg, S.D. (1993). Cognitive dysfunction and central nervous system lupus. Lupus News, 13(2).

Denburg, S.D., Carbotte, R.M., & Denburg, J.A. (1987). Cognitive impairment in systemic lupus erythematosus: A neuropsychological study of individual and group deficits. Journal of Clinical and Experimental Neuropsychology, 9, 323-339.

Denburg, S.D., Carbotte, R.M., Long, A.A., & Denburg, J.A. (1988). Neuropsychological correlates of serum lymphocytoxic antibodies in systemic lupus erythematosus. Brain, Behavior and Immunity, 2, 222-234.

Devins, G.M. (1989). Enhancing personal control and minimizing illness intrusiveness. In N.G. Kutner, D.D. Cardenas, & J. D. Bower (Eds.), Maximizing rehabilitation in chronic renal disease (pp.109-136). New York: PMA Publishing Corporation.

Devins, G.M., Orme, C.M., Costello, G., Binik, Y.M., Frizzel, B., Stam, H.J., & Pullin, W.M. (1988). Measuring depressive symptoms in illness populations: Psychometric properties of the Center for Epidemiologic Studies Depression (CES-D) Scale. Psychology and Health, 2, 139-156.

Dubois, E.L., Wierchowiecki, M., Cox, M.B., & Weiner, J.M. (1974). Duration and death in systemic lupus erythematosus. Journal of the American Medical Association, 227, 1399-1402.

Earle-Boyer, E.A., Derper, M.R., Davidson, M., & Harvey, P.D. (1991). Continuous performance tests in schizophrenic patients: Stimulus and medication effects on performance. Psychiatry Research, 37, 47-56.

Edworthy, S.M., Zatarin, E., McShane, D.J., & Bloch, D.A. (1988). Analysis of the 1982 ARA lupus criteria data set by recursive partitioning methodology: New insights into the relative merit of individual criteria. Journal of Rheumatology, 15, 1493-1498.

Fava, G.A., & Molar, G. (1987). Criteria for diagnosing depression in the setting of medical disease. Psychotherapy and Psychosomatics, 48, 21-25.

Feinglass, E.L., Arnett, F.C., Dorsch, C.A., Zizic, T.M., & Stevens, M.B. (1976). Neuropsychiatric manifestations of systemic lupus erythematosus: Diagnosis, clinical spectrum and relationship to other features of the disease. Medicine, 55, 323-339.

Felton, B.J., & Revenson, T.A. (1987). Age differences in coping with chronic illness. Psychology and Aging, 2, 164-170.

Felton, B.J., Revenson, T.A., & Hinrichsen, G.A. (1984). Stress and coping in the explanation of psychological adjustment among chronically ill adults. Social Science and Medicine, 18, 889-898.

Fisk, A.D., & M.W. Scerbo (1987). Automatic and control processing approach to interpreting vigilance performance: A review and reevaluation. Human Factor, 29, 653-660.

Fisk, J.D., Eastwood, B., Sherwood, G., & Hanly, J.G. (1993). Patterns of cognitive impairment patients with systemic lupus erythematosus. British Journal of Rheumatology, 32, 458-462.

Giang, D.W. (1991). Systemic Lupus Erythematosus and depression. Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 4, 78-82.

Ginsburg, K.S., Wright, E.A., Larson, M.G., Fossel, A.H. Albert, M., Schur, P.H., & Liang, M.H. (1992). A controlled study of the prevalence of cognitive dysfunction in randomly selected patients with system lupus erythematosus. Arthritis and Rheumatism, 35, 776-782.

Golinkoff, M., & Sweeney, J.A. (1989). Cognitive impairments in depression. Journal of Affective Disorders, 17, 105-112.

Goodglass, H. (1986). The flexible battery in neuropsychological assessment. In T. Incagnoli, G. Goldstein and C.J. Golden (Eds.), Clinical application of neuropsychological test batteries. New York: Plenum Press.

Gordon, M. (1991). Instruction Manual for the Gordon Diagnostic System (GDS) Model III-R. DeWitt, New York: Gordon, Systems, Inc.

Gordon, M., McClure, F.D., & Post, E.M. (1986). Interpretive guide to the Gordon Diagnostic System. DeWitt, New York: Gordon Systems, Inc.

Gordon, M., & Mettelman, B.B. (1988). The assessment of attention: I. Standardization and reliability of a behavior-based measure. Journal of Clinical Psychology, 44, 682-690.

Grigor, R., Edmonds, J. Lewkonia, R., Bresnihan, B., & Hughes, G.R. (1978). Systemic lupus erythematosus. Annals of the Rheumatic Diseases, 37, 121-128.

Gronwall, D.M.A., & Sampson, H. (1974). The psychological effects of concussion. New York: Oxford University Press.

Guze, S.B. (1967). The occurrence of psychiatric illness in systemic lupus erythematosus. American Journal of Psychiatry, 123, 1562-1520.

Hall, R.C.W., & Beresford, T.P. (1985). Physical illness in psychiatric patients: Areas of Inquiry. Psychiatric Medicine, 2, 401-415.

Hall, R.C.W., Popkin, M.K., Stickney, S.K., & Gardner, E.R. (1979). Presentation of the steroid psychosis. Journal of Nervous and Mental Disease, 167, 229-235.

Hall, R.C.W., & Stickney, S.K. (1984). Medical and psychiatric features of systemic lupus erythematosus. Psychiatric Medicine, 1, 287-301.

Hall, R.C.W., Stickney, S.K., & Gardner, E.R. (1981). Psychiatric symptoms in patients with systemic lupus erythematosus. Psychosomatics, 22, 15-24.

Hanly, J.G. (1992). Personal correspondence, September 15.

Hanly, J.G., Fisk, J.D., Sherwood, G., Jones, E., Jones, J.V., & Eastwood, B. (1992). Cognitive impairment in Patients with systemic lupus erythematous. Journal of Rheumatology, 19, 562-567.

Harris, E.N., & Hughes, G.R.V. (1985). Cerebral disease in systemic lupus erythematosus. Springer Seminars in Immunopathology, 8, 251-266.

Hasher, L., & Zacks, R.T. (1979). Automatic and effortful processes in memory. Journal of Experimental Psychology: General, 108 (3), 356-388.

Hay, E.M., Black, D., Huddy, A., Creed, F., Tomenson, B., Bersen, R.M., & Holt, P.J.L. (1992). Psychiatric disorder and cognitive impairment in Systemic Lupus Erythematosus. Arthritis and Rheumatism, 35, 411-416.

Houtz, A. (1990). Alzheimer's disease and attention: An investigation into the initial stage of information processing. Unpublished doctoral dissertation, University of North Texas, Denton.

Huapaya, L., & Ananth, J. (1980). Depression associated with Hypertension: A review. Journal of the University of Ottawa, 5, 58-62.

Hughes, G.R.V. (1980). Central nervous systemic lupus - diagnosis and treatment. The Journal of Rheumatology, 17, 405-411.

Kahneman, D. (1973). Attention and effort. Englewood Cliffs, NJ: Prentice Hall.

Kaplan, H.I., & Sadock, B.J. (1991). Comprehensive glossary of psychiatry and psychology. Baltimore: Williams & Wilkins.

Kassen, S.S., & Lockshin, M.D. (1979). Central nervous system lupus erythematosus: The need for classification. Arthritis and Rheumatism, 22, 1382-1385.

Kenny, J.T., & Meltzer, H.Y. (1991). Attentional and higher cortical functions in Schizophrenia. Journal of Neuropsychiatry, 3, 269-275.

Kerlinger, F.N. (1986). Foundations of behavioral research. Toronto: Holt, Rinehart and Winston.

Kershner, P., & Wang-Cheng, R. (1989). Psychiatric side effects of steroid therapy. Psychosomatics, 30, 135-139.

Kinash, A.G. (1982). Systemic Lupus Erythematosus: The psychosocial dimension. Canada's Mental Health, June, 19-22.

Klippel, J.H., & Zvaifler, N.J. (1975). Neuropsychiatric abnormalities in systemic lupus erythematosus. Clinics in Rheumatic Diseases, 1, 621-638.

Koffler, S. (1987). The role of neuropsychological testing in systemic lupus erythematosus. In R.G. Lahita (Ed.), Systemic Lupus Erythematosus. New York: John Wiley & Sons.

Kutner, K.C., Busch, H.M., Racis, S.P., & Krey, P.R. (1988). Neuropsychological functioning in systemic lupus erythematosus. Neuropsychology, 2, 119-126.

Lewis, D.A., & Smith, R.E. (1983). Steroid-induced psychiatric syndromes. Journal of Affective Disorders, 5, 664-654.

Lezak, M.D. (1983). Neuropsychological Assessment (2nd Ed.). New York: Oxford University Press.

Liang, M.H., Socher, S.A., Larson, M.G., & Schur, P.H. (1989). Reliability and validity of six systems for the clinical assessment of disease activity in system lupus erythematosus. Arthritis and Rheumatism, 32, 1107-1118.

Lim, L., Ron, M.A., Ormerod, I.E.C., David, J., Miller, D.H., Lodsdail, S.J., Walport, W.J., & Harding, A.E. (1988). Psychiatric and neurological manifestations in systemic lupus erythematosus. Quarterly Journal of Medicine, 66, 27-38.

Ling, M.H.M., Perry, P.J., Tsuang, M.T. (1981). Side effects of corticosteroid therapy. Archives of General Psychiatry, 38, 471-477.

Lipkin, M., (1989). Psychiatry and medicine. In H.I. Kaplan & B.J. Sadock (Eds.), Comprehensive textbook of psychiatry (Vol 2, pp. 1280-1296).

Lishman, W.A. (1988). Organic psychiatry: The psychosocial consequences of cerebral disorder. (pp. 361-366) Boston: Blackwell Scientific Publications.

Magner, M.B. (1991). Psychiatric morbidity in outpatients with systemic lupus erythematosus. South African Medical Journal, 80, 291-293.

McCune, W.J., & Golbus, J. (1988). Neuropsychiatric lupus. Rheumatic Disease Clinics of North America, 14, 149-167.

McCune, W.J., MacGuire, A., Aisen, A., & Gebarski, S. (1988). Identification of brain lesions in neuropsychiatric systemic lupus erythematosus by magnetic resonance scanning. Arthritis and Rheumatism, 31, 159-166.

Miller, B.F., & Keane, C.B. (Eds.) Encyclopedia and dictionary of medicine, nursing, and allied health. Toronto: W.B. Saunders Company.

Miller, W.R. (1975). Psychological Deficit in Depression. Psychological Bulletin, 82, 238-260.

Mitchell, D.M., & Collins, J.V. (1984). Do corticosteroids really alter mood? Postgraduate Medical Journal, 60, 467-470.

Moscovitch, M. (1979). Information processing and the cerebral hemispheres. In M.S. Gazzaniga (Ed.), Handbook of behavioral neurobiology:Vol 2. Neuropsychology. New York: Plenum.

Naglieri, J.A., & Das, J.P. (1990). Planning, attention, simultaneous, and successive (PASS) cognitive processes as a model for intelligence. Journal of Psychoeducational Assessment, 8, 303-337.

Newman, S., Fitzpatrick, R., Lamb, R., & Shipley, M. (1990). Patterns of coping in rheumatoid arthritis. Psychology and Health, 4, 187-200.

Orme, J.G., Reis, J., & Herz, E.J. (1986). Factorial and discriminant validity of the Center for Epidemiological Studies Depression (CES-D) Scale. Journal of Clinical Psychology, 42, 28-33.

Pakaslahti, P.A., & Achte, A.K. (1982). Psychiatric complications of chronic physical disease. In E.K. Korany (Ed.), Physical illness in the psychiatric patient (pp. 59-77). Springfield: Charles C. Thomas.

Papero, P.H., Bluestein, H.G., White, P., & Lipnick, R.N. (1990). Neuropsychological deficits and antineuronal antibodies in pediatric systemic lupus erythematosus. Clinical and Experimental Rheumatology, 8, 417-424.

Papero, P.H., & Lipnick, R. (1988). Neuropsychological (NP) deficits in adolescents/young adults with Lupus (SLE). Journal of Clinical and Experimental Neuropsychology, 10, 89.

Peck, E.A., Stephens, V., & Martelli, M.F. (1987). A descriptive summary of essential neuropsychological tests. In L.C. Hartlage, M.J. Asken and J.L. Hornsby (Eds.), Essentials of neuropsychological assessment. New York: Springer Publishing Company.

Posner, M.I. (1978). Chronometric explorations of mind. Toronto: John Wiley & Sons.

Posner, M.I., & Presti, D.E. (1987). Selective attention and cognitive control. Trends in Neuroscience, 10, 13-17.

Posner, M.I., & Synder, C.R.P. (1975). Attention and cognitive control. In R.L. Solso (Ed.), Information processing and cognition. Hillsdale, NJ: Erlbaum.

Radloff, L.S. (1977). The CES-D scale: A self-report depression scale for research i the general population. Applied Psychological Measurement, 1, 385-401.

Rasile, D.A., Burg, J.S., Rumsey, R.L., Burright, R.G., & Donovick, P.J. (1993). The relationship between GDS scores and other measures of attention in MS patients and "healthy" adults. ADHD/Hyperactivity Newsletter, 19, 10-11.

Reeves, W.H., & Lahita, R.G. (1987). Clinical presentation of systemic lupus erythematosus in the adult. In R.G. Lahita (Ed.), Systemic Lupus Erythematosus (pp. 355-382). New York: John Wiley & Sons.

Rimon, R., Kronqvist, K., & Helve, T. (1988). Overt psychopathology in systemic lupus erythematosus. Scandinavian Journal of Rheumatology, 17, 143-146.

Roberts, D.M., & Hughes, W.M. (1989). Systemic lupus erythematosus. How to manage this chronic complicated disorder. Postgraduate Medicine, 86, 191-194.

Rosvold, H.E., Mirsky, A., Saason, L., Bransome, E.D., Jr., & Beck, L.H. (1956). A continuous performance test of brain damage. Journal of Consulting Psychology, 20, 343-350.

Rothfield, N. (1985). Clinical features of systemic lupus erythematosus. In W.N. Kelley, E.D. Harris, S. Ruddy, & C.B. Sledge (Eds.), Textbook of rheumatology 2nd ed.. Toronto: W.B. Saunders Company. (1070-1097).

Rothfield, N. (1989). The diagnostic features of SLE. Hospital Practice, Jan, 37-46.

Roubenoff, R. & Hochberg, M.C. (1991). Systemic lupus erythematosus. In N. Bellamy (Ed.), Prognosis in the rheumatic diseases. Boston: Kluwer Academic Publishers. (193-212).

Rourke, B.P., Bakker, D.J., Fisk, J.L., & Strang, J.D. (1983). Child neuropsychology: An introduction to theory, research, and clinical practice. New York: Guildford Press.

Roy-Bryne, P.P., Weingartner, H., Bierer, L.M. Thompson, K., & Post, R.M. (1986). Effortful and automatic cognitive processes in depression. Archives of General Psychiatry, 43, 265-267.

Sano, M. (1988). Using computers to understand attention in the elderly. American Behavioral Scientist, 31(5). 588-594.

Schneider, W., & Shiffrin, R.M. (1977). Controlled and automatic human information processing: I. Detection, search, and attention. Psychological Review, 84, 1-66.

Shiffrin, R.M., & Schneider, W. (1977). Controlled and automatic human information processing: II. Perceptual learning, automatic attending, and a general theory. Psychological Review, 84, 127-190.

Shum, D.H.K., McFarland, K.A., & Bain, J.D. (1990). Construct validity of eight tests of attention: Comparison of normal and closed head injured samples. The Clinical Neuropsychologist, 4, 151-162.

Singer, J., Denburg, J.A., & the Ad Hoc Neuropsychiatric Workshop Group. (1990). Diagnostic criteria for neuropsychiatric systemic lupus erythematosus: The results of a consensus meeting. The Journal of Rheumatology, 17, 1397-1402.

Smith, C.A., Dobbins, C.J., & Wallston, K.A. (1991). The mediational role of perceived competence in psychological adjustment to rheumatoid arthritis. Journal of Applied Social Psychology, 21, 1218-1247.

Sohlberg, M.M., & Mateer, C.A. (1987). Effectiveness of an Attention-training Program. Journal of Clinical and Experimental Neuropsychology, 9, 117-130.

Spreen, O., & Strauss, E. (1991). A compendium of neuropsychological tests. New York: Oxford University Press.

Stuss, D.I., Ely, B.A., Hugenholtz, H., Richard, M.T., LaRochelle, S., Poirier, C.A., & Bell, I. (1985). Subtle neuropsychological deficits in patients with good recovery after closed head injury. Neurosurgery, 17, 41-47.

Sutton, J.D., Navarro, A., & Stevens, M.B. (1984). Systemic lupus erythematosus XI: Nonpharmacological management. Md State Medical Journal, 33, 469-471.

Sweet, J.J., Newman, P., Bell, B. (1992). Significance of depression in clinical neuropsychological assessment. Clinical Psychology Review, 12, 21-45.

Tan, E., Cohen, A., Fries, J., Masi, A.T., McShane, D.J., Rothfield, N., Schaller, J.G., Talal, N., & Winchester, R.J. (1982). The revised criteria for the classification of systemic lupus erythematosus (SLE). Arthritis and Rheumatism, 25, 1271-1277.

Tancer, M.E., Brown, T.M., Evans, D.L., Ekstrom, D., Haggarty, J.J., Pedersen, C., & Golden, R.N. (1990). Impaired effortful cognition in depression. Psychiatry Research, 31, 161-168.

Tariot, P.N., & Weingartner, H. (1986). A psychobiologic analysis of cognitive failures. Archives of General Psychiatry, 43, 1183-1188.

van Dam, A.P., Wekking, E.M., & Oomen, H.A.P.C. (1991). Psychiatric systemic lupus erythematosus. Psychotherapy and Psychosomatics, 55, 132-140.

Van Zomeren, A.H., Brouwer, W.H., & Deelman, B.G. (1984). Attentional deficits: The riddles of selectivity, speed, and alertness. In N.Brooks (Ed.), Closed head injury: Psychological, social, and family consequences. New York: Oxford University Press.

Varney, N.R., Alexander, B., & MacIndoe, J.H. (1984). Reversible steroid dementia in patients without steroid psychosis. American Journal of Psychiatry, 141, 369-372.

Vaughan, J.H. (1993). Pathogenetic concepts and origins of rheumatoid factor in rheumatoid arthritis. Arthritis and Rheumatism, 36, 1-6.

Weber, A.M. (1986). Measuring attentional capacity. Unpublished doctoral dissertation, University of Victoria, Victoria.

Weber, A.M. (1988). A new clinical measure of attention: the attentional capacity test. Neuropsychology, 2, 59-71.

Weber, A.M. (1990). A practical clinical approach to understanding and treating attentional problems. Journal of Head Trauma Rehabilitation, 5, 73-85.

Weber, A.M., & Segalowitz, S.J. (1990). A measure of children's attentional capacity. Developmental Neuropsychology, 6(1), 13-23.

Weingartner, H. (1988). Models of memory dysfunction. Annals of the New York Academy of Science, 444, 359-369.

Weingartner, H., Cohen, R.M., Murphy, D.L., Martello, J., & Gerdt, C. (1981). Cognitive processes in depression. Archives of General Psychiatry, 38, 42-47.

Weiss, L. (1992). Attention deficit disorder in adults. Dallas: Taylor Publishing Company.

Wekking, E.M. (1993). Psychiatric Symptoms in Systemic Lupus Erythematosus: An Update. Psychosomatic Medicine, 55, 219-228.

Wekking, E.M., Nossent, J.C., van Dam, A.P., & Swaak, A.J.J.G. (1991). Cognitive and emotional disturbances in systemic lupus erythematosus. Psychotherapy and Psychosomatics, 55, 126-131.

Westbrook, M.T., & Viney, L.L. (1982). Psychological reactions to the onset of chronic illness. Social Science and Medicine, 16, 899-905.

Willner, P. (1984). Cognitive functioning in depression: a review of theory and research. Psychological Medicine, 14, 807-823.

Wolkowitz, O.M., Reus, V.I., Weingartner, H., Thompson, K., Breier, A., Doran, A., Rubinow, D., & Pickar, D. (1990a). Cognitive effects of corticosteroids. American Journal of Psychiatry, 147, 1297-1303.

Wolkowitz, O.M., Rubinow, D., Doran, A.R., Braier, A., Berrettini, W.H., Kling, M.A., & Pickar, D. (1990b). Prednisone effects on neurochemistry and behavior. Archives of General Psychiatry, 47, 963-968.

Wolkowitz, O.M., Tinklenberg, J.R., & Weingartner, H. (1985). A psychopharmacological perspective of cognitive functions. Neuropsychobiology, 14, 88-96.

Wolkowitz, O.M., & Weingartner, H. (1988). Defining cognitive changes in depression and anxiety: a psychobiological analysis. Psychiatry and Psychobiology, 3, 131s-138s.

Yancey, C.C., Doughty, R.A., & Arthreya, B.H. (1981). Central nervous system involvement in childhood systemic lupus erythematosus. Arthritis and Rheumatism, 24, 1389-1395.

Zvaifler, N.J., & Woods, V.L. (1985). Etiology and pathogenesis of systemic lupus erythematosus. In W.N. Kelley, E.D. Harris, S. Ruddy, & C.B. Sledge (Eds.), Textbook of rheumatology, Toronto: W.B. Saunders Company, 1042-1069.

APPENDIX A

Advertisements for Control Subjects

1) Mail-out to Rheumatoid Arthritis Patients

2) Newspaper Advertisement for Healthy Controls

The following notice, printed on University of Calgary, Faculty of Medicine letterhead, was sent to 24 patients with Rheumatoid arthritis:

ATTENTION STUDY

PATIENTS WITH RHEUMATOID ARTHRITIS:

The University of Calgary is conducting a study to investigate the effects of disease on attention in patients with Rheumatic Diseases.

You are invited to participate in this research project.

Your participation would entail one 60-minute session. During this session you would be asked to complete a brief questionnaire, a visual attention task, and an auditory attention task.

If you would like to participate in this study, please contact Elizabeth Kerr at 283-1027.

The following advertisement ran regularly, although not weekly, in the "Helping Hands" section of the Neighbours supplement to Thursday's Calgary Herald. The Neighbours section is also distributed to mail boxes in some of Calgary's neighbourhoods.

"The University of Calgary Department of Educational Psychology needs female volunteers without a history of chronic illness to serve as control subjects in a study investigating attention in chronically ill women. Approximately one hour will be required. Study is being conducted by a supervised PhD student. Call 283-1027."

APPENDIX B

Letters of Informed Consent:

(a) Letter for SLE and RA Subjects

(b) Letter for Healthy Control Subjects

LETTER OF INFORMED CONSENT

(Printed on University of Calgary, Department of Educational Psychology letterhead)

Research Project: Attentional processing in patients with Systemic Lupus Erythematosus

Investigator: Elizabeth Kerr - Doctoral student in Clinical (community) Psychology

Supervisors: Dr. S.M. Edworthy - Faculty of Medicine
Dr. M. Samuels - Department of Educational Psychology

This consent form, a copy of which has been given to you, is only part of the process of informed consent. It should give you the basic idea of what the research project is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, you should feel free to ask. Please take the time to read this carefully.

The purpose of this study is to investigate the effects of disease on the nature of attention in patients with Systemic Lupus Erythematosus. Women suffering from Systemic Lupus Erythematosus, those suffering from Rheumatoid Arthritis as well as those who have no past history of a chronic disease will be assessed. It is hoped that this study will provide new information that may aid in the understanding of Systemic Lupus Erythematosus, and early diagnosis of possible involvement of the central nervous system.

You are invited to participate in this research project. Your participation would entail a meeting with Miss Kerr on one occasion for approximately 60 minutes. The session will involve a brief questionnaire about your background history and current concerns, followed by the completion of attention tasks. Miss Kerr will explain the instructions to you and will be present during task completion. This session would need to be arranged within 2 weeks of your clinic visit in order to obtain up to date information about disease activity.

In order to assess the relationship between disease state and performance on attention tasks, Miss Kerr will require access to your medical files to obtain specific information regarding the date of disease diagnosis, medication dose, system involvement and results of haematologic and serological tests.

As a participant, complete anonymity is assured. Once written consent is obtained by you, any information gathered from you will be coded and accessible only to Miss Kerr and her supervisory committee. The results of this study may be published, however, at no time will your name appear in the study. Furthermore, data will not be identified with a particular individual.

You will be provided with your individual results, as well as a copy of the group results of the study, should you desire. If you wish, and only with your written permission, your individual results will be forwarded to your physician.

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigator, sponsors, or involved institutions from their legal and professional responsibilities. Participation in this study is completely voluntary. Your decision of whether to participate will in no way affect your access to treatment. You are free to withdraw from the study at any time without jeopardizing your health care. Your continued participation should be as informed as your initial consent, so you should feel free to ask for clarification or new information throughout your participation. If you have further questions concerning matters related to this research, please contact: Elizabeth Kerr at 220-5659.

If you have any questions concerning your rights as a possible participant in this research, please contact the Office of Medical Bioethics, Faculty of Medicine, The University of Calgary, at 220-7990.

_____
DATE

_____
NAME

_____
SIGNATURE

_____
WITNESS

_____
SIGNATURE

I wish to receive my individual results. _____ YES _____ NO

I wish a summary of the group results. _____ YES _____ NO

My mailing address is:

A copy of this consent form will be given to you. Please keep it for your records and future reference.

LETTER OF INFORMED CONSENT

(Printed on University of Calgary, Department of Educational Psychology LetterHead)

Research Project: Attentional processing in patients with Systemic Lupus Erythematosus

Investigator: Elizabeth Kerr - Doctoral student in Clinical (community) Psychology

Supervisors: Dr. S.M. Edworthy - Faculty of Medicine
Dr. M. Samuels - Department of Educational Psychology

This consent form, a copy of which has been given to you, is only part of the process of informed consent. It should give you the basic idea of what the research project is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, you should feel free to ask. Please take the time to read this carefully.

The purpose of this study is to investigate the effects of disease on the nature of attention in patients with Systemic Lupus Erythematosus. Women suffering from Systemic Lupus Erythematosus, those suffering from Rheumatoid Arthritis as well as those who have no past history of a chronic disease will be assessed. It is hoped that this study will provide new information that may aid in the understanding of Systemic Lupus Erythematosus and early diagnosis of possible involvement of the central nervous system.

You are invited to participate in this research project. Your participation would entail a meeting with Miss Kerr on one occasion for approximately 60 minutes. The session will involve a brief questionnaire about your background history and current concerns, followed by the completion of attention tasks. Miss Kerr will explain the instructions to you and will be present during task completion.

As a participant, complete anonymity is assured. Once written consent is obtained by you, any information gathered from you will be coded and accessible only to Miss Kerr and her supervisory committee. The results of this study may be published, however, at no time will your name appear in the study. Furthermore, data will not be identified with a particular individual.

You will be provided with your individual results as well as a copy of the group results of the study, should you desire. If you wish, and only with your written permission, your individual results will be forwarded to your physician.

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigator, sponsors, or involved institutions from their legal and professional responsibilities. Participation in this study is completely voluntary. Your decision of whether to participate will in no way affect your access to treatment. You are free to withdraw from the study at any time without jeopardizing your health care. Your continued participation should be as informed as your initial consent, so you should feel free to ask for clarification or new information throughout your participation. If you have further questions concerning matters related to this research, please contact: Elizabeth Kerr at 220-5659.

If you have any questions concerning your rights as a possible participant in this research, please contact the Office of Medical Bioethics, Faculty of Medicine, The University of Calgary, at 220-7990.

_____ _____

DATE NAME

_____

SIGNATURE

_____

WITNESS

_____

SIGNATURE

I wish to receive my individual results. _____ YES _____ NO

I wish a summary of the group results. _____ YES _____ NO

My mailing address is:

A copy of this consent form will be given to you. Please keep it for your records and future reference.

APPENDIX C

Personal Questionnaires:

(a) Questionnaire for SLE/RA Subjects

(b) Questionnaire for Healthy Subjects

Questionnaire
(SLE)

Name: _____ Date: _____ / _____ / _____
Day Month Year

Date of Birth: _____ / _____ / _____
Day Month Year

Please indicate the highest level of education you have received:

Grade School (grades 1 2 3 4 5 6 7 8) _____

High School (grades 9 10 11 12) _____

Additional Education (i.e beyond high school) _____
Please list # of years beyond

1) When were you diagnosed with Lupus?

_____ /_____ /_____
Day Month Year

2) When was the first time you recall thinking that something was wrong with your health? Please provide approximate date.

_____ / _____
Month Year

3) How many times have you been hospitalized for complications related SLE over the last year? _____

4) Are you currently taking prednisone? _____ _____
Yes No

Please indicate the degree to which the following statements apply to you.

(1) Fluctuations in my mood now, compared to before I had a diagnosis of Lupus are:

_____	_____	_____	_____
Don't know	less frequent	about the same	more frequent

(2) Fluctuations in my mood when I am experiencing symptom exacerbations, compared to when my disease is inactive are:

_____	_____	_____	_____
Don't know	less frequent	about the same	more frequent

(3) Compared to most weeks, in the last week fluctuations in my mood have been:

_____	_____	_____	_____
Don't know	less frequent	about the same	more frequent

(4) Compared to my behaviour before being diagnosed with Lupus, I am tense or angry:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(5) Compared to periods of disease inactivity, during active periods I am tense or angry:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(6) Compared to most weeks, in the last week I am tense or angry:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(7) Compared to my behaviour before being diagnosed with Lupus, my spirit is very high:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(8) Compared to periods of disease inactivity, during active periods my spirit is very high:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(9) Compared to most weeks, in the last week my spirits has been very high:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(10) Compared to my behaviour before being diagnosed with Lupus, I am depressed:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(11) Compared to periods of disease inactivity, during active periods I am depressed:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(12) Compared to most weeks, in the last week I have been depressed:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(13) Compared to my behaviour before being diagnosed with Lupus, I frustrated:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(14) Compared to periods of disease inactivity, during active periods I frustrated:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(15) Compared to most weeks, in the last week I am frustrated:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(16) Compared to my ability to concentrate before being diagnosed with Lupus, my ability to concentrate is:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(17) Compared to periods of disease inactivity, during active periods my ability to concentrate is:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(18) Compared to most weeks, in the last week my ability to concentrate was:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(19) Compared to my memory ability before being diagnosed with Lupus, my ability to remember is:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(20) Compared to periods of disease inactivity, during active periods my ability to remember is:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(21) Compared to most weeks, in the last week my ability to remember was:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

Questionnaire
(Healthy Controls)

Name: _____ Date: _____ / _____ / _____
Day Month Year

Date of Birth: _____ / _____ / _____
Day Month Year

Please indicate the highest level of education you have received:

Grade School (grades 1 2 3 4 5 6 7 8) _____

High School (grades 9 10 11 12) _____

Additional Education (i.e. beyond high school) _____
Please list # of years beyond

Are you currently taking prednisone? _____ _____
Yes No

Do you suffer from any type of chronic illness?

_____ _____ _____
Yes No If yes please give name of illness

Please list current prescribed medications:

Were you considered to have an attention deficit as a child?

_____ _____
Yes No

Please indicate the degree to which the following statements apply to you.

(1) Compared to most weeks, in the last week fluctuations in my mood have been:

_____	_____	_____	_____
Don't know	less frequent	about the same	more frequent

(2) Compared to most weeks, in the last week I have been tense or angry:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(3) Compared to most weeks, in the last week my spirits have been very high:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(4) Compared to most weeks, in the last week I have been depressed:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(5) Compared to most weeks, in the last week I have been frustrated:

_____	_____	_____	_____
Don't know	less frequently	about the same	more frequently

(6) Compared to most weeks, in the last week my ability to concentrate has been:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

(7) Compared to most weeks, in the last week my ability to remember has been:

_____	_____	_____	_____
Don't know	Not as good	about the same	Better

APPENDIX D

Attention Deficit Screening Questionnaire

Please indicate which of the following statements currently apply to you. In addition, if they applied to you during your childhood please put a check under the child column.

	YES	SOME	NO	CHILD
Often fail to finish things started	____	____	____	____
Often do not seem to listen	____	____	____	____
Easily distracted	____	____	____	____
Have difficulty concentrating on sustained-attention tasks	____	____	____	____
Often act before thinking	____	____	____	____
Shift excessively from one activity to another	____	____	____	____
Have difficulty organizing work or become disorganized if not following a schedule	____	____	____	____
Benefit from a structured environment	____	____	____	____
Frequently call and talk out, interrupting conversations	____	____	____	____
Have difficulty waiting turn in group situations	____	____	____	____
Impatient	____	____	____	____
Excessively on the move, often falling asleep when still	____	____	____	____
Have difficulty sitting still or fidget excessively	____	____	____	____
Move about excessively during sleep	____	____	____	____

YES SOME NO CHILD

Always "on the go"	____	____	____	____
Have difficulty staying seated	____	____	____	____
Engage in more than one activity at a time	____	____	____	____
Very sensitive to rejection, teasing, criticism, and frustration	____	____	____	____
Shift moods suddenly and unexpectedly but based on events	____	____	____	____
Hot temper that disappears quickly (don't hold grudges)	____	____	____	____
Frequent negative thinking after excitement	____	____	____	____
Hard to give and take soothing and holding	____	____	____	____
Am soothed and/or aided in focusing by use of TV, radio, or fan	____	____	____	____
Tend to blame others	____	____	____	____
Stand-up comedy tendencies	____	____	____	____
Respond to asking better than being told	____	____	____	____

APPENDIX E

Written Permission for Reproduction of Table

Dec 28, 1993

3005 NW 50, Apt 214
Oklahoma City, OK, USA 73112
Tel. (405) 943-4941.

Elizabeth N Kerr, M.A.
206-934 2nd Ave, N.W.
CALGARY, Alberta T2N-0E6
CANADA.

Dear Ms Kerr,

I am happy to give you permission to reproduce the "task requirements" table regarding the Attentional Capacity Test in your dissertation. Good luck with your research efforts. Sorry about the delay in replying.

Sincerely,

Alison Mary Weber.