

CHAPTER 1

INTRODUCTION

1.1. OVERVIEW

Multiple Sclerosis (MS) is the most common inflammatory demyelinating disease of the central nervous system. The onset is mainly between the ages of 20 and 40 years and it occurs more frequently in females than in males. This disease has grave implications for the quality of life of the sufferer. The symptoms are both physical and psychological and the disease is incurable (Keegan & Noseworthy, 2002; Mohr & Cox, 2001).

Numerous neuropsychological studies have been undertaken to establish the extent of cognitive changes accompanying MS, as these are a major factor determining the quality of life of patients with MS (Beatty, Goodkin & Monson, 1989; Brassington & Marsh, 1998; Franklin, Nelson, Filley, & Heaton, 1989; Rao, Leo, Bernardin & Unverzagt, 1991; McIntosh-Michaelis, Roberts, Wilkinson, Diamond, McLellan, Martin & Spackman, 1991; Rao, Leo, Ellington, Nauertz, Bernardin, & Unverzagt, 1991; Rao, 1990). Although some of these studies, like the one done by Rao et al. (1991) found some relationships between the nature and severity of impairment of cognitive functions and some aspects of psychosocial functioning of the individual with MS (in this specific study the aspects being higher unemployment, engagement in fewer social activities, higher levels of sexual dysfunction, greater difficulty performing routine household tasks and increased occurrences of psychological difficulties), very few studies have attempted to gain an overall picture of the life world of the MS sufferer and the myriad of difficulties that these individuals face on a daily basis.

Additionally, other symptoms not adequately explained in terms of pure cognitive dysfunction are clearly also prevalent in MS. These symptoms are often described as psychological symptoms, behavioural symptoms, or personality symptoms and may have even more serious and far-reaching implications for the quality of life and

adaptation of the MS sufferers. Apathy or behavioural inertia, impulsivity, confusion, emotional lability, inappropriate sexual comments and behaviour, failure to comply with medical or rehabilitative treatment and diminished interest in social and employment activities as reported by Grigsby, Kravcisin, Ayarbe, and Busenbark, (1993) and Rao (1990) are examples of such symptoms.

I believe the involvement of the frontal lobes in the disease course of these patients might provide an explanation for the great number of psychological, behavioural and personality symptoms that are manifested in MS. Impairments in executive functioning, traditionally ascribed to dysfunction of the frontal lobes, are common to the neuropsychological deficits found in MS (Huber, Bornstein, Rammohan, Christy, Chakeres & McGhee, 1992) and further serve to support the involvement of the frontal lobes in the MS disease course. Symptoms often erroneously construed as resulting from psychological or personality problems might in fact have at its core a dysfunction in the regulation of behaviour (or behavioural pathology) – the essential feature of frontal lobe dysfunction. Support for the existence of the relationship between these ‘psychosocial’ symptoms and the impairment of frontal lobe function (i.e. executive dysfunction) are provided by Grigsby et al. (1993, p.1350) when they state that the ”problematic behaviour manifested in patients with neurological disorders are especially found in patients where the lesions are of the prefrontal cortex or of the kind that disrupts the fiber tracts connecting the frontal cortex with other areas of the brain”.

Further support for the above relationship is found in the fact that these ‘problematic behavioural symptoms’ closely resemble the symptoms of frontal lobe dysfunction (executive dysfunction) as described by Damasio (in Heilman and Valenstein, 1985; Lezak, 1995; Russell & Roxanas, 1990). Stuss, Gow and Hetherington (1992) furthermore propose that the primary change after frontal lobe pathology constitutes a disorder of personality. They state that this disorder of personality implies “a change in the stable response pattern that defines an individual as a unique self” (Stuss et al., 1992, p.349). It thus appears that the frontal lobe symptoms account for a great majority of behavioural, psychological, and personality problems encountered by the MS patient.

Symptoms of frontal lobe dysfunction are often overlooked as they do not readily show up on standard neurological investigations and considering that intellectual (as measured by standardised tests) and verbal abilities often stay relatively intact in the presence of this kind of dysfunction complicates matters further (Damasio, in Heilman & Valenstein, 1985). It becomes clear how the nature of frontal lobe symptoms might pervade the life world of the MS sufferer causing a wide variety of difficulties that the MS sufferer faces during the course of the disease.

These psychosocial and behavioural symptoms may furthermore occur due to the emotional reaction towards, and the process of adaptation to the disease, not unlike the process of bereavement. In this case patients have lost something very dear to them, namely the sense of self as a healthy, productive and independent human being. They are forced to re-evaluate their automatic assumptions of, and hopes for a healthy and extended future. They are often reminded of this fact when they are brought face to face with the disease symptoms which might crop up at the most unexpected times. They are further reminded of their loss when they are not able to perform duties of daily living as they had done before which lead to feelings of uselessness and dependency, resulting in great emotional distress. It is therefore very important to take cognisance of the individuals' emotional state, including their emotional reaction toward the illness.

The symptoms that result from MS not only cause great distress and difficulties for the patients themselves, but also negatively influence their interpersonal relationships and subsequently place great demands on their loved-ones, caregivers, and health professionals. This is especially true if insufficient knowledge about the process of MS exists and the behaviours that the patients manifest are viewed plainly as the patient being difficult, lazy or deliberately insensitive, instead of as a result of central nervous system dysfunction (McIntosh-Michaelis et al., 1991). It is therefore also crucial that the significant others in the patient's life should be involved in research to examine the many and varied changes and difficulties brought about as a result of MS.

I believe that an understanding of the problems resulting from the interactions between the neurological, cognitive and affective factors involved in the course of MS

can result in a more accurate and holistic picture of the life world of the MS sufferer. This will hopefully lead to a greater understanding of the daily difficulties faced by both those individuals with MS and their loved ones and associates. It is clear that adequate patient counselling and education is important in making the disease process less alien. By disseminating adequate and relevant information many of the problems that the affected individuals, as well as their relatives and caregivers will potentially face, could be greatly alleviated if not completely averted, making the MS disease process more manageable and less traumatic. For this type of preventative strategy to be successful a thorough understanding of all the consequences of MS is necessary and should not only include counselling on the physical symptoms and problems that could be expected, but also very importantly should include counselling concerning the neuropsychological (i.e. the cognitive, emotional, behavioural) and psychosocial implications of MS.

1.2. THE CURRENT STUDY

The main objective of the study is to explore the involvement of certain demographic (gender, age and education), cognitive (specifically executive functions) and psychological factors (personality changes and other psychosocial issues) in the disease process in a group of MS patients. This exploration is done in an attempt to gain a general and hopefully more holistic picture of the life world of the individual with MS. This study will attempt to not only describe the picture as it emerges but also to start to investigate how these different factors involved in the disease process, interrelate to form the fabric from which this emerged picture is woven.

This dissertation is divided into three broad sections. The first section consists of chapters 2 to 5 and contains the literature review. Chapter 2 provides an overview of relevant factors concerning MS as a medical condition. Chapter 3 discusses the functional brain anatomy that is important for understanding the effects of MS on cognitive functioning, as well as personality and behaviour. In Chapter 4 the psychosocial implications of MS are discussed, including the emotional "experiencing" of MS, the process of adaptation to the disease and the relationship between aspects of affect and cognition. The effect of MS on the family and

caregivers are also briefly mentioned. Chapter 5 contains a discussion of the cognitive implications of MS.

The second section, comprising chapters 6 and 7, presents the methodology, results and discussion of the current study. Chapter 8 comprises the third section and contains a discussion of the results of this current study, a formulation of the conclusions that can be drawn from it, a critical overview of the study and some suggestions for future research.

CHAPTER 2

MULTIPLE SCLEROSIS

2.1. INTRODUCTION

Multiple Sclerosis (MS) is a degenerative disease of the central nervous system and the most prevalent of the demyelinating diseases. Since MS strikes people in their prime when careers and families are being established, it has singularly tragic repercussions. The quality of life of both sufferers and their associates are irretrievably changed (Keegan & Noseworthy, 2002; Mohr & Cox, 2001; Rao, 1986). Due to the nature of MS, the disease does not affect all individuals in exactly the same way and there is no typical progression of MS for all individuals. This uncertainty concerning personal disease process and outcome thus leads to a wide range of emotional reactions (such as distress, anger, fear and anxiety) in the afflicted individuals. The disease is multi-focal, thus having effects on the cognitive, affective and physical spheres of the patients' life, and as such poses unique problems not associated with other diseases.

2.2. ETIOLOGY AND INCIDENCE

Multiple sclerosis (MS) is a chronic progressive neurological disease characterized by disseminating demyelination of the nerve fibres of the brain and spinal cord. In a healthy nerve, the myelin sheath protects and nourishes the nerve fibre. The consequences of the breakdown of this sheath and its replacement by sclerotic tissue plaques, mainly contribute to difficulties with impulse conduction by blocking or distorting normal transmission of nerve impulses. Until recently it was believed that any damage to the nerve fibres (axons) themselves were secondary to, and substantially less than the damage to the myelin sheath. However recent research has shown that the axons can become irreversibly damaged as a consequence of the immune system's attack on the myelin and the resulting inflammation (Trapp, Peterson & Ransohoff, 1998).

The sclerotic plaques are found predominantly in the white matter of the brain and the spinal cord, and to a lesser degree in the grey matter of the cerebral cortex and in the cranial or spinal nerve roots. The specific areas typically populated by these plaques are 1) the optic nerves and chiasm, 2) the periventricular regions of the brain and 3) the supial region of the spinal cord (Walton, 1985).

According to a spokesperson for 'Multiple Sclerosis South Africa' (personal communication, 2001) the estimated incidence of MS in South Africa is approximately one person in every 100 000. This seems to be in accordance with findings by Kurtze, Beebe and Norman (1979) of prevalence figures for MS in equatorial countries around 1/100 000. Kurtz et al. (1979) furthermore found the incidence rates for the southern United States and southern European countries to be around 6-14/100 000, and for the northern United States, northern European countries and Canada to be around 30-80/100 000. The incidence of MS in South Africa is higher in the white population than in other population groups. It is not yet clear whether this is because it is more common amongst Caucasians or whether it is due to misdiagnoses in other populations. It does however seem to be relatively rare in the black community. Research done in the U.S.A. by Matthews, Compston, Allen and Martyn (1991), in which steps were taken to prevent bias of under diagnosis in the black male population, showed that the incidence of MS was in fact lower in the African-American sub-population than in the Caucasian sub-population. Interestingly enough, this study also showed that the occurrence of MS in the African-American sub-population in the U.S.A. was still higher than in the black populations of Africa. This led Matthews et al. (1991) to conclude that even though the "black" populations were relatively protected from developing MS by their genetic constitution, it still seemed that the environmental factors that played a role in the development of MS seemed to be similar to those for the 'white' population.

MS produces a varied clinical picture. Symptoms most often experienced include: weakness or loss of motor control over limbs, visual symptoms (such as blindness in one eye, double vision, dimness of vision and loss of field of vision), numbness, vertigo, tremor, loss of taste, epilepsy, impotence, and difficulties with sphincter

control. In most cases, abnormalities are also found in the cerebro-spinal fluid (Walton, 1985).

The severity, duration, and prognosis of MS vary and the survival rate for sufferers is approximately 85% of that for the general population (Chipps, Clanin & Campbell, 1992). Diagnosis of the disorder is made on the presence of multiple lesions in the central nervous system and dissemination over time.

There is an association between the prevalence of MS and distance from the equator. The greater the distance from the equator the higher the incidence of MS. The highest incidence of MS is in Western Europe, Southern Canada, Southern Australia and New Zealand. As seen from the correlation between incidence rates and area of origin (Berkow, 1977; Chipps et al., 1992), the possibility of a critical window period during which environmental factors may exert an effect, should also be kept in mind. When moving from an area of higher prevalence to areas of lower prevalence after the age of 15 years, the person retains the risk of MS of the previous area. When moving before the age of 15 years, the individual acquires the risk prevalence of the new area (Berkow, 1977; Chipps et al., 1992).

Women are affected more often than men. In 75% of cases the onset of symptoms occurs between the age of 20 and 40 years. MS is rare in childhood and fairly uncommon in old age (Berkow, 1977; Chipps et al., 1992).

2.3. PATHOPHYSIOLOGY

The precise cause of MS is still unknown. Various hypotheses have been put forward and research efforts have implicated genetic, environmental, and immunological variables. Some explanations for the cause of MS include (a) a slow-acting virus, (b) a delayed reaction to a virus, (c) local hypoxia from toxic agents, (d) an autoimmune reaction where the body attacks its own tissue, (e) myelinolysis by enzymes, (f) trauma, (g) vascular lesions due to blood clotting abnormalities and (h) excesses or deficiencies of various nutrients (Berkow, 1977; Brassington & Marsh, 1998).

The explanation that seems to be prevalent is that MS is caused by a viral agent working in combination with a genetic susceptibility for the development of the disease. However, researchers have as yet not been able to isolate an actual virus and viral hypotheses are mostly based on circumstantial evidence. The genetic explanations on the other hand, are based on the assumption that MS is an autoimmune disease. Research has focused on human leukocyte antigen (HLA) genes, T-cell receptor genes, and immunoglobulin, all of which are the genetic loci that have been proven to play a part in the autoimmune responses (Brassington & Marsh, 1998). It is interesting to note that the specific type of HLA gene, namely the HLA-DR2 haplotype, which is considered to play a role in the genetic inheritance of MS, is most commonly found in Caucasians. The possibility that this may serve as proof for the greater incidence of MS amongst Caucasians, should be considered.

There is a substantial body of research evidence concerning a genetic basis for MS. Ebers et al. (1986) found a MS concordance rate for monozygotic twins of 30% whereas the rate for dizygotic twins was 3% - the risk decreased as the degree of relatedness decreased. In addition, first degree relatives of persons with MS have between 15 – 20 times (Chipps et al., 1992) greater incidence of the disease than the general population, with siblings being at most risk (White, 1990).

In MS some characteristics of an autoimmune disease seem to be present. An autoimmune disease results when the body's immune system loses the ability to discriminate between the body's own and foreign agents and then proceeds to attack the body's own tissue as if they were foreign agents invading the body and requiring elimination. It appears that alterations in the function of the suppressor lymphocytes are responsible for this attack on the body's own structures. Defective immunoregulation accompanies, and even perhaps precedes, acute deterioration in the health of the individual suffering from MS, during which time unimpeded damage of the myelin membranes and oligodendrocytes occur. It is further evident that times of remission during the disease course are accompanied by rebound elevation of suppressor function, whereby the destruction of body-own structures, such as the myelin membranes, is inhibited.

An important factor to remember here is the role that psychosocial stressors play in amending the human immune function. Research relating the connection between psychosocial factors (such as stress, depression, and anxiety) and changes in the immune function are abundant (Ader, Felten & Cohen, 1991). Rogers, Dubey and Reich (1979) state that stress increases the individual's vulnerability to disease by suppressing the immune system. Rogers et al. (1979), as well as Ader et al. (1991), state that diseases closely associated with immunological mechanisms such as infection, malignancy and autoimmune diseases are influenced by psychosocial factors. Ader et al. (1991, p.969) however warn that "all speculations about the role of psychosocial factors in autoimmune disease must be tentative". The precise way in which psychosocial factors influence autoimmune disease is not yet clear. Ader et al. (1991) state that these psychosocial factors might contribute to, interact with, or exacerbate an initial infection or intolerance to body own antigens, or they may intervene at some stage in the ensuing cascade of immunological changes that follow the onset of a disease. When considering MS as an autoimmune disease it thus seems plausible that the psychological state of the sufferers will have an effect on the status of the disease and vice versa. There is a high incidence of depression in MS sufferers, between 25 – 54% (Minden & Schiffer, 1990). In addition, Feinstein (1995) found a direct relationship between increased rates of depression and increased rates of deterioration of lesion loads in the brains of MS sufferers. Therefore the possibility for a psychoneuroimmunological mechanism in MS seems worthy of investigation.

Taken together, all these hypotheses concerning the possible causes of MS point to the importance of considering a multi-factor model in explaining the etiology of MS.

2.4. CLINICAL MANIFESTATIONS AND DISEASE COURSE

The clinical signs and symptoms of MS vary considerably and are typical of the chronic, yet unpredictable nature of the disease. During a flare up of the disease, symptoms may last several weeks or only brief moments. Subjective physical symptoms are described as bizarre and may be unsubstantiated by physical examination, making diagnosis more difficult.

Neuropathologic changes in MS include multifocal plaques of demyelination distributed within the brainstem, cerebellum, spinal cord, optic nerve and cerebrum. During the demyelinating process (primary demyelination), the myelin sheath and the myelin-sheath cells are destroyed. This demyelination process leads to four significant central disturbances namely:

- * a decrease in nerve **conduction speed**;
- * nerve **conduction block** (frequency related);
- * **differential rate of transmission** of impulses; and
- * **complete failure** of impulse transmission.

The above disturbances account for the variety of clinical signs and symptoms. Symptom remission occurs when demyelinated areas are healed by scar tissue. Due to the subsequent difficulties brought about by these scar tissues (for example impaired impulse conduction, impaired blood flow and immune reaction to inflammation) the nerve fibres (axons) themselves degenerate and the damage becomes permanent.

The disease course of MS is as varied as are the symptoms and the individuals suffering from it. Disease course classifications also vary considerably. Table 2.1 contains a comparison of two of these classification systems namely those proposed by Chipps et al. (1992) and Lubin and Reingold (1996).

TABLE 2.1: CLASSIFICATION OF MS DISEASE COURSE

Chipps et al. (1992)		Lubin and Reingold (1996) and Keegan and Noseworthy (2002)	
Type	Symptoms	Type	Symptoms
(i) Benign	<ul style="list-style-type: none"> - 20% of cases - mild exacerbations with complete or near complete remissions - minimal or no disability 	(i) Relapsing-remitting MS (RRMS)	<ul style="list-style-type: none"> - approximately 70 – 75% of MS suffers - clearly defined attacks with full recovery or with residual deficit upon recovery - periods between disease relapses characterised by lack of disease progression.
(ii) Exacerbation - Remitting	<ul style="list-style-type: none"> - 25% of cases - there are more frequent attacks early in the illness - less complete remissions - long periods of stability - some disability 	(ii) Secondary-progressive MS (SPMS)	<ul style="list-style-type: none"> - of the 70-75% of suffers that start with a RRMS disease course, more than 50% develop SPMS within 10 years and 90% within 25 years - begins with RRMS disease course but

			followed by progression of variable rate - may include occasional relapses and minor remissions and plateaus
(iii)Chronic – relapsing	- 40% of cases - fewer remissions as the disease progresses - disability becomes progressive as the disease progresses.	(iii)Progressive-Relapsing MS (PRMS)	- approximately 6-10% of MS suffers - least common disease course - progressions from onset but with clear acute relapses, with or without full recovery
(iv)Chronic – progressive	- in 15% of cases - insidious onset - steady progression of symptoms - no remissions	(iv)Primary-progressive MS (PPMS)	- 15% of MS suffers - progression of disability from onset, without plateaus or remissions, or - with occasional plateaus and temporary minor improvements.

Pryse-Phillips (2001) however is critical of these differentiations of MS into different subtypes. He especially views the distinction between the ‘relapsing-remitting’ (RR) and ‘secondary progressive’ (SP) subtypes of MS as problematic. He suggests that by viewing the symptomatic course of the disease one would notice that these so-called subtypes in actual fact represent different stages in the same disease course. He points out that when one considers the “cumulative burden” of the disease (as represented on MRI scans and subjectively experienced as symptoms) one sees a “trend towards progression with intermittent elevations corresponding to clinical ‘attacks’. Then at some arbitrary point ... the persisting, accumulated burden of symptoms and signs makes it impossible to distinguish future ‘attacks’ which impair the function of neurological systems already impaired by preceding disease activity” and thus the RR ‘subtype’ in actual fact represents the earlier stages whereas the SP ‘subtype’ represents the later stages in the MS disease course (Pryse-Phillips, 2001, p.188). This view is supported by Keegan and Noseworthy (2002) who also describe the course of MS as progressing from the RRMS (the major presentation seen in younger adults) to the SPMS presentation in a majority of patients. They further describe primary progressive MS (PPMS) in a minority of patients (about 15% of patients) and the progressive relapsing MS (PRMS) in an even smaller proportion of MS patients.

Chipps et al. (1992) also identify more specific syndromes according to the particular area of the central nervous system that is affected. These syndromes of MS are as follows:

- Cerebral syndrome
 - optic neuritis (visual clouding, loss of part of the visual field, and pain) – often an early sign of MS.
 - intellectual and emotional changes.
 - seizures.
 - hemiparesis, hemisensory loss, dysphasia.

- Cerebellar syndrome
 - motor ataxia
 - hypotonia
 - asthenia

- Brainstem syndrome
 - symptoms that reflect damage to spinal nerves III through XII.
 - intranuclear ophthalmoplegia (INO)
 - nystagmus
 - dysarthria
 - scanning speech (slow speech with pauses between syllables) in later stages of the disease.

- Spinal syndrome
 - damage to the corticospinal tracts and dorsal column.
 - spastic paresis
 - bowel and bladder dysfunction
 - paresthesia

Exacerbations of symptoms in MS have been correlated with several factors such as infection, emotional stress, pregnancy, physical injury, cold temperatures, hot baths and fatigue (Chipps et al., 1992).

2.5. MEDICAL MANAGEMENT

Currently there is no definitive cure for MS. Treatment is aimed at lengthening the intervals between exacerbations (thus lengthening periods of remissions) and alleviating the symptoms. Treatments normally used today include immune suppression, typically using corticosteroids, the use of drugs to improve conduction in demyelinated tissue and attempts toward remyelination.

According to a report by the Consortium of Multiple Sclerosis Centers (United States of America and Canada) (2000), treatment strategies fall into five general categories:

- Treatment of acute exacerbations
- Symptom management
- Disease modification
- Rehabilitation (to enhance and maintain physical function), and
- Psychosocial support.

2.5.1. Treatment of Acute Exacerbations

During this phase of treatment the corticosteroids take center stage in the treatment regime. Although precise treatment protocols differ they all seem to follow a 3 to 5 day course of high-dose intravenous (IV) corticosteroids (such as methylprednisolone), and then possibly a period during which a gradual tapering down of the dosage of corticosteroids using oral dosages of corticosteroids (such as prednisone). Corticosteroids act to decrease acute inflammation in the central nervous system (CNS) but have no long-term benefits in MS. Many individuals report “feeling better” when taking steroids and this is in part due to the fact that steroids sometimes have a mood-elevating effect.

Even though most people seem to tolerate short courses of steroids well, chronic use of corticosteroids cause many serious side effects such as hypertension, diabetes, bone loss (osteoporosis), and ulcers. Mood changes (as mentioned above) are relatively common. Individuals report feeling “high”, energetic, and unable to sleep while on corticosteroids and/or depressed and unable to sleep as they come off the medication. A small percentage of people may experience quite severe disturbances in mood or

behaviour and in these instances, lithium and carbamazepine have been shown to be effective in preventing or managing the symptoms. Once again the importance of adequate and relevant patient education/counselling comes to the fore. Patients should be educated as to the possibility of these side effects of corticosteroids and reminded that a person can react very differently to corticosteroids from one course to the next.

2.5.2. Symptom Management

Table 2.1 presents the symptoms of MS, the treatments recommended to manage these symptoms and the potential emotional and social impact of these symptoms on the individuals' lives.

TABLE 2.2: SYMPTOMS OF MS - TREATMENTS AND PSYCHOSOCIAL IMPACT

SYMPTOM	TREATMENT	PSYCHOSOCIAL IMPLICATIONS
<p><i>Ambulation Problems</i></p> <ul style="list-style-type: none"> • Spasticity • Impaired balance • Weakness 	<p><i>See:</i> Spasticity Mobility aids and exercise Mobility aids and exercise</p>	<p><i>See:</i> Spasticity Resistance to use of mobility aids:</p> <ul style="list-style-type: none"> • Perceptions of self: damaged, weak; giving in • Others' perceptions: less intelligent; less competent
<p><i>Bladder Dysfunction*</i></p> <ul style="list-style-type: none"> • Failure to store (urgency, frequency, incontinence. Nocturia) • Failure to empty (urgency, hesitancy, double voiding, feelings of incomplete emptying) • Combined failure to store/failure to empty 	<p>Anti-cholinergic agents or anti-muscarinic agents; schedule voiding; avoidance of diuretics</p> <p>Intermittent self-catheterization (ISC); may require indwelling catheter</p> <p>Combination of the above</p>	<p>Fear of drinking liquids; anxiety over loss of control; fear of leaving vicinity of bathroom; embarrassment/shame; fear of incontinence during intercourse; increased fatigue due to interrupted sleep</p> <p>Anxiety about less of control; fear of ISC</p> <p>Same as above</p>
<p><i>Bowel Dysfunction*</i></p> <ul style="list-style-type: none"> • Constipation • Fecal impaction • Diarrhea (usually from constipation) • Fecal incontinence 	<p>Bowel training; high-fiber diet; digital stimulation; exercise; medication (e.g., softeners, mild laxatives, mini-enemas)</p> <p>Manual disimpaction</p> <p>Disimpact and relieve constipation</p> <p>Bowel program; anti-cholinergic medication (for hyper-reflexic bowel)</p>	<p>Discomfort; exacerbation of spasticity</p> <p>Discomfort; embarrassment</p> <p>Discomfort; embarrassment</p> <p>Loss of control; anxiety about leaving home/being around others; shame</p>
<p><i>Cognitive Symptoms*</i></p> <ul style="list-style-type: none"> • Memory impairment • Impaired attention/concentration • Slowed processing speed • Impaired executive functions • Impaired spatial relations • Impaired word-finding ability <p><i>Note: Cognitive deficits are often missed in a standard neurologic exam</i></p>	<p><i>Non-medical:</i> cognitive rehabilitation</p> <ul style="list-style-type: none"> • Restorative approach: direct retraining exercises (have only limited benefit for daily activities) • Compensatory approach: aims to improve function via substitution of compensatory strategies/tools for the impaired function <p><i>Medical:</i> Medication may be useful; disease-modifying agents may be beneficial</p>	<p><i>Individual:</i> denial; anxiety; loss of self-esteem/self-confidence; depression; may interfere with self-care and independence.</p> <p><i>Interpersonal:</i> family strain; marital strain; impaired communication; role shifts within the family</p> <p><i>Employment:</i> major cause of high unemployment rate in people with MS</p> <p><i>Healthcare:</i> may affect communication with providers and compliance with treatment</p>

<p><i>Fatigue</i></p> <ul style="list-style-type: none"> • <i>Primary</i> (neurologic): overwhelming lassitude or tiredness that can strike at any time of day • <i>Secondary</i>: resulting from disturbed sleep; depression; extra exertion due to impairments; medications 	<p><i>Non-medical</i>: naps; moderate aerobic exercise; work simplification; use of assistive devices (e.g., electric scooter); cooling strategies/devices</p> <p><i>Medical</i>: Medication</p>	<p>Inability to carry out activities at home and at work; fatigue of this magnitude is depressing; invisible symptom that is easily misinterpreted by others</p>
<p><i>Sensory Problems/Pain*</i></p> <ul style="list-style-type: none"> • <i>Sensory symptoms</i> (from loss of myelin): numbness, tingling • <i>Primary pain</i> (from loss of myelin): <ul style="list-style-type: none"> - trigeminal neuralgia (sharp facial pain); - dysesthesias (electric shock-like sensations in trunk or extremities); - retro-orbital pain (with optic neuritis) • <i>Secondary pain</i> (musculoskeletal): resulting from poor posture/balance in ambulatory individuals or improper use/fitting of wheelchair 	<p>No treatment required unless bothersome; medication of necessary</p> <p>Medication Surgery Medications or topical application of capsaicin cream High-dose IV steroids</p> <p>Analgesics; gait training; wheelchair assessment; exercise</p>	<p>Anxiety; discomfort; clumsiness; fatigue increased by medications and interrupted sleep</p> <p>Medications increase fatigue</p> <p>Medications increase fatigue</p> <p>Steroid can affect mood</p> <p>Discomfort <i>Note: People often told by doctors that MS does not cause pain</i></p>
<p><i>Sexual Dysfunction*</i></p> <ul style="list-style-type: none"> • <i>Primary</i> (result of neurologic impairment): impaired arousal, sensory changes, reduced vaginal lubrication, erectile dysfunction, inability of reach orgasm • <i>Secondary</i> (resulting from other MS symptoms): fatigue, spasticity, bladder/bowel problems, sensory changes interfere with sexual activity. <i>[Note: impaired arousal, erectile dysfunction, and inability to orgasm can also result from medications taken to relieve other symptoms, most notably antidepressants]</i> • <i>Tertiary</i> (resulting from disability-related attitudes/feelings): feeling unattractive; unable to attract a partner; believing that sexuality is incompatible with disability 	<p>Evaluation of medications that might be interfering with sexual function <i>Men</i>: Oral medication; injectable or insertable medication, prosthetic devices, <i>Women</i>: lubricating substances; enhanced stimulation</p> <p>Effective management of MS symptoms to reduce impact on sexual function</p> <p>Individual and couple's counseling and education</p>	<p><i>Individual</i>: Significant impact on gratification, self-esteem, self-confidence, difficult/ embarrassing to discuss with healthcare providers</p> <p><i>Interpersonal</i>: Significant impact on all intimate relationships:</p> <ul style="list-style-type: none"> • Sexual activity can be difficult, exhausting, painful, and unsatisfying • Lack of arousal can be misunderstood and resented by partner • Learning new ways to be intimate can be frightening and difficult • Caregivers may become disinterested in, or uncomfortable, with their disabled partner <p>Person with MS may be reluctant to become intimate with new partner</p>
<p><i>Spasticity</i></p> <ul style="list-style-type: none"> • Phasic spasms (flexor or extensor) 	<ol style="list-style-type: none"> 1. Rehabilitative PT (stretching) 2. Oral medications 	<p>Oral medications increase fatigue and weakness Surgical implantation of pump</p>

<ul style="list-style-type: none"> Sustained increase in muscle tone <p>Spasticity can range from relatively mild to quite severe, and treatment is approached in a step-wise fashion.</p> <p><i>Note: Some degree of spasticity may be required to support weakened limbs</i></p>	<p>3. Intrathecal baclofen pump</p> <p>4. Surgery</p>	<p>in abdomen can be frightening</p> <p>Severing of tendons is irreversible</p>
<p><i>Speech/Swallowing Problems</i></p> <ul style="list-style-type: none"> <i>Dysarthria</i>: poorly articulated, slurred speech <i>Dysphagia</i>: difficulty in swallowing that can lead to aspiration and/or inadequate nutrition 	<p>Assessment, exercise program, training with augmentative or alternative communication devices, if needed</p> <p>Assessment, exercise program, modified diet, non-oral feeding strategies, if needed</p>	<p>Slurring can be misinterpreted as drunkenness or lack of intelligence</p> <p>Slow, slurred speech interferes with communication</p> <p>Fear of loss of control, choking</p> <p>Food needs to be blended</p> <p>Eating is exhausting</p> <p>Loss of pleasurable mealtimes</p> <p>Loss of ability to eat orally</p>
<p><i>Tremor</i></p> <ul style="list-style-type: none"> Involuntary movements of the arms, legs, or head; tremor can be the least treatable and most debilitating symptom of MS 	<p><i>Non-medical</i>: balance/co-ordination exercises; weights on limbs or utensils</p> <p><i>Medical</i>: Medications</p>	<p>Fear of loss of control— severe tremor is a major threat to independence</p> <p>Medications can increase fatigue</p>
<p><i>Vertigo</i></p> <ul style="list-style-type: none"> Severe dizziness and nausea caused by inflammation in the brainstem 	<p>Oral medication, fluids and high-dose corticosteroids if nausea prevents the use of oral medications</p>	<p>Interferes with functioning at home and at work</p> <p>Steroids can impact mood</p>
<p><i>Visual Impairment*</i></p> <ul style="list-style-type: none"> Optic neuritis (temporary loss of disturbance of vision, often accompanied by pain; may also cause a “blind spot” (scotoma) in center of vision. Diplopia (double vision) Nystagmus (rhythmic jerkiness or bounce in one or both eyes) 	<p>High-dose corticosteroids</p> <p>High-dose corticosteroids</p> <p>Medication if necessary</p>	<p>Visual symptoms can threaten independent functioning (e.g., driving), increase fatigue, and interfere with activities at work and at home</p> <p>Steroids can impact mood</p> <p>Medication can increase fatigue</p>
<p><i>* Invisible symptoms can be stressful since they tend to be ignored, misunderstood, or misinterpreted by other people</i></p>		

(* Table adapted from National MS Society, 2000)

2.5.3. Disease Modification

Although there are no medications or treatments that cure the disease some medications have proven to alter the process of MS significantly.

According to the National MS Society (2000), clinical trials have shown the following medications to have an influence on the disease process of the relapsing-remitting type MS:

- interferon beta 1b reduces the frequency and severity of exacerbations, reduces new or active lesions on MRI, reduces attack frequency, and may slow progression of disability,
- interferon beta 1a reduces the frequency of relapses, reduces new or active lesions on MRI, and may slow disease progression, while
- glatiramer acetate reduces the frequency of exacerbations and the number of new or active lesions on MRI.

There have been contradictory results as to the effectiveness of current available medication to positively influence the disease process of the progressive type of MS. To date there have been no medications approved in the United States of America for treatment of the primary- or secondary-progressive type MS. Clinical trials conducted in Canada and Europe found that interferon beta 1b proved no more effective than a placebo in slowing progression of disability. Clinical trials concerning interferon beta 1a and glatiramer acetate for primary-progressive and secondary-progressive MS are currently underway in North America and Europe. Mitoxantrone, a potent immunosuppressant usually used in adult myeloid leukaemia, was shown to slow progression of disability, reduce relapse rate, and reduce the numbers of inflammatory lesions in the brain, in secondary-progressive type MS. Other immunosuppressive medications are also being used to treat progressive type MS, but these treatments are viewed with a great deal of anxiety, since many patients associate these chemotherapies with cancer. “People resist the idea that their MS is ‘as bad as cancer’, and have a genuine fear of the side effects” (National MS Society, 2000, p.37). Although much lower dosages of these medications are used for treatment of MS the concerns relating to the short-term side effects (e.g. nausea and hair loss) and the long-term side effects (e.g. sterility, cardiotoxicity, liver toxicity) are valid concerns.

Considering these different treatment options, possible side effects and varied treatment results, the importance of adequate patient education/counselling once again becomes very relevant. The medical and mental health professionals need to assist patients to weigh their options and make informed decisions regarding their treatment. This will ensure adherence to disease modifying therapies and also curtail patient

despair resulting from the non-compliance of initial unrealistic treatment expectations.

2.5.4. Rehabilitation

Rehabilitation in MS should be a constantly evolving process directed toward helping the individual recover and/or maintain the highest possible level of functioning and realise his or her optimal physical, mental, and social potential. Most individuals with MS continue to have limitations even though there are disease-modifying medications available that help slow the disease progression and MS rehabilitation should therefore involve the intermittent and ongoing use of multidisciplinary strategies to promote functional independence, prevent complications and enhance overall quality of life of the individual with MS.

The rehabilitation process, according to the National MS Society (2000), usually targets the following impairments in individuals with MS: spasticity, movement disorders, weakness, imbalance, fatigue, paralysis, bowel and bladder problems, sexual dysfunction, visual disturbance, pain, sensory loss, speech and swallowing problems, and cognitive impairments. Although interventions can not restore the neurological damage caused by MS it can reduce disablement by “minimising the impact of existing impairment(s) on day-to-day functioning, and enhancing the person’s ability to carry out daily activities and participate to the fullest extent possible in all of his or her life roles” (National MS Society, 2000, p. 40).

2.5.5. Psychosocial Support

Effective and successful psychosocial support in MS requires a thorough understanding of the myriad and varied aspects related to MS. Most of these psychosocial aspects will be discussed in Chapter 4 of this dissertation and will thus not be covered at this stage. However one should note that there are a few objectives that any attempt at providing any psychosocial support to individuals affected by MS (be it official organised programmes on national scale or personal individual attempts) should aim to achieve. These are:

- disease-related education should be given as part of a supportive educational process designed to enhance individuals’ understanding of the disease, of adaptive coping strategies, and of available resources.

- diagnose and/or treat emotional and cognitive problems.
- design family interventions aimed at supporting family members' efforts to cope with the impact that MS has made on their lives.
- support MS sufferers to remain productively employed as long as possible
- help with the transition out of the workforce when and if it becomes necessary.
- help individuals with MS and their families to utilise all the possible available resources to their disposal.

Treatment of a MS patient should be an interdisciplinarian team approach as MS is a multi-focal disease, affecting various levels of an individual's functioning and involving not only the sufferer but also his or her significant others, as well as the medical team.

2.6. CONCLUSION

MS is a complex disease and is as varied as the individuals suffering from it. It exerts its effects over a large spectrum of human functioning and possesses the potential to disrupt not only the lives of affected individuals, but also those of the individual's family and friends. The broader medical fraternity is expected to possess adequate knowledge of the disease but the complex nature of this condition confounds this task immensely. The importance of thorough patient education, not only of the expected physical symptoms, but also symptoms of a psychological and social nature, becomes abundantly clear if the affected individual is to adapt successfully to the disease and if the disease is to be managed appropriately.

CHAPTER 3

FUNCTIONAL BRAIN ANATOMY RELEVANT TO THE CURRENT STUDY

3.1. INTRODUCTION

Residual problems such as decreased insight, judgement, impaired thought, organisation and apathy, have greater limitations on the social adjustment of an individual with brain injury than the effects of physical factors (Bond, 1975, as cited in Walsh, 1991; Benedict, Shapiro, Priore, Miller, Munschauer, Jacobs, 2000). This is why it is important, within the scope of the current research, to include a discussion of the functional anatomy of the brain with specific focus on the areas mostly involved with the cognitive (specifically executive functions) and psychological factors (e.g. personality changes and other psychosocial issues) involved in adaptation to MS.

When discussing psychological and behavioural change in relation to chronic disease, it is important to differentiate between factors that are due to organic dysfunction and those that are reactive to the nature of the disease. According to Walsh (1991) some of these reactive difficulties are depression, anxiety and irritability as they accompany lesions of the cortex in a large variety of localisations. Other difficulties, however, seem only to accompany lesions in certain localities, and these are therefore due to the organic condition. An example of such changes, which are frequently found in association with frontal lobe damage, is the set of changes Walsh (1991) calls a modification of personality.

3.2. GENERAL ORGANISATION OF THE BRAIN

Although the theory of Luria (1973) is more than twenty years old, it is still considered the primary theory concerning the functional anatomy and organisation of the brain. It is considered the fundamental basis for any knowledge concerning neuropsychology. Most current theories of the brain and the relation between its anatomy and function, is still based on the work of Luria. Therefore I have also made

use of this theory as starting point for the discussion on the brain's functional anatomy and how dysfunction (due to MS lesions) of these areas may lead to certain alterations in cognition, personality and social behaviour.

Luria (1973) distinguishes three principal functional units of the brain. Any type of mental activity requires the integrated functioning of all three these units. These are: (a) the unit for regulating tone and waking and mental states (consisting of the brain stem, the diencephalon and medial regions of the cortex), (b) the unit for obtaining, processing and storing information (consisting of the lateral regions of the neocortex where it occupies the posterior regions, including the visual (occipital), auditory (temporal) and general sensory (parietal) regions) and lastly (c) the unit for programming, regulating and verifying mental activity (consisting of the anterior regions of the hemispheres, anteriorly to the precentral gyrus).

All mental processes in humans, especially their conscious activities, take place with the participation of all three these units. Each form of conscious activity is always the result of a complex functional system with all three functional brain units taking part, be it in varying degrees. All three units are in themselves hierarchical in structure and each is made up of at least three cortical zones namely, the primary (projection) area which receives impulses from or sends impulses to the periphery, the secondary (projection-association) area where incoming information is processed or programmes are prepared, and finally, the tertiary area (zones of overlapping) responsible for the most complex forms of mental activity requiring the cooperative participation of many cortical areas.

3.2.1. First Functional Unit of the Brain

The first functional unit, regulating tone and waking and mental states, is responsible for maintaining an optimal level of cortical tone which is necessary for organised, goal directed activity. To maintain this level of excitation certain theoretical concepts become important. Firstly the law of strength should be functional, i.e. that the strength of the response is directly correlated to the strength of the stimulus; secondly a certain concentration of nervous processes should be maintained and a balance in the relationships between excitation and inhibition upheld; and thirdly the nervous processes should also be of high mobility, that is, it should be easy to change from

one activity to another. In a state of sleep these factors are not upheld and in this state of inhibition (Luria, 1973) an organised course of mental activity is not possible. This unit, however, cannot maintain cortical tone without the structures of the subcortex and brainstem. The most central of these structures is the reticular formation. It serves as a nerve net gradually increasing the excitation level of the unit, ultimately modulating the state of the entire nervous system. The ascending reticular formation consists of fibres running upward from the reticular formation connecting it to the thalamus, caudate nucleus, archicortex and lastly the neocortex, activating the cortex and regulating its activity. On the other hand, the descending reticular formation runs in the opposite direction originating in the neocortex and ending in the brain stem. It has the function of modulating the state of waking as required by the initiated programs in the cortex that require these modulations for their performance. The ascending and descending reticular formation thus forms a reciprocal relationship between the reticular formation and the cortex, causing the reticular formation to both influence the tone of the cortex, as well as being regulated by it.

3.2.2. Second Functional Unit of the Brain

The second functional unit of the brain, the unit for receiving, analysing and storing information is characterised by modality specific zones that are hierarchically organised. The primary and secondary zones are responsible for receiving and processing of incoming information and the tertiary zone for converting concrete perception into abstract thinking, this includes symbolic representation as well as memorising organised experience. This second unit does not serve as a nerve net, as does the first unit, but is organised into isolated neurons obeying the “all-or-nothing” rule. Luria (1973) distinguishes three basic laws governing the workings of the second and third functional units of the brain. They are the law of hierarchical structure of the cortical zones, the law of diminishing specificity of the hierarchically arranged cortical zones and the law of progressive lateralisation of functions.

3.2.3. Third Functional Unit of the Brain

The third functional unit of the brain is the unit for programming, regulating and verifying activity. It has the function of organising conscious activity. It is involved in the process of forming intentions and plans and in programming actions, as well as

regulating behaviour so that it conforms to these prior formed plans and intentions. This unit is also involved in the subsequent verification of these actions.

These processes require functionally different brain structures and it is for this reason that the third brain unit is functionally different to both the first and second units. It is situated in the anterior regions of the brain i.e. anterior to the precentral gyrus thus comprising the frontal lobes. The outlet channel for this brain unit is the motor cortex, involving also the great pyramidal tract (for motor activation) as well as the extra-pyramidal system (for providing a tonic background).

Impulses sent by the primary motor cortex to the muscles are first converted into appropriate motor programmes in the structures of the precentral gyrus (such as the extracellular grey matter) and the secondary and tertiary areas of the motor cortex. This unit also obeys the principles of hierarchical organisation and diminishing specificity governing the organisation of the second functional unit of the brain, but in this unit the impulses move from the tertiary and secondary areas to the primary areas for conduction to the body.

As mentioned earlier the frontal lobes are a very important part of this third functional unit of the brain. They play a decisive role in the processes associated with the third unit of the brain. An indication of this role is the many rich two-way connections that the frontal lobes have with both lower levels of the brain (such as the medial and ventral nuclei and the pulvinar of the thalamus) as well as with most other parts of the cortex (such as the occipital, temporal and parietal regions as well as with the limbic regions). A particularly important connection of the medial and basal regions of the frontal lobes are with the reticular formation which in effect connects the third functional unit with the first functional unit of the brain. It has been shown that these regions of the frontal lobes exert their regulative influence on the higher forms of activation in close association with speech. In other words, the higher mental processes of human beings are based on the activity of speech. The importance of the frontal lobes in the processes of the third functional unit of the brain is summarised by Luria when he states that “it can thus be concluded that the frontal lobes of the brain are among the vital structures responsible for the orientation of an animal’s behaviour

not only to the present, but also to the future, and that they thus are responsible for the most complex forms of active behaviour.” (Luria, 1973, p.91)

3.3. THE FRONTAL LOBES

3.3.1. The Role of the Frontal Lobes in Adaptive Behaviour

"For behaviour to be effective, it must meet environmental conditions. It must be appropriate, modifiable, energised or motivated and be free from disruptive internal influences. Effective behaviour requires an anticipatory relationship to the goal in the form of planning. It requires the ability to monitor ongoing actions as to effect change, should deviations from the plan occur, and the effectiveness of action must finally be checked against the anticipated outcome and any necessary adjustments made." (Walsh, 1991, p.170)

The actions as described above are impossible if the frontal lobes are not intact. Damasio (in Heilman & Valenstein, 1985) furthermore states that dysfunction of the frontal lobes do not lend themselves easily to quantitative measurement for they are more readily described as changes in quality. He states that while patients with frontal lobe dysfunction often do not show significant impairments in objective measures of language and allied abilities, it does not mean that the individual's personality has not been affected. Often the most prominent signs of frontal lobe dysfunction are subtle changes in alertness, affect, emotional response, appropriate control of regulatory behaviours and high-level problem solving.

Considering that the main objective of this study is to explore the involvement of certain cognitive (especially executive functions) and psychological factors (personality changes and other psychosocial issues) in the disease process in a group of MS patients, it is necessary to include a discussion of the functional integrity of the frontal lobes.

Walsh (1991) describes three functional areas of the frontal cortex each of which is responsible for qualitatively different modes of behaviour. Firstly the dorsolateral cortex which has to do with the preparation and execution of actions, then the medial

frontal cortex which mediates self-initiated actions and also sustains behaviour at an appropriate level and lastly the basal/basomedial cortex which is in control of inhibition and excitation and the emotional control of behaviour.

The *dorsolateral frontal cortex* can be divided into three subzones, namely pre-frontal cortex which is related to ideation or intellectual control of actions, the premotor cortex which serves as an integration centre for complex movements and the motor zone for the implementation of movements. Two specialised areas are also situated within this division of the frontal cortex. They are Broca's area serving a language function and the frontal eye fields which have to do with visual scanning and perceptual integration. Damage to this dorsolateral area of the frontal cortex leads to problems in planning, learning, conceptual behaviour and problem solving. It can be seen in the uncritical attitude which frontal patients show to their own actions, but more significantly to their own errors. This is an example of the frontal lobe paradox where the individual's intelligence is seemingly preserved or restored but these individuals fail to cope with the demands of their occupations or professions. The person seems to know what is to be done, yet does not do it.

Walsh (1991) puts forward a controversial hypothesis as explanation for the above occurrence. He states that it is as a result of 'imperfect learning' where the individual has trouble adapting old programmes of learning to new situations or show insufficient new learning due to the lack of organisation of the material to be learned. Some of these difficulties also seem to be a result of the individuals' lack of inhibition causing them to respond in previously appropriate modes and lead to frustration when they find themselves doing so. This lack of inhibition is however more related to the basal or orbital cortex than to the dorsolateral cortex. These individuals also show a shift from a conscious mode of behaviour based on abstract thought processes to a "concrete determination of behaviour by aspects of the present situation" (Walsh, 1991, p.174). This implies that the individuals show little concern for the past or the future. They are unable to construct goals in the form of planning and check ongoing actions to ascertain whether they are effective and, if not, to adapt these actions. All these processes have been described as the individual having undergone a personality change.

Dysfunction in the *basal and basomedial frontal cortex* seems to be the more prominent area when discussing personality change due to frontal lobe damage. The core underlying personality changes which lead to disability seems to be the loss of inhibition. The behaviour of such individuals place great strain on their families, friends and caregivers. To lack inhibition means that an individual loses the ability of intellectual selectivity, i.e. lacks the function of suppressing inappropriate responses.

The major problem related to *medial cortex* lesions is a state of adynamia. It is obvious what the impact of this state has on the individual and his/her relationships with significant others. The reason being that this state of passivity and lack of ability to initiate and sustain action could be construed by the uninformed as being of a psychological nature and is thus seen as problems of resistance, apathy and depression.

3.3.2. The Frontal Lobes and Multiple Sclerosis

Multiple Sclerosis has a devastating impact on the cognitive functioning of the individual. However, this is not the only area in which the patient encounters difficulty. Benedict et al. (2000) state that although little is known about the neuroimaging correlates of personality change in MS, behaviours such as behavioural disinhibition, social aggression and euphoria seem to be associated with personality changes in these individuals. These symptoms in turn are also correlated with executive dysfunction and thus seem to be related to frontal lobe involvement in MS. They further cite research which supports the notion that these symptoms have a devastating impact on the quality of life of both the individual with MS and their caregivers. These frontal lobe symptoms are however not easily detected on standard neuropsychological screening and are often misconstrued as wilful behaviour thereby complicating interpersonal relationships and attempts at rehabilitation. Add to this the fact that these types of symptoms are resistant to standard behavioural or psychiatric treatment and it becomes clear how complicated the situation becomes if not accurately assessed and managed.

Rao et al. (1991) furthermore conclude that multiple sclerosis has a devastating impact on the patient's psychosocial functioning. In their research, Rao et al. (1991)

made use of close relatives or friends of the MS patients, to rate the patients' personality. These informants viewed the patients as confused and emotionally unstable. This pattern of behavioural disturbance appeared to be unrelated to clinical depression. These patients showed apathy, confusion and diminished interest in social and employment activities.

When studied closely, the above symptoms as discussed by Rao et al. (1991) and Benedict et al. (2000), resemble the symptoms of the frontal lobe syndrome as described by Russell and Roxanas (1990). She states that changes occur primarily in the personality of the patient and result in altered behaviour and social awareness along with changes in activity level, motivation and habitual mood. She goes on to state that the "associated cognitive deterioration is more apparent than real, although the lack of real insight is usually striking as is the inability to apply knowledge to real life situations and the difficulties in planning, organising and sequencing. In addition there may be a diminution of spontaneity and initiative along with distractibility, short attention span and difficulty with goal directed activity, resulting in impaired efficiency. Alternatively, presentation may be more one of apathy and indifference, slow thought, lethargy, psychomotor retardation and a lack of motivation and facial expression. The patient may appear to be depressed but may engage in short bouts of aggressive behaviour if irritated" (Russell & Roxanas, 1990, p.118)

It is also proposed by Stuss et al. (1992) that the primary aspect of frontal lobe pathology is a disorder of personality. This implies a change in the stable response patterns that define an individual as a unique self. Within this view, we find the relationship between cognitive abilities and personality. They state that "dysfunction of personality includes cognitive abilities, with a disorder of self-reflective awareness as a key deficit." (Stuss et al., 1992,p.349)

It would then seem that frontal lobe symptoms might account for a great majority of personality and other psychological problems encountered by the MS patient. It is thus not just a simple matter of superficially attributing these difficulties to mere psychological states of mind, depression or inability to cope (Peyser, 1984). Furthermore, the symptoms of frontal lobe dysfunction are often so subtle that they are overlooked during the routine neurological examination.

It is at this stage that the accurate assessment of the cognitive deficits directly related to frontal lobe dysfunction become important because of their possible influence on these types of personality and other psychological difficulties. Reasons for suggesting this originate from the research findings stated above, as well as in the sighting of the literature that follows:

- Grigsby et al. (1993) hypothesises that MS patients whose lesions have essentially isolated the frontal cortex may present behaviour management problems and are often described by caregivers as unmotivated or excessively impulsive. These lesions may also cause cognitive functioning to have a passive quality, with an associated decrease in ability to direct attention and information processing resources actively.
- Huber et al. (1992) states that impairments in executive function traditionally linked to frontal lobe lesions, are common to neuropsychological deficits in MS.
- According to the research of Mendozzi, Pugnetti, Saccani, and Motta (1993), patients who have specific impairments on tests sensitive to frontal lobe deficits have shorter disease duration and are less physically disabled than those failing on the parietal tasks or those with combined deficits. This is extremely important as the earlier the detection and thus, the diagnosis, the more effective the action that can be taken for treatment and rehabilitation.
- Benedict et al. (2000, p.395) state that “personality change and pathological affect are known to be associated with neuropsychological measures of executive ability” and that these symptoms as well as impaired social behaviour were mainly associated with reduced metabolism in the inferior aspects of the frontal lobes.
- Further research also shows that, relative to individuals without MS, deficits on tests sensitive to frontal lobe damage were more severe in patients with clinical onset around age 20 than those patients with later onset. It is thus proposed that

greater disease activity interacting with developmental factors are responsible for the appearance of temporary frontal deficits in several young MS patients (Mendozzi et al., 1993)

- Frontal lobe dysfunction is also inherent in the personal experience of the MS sufferer. Taylor (1990) found discrepant ratings on everyday cognitive difficulties between patients themselves and those of informants. This discrepancy related to the performance on tests considered sensitive to frontal lobe dysfunction. It goes to show that neuropsychological assessment on these deficits is very important for positive diagnosis.
- According to Beatty et al. (1989), MS patients fail to make effective use of semantic encoding to aid memory and perform poorly on verbal fluency and concept formation tests that are sensitive to frontal lobe damage.

The psychological changes (especially those of personality and lack of insight) that occur in patients cause great distress for the patients, their caregivers and relatives. This is especially so if such behaviour is viewed not as a result of brain dysfunction, but as the patient being 'difficult', lazy or deliberately insensitive (McIntosh-Michaelis et al., 1991). It is therefore crucial that the significant others in the patients' lives should be involved in research done to examine the MS patients' daily difficulties due to these psychological changes.

3.3.3. The Frontal Lobe Syndrome

In an attempt to describe to set of symptoms that manifested with frontal lobe dysfunction, Luria (1973) coined the term 'frontal lobe syndrome'. Depending on the locale of the affected part of the frontal lobes, the symptoms of the 'frontal lobe syndrome' involve the following:

- a marked disturbances of the organisation of movements and actions,
- disintegration of motor programmes,
- disturbance of the comparison of human motor behaviour with the original plan,

- disintegration of speech activity itself (e.g. pathological inertia of speech) and of behavioural acts which especially depend upon participation of speech for their regulation,
- distinctive inactivity of the speech processes,
- difficulty in expressing a thought in discursive speech,
- generalised disinhibition,
- gross changes in affective processes,
- sharp decrease in cortical tone, leading to disturbance of the working state and sometimes to oneiroid (dream) states,
- gross disturbance of memory,
- disturbance of the selectivity of mental processes in which the patients are no longer clearly oriented relative to their surroundings or their past. As a result they utter uncontrollable confabulations and their consciousness become disturbed.

Furthermore, although patients' intellectual abilities remain potentially intact, they are severely disturbed by this increased disinhibition of their mental processes. This leads to uncontrollable impulsiveness and fragmentation so that they cannot carry out planned and organised intellectual activity (Luria, 1973).

Damasio (in Heilman & Valenstein, 1985) is however sceptical of the use of the term 'frontal lobe syndrome' as he states that "the notion of a single frontal lobe syndrome is just as absurd as the notion of a single frontal lobe function" (Heilman & Valenstein, 1985, p.369). He alternatively proposes the use of "symptom clusters that derive manifestations from different structural sectors of the frontal lobes" (Damasio in Heilman & Valenstein, 1985, p.369). However, Damasio does describe symptoms resulting from damage to the orbital sector of the frontal lobes and states that these symptoms are those usually associated with the concept of the 'frontal lobe syndrome'. This clinical picture is dominated by a major disturbance of personality, although basic memory function and other intellectual abilities are preserved (Heilman & Valenstein, 1985).

3.4. BRAIN STRUCTURES RELATED TO AFFECT

The term *limbic system* refers to an extensive grouping of structures including the limbic lobe (cingulate gyrus and the parahippocampal gyrus, as well as the subcallosal gyrus, the hippocampal formation and the dentate gyrus), the temporal lobe, the anterior portion of the insula, the posterior orbital surface of the frontal lobe and a number of subcortical nuclei such as the thalamic, hypothalamic, septal and amygdaloid nuclei. It is also believed that there is a close relationship between the limbic system and the midbrain's reticular formation and the reticular nucleus of the thalamus (Walsh, 1994). The limbic system receives input from many areas of the neocortex and in turn is extensively interconnected with the hypothalamic centres involved in basic drives as well as endocrine and autonomic function¹ (Heilman & Valenstein, 1985).

According to Damasio (1994), the limbic system plays an important role in emotions and feelings, as well as in the enactment of drives and instincts and in participating in the regulation of the brain stem and hypothalamus. Historically, a pathway in the limbic lobe (i.e. cingulate hippocampus fornix mammillary bodies anterior thalamus cingulate) has been described as an important central mechanism serving emotional feeling and expression and the hypothalamus has been described as the effector of emotion (Papez, 1937 in Heilman & Valenstein, 1985). Furthermore, Bard (1934, in Heilman & Valenstein, 1985) demonstrated that the hypothalamus played an important role in mediating the rage response.

It is important to note that the frontal lobes have particularly strong limbic connections and frontal lobe lesions can cause prominent emotional changes, especially damage to the mesial area of the frontal lobe which is associated with, amongst others, a major disruption of the expression and experience of affect (Damasio in Heilman and Valenstein, 1985).

¹This explains the physiological changes in endocrine and autonomic functioning associated with emotional reactions.

According to Heilman & Valenstein (1985), both the subcortical (brainstem, thalamic, basal ganglionic) and the cortical regions are necessary for normal arousal responses. The limbic and hypothalamic areas, furthermore, mediate the expression of particular emotions with their characteristic motor, autonomic, and endocrine components. They go on to state that cortical lesions may influence emotion in different ways by either interfering with the cognitive aspects of emotion, or by impairing the arousal mechanisms, or by disconnecting intact cognitive capacities from the limbic-hypothalamic systems (which provide information about basic needs and which mediate emotional expression) with resultant emotional flatness or the disinhibition of emotions.

Right hemisphere lesions seem to interfere with emotions more profoundly than lesions in the left hemisphere. Mainly because the right hemisphere lesions reduce arousal and possibly because the right hemisphere is specialised for the cognitive processes necessary for the perception and expression of emotions. It is, however, not known whether the right and left hemispheres differ in their anatomical relationships with the limbic system (Heilman & Valenstein, 1985).

3.5. CONCLUSION

From the discussion above it is clear that the relationship between the anatomy of the central nervous system and its function is complex and by no means completely understood. It is a grave mistake to assume that the nature of the relationship between a structure's anatomy and its function is a single, linear cause-and-effect relationship. The structures of the brain are enveloped by numerous interconnections and to exhibit a single neurological function the input from various structures, in various areas are required.

The frontal lobes especially pose a problem when attempts are made to quantify and objectively measure their functions. These functions are often called the higher or executive functions and makes up a great part of those functions that make individuals unique, in other words their individual personalities. Considering the nature of the frontal lobe functions, as well as the enormous amount of interconnections between

these lobes and all other areas of the brain, it becomes clear why dysfunction of these lobes have such far reaching effects and why these effects are so difficult to study.

Even more complex is the relationship between emotion and functional anatomy. While we know that the limbic system has a big role to play in the experiencing and expression of emotion, we are also aware that emotion is not only made up of neurological components but also endocrine and humeral components. This implies that not only does the limbic system receive input from many areas of the neocortex but in turn exerts influences on the hypothalamic centres involved in basic drives, as well as the endocrine and autonomic nervous systems.

An attempt has been made to demonstrate the interconnectedness of the functional anatomy of the central nervous system not only within itself but also concerning its effects on the individual's neurological functioning, personality, emotions, and behaviour.

CHAPTER 4

THE PSYCHOSOCIAL EFFECTS OF MULTIPLE SCLEROSIS

4.1. INTRODUCTION

MS has many effects on the life and functioning of patients and their families. As discussed in Chapter 2, MS pervades the entire scope of the affected individual's life - physical, cognitive, psychological, and social. Not only does MS present the patients and their families with difficulties similar to those associated with many other neurological disorders, but due to its uncertain, yet pervasive onset and disease course also present the patients and their families with many unique and varied challenges (Feinstein, 2004; Hakim et al., 2000).

In this chapter some of the psychosocial effects of MS are considered and discussed. The term 'psychosocial' is used in the broadest sense of the word. It includes aspects that vary from the very personal or internal, such as the patients' personal life and life-plans, self-confidence and self-esteem, personality, and emotional state, as well as the more external effects such as the patients' relationships with their families, their employment and economic status and aspects of their future (Simons, 1984 in Murray 1995). It is also important to keep in mind that the individual's psychosocial status should not be viewed in isolation and that it is influenced by various other aspects such as the individual's mobility, bladder and bowel control, mood, sexual functioning and mental changes (Murray, 1995).

The importance of considering the possible manifestation of affective disorders in MS, as well as the influence these disorders have on the individual's functioning, is highlighted by Rodgers and Bland (1996, p.441) when they state that "changes in mood, personality and cognitive functioning are amongst the most disabling and distressing symptoms for individuals diagnosed with MS, yet patients and their families receive little understanding or help with these problems. When behavioural changes are addressed, the changes are described simply as emotional reactions to the life situation or poor adjustment to chronic illness."

These psychosocial factors furthermore differ from the physical, neurological and cognitive factors involved in MS with regard to their relationship with the disease course. The neurological indicators progress in line with the progression of the disease course. However, the psychosocial indicators such as coping and emotional factors often do not show this similar progressive relationship because "...personality traits, emotional problems, and coping behaviours are present before the onset of the disease and may worsen, stay the same or improve as the disease progresses." (Murray, 1995, p.198).

It is no longer acceptable to view affective disorders merely as a psychological reaction to illness. Matters are more complex and recent research has shown that there are other possible variants that play a role in the manifestation of these affective disorders in MS. Affective symptoms might occur as a side-effect of steroids used to manage the symptoms (especially during exacerbations) of MS and, more importantly research is showing that the occurrence of affective symptoms most likely has a neurological etiology due to factors such as the precise location of brain demyelination with resultant specific brain lesion areas that are associated with affective symptoms in MS (Rodgers & Bland, 1996).

4.2. EMOTIONAL STATUS

4.2.1. Stress

It seems plausible to assume that anyone with a chronic progressive disease like MS experiences a great deal of stress regarding the diagnosis and may subsequently experience varying degrees of stress at various times during the disease course. Murray (1995) states that it is always stressful for a person to hear the diagnosis of MS. After diagnosis the individual who was previously healthy must now adapt to the reality of symptoms and problems, the future becomes uncertain, expectations and plans need to be reviewed, and an extreme likelihood of increased neurological deficit and disability is anticipated. Burnfield and Burnfield (1984, in Murray 1995) state that MS patients go through a process similar to bereavement.

According to Murray (1995), the period during which the individual's symptoms are being investigated, but the cause has not yet been identified, is especially stressful to the individual. During this period the patient often experiences definite symptoms and they know something is seriously wrong, but due to the nature (vague, insidious, and non-specific) of these symptoms, and sadly sometimes due to the inexperience of medical professionals, a specific diagnosis is forever forthcoming. At worst the symptoms are considered to be due to some psychosomatic condition and this causes extended psychological and physical suffering and resultant stress for the patient, until a correct diagnosis of MS is made. Often doctors think that it is kinder to keep the diagnosis and explanations vague or not to tell the patient of the diagnosis at all or even worse to not tell the patient but to tell their families about the diagnosis. Although this is done with the best intentions, research (Sencer, 1988; Burnfield, 1984; Elain, 1985; all in Murray, 1995) has shown that this causes significant additional stress to the patient. The patient might experience anxiety due to experiencing symptoms that are clearly serious with the additional suspicions that the doctor is not telling them the truth. Also, patients might be expected to function normally i.e. in the absence of a diagnosis, and might even be suspected of being hypochondriacs or malingerers by loved ones, employers and even the patients themselves. This may furthermore lead to patients becoming more active in trying to establish their own diagnosis which could increase conflicts with family, friends and doctors (Murray, 1995).

Research concerning the role of stress in MS has mainly focussed on two aspects namely, whether stress contributes to the onset of the disease and whether it precipitates exacerbations (Rao, 1990). Case study investigations have indicated an association between stress and MS in general but controlled clinical studies have failed to indicate a distinct relationship between stress and either the onset of MS or the exacerbation of MS (Murray, 1995; Rao, 1990). Possible reasons why clinical studies have failed might be related to the myriad of methodological difficulties involved in studying such a relationship (e.g. difficulties in defining and assessing 'stressfulness' or stress events (La Rocca, 1984; Murray, 1995) or might be ascribed to the fact that the relationship between stress and MS might not necessarily be a direct causal relationship. Murray (1995), as well as Rao (1990) state that stress might indirectly exert its influence on the course of MS via modulation of immune function.

This statement become even more important if we consider the fact that the immune response is involved in the pathophysiology of MS. It thus seems reasonable to assume an underlying physiological relationship between the occurrence of stress and the onset or exacerbation of MS symptoms.

The discussion above requires an elaboration of the role and mechanisms through which psychosocial factors, and stress in particular, influence immune function. The specialised field of psychoneuroimmunology² (PNI) is producing a growing body of evidence (Ader, Felten and Cohen, 1991; Daruna & Morgan, 1990) regarding the influence (mostly detrimental) that psychosocial factors have on immune function. Although it is not within the scope of this study to venture into the vast field of PNI, it is important to consider the relationship between these factors and understand the possible mechanism by which this relationship is effected.

4.2.1.1. Mechanisms through which psychosocial factors influence immune function.

Psychosocial factors exert an influence on the functioning of the immune system via four major pathways namely: (i) via lymphocyte-mediated immune-effector activity, (ii) by endocrinological activity, (iii) directly via peripheral nervous system innervation of lymphoid glands, and (iv) through hypothalamic integration (Daruna & Morgan, 1990). The *first pathway* entails the immune system's identification of potential pathogens by detecting alien macromolecules or antigens (located on the surface membranes of the foreign objects). The lymphocytes respond to these alien antigens after the antigens have been processed by antigen-presenting cells such as the monocytes and macrophages (the first line of defence of the immune system). Antigen-presenting cells display fragments of the alien antigens on their surfaces and physical interactions between these antigen-bearing cells and lymphocytes lead to lymphocyte activation. The process of lymphocyte activation is facilitated by interleukin-1 (a monokine released by macrophages). Activated T-lymphocytes produce lymphokines (such as B-cell growth factor, B-cell differentiating factor, interleukin-2 and interleukin-4) which facilitate immune-effector activity with subsequent elimination of the alien antigen by firstly promoting maturation of B-

² Psychoneuroimmunology is a specialist field that aims to study the interconnectedness and reciprocal influence of psychological, neurological and immune factors on one another.

lymphocytes into anti-body producing plasma cells, and secondly by enhancing the cytotoxicity of natural-killer cells and cytotoxic T lymphocytes (both these cell types attack the alien antigen directly through phagocytosis).

The *second pathway* relies on the eventual release of hormones that either increase or decrease immune function. The pituitary, adrenal cortex, thyroid and gonads are all centres involved in the functioning of this mechanism. Peptides (such as adrenocorticotrophic hormone (ACTH), luteinizing hormone, beta-endorphin, follicle-stimulation hormone, growth hormone, oxytocin, prolactin, thyroid-stimulating hormone (TSH) and vasopressin) that are released by the pituitary exert their actions on lymphocytes either directly, by binding to the cell (beta-endorphins, beta-endorphin, growth hormone, oxytocin, prolactin, and vasopressin), indirectly, by stimulating endocrine gland secretions i.e. hormones (luteinizing hormone) or by means of both these actions above (ACTH and TSH). Endocrine-gland hormones known to influence immunity include the corticosteroids, thyroxine, and steroids produced in the gonads (testosterone, estrogen, and progesterone). Just like the peptides, the hormones also influence the lymphocytes either directly, by binding directly to lymphocytes (corticosteroids, thyroxine, and progesterone) or indirectly, by affecting the release of thymosins from the thyroid (testosterone and estrogen). It is important to note that the influence of the endocrine system on the immune system is subject to regulatory feedback originating in the immune system. A two-way relationship thus exists between the endocrine and immune systems. Peptides derived from the thymus and macrophages (thymosins and interleukin-1, respectively) seem to modulate endocrine activity through the hypothalamus. Lymphocytes also release neuroendocrine peptides (such as ACTH, beta-endorphin and TSH) and could therefore further also influence endocrine activity directly.

The *third pathway* is via the direct innervation of the lymphoid organs and adrenal medulla via nerve fibres of the autonomic nervous system. These nerve fibres and adrenal medulla release various neurotransmitters (such as acetylcholine, epinephrine, and norepinephrine) and peptides (such as vasoactive intestinal peptide and neuropeptide Y) that modulate immune function.

The *fourth pathway* entails the hypothalamus' integration of endocrine and neural influences on immune function. The hypothalamus is able to achieve this integrative function largely due to the characteristic functioning of the paraventricular nucleus which is found within the hypothalamus. The paraventricular nucleus is considered the "... most likely site through which psychosocially induced alterations in neocortical and limbic patterns of activity could produce changes in immune responsiveness" (Daruna& Morgan, 1990, p.9). This function is made possible by (i) the neural projections that the paraventricular nucleus has to the autonomic centres in the medulla (parasympathetic) and the spinal cord (sympathetic) - neurons containing peptides released by the posterior pituitary (oxytocin and vasopressin) and neurons containing corticotrophin-releasing factor and thyrotropin-releasing hormone (which control release of ACTH, beta-endorphin, and thyroid-stimulating hormone from the anterior pituitary) are found in the paraventricular nucleus, (ii) the direct projections from the nuclei in the medulla oblongata (which transmit visceral afferent feedback originating partially in lymphoid tissue) and subfornical organ (which is capable of responding to macro-molecular bloodborne factors that originate from sites of immunological activity due to the absence of a blood-brain barrier) that the paraventricular nucleus receives, and by (iii) the fact that the paraventricular nucleus appears to be under direct control of higher-order neural systems - the paraventricular nucleus receives a major projection from the bed nucleus of the stria terminales and is thus subject to modulation by the neocortex and limbic system (including the amygdala and hippocampus).

All said and done, the fact still remains that the precise nature of the relationship between stress, specifically, and either the onset or exacerbation of MS still remains unclear. However, what is important is to remember that stress may be either a causal factor or a consequence of the MS disease course. La Rocca (1984) suggests that a more accurate model for understanding the role of stress in MS may be to consider this relationship as circular - i.e. MS produces stress and enhances the impact of other events, in turn precipitating disease activity.

Pulton (1977, in Rao, 1990, p.206) notes that since "... MS patients cannot be isolated from stress, some type of intervention to help individuals cope more effectively might be useful". This seems to reiterate the importance of supportive structures such as

support groups, not only for assisting the patients themselves but also for supporting the caregivers and the families of those individuals with MS. It could furthermore be useful to be able to identify possible sources of stress for individuals with MS if supportive structures and therapeutic interventions are to be successful in reducing the influence of stress on disease course.

Box 4.1 contains some factors that might be considered when implementing any of the supportive measures discussed above.

BOX 4.1: FACTORS THAT LEAD TO RECURRING STRESS IN MS
1. A lack of short-term memory and problems with judgement, such as some loss of the person they once were. This is important for both the patient and his/her significant others.
2. The patient quite often suffers from incontinence which leads to embarrassment and frustration.
3. Anxiety because of the uncertainty inherent in the disease, life expectancy and so forth. Will they wake up tomorrow with the loss of another functional ability?
4. The patient might suffer from sexual abnormalities.
5. Quite often the patient suffers either from a lack of income due to inability to work, or a shortage of funds due to MS related expenses.
6. The worry about possible nursing home placement and the feeling that they are a burden.
7. The patient often feels a lack of personal space and a lack of time and ability to do things.
8. The patient is quickly exhausted and does not have much energy left to have fun and relax.
9. The nature of the illness often results in the fact that the patient can no longer take part in social activities and thus loses friends and becomes isolated.
10. The mere practical implications of losing his/her drivers licence, and thus the lack of individual freedom and the dependency on others for transportation, can lead to great stress.
11. The loss or re-defining of the home role of the patient.
12. Loss of the ability to be physically active, especially if this was important to the person in their life before MS.
13. Loss of the ability to give help to others.
14. Stress over the way they view their body image is a very serious factor.

(Soderberg, 1993)

4.2.2. Disturbances of Affect

Changes in the mental status (cognitive and emotional aspects) of patients with MS may be common but they may be overlooked because of the emphasis on the physical symptoms. Affective disturbances such as depression, bipolar affective disorder, late-stage euphoria, and pathological laughing and weeping frequently occur in MS (Rodgers & Bland, 1996) with depression seemingly having the highest incidence and prevalence in MS (Kesselring & Klement, 2001; Feinstein, 1995 and 2001; Brassington & Marsh, 1998; Minden, Orav & Reich, 1987; Whitlock & Siskin, 1980) followed by bipolar affective disorder (Joffe, Lippert, Gray, Sawa & Horvath, 1987). Generally speaking these affective disturbances seem to be more common during exacerbations and in the chronic progressive disease course (Rodgers & Bland, 1996). There also seems to be a dissociation between affect and disability (Rodgers & Bland,

1996; Petersen & Kokmen, 1989) thus pointing to the possibility that changes in affect may not merely be a reaction to the disability brought about by MS.

Lyon-Caen et al. (1986) found abnormalities of affect such as affective incontinence, lability and over-sensitivity to emotional stimuli which were unrelated to depression but were however closely correlated with the presence of cognitive and memory disturbances. Rao (1990) found the incidence of depression in individuals with MS to be greater than in controls with comparable neurological conditions suggesting that the etiology of affective disturbance (especially depression) in MS might be more than just a reactive response to a disabling disease. Joffe et al. (1987) furthermore found the incidence of bipolar affective disorder to be approximately 13 times higher in their MS research sample than would be expected for the general population.

The precise relationship between affective disturbance and MS remains unclear but Joffe et al. (1987) suggest three possible reasons for this relationship. Firstly, they consider that the manifestation of a disorder of affect could be construed as a psychological response to a disabling disease. Secondly, they consider the possibility that these affective disturbances and MS share a common neurological substrate and thirdly, that an unknown factor involved or related in some way to immune function (note here the inflammatory reaction underlying demyelination, as well as the autoimmune nature of MS, as discussed in chapter 2 of this document), might serve as a common etiological agent for both conditions. Fassbender et al. (1998) add a fourth possibility, namely that affective disturbances in MS could causally be related to brain abnormalities occurring as a result of the MS disease process. Garland and Zis (1991) suggest further explanations for the relationship between affective disturbances and MS. As Joffe et al. (1987), these authors suggest that structural lesions produced by MS may cause affective disorders. However, they also suggest two additional possibilities namely, that (i) MS acts as psychosocial stressor in individuals who might be either biological and/or psychologically predisposed to major depressive or manic episodes, and (ii) a possible genetic link in susceptibility to MS and affective disorders might exist.

Whatever the cause might be, it remains undeniable that the occurrence of affective disorders in MS cause great additional stress for both the individuals with MS and

their significant others, and more often entail negative implications for these individuals' psychosocial, employment and rehabilitative processes.

Rao (1990) suggests that it is advisable to make a distinction between the affective disturbances of depression (thus unipolar) and bipolar affective disorder on the one hand, and euphoria and pathological laughing and weeping on the other, when discussing affective disturbances associated with MS. He maintains that these two categories of affective disturbances differ from each other in mainly two ways. Firstly, he states that euphoria and pathological weeping and laughing seem clearly attributable to structural brain disease as these symptoms are also found in other neurological conditions such as stroke, amyotrophic lateral sclerosis and other diseases that damage the subcortical forebrain structures, whereas the relationship between neurological substrates and unipolar and bipolar affective disorders still remain cloudy (the ever present fact that these symptoms could additionally be ascribed to being a psychological reaction to having a disease).

Secondly, he states that the emotional dysregulation seen in MS differs in nature to that seen in psychiatric patient populations. In psychiatric patient populations the emotional fluctuations are more a matter of emotional lability (“rapid oscillations of feeling states” (Rao, 1990, p.190)) such as seen in borderline personality disorder, as opposed to the emotional fluctuations seen in MS patients which is an “emotional dysregulation syndrome” in which the subjective emotional state of the individual might remain stable but the displayed emotional state fluctuates. He is of the opinion that a disconnection between the neurological centres governing perceiving of emotion and those expressing emotion seems to have occurred in these individuals.

4.2.2.1. Depressive disorder.

Depression is the most common of a grouping of four disorders of affect (the others being euphoria, mania and pathological laughing and weeping) that are found to be associated with MS (Feinstein, 1995). The incidence rate of depression in MS is considered approximately in the range of 27% and 54% (Minden & Schiffer, 1990) and 53.4% (Zorzon et al., 2002). The risk for suicide is elevated for individuals with MS (around 30%) and is linked to the presence and severity of depression and social isolation (Feinstein, 2004). Rodgers and Bland (1996) found that the population of

young men during their first five years of MS diagnosis were especially at risk for suicide. Depression may also affect MS disease course either directly by affecting immune system functioning or indirectly by affecting behaviours that promote disease exacerbation or progression (Mohr & Cox, 2001).

Minden and Schiffer (1990) state that the depression in MS is moderately severe. The characteristic symptoms of depression in MS lean towards anger, irritability, worry and discouragement rather than withdrawal, self-criticism and disinterest (Minden et al., 1987) and inability to mourn, loss of hope, and pessimism (Kesselring & Klement, 2001). Feinstein and Feinstein (2001) also found that complaints of irritability, sadness and tearfulness, in a sample of MS patients, all symptoms of affective instability, were indicative of general psychological distress.

To estimate the incidence of depression in MS is not as simple as it may seem. Many symptoms that are common criteria for the diagnosis of depression, are also primary symptoms of MS. Fatigue for example, is a major primary symptom of MS (fatigue will be discussed in greater depth later in this chapter), and may lead to many symptoms and difficulties generally attributed to the presence of depression e.g. difficulty concentrating, irritability, tiredness, forgetfulness etc. This consideration is underscored by the findings of Voss et al. (2002) of fatigue being significantly predictive of depressed mood in MS (this relationship occurring independent of degree of physical disability). Distinguishing between fatigue as a result of MS and as an indication of the presence of depression is thus very important and suggestions on how this differentiation could be achieved are presented when fatigue is discussed in more depth.

Various research results have shown a number of correlations between depression and various other variables relevant to MS. Murray (1995) found correlations between depression in MS and aspects such as age, gender and education. Brassington and Marsh (1998) reported a correlation between depressive symptoms in individuals with MS, disability, and lack of social support, whilst depressive episodes seemed to be a result of structural lesions. Feinstein (1995) noted that there was a positive association between depression and brain lesion load and the incidence of depression seemed to increase with the deterioration of these lesion loads. Contrary to these findings Zorzon

et al. (2002) found that measurements of lesion load showed no significant difference between depressed and non-depressed MS patients.

4.2.2.1.1. Etiology of depression in MS.

The precise etiology of depression in MS remains unclear. Research findings regarding the relationship between, firstly depression and disease severity, and secondly depression and cerebral involvement in MS, have provided contradictory results (Murray, 1995). Some studies have shown a definite neurological substrate for depression in MS. Schiffer, Caine, Bamford and Levy (1983) found significantly more depressive episodes in their sample of MS patients with cerebral lesion involvement, than in their sample of MS patients with only spinal involvement. The fact that the degree of cognitive impairment was the same for both these groups suggests that depressive symptoms in MS were the result of specific lesions rather than a general impairment in cognitive functioning.

Schiffer et al. (1983) furthermore found higher rates of depression in MS as compared to either temporal lobe epilepsy or amyotrophic lateral sclerosis patients. Whitlock and Siskind (1980) also found that depression occurred more frequently in patients with MS than in patients with other disabling neurological conditions such as muscular dystrophy, motor neurone disease and dystrophica myotonica. These types of findings seem to suggest that the occurrence of depression in MS does in fact have a neurological substrate and should not only be viewed as resulting primarily from a psychological reaction to an illness.

However, other studies have failed to show an association between depression in MS and aspects of brain involvement (Ron & Logsdail, 1989; Feinstein, 2004), whilst yet others have shown strong correlations between the occurrence of depression in MS and psychosocial factors. Studies by Ron and Logsdail (1989) have showed a strong association between patients' perceived levels of social stress and support and the occurrence of depression and a study by Voss et al. (2002) which found that fatigue and physical disability contributed to depressed mood in MS (this association with depression being at least partially mediated by the individual's inability to partake in recreational activities). According to Feinstein (1995) the possible reasons for these contradictory results regarding the relationship between depression and neurological

involvement in MS, are (i) the dynamic nature of the MS disease process (variability in disease activity with resultant variability in lesions distribution and size, thus changing lesion pattern), (ii) methodological problems of these studies (varied use of techniques for the assessment of depression and lesions involvement), and (iii) varying sensitivity of older versus newer MRI machines for accurate detection of brain lesions.

If depression in MS does in fact have neurological substrates it seems relevant to consider whether there might be specific lesion locations that might be more implicated in the development of depression. Robinson et al. (1984, in Feinstein, 1995) found that left (dominant) anterior frontal lesions were associated with the increased occurrence of depression in stroke patients. These results were partly supported by the findings of Reischies et al. (1988, in Feinstein, 1995, p.574) that "periventricular and discrete frontal, as opposed to temporal areas, were identified as the discriminant regions" for the occurrence of depression in MS patients. Zorzon et al. (2002) found that brain dystrophy for depressed MS patients seemed to be more pronounced in both frontal lobes (especially the left frontal lobe) and both temporal lobes (especially the right temporal lobe) implicating these areas and especially the right temporal lobes in the etiology of depression.

Whatever the case may be, it seems that the most accurate route to take in explaining the etiology of depression in MS would be a "multifactorial" one, where both neurological and psychosocial factors are included (Feinstein, 1995). This view is echoed by Murray (1995, p.201) when he states that "although one might suspect that depression could be related to the neurological dysfunction of MS as suggested by Whitlock and Siskin (1980), it is likely to be a more complex, multifactorial process, involving both psychological and neurological factors (Minden & Schiffer, 1990)."

4.2.2.1.2. Depression and physical disability.

According to Voss et al. (2002), research concerning the relationship between depression in MS and physical disability have been mixed. Fischer et al. (1994, in Voss et al., 2002) has shown that physical disability is independent of depression in patients with MS. Rabins et al. (1986) also found that depression was correlated with the degree of neurological impairment but not with the degree of functional disability.

Brassington and Marsh (1998) on the other hand, reported a correlation between depressive symptoms in individuals with MS and degree of disability. According to Voss et al. (2002), these contradictory results could be ascribed to mainly two methodological factors concerning studies of this kind, namely, reduced measurement specificity (different studies utilising different measures to ascertain degree of disability) and the unique considerations when diagnosing depression in individuals with MS (due to overlapping symptoms of MS e.g. fatigue and depression). Symptoms such as sleep abnormalities, sexual dysfunction, and concentration difficulties might be ascribed to depression when they are in actual fact symptoms of MS, thus inflating the estimated prevalence of depression in MS populations. Garland & Zis (1991) furthermore propose that these contradictory results might occur due to the fact that just as there is evidence for a neurological substrate for depression in MS patients, so too evidence exists for the development of chronic depressive symptoms following on the progressive disability caused by the MS disease process. Important to note here is that MS disease duration alone, showed no correlation with the presence of depression (Murray, 1995; Feinstein, 1995). It thus seems that these results imply that the physical disability resulting from the progression of MS and not merely the duration of MS might show an association with the occurrence of depression.

4.2.2.1.3. Depression and cognitive impairment.

Contradictory results regarding the relationship between depression and cognitive functioning exist. Rao and Hammeke (1984) found that MS patients with mild to moderate cognitive impairment reported more depressive symptoms than those patients without cognitive impairment or those with severe cognitive impairment. (A possible reason for the lack of reporting of depressive symptoms in the cognitively severely impaired group could be ascribed to the degree of impaired personal insight brought about by severe cognitive impairment, especially referring to impairment of executive cognitive abilities). On the other hand, Lyon-Caen et al. (1986) found no correlation between depressive status and the presence of cognitive impairment. Furthermore, Schiffer (1983, in Garland & Zis, 1991) compared individuals with cerebral MS with non-cerebral MS individuals and found that cerebral structural damage was involved with the development of depression. The degree of cognitive impairment was the same for both these groups suggesting that depressive symptoms

in MS are the result of specific lesions rather than a general impairment in cognitive functioning. The results of this study thus suggest that depression in MS is unrelated to the degree of cognitive impairment. Possible reasons for this, according to Feinstein (1995), could be aspects such as methodological weaknesses of such studies, aspects associated with the complexities involved in the demyelination process, and the difficulties that exist in accurately detecting the extent and severity of cerebral involvement.

It seems that depression in patients with MS cannot be predicted by any of the manifestations of the underlying disease process such as duration of the disease symptoms, degree of disability, illness pattern or family history of an affective disorder (Minden & Schiffer, 1990). Even though research has so far provided no definite answers as to the biological versus psychological determinants of depression in MS, the fact remains that depression has a significant adverse effect on patients' work functioning, their family and social lives and adaptation in MS and thus must at all times receive careful consideration when dealing with individuals with MS.

4.2.2.2. Bipolar affective disorder.

As mentioned earlier the incidence rate of bipolar affective disorder in the MS patient population seems to be approximately 13% as opposed to the expected 1% for the general population (Joffe et al., 1987). Schiffer et al. (1986, as reported in Minden & Schiffer, 1990) as well as Rao (1990), found the incidence rate of bipolar affective disorder in the MS population was double the expected incidence rate for the normal population. Just as in the case of depression, this higher than expected incidence of bipolar affective disorder in MS may be associated with an underlying biological mechanism such as a shared genetic vulnerability similar to that which were discussed earlier for depression. However, what makes findings regarding bipolar affective disorder slightly different from that of depression, is the fact that the findings for bipolar affective disorder are not so complicated by the evidence that are in favour of the incidence of these affective disorders as merely psychological reactions to an illness, as opposed to these affective disorders having neurological underpinnings in their occurrence in MS.

Research findings concerning the etiology of bipolar affective disorder in general, tend to lean towards biological explanations, mostly ascribing the etiology of bipolar affective disorder to genetic factors (Kaplan & Sadock, 1998; Rosenhan & Seligman, 1995; Soreff, 2002). Rao (1990) reports on studies where vulnerability genes were found on chromosomes X and XI in family studies regarding bipolar affective disorder.

Soreff (2002) reports on neuroimaging studies of individuals with bipolar affective disorder that suggest that cell loss in the frontal lobes and hippocampus are associated with the occurrence of mood disorders and bipolar affective disorder specifically. It seems reasonable to suspect a neurological cause for these increased incidences of bipolar affective disorder (as well as depression) in individuals with MS when considering that Filley et al. (1989, in Rodgers & Bland, 1996) state that the characteristic patchy, multifocal demyelination caused by MS appears to mostly involve the frontal lobes. Rodgers & Bland (1996) further state that compromise of these brain areas result in symptoms of dementia, personality alterations and psychosis. Another aspect that needs to be considered when investigating the etiology of bipolar affective disorder in MS is that bipolar affective disorder is not automatically assumed to be the result of a psychological reaction to having a disease such as MS, as is assumed when dealing with depressive symptoms.

As mentioned earlier, mania and hypomania may occur secondary to the treatment with corticotropin releasing medications (corticotropin is a hormone secreted by the anterior pituitary gland during an immune reaction) and prednisone (a steroid that is used in the treatment of MS symptoms) and this should be kept in mind when evaluating the occurrence of bipolar affective disorder in MS (Minden & Schiffer, 1990; Rodgers & Bland, 1996).

Hutchinson et al. (1993, in Rodgers & Bland, 1996) reported on patients who presented with bipolar affective disorder prior to being diagnosed with MS. They proposed that bipolar affective disorder might be an initial symptom of MS preceding the other neurological symptoms, or that there might be a shared genetic predisposition to bipolar affective disorder and MS. Although research has been done regarding the subcortical abnormalities of individuals with bipolar affective disorder

(Dupont et al., 1990, in Rodgers & Bland, 1996) further research is needed to investigate a possible shared etiology (possibly a shared genetic etiology for anatomical similar demyelination) for bipolar affective disorder and MS. Supporting evidence for the shared genetic link for MS and bipolar affective disorder is found in Minden & Schiffer's (1990) accounts of research findings where familial clustering of MS and bipolar affective disorder occurred. They mention the "possibly non random inheritance of certain major histocompatibility class II markers" among these patients (Minden & Schiffer, 1990, p.102).

Murray (1995) states that although psychiatric symptoms such as depression and bipolar affective disorder occur more often in individuals with MS than the healthy population, they seem to be uncorrelated with aspects such as sub type of disease, the degree of cognitive deficits, and neurological evidence of ventricular enlargement.

Even though research findings indicating an association between bipolar affective disorder and MS are much more limited than research regarding the association between depression and MS, it is clear that there is an undeniable association between bipolar affective disorder and MS. The fact that limited research findings regarding bipolar affective disorder in MS exist does not necessarily imply that the association between depression and MS is stronger than the association between bipolar affective disorder and MS. Bipolar affective disorder is less common than depressive disorder and additionally to this, one should consider that the symptoms of mania and hypomania are less likely to be confused with symptoms such as fatigue, low energy levels and weaknesses resulting from the MS disease process and not depression (thus resulting in possible over reporting of depression in MS).

Whatever the reason might be for these limited research findings the fact remains that the symptoms of bipolar affective disorder, just as that of depression, clearly has wide reaching implications for the daily life of those individuals with MS, their families and those involved in managing the disease course. With the limited research evidence so strongly suggestive of shared genetic and/or neurological etiology for these two conditions this field of research could hold great promise for our increased understanding of the MS disease process.

4.2.2.3.Euphoria

Little consensus exists on the prevalence of euphoria in MS. La Rocca and King (2002) estimates the incidence of euphoria in MS at around 10 percent, but estimates range from 63% to 0% (Minden & Schiffer, 1990). Murray (1995) is of the opinion that early research of euphoria in MS have overrated the incidence rates – it is not quite clear why he holds this opinion. One of the possible causes for these divergent incidence rates for euphoria in MS seems to be the lack of a single, clear definition of euphoria. Different studies seem to use different descriptions and criteria for what they consider to be euphoria. The implications that this methodological issue has for our evaluation of research, and thus for our estimated incidence rates of euphoria in MS, is made clear by the research of Cottrell and Wilson (1926, as discussed by Rao, 1990). Although this research is dated the implications of the findings still hold true for the matter at hand. Rao (1990) cites the research done by Cottrell & Wilson (1926) in which they systematically examined 100 patients with MS (then still termed ‘disseminated sclerosis’) in which they identified four states of well-being that could serve as some indication of the different facets of what subsequent research considers euphoria. These two states are what they termed (i) ‘euphoria sclerotica’ (mental well-being) and (ii) ‘eutonia sclerotica’ (physical well-being). In ‘euphoria sclerotica’ the individual consistently has a cheerful mood and in ‘eutonia sclerotica’ the patient is unaware or unconcerned about their physical disability (this description seems to be that of anosognia). In this research the ‘eutonia sclerotica’ was distinguished from another state which Cottrell & Wilson (1926, in Rao, 1990) termed ‘*spes sclerotica*’ which is characterised by “optimism as to the future and the prospects of ultimate recovery which is out of place and incongruous” (Rao, 1990, p.181). Cottrell & Wilson (1926, in Rao, 1990) considered eutonia a unique symptom of MS. Considering this it is clear how the different facets of what is generally termed euphoria can influence incidence rates for euphoria in MS. Cottrell & Wilson (1926, in Rao, 1990) found that when their subjects were considered on these different subdivisions of the general term euphoria, 63% were euphoric (in terms of their classification, i.e. mental well-being) as opposed to 84% that were eutonic (physical well-being). Interestingly enough they found that only 10% were depressed and 4% had mixed feelings of “well-being and ill-being” (Rao, 1990, p.181). Overall 84% of their subject group had a shift towards a more optimistic outlook and 96% had

symptoms of “emotional overreaction”. Considering previous research as well as his own studies, Rao (1990) concludes that when a distinction is made between euphoria (in terms of the individual experiencing a persistent elevation in mood) and eutonia (where patients seem to lack cognisance of the severity of their disability) in evaluating research findings regarding incidence rates of euphoria in MS, the rates for the presence of euphoria drop dramatically. He reported that fewer than 10% of MS patients experience a persistent elevation in mood.

Another reason for the different findings for the incidence of euphoria in MS might entail the fact that researchers often do not adequately distinguish euphoria from firstly, the symptoms of pathological laughing and weeping (where patients are unable to control their outward expression of emotion) and secondly, mania and hypomania with their associated symptoms of hyperactivity, pressured speech and racing thoughts (Minden & Schiffer, 1990). Rao (1990) states that the euphoria described in MS patients is distinguishable from the manic or hypomanic phases of bipolar affective disorder in as far as the euphoria in MS does not seem to be a sustained mood state as is the case of mania and hypomania in bipolar affective disorder.

When euphoria is manifested in MS it seems to be in the later stages of the disease and in those individuals who have greater cognitive deficits and subcortical changes (Murray, 1995). These conclusions are substantiated by Rao when he states that “euphoric mood in MS patients, as defined in the broader sense, correlates with the extent of brain involvement (particularly of periventricular structures)” (Rao, 1990, pp.181-182). SurrIDGE (1969) also concluded that euphoria was determined by the extent of neurological disability and thus per implication that structural brain involvement causes euphoria in MS. Rao (1990) hypothesises that this euphoria (and the pathological laughing and weeping which is discussed later) could be one of the aspects of the so-called ‘frontal lobe disconnection syndrome’ (or in the words of Luria (1973) the ‘frontal lobe syndrome’) which results from lesions in the periventricular bi-directional pathways of the frontal lobes.

The nature of the euphoria presenting in MS seems to be most recognisable as a cheerful acceptance of circumstances that would lead to great distress, sadness, and worry in other individuals (Murray, 1995) and a “persistent cheerfulness and

optimism about the future despite awareness of disability” (Rodgers & Bland, 1996, p.442). Minden and Schiffer (1990, p.98) describe euphoria in MS as not being “a fluctuating emotional state or reversible mood but rather a persistent frame of mind and outlook, an apparent and permanent change in personality”. This description reminds of an earlier discussion in this document, regarding MS presenting as a subcortical dementia with the symptoms of forgetfulness, diminished insight and personality changes presenting accordingly (Brassington & Marsh, 1998), and more directly with Rao’s (1990) conclusion that euphoria correlates with dementia. Therefore the possibility that the euphoria seen in MS might be secondary to subcortical dementia rather than a primary symptom of MS should also be considered.

Minden and Schiffer (1990) further comment that the most striking feature of euphoria in MS is the apparent dissociation between cognition and emotion. For example, an individual with MS might be fully aware of the incapacitating effects of his/her disease but would not display any distress or worry concerning their situation (see the earlier discussion of the nature of euphoria, as well as the research of Cottrell and Wilson (1926) as discussed by Rao, 1990). This fact might subsequently lead to underlying emotional disturbance such as depression, being overlooked as the symptoms of the euphoria might mask the individual’s true inner feelings. This point is underscored by the observations of Surridge (1969) where he noted that many of the subjects who initially appeared euphoric often appeared less so as the interview proceeded, concluding that it might be the outward appearance of mood rather than an emotional lability that was common in MS patients.

Other reasons that might explain the varied incidence rates of euphoria in MS might be biological in nature. Factors such as the diverse neurological characteristics of the demyelinating disease process and factors relating to methodological issues regarding the diversity in research samples regarding variables such as the disease process and the disease duration and intensity, comes to mind.

Whatever the case may be regarding the incidence rates of euphoria in MS, some factors regarding the nature of the association between euphoria and MS seem quite clear. Research reports agree that euphoria in MS is a neurologically based emotional state, resulting directly from the demyelination process and is not merely a

psychological response to an illness (Rabins et al., 1986; SurrIDGE, 1969; Minden & Schiffer, 1990). Lesions in the frontal lobes, basal ganglia and parts of the limbic system seem most involved in producing euphoria in MS.

Euphoria in MS is associated with disease characteristics such as the severity of the disability, longer duration of symptoms, the chronic progressive sub type of MS, cognitive deficits and enlarged ventricles, but shows no relationship to a disease course involving only spinal demyelination (Minden & Schiffer, 1990; Rao, 1990).

It ought to be clear that the presence of euphoria (and eutonia) in an individual with MS will have certain implications for the way the patients and their families will cope with the disease process. If an individual lacks concern regarding their disability, they will be less motivated to change and participate in rehabilitation programmes. Also, if the patient's family does not understand that this lack of concern is organically based and not merely a psychological attitude, they will become very frustrated, demoralised and angry with the patient and this could subsequently lead to unnecessary conflict and difficulties in coping with the disease, both for the patients and their families.

4.2.2.4. Pathological laughing and weeping.

A condition similar in its neurological etiology, and often confused with euphoria is what is termed "pathological/pseudobulbar laughing and weeping/crying". This condition comprises of sudden outbursts of crying or laughing, either with or without a precipitating event. What is very important here is that the expressed emotion is not an expression of the subjective mood state the patient is experiencing. It is often described as the 'emotional dysregulation syndrome' of MS (Minden & Schiffer, 1990). Pathological weeping and laughing may even overlap with euphoria, but often also occurs on its own (Minden & Schiffer, 1990).

Although researchers seem to accept as fact that this condition has neurological substrates, the precise mechanism underlying pathological laughing and weeping is still unclear. Baretz and Stephanson (2002) state that this condition "occurs with severe brainstem involvement and reflects a physiological defect in the control of affective expression rather than a psychological mode of adaptation to stress". Minden

and Schiffer (1990) state that the condition seems to result from a disconnection of diencephalic or brain-stem centres from the right hemisphere or mechanisms of frontal control. Rao (1990) also states that this condition seems to be associated with bilateral corticobulbar fibre lesions, although it is still not certain whether bilateral involvement is necessary, as research done by Sackheim et al. (1982, in Minden & Schiffer, 1990) found 'pathological emotionality' resulting from unilateral (right hemisphere) involvement alone.

Prevalence rates for pathological laughing and weeping in MS seem to be around 7 to 10% (SurrIDGE, 1969; Minden & Schiffer, 1990). Murray (1995) states that although this condition also manifests in other neurological conditions, its manifestation in MS is often transient (clearing spontaneously in a matter of months) and is often responsive to treatment with tricyclic antidepressants.

The symptom of pathological laughing and weeping clearly has similar implications as euphoria for the experience and management of the MS disease process. A great deal of pain and confusion can occur if this symptom is not clearly understood and the often inappropriate emotions seemingly expressed by the patient, are misconstrued as an accurate representation of the patients true feelings. Apart from coping with the disease process itself, the patient must now also deal with their own confusion regarding the incongruity between their emotional expressiveness and actual underlying feelings. This incongruence between expressed and subjective mood states will most likely be misinterpreted by uninformed care-givers who will attempt to provide the kind of care and support that they assume is in accordance with the needs which the patient has expressed. These symptoms may also set the stage for great uncertainty as neither the patient nor his/her care-givers will know what to expect regarding the patients reactions, confounding an already complicated situation.

4.3. FATIGUE

Fatigue is the one most common complaint of individuals with MS. Research regarding fatigue in MS show that fatigue is a major factor in the psychological and social well-being of individuals with MS, thus a very important determinant of their

quality of life (Murray, 1995). Murray (1995) reports that fatigue was rated the most troubling symptom in 40 % of the MS cases in their study. Ford, Trigwell and Johnson (1998) reported this number to be around 85% of the MS cases in their study. In other studies, as reported by Murray (1995), 96% of MS patients reported that fatigue was either their worst symptom (14%) or one of their worst symptoms (55%). Not only is fatigue a problem in itself, but it also affects the other symptoms of MS either directly, making it worse (reported by 60% of individuals with MS in the study by Murray, 1995), or affects the individual's ability to cope and manage the other symptoms of MS.

Murray (1995) reports that 84% of the cases they studied reported that they experienced increased fatigue when exposed to higher temperatures (the reason for this is discussed later in this section) and 51% of the cases reported that they noticed increased fatigue before any other symptoms of MS. In this same study 40% of cases reported that they experienced daily fatigue that lasted six or less hours (44,7%) or experienced fatigue continuously (25,9%).

Research of fatigue in MS is complicated by similar issues as those involved in relation to e.g. research of euphoria in MS. Firstly, the definition of fatigue poses a problem. Different research projects use different definitions for what they consider fatigue and as such the research findings vary as well. Herndon (1999, p.7) suggests that fatigue be defined as “a subjective lack of physical and/or mental energy that is perceived by the individual or care-giver to interfere with usual and desired activities.” This definition is in accordance with the research findings of Ford et al. (1998) in which they investigated whether individuals with MS differentially experienced physical and mental fatigue. They proposed that fatigue should be considered as a continuous concept including both physical and mental components, instead of a discrete variable. In their study Ford et al. (1998) found a significant correlation between mental and physical fatigue but only the mental fatigue was found to correlate with scores of depression and anxiety.

Secondly the comorbidity (and thus confusion of the symptoms) of fatigue and of other affective disturbances (especially depression) poses a problem. The symptoms of depression and of fatigue are very similar (fatigue is also a very important

characteristic of depression) and these two conditions could easily be confused, ascribing the manifested symptoms to a depressive state when in fact the symptoms are that of fatigue due to MS. This aspect is complicated even more by research findings (Ritvo et al., 1996, in Voss et al., 2002) that found fatigue to be a significant predictor of depressed mood in MS. Fatigue predicted depressed mood independent of physical disability, so the association between depressed mood and fatigue in MS cannot be ascribed to physical disability alone. Whether the association between depressed mood and fatigue is real, or a result of confusing the symptoms of these two conditions, is unclear. It is thus very important to accurately differentiate between depression and fatigue when research is done in MS. Patten and Metz (2000) suggest that fatigue associated with MS can be distinguished from the fatigue associated with depression on the following grounds: (i) the fatigue resulting from MS is aggravated by heat which is not typically the case for fatigue due to depression; (ii) the fatigue resulting from MS seems to be alleviated by rest and/or sleep and as such individuals with MS often become very adept at managing their fatigue by monitoring and modifying their activity levels and life-style, whereas the fatigue associated with depression is not predictably alleviated by rest; and (iii) the fatigue resulting from MS in most cases seem to last for only a few hours at a time, whereas the fatigue due to depression is more chronic and persistent.

Voss et al. (2001) and Ford et al. (1998) state that the precise cause of fatigue in MS is unclear, whilst Herndon (1999) states that fatigue in MS is a complex problem caused by a variety of factors. He proposes the following possible etiological factors of fatigue in MS.

(i) MS disease process related fatigue.

Herndon (1999) considers this type of fatigue as related to the inflammatory process in the brain during the MS disease process with the associated secretion of lymphokines and cytokines (substances secreted by the immune system during an inflammatory process and discussed earlier in this chapter). Fatigue is caused by the immune response in which the body fights the infection and although it is not known exactly which of these substances secreted during the immune response are responsible for the fatigue, these substances are the most probable agents for disease related fatigue. Disease related fatigue similar to fatigue in MS is also seen in other

autoimmune diseases such as lupus and rheumatoid arthritis (Krupp et al., 1989 and Belza et al., 1993, both in Herndon, 1999), and this fatigue seems to improve when immunomodulatory medication (such as high dosages of steroids used during exacerbations) are applied.

Herndon (1999, p.2) considers fatigue of this nature (i.e. related to infection) as "a signal from the immune system to the nervous system telling the individual to slow down and rest while the system fights the infection". In MS this type of fatigue presents at its worst in the early to mid-afternoon. It is usually absent or mild during the morning and often improves toward the evening. It seems to mostly impair the individual's cognitive abilities (especially executive and decision making abilities) and is more prominent in individuals with a more active disease course. Herndon (1999) goes so far as to state that severe fatigue in the absence of new disease symptoms suggests the presence of neuronal changes on the micro level as seen using MRI.

(ii) Fatigue related to other infection.

Fatigue can also appear as a result of infection other than that of the inflammatory nature of the MS disease process itself. Conditions such as urinary tract infection is often the culprit and once this infection has been treated and cleared the fatigue also dissipates. This kind of fatigue is thus more transient and is usually worse if the infection is accompanied by a fever. Herndon (1999) suggests that two aspects should be considered if there is an acute worsening of fatigue in an individual with MS. Firstly the possibility of new MS symptoms should be investigated in which case the fatigue is related to the inflammatory MS disease process itself, and secondly a thorough examination for the presence of a secondary infection should be undertaken, as both these instances increase fatigue.

(iii) Fatigue caused by medications (thus iatrogenic fatigue).

Quite a number of medications used in the treatment of MS and its related symptoms may produce fatigue as side effect. Medications such as benzodiazepines and tricyclic antidepressants, used to treat sleep disturbances may cause drowsiness and sedation. Also medications such as analgesics, anticonvulsants, antihistamines, antihypertensives, and muscle relaxants to name a few, might produce symptoms

similar to that of fatigue as side effects.

(iv) Fatigue due to physical disability.

MS produces a variety of physical disabilities. Individuals who have these disabilities may have to exert extra effort and energy to accomplish the same physical results than would an individual without a physical disability. Herndon (1999) states that metabolic studies have shown that an individual with a spastic gait can expend twice as much energy walking as would a healthy individual. Individuals with weak muscles will use different muscle groups to compensate for the weaknesses and so overwork the muscles that are still functional. Often the muscles used as compensation weren't really the intended producers of the activities they are now used for and as such not ideally suited for these actions and will thus tire at a faster rate, leading to increased levels of fatigue.

(v) Fatigue due to disruption/disorder of sleep patterns.

Fatigue due to sleep difficulties is relatively common in MS. Aspect such as involuntary limb movements, sleep apnea, and urinary frequency may be present and disturb the sleep pattern of MS sufferers. Fatigue thus being caused by sleep deprivation. According to Herndon (1999) a large variety of factors cause sleep disturbances in MS. Apart from those mentioned above, demyelination of parts of the brainstem controlling both sleep and wakefulness cycles, as well as breathing, may further lead to altered respiratory patterns and thus interrupted sleep patterns. Secondary to the effects of the MS disease process itself, individuals might experience affective disturbance such as depression. Sleep disturbance is a well-known symptom of depression and this condition in itself might lead to disturbed sleep patterns in an individual with MS. These individuals may not be able to fall asleep or they might awake in the early hours of the morning and not be able to fall asleep again thus not getting adequate rest and sleep leading to fatigue during the day (Herndon, 1999).

When all these conditions are considered it becomes clear that the degree of sleep disturbance in MS might indeed require serious consideration as one of the causes of fatigue as noted in MS.

(vi) Fatigue associated with depression.

As discussed earlier, certain symptoms related to depression might interfere with the normal sleeping patterns of those individuals with MS and as such lead to fatigue during the day. Other symptoms of depression such as inability to concentrate, lack of interest and motivation may also pose a problem when fatigue in MS is considered. These symptoms lead to the individual not having the energy and or the interest to do what they need to do during the day. These symptoms as well as the psychomotor and cognitive slowing found in severe depression as reported in the DSM-IV-TR classification criteria for depressive disorder (APA, 2000) may often be misconstrued as relating to fatigue instead of resulting from depression.

(vii) Nerve fibre fatigue.

Herndon (1999, p.3) describes nerve fibre fatigue as "an activity and/or temperature related failure of the demyelinated nerve fibres to conduct impulses". This type of fatigue is often overlooked even though it severely affects function and contributes to the overall fatigue experienced by MS sufferers. This type of fatigue has its own specific characteristics and follows a diurnal pattern similar to disease process related fatigue discussed earlier. Herndon (1999) states that nerve fibre fatigue is seen in most MS patients and its influence increases as the disease progresses.

It seems that during an exacerbation the conduction of impulses in the nerves fail as these nerves are demyelinated. These conduction failures possibly exist as a result of damage to the nodal sodium channels or absence of sodium channels from the internodal membranes (Kasckow et al., 1986 and Ritchie et al., 1977 both in Herndon, 1999). It is a well-known fact that the nerve conducts impulses by regulating the exchange of, amongst other chemicals, sodium and potassium across the cell membrane via the sodium-potassium pump (Martin, 1998). It appears that the composition of the extracellular fluid is disturbed during the inflammatory process (which causes the demyelination of the nerve fibres) by the by-products (possibly enzymes such as proteases, lipases, neuraminidase, phosphatases and glycosidases) of the demyelination process which in turn results in interference of the normal exchange of sodium and potassium across the cell membrane during impulse conduction. Additionally to this, research mentioned by Herndon (1999) shows that not only does phospholipase exert the most rapid and extensive damage to myelin, but it also

destroys the sodium channels specifically. All these factors then culminate to produce the impulse conduction failure seen in the demyelinated nerve fibres.

With time conduction in most of the surviving nerves fibres are restored. This is accomplished by insertion of additional sodium channels in the axonal membrane of the nerve fibre. This alone will however not ensure that impulse conduction will occur. For the impulse to pass from the myelinated section of the nerve fibre and continue along the demyelinated section a larger electrical current is required, as the demyelinated section of the nerve fibre has an increased membrane capacitance (due to lack of a myelin sheath) and as such requires a larger charge to depolarise the membrane for impulse conduction. So, even though the amount of sodium channels have been increased a larger impulse is required to depolarise this section of the nerve membrane and subsequently to activate the exchange of sodium and potassium across the cell membrane for impulse conduction. One of the consequences of these adaptations of the nerve membrane after demyelination is that the nerve fibres become temperature sensitive (Rasminsky, 1972 in Herndon, 1999). This temperature sensitivity results from the "low safety margin for conduction and the sodium channel response to temperature" (Herndon, 1999, p.6). So when an impulse triggers a node the sodium channels open and sodium pours into the cell membrane depolarising the membrane. The rate at which the sodium channels close are temperature dependent, closing at a faster rate with an increase in temperature resulting in a decrease in the time the current can flow and thus causing conduction failure. Cooling on the other hand has an opposite effect increasing the time the sodium channels are open and thus improving conduction. Research mentioned by Herndon (1999), have found that temperature changes as small as 0.5 degrees Celsius above normal can cause conduction failure.

The above discussion explains the underlying 'mechanics' of nerve fibre fatigue which is experienced by most individuals with MS and which is most evident in difficulty walking more than short distances and sensitivity for increased temperatures. In this respect Herndon (1999, p.6) states "when nerve fibre fatigue occurs and the fibres stop conducting, the legs simply will not move until the nerve fibres are rested enough to begin conducting again".

From the above discussion of fatigue in MS, it is apparent that fatigue is a complex symptom and requires careful investigation when presented. Since fatigue has many contributing factors the management of fatigue will require a multifaceted approach. To effectively treat fatigue the precise causes of the fatigue need to be clear. According to Herndon (1999), fatigue related to the disease process often responds well to medication and specifically to treatment with amantadine. Other medications that have been reported to alleviate fatigue in MS are high dosages of aspirin and the newer serotonin reuptake inhibitor type antidepressants such as fluoxetine (Prozac) or sertraline (Zoloft), although the effectiveness of these medications still need further investigation. Apart from drug therapy there are additional strategies that might prove useful in the management of fatigue in MS. These rely on the management of the secondary symptoms of MS (such as depression, sleep disturbances and other infections) that could lead to fatigue such as periodic rest and scheduling strategies, reconsidering medication regimes, addressing and treating infections, utilising assistive equipment and rehabilitative exercises and home and work environment modifications.

It is clear that fatigue can impose great additional difficulties on the individual trying to manage and cope with MS. Fatigue can exert a negative influence on many levels of an individual's functioning be it cognitive, physical, psychological, behavioural or social and as such needs to be managed and controlled effectively. However, fatigue is a multifaceted and complex symptom and its treatment should be no less. The effective treatment of this most reported and disturbing symptom of MS can significantly improve the overall function of the individual with MS and in doing so greatly improve their overall quality of life.

4.4. ASPECTS RELATING TO PERSONAL LIFE: SELF-ESTEEM, RELATIONSHIPS, ROLES AND EMPLOYMENT

Jiwa (1995, p.87) defines self-esteem as “the degree to which one likes oneself and feels competent to cope with life’s tasks” and Plug, Meyer, Louw and Gouws (1988) define self-concept (synonym: self-image) as an individual’s perception and evaluation of him-/herself and including cognitive, emotional and evaluative elements

– self-esteem representing the evaluative element. For the purpose of this discussion self-concept, self-image and self-esteem will be used as synonyms and the definitions as mentioned above will be followed.

MS mostly affects individuals in early and middle adulthood when these individuals' focus is their career, relationships and the establishment of a family of their own. These individuals' most likely perceive themselves as vibrant, healthy and possibly somewhat invincible beings. They might not have given much thought to their mortality and the psychosocial environment in which they find themselves aims to reinforce these views. However, when MS strikes these individuals are forced to face illness, disability and mortality head-on which could result in serious problems relating to the way these individuals view themselves, their abilities, the state of their future hopes and dreams and their existence as a whole.

The symptoms of MS may place many restrictions on the individual and this may leave the individual extremely frustrated, placing even greater demands on their coping abilities and those of their loved ones. Both employment and social activities (such as leisure activities) might be adversely affected due to aspects such as cognitive, physical and economic limitations. Individuals with MS might feel self-conscious or embarrassed to appear in public as the symptoms of MS might be very visible making them extremely self-conscious and open to public scrutiny (Murray, 1995; Jiwa, 1995). Onlookers might for example, perceive these individuals as being intoxicated due to the ataxia and the sufferer might be ashamed of having to use walking aids when previously they didn't give much thought as to how they got around (Murray, 1995). Additionally these individuals might feel that they are a burden on others (Jiwa, 1995). These feelings of uselessness cause self-doubt regarding their competence and abilities and skills, thus affecting levels of self-esteem.

Additionally to having to face all their own emotions, disease symptoms and relational problems, these individuals often need to deal with being stigmatised by society or being labelled 'disabled', which often implies a shift in how they perceive themselves and their identity as independent human beings (Murray, 1995).

In addition to the other physical symptoms of MS, fatigue also has detrimental effects on the MS sufferer. Fatigue places extra strain on the individual and makes activity much more difficult, requiring increased effort to accomplish even simple tasks. What complicates the effects of fatigue is that fatigue as such, is a subjective experience and not objectively visible. This often makes it very difficult for the individual to express the nature of their difficulties and to elicit understanding and gather support from bosses, colleagues, marital partners and other loved ones, making it extremely difficult to cope successfully in their career and family life.

Due to the symptoms of MS (such as fatigue and cognitive and physical disability) these individuals can possibly no longer successfully fulfil their roles and obligations both regarding their own expectations such as functioning successfully in their occupation, as well as the expectations of others regarding their roles as marital partners, parents and employees, which help to lower their levels of self-esteem (Murray, 1995; Jiwa, 1995).

Losing employment so often leads to feelings of worthlessness and dependency (as gainful employment is so often equated with contributing to society and being a successful human being) leaving the individual feeling helpless and as though they have lost control of their lives (Jiwa, 1995). Murray (1995) reports on a study done in the USA (Inman, 1984) that found that 1 in every 10 MS patients had to change their jobs due to their disease. This study also found that the chances of being gainfully employed decreased as the disease progressed, which was especially relevant to males. Murray (1995) states that only approximately 17 to 25% of MS sufferers are able to maintain their employment throughout the course of their disease. The major factors, according to La Rocca et al. (1985, reported by Murray, 1995) that seem to influence employment rates for those with MS are mobility and age. Additional aspects such as the “work site characteristics, control over work space, and personal schedule freedom on the job, plus willingness of the employer to make modifications for a disabled worker” all play an important role (Murray, 1995, p.215).

The symptoms of MS may lead to problems regarding intimacy and sexual functioning in intimate relationships. The individual with MS might feel that they are no longer attractive to their partner due to their disabilities. They may also no longer

physically be able to continue sexual relations with their partners due to the symptoms of MS such as loss of sensation, loss of libido (often a side-effect of medication), erectile dysfunction and bladder control difficulties. Zorzon et al. (2001) found that 73.1% of the individuals with MS in their study reported sexual dysfunction. Their research found that bladder dysfunction, degree of disability, anxiety, and age (significant but weak), were correlated with sexual dysfunction over a two-year period. These sexual difficulties often cause the individuals with MS to distance themselves from their partners leading to conflict and miscommunication, diminishing their self-esteem in the process and limiting their sources of social support and subsequently their ability to cope effectively with the disease.

Parenting may also pose serious problems. If there isn't adequate support and the individuals with MS has difficulty accepting their limitations (or doesn't have a clear understanding of their limitations) they may over-extend themselves in an attempt to remain a competent parent. This is especially the case where role reversal has occurred and the child is now taking care of the parent with MS. This may lead to the parent feeling frustrated, sad and guilty as they are no longer as capable as they were, thus once again having detrimental effects regarding the individual's self-esteem (Jiwa, 1995).

It is thus understandable that the MS sufferer might opt for withdrawing from society and might often even attempt to, in a manner of speaking, withdraw from their own lives. Lyons (1987, in Murray, 1995) found that adults with disabilities, including those with MS, were often lonely, isolated and had low self-esteem. They often seem to lead boring, lonely, inactive lives feeling that "they lack the skills or ability to be more active and have difficulty making the adjustments needed to continue activities when disability limits function" (Murray, 1995, p.210).

What makes adapting to MS even more difficult is the unpredictable and progressive nature of the disease. It requires continuous adjustment from the sufferer for as soon as the sufferer has adjusted to the disabilities the disease caused, they might have another exacerbation or experience further progression of the disease, leaving them without those abilities that they utilised to adjust to the disease previously, making their coping methods and strategies ineffective (Murray, 1995). This leads to

increased lowering of their self-esteem and perceptions of themselves as functional members of society as they are trying to adapt to an ever-lowering level of ability.

Walsh and Walsh (1989) found that individuals suffering from MS had significantly lowered self-esteem. Even the mere fact that one had a diagnosis of MS seemed to affect self-esteem levels. They furthermore found that the degree of physical restriction also exerted a negative effect on levels of self-esteem. They found that individuals suffering from MS who used no walking aids scored much higher on indexes of self-esteem (only 1 point lower than the student control group used in their study). A further fact to consider regarding this study, as noted by Walsh & Walsh (1989), is that the severity of the symptoms of MS, are inter-correlated. Thus as the severity of physical symptoms such as the ability to walk increases so too does the severity of other symptoms (for example incontinence). These symptoms then additionally exert their effects on the sufferer causing the individual to become increasingly dependent on rehabilitative aids, and on other people, and so serve to diminish their levels of self-esteem. Walsh and Walsh (1989) found that levels of self-esteem was increased when individuals suffering from MS was able to integrate the reality of the disease into their self-concept and by doing so was able to more effectively adjust to, and manage the disease and its effects.

Jiwa summarises it well when she states that “the net effect of all the changes MS brings to a person’s life can result in an alteration of that person’s sense of self in relation to the world. Now the person takes on the identity of a disabled person. They feel physically unattractive, financially and emotionally burdensome, and generally inadequate. Guilt about past acts can be present if the person views the MS as punishment. The person with MS often claims to feel out of control as the fears of increasing dependence mount. Coupled with the fears of losing the support of loved ones. They begin to see themselves as very alone in the world – alone with a wounded self-esteem.” (Jiwa, 1995, p.88-89)

Much more can be said about the myriad of difficulties relating to the personal life of those suffering from MS, but it goes beyond the scope of this document. However, it is important to note how all these various types or categories of symptoms and effects of MS are inter-related. For example, not only is the level of self-esteem influenced

by symptoms such as physical disability and the use of aids, but the level of an individual's self-esteem is also a very important determining factor in the individual's ability to successfully adjust to, and manage MS.

4.5. ASPECTS RELATED TO ADAPTATION AND COPING

Research regarding coping with and adaptation to chronic disease have, partly due to the traditional tendency of medical science to overlook the link between body and mind, to a large extent neglected to investigate the association between the somatic and psychosocial aspects of chronic illness. Physical disease, whether acute or chronic, imposes certain demands and limitations on the patients, and in chronic disease, such as MS, the consequences are both profound and long-term.

When an individual is diagnosed with a specific chronic illness, the implication is that a specific pattern of symptoms is present and additional symptoms could most likely be expected as the disease progresses. This aspect is often discussed (albeit mostly very superficially) and the patients and their disease are then medically managed. However, what this diagnosis does not tell us, and as such an aspect that is overlooked and ignored in most cases, is what meaning this specific disease holds for the individual who has been diagnosed. The fact that this aspect of chronic disease is greatly ignored (the medical fraternity being the major culprit) is extremely unfortunate as this aspect is one of the most important (if not *the* most important) factors that will influence how the patients cope with and adapt to their disease.

Since disease and illness occur within the context of patients' lives, one can expect psychological reactions from both the patients and those around them. Although no clearly established uniform psychological criteria for adjustment to chronic disease are apparent in all patients, several factors, both outside and from within the individual patient can affect adaptation (Schlebusch, 1987).

Apart from the stresses arising from the immediate health-care issues, there are also many stresses associated with day-to-day living that are not exclusively related to a specific disease and its treatment. This must have a significant psychological impact

on the patients' coping ability. According to Schlebusch (1987), the degree of adaptation to disease will vary with factors such as the individual's self-concept before the illness, the severity of the illness and change in living pattern it necessitates, and the meaning that the altered function has to the person and those close to him or her (Redman, 1988). Additionally, different disease processes might lead to slightly different patterns of reaction and adaptation to the disease. In this regard you are reminded of an earlier discussion (previous section) regarding the unique difficulties the MS disease process poses due to its uncertain progressive nature and the subsequent continued adjustment and adaptation it requires from the patient.

Livneh and Antonak (1997) state that although many authors use the terms 'adaptation' and 'adjustment' interchangeably, they prefer to distinguish between them since it is their opinion that these two terms refer to separate aspects regarding the response to chronic illness and disability. These authors describe adaptation to chronic illness and disability as "an evolving, dynamic, general process through which the individual gradually approaches an optimal state of person-environment congruence manifested by (1) active participation in social, vocational, and avocational pursuits; (2) successful negotiation of the physical environment; and (3) awareness of remaining strengths and assets as well as existing functional limitations" (Livneh & Antonak, 1997, p.8). They state that adjustment refers to a particular phase in this adaptation process, more precisely that adjustment is "the clinically and phenomenologically hypothesized final phase – elusive as it may be – of the unfolding process of adaptation to crisis situations including the onset of chronic illness and disability" (Livneh & Antonak, 1997, p.8).

Many theories exist regarding the nature of the adaptation process to chronic illness and disability but very few of these theories actually agree on the precise nature of the concept and the process of adaptation. Some authors (Kübler-Ross, 1969; Bowlby, 1980; Parkes, 1975; Horowitz, 1986; all in Livneh & Antonak (1997)) view adaptation to chronic illness as being a sequence of phases during which the individual gradually progresses to acceptance of the disease or disability. These phase theories commonly entail the description of the reactions (such as anger, anxiety and depression) the individuals manifests at various times during this adaptation process

(Livneh & Antonak, 1997).

Suchman (1965) describes the stages of adaptation to disease as follows. In the first stage (the 'symptom experience' stage) the patients make a decision that something is wrong. This decision is made according to various experiences and aspects: (i) physical experience such as pain, discomfort, change of appearance; (ii) the cognitive aspect which is the interpretation of the physical experience; and (iii) the emotional response of fear or anxiety. There is often denial of illness. During the second stage ('assumption of sick role' stage) the individuals decide that they are sick and need professional care. They seek symptom alleviation, advice and information and temporary acceptance of their condition from family and friends. The reaction of the family and friends are very important in determining the sick role the patients then take on. They want confirmation of their feelings and permission to suspend normal duties. During the third stage ('medical care contact' stage) the patients seek professional medical diagnosis and a course of treatment. They seek authoritative sanction to become 'legitimately' ill or to return to normal activities. If they refuse to accept diagnosis this stage is prolonged as they search for another diagnosis. When the patients make the decision (either conscious or unconsciously) to transfer control to the physician and to accept and follow prescribed treatment the fourth stage ('dependent patient role' stage) is entered. In the final stage ('recovery or rehabilitation' stage) the person relinquishes the patient role. For many with chronic illnesses or physical impairments, this is a long and demanding stage with recurring episodes of illness. The person re-establishes relationships changed by the illness.

Regarding MS patients' adaptation to their disease, Matson and Brookes (1977) found that the adaptation process entailed mainly four subsequent stages that they describe as follows:

Stage 1 - Denial

The patients deny that this can be happening to them. They try to conceal their symptoms and seek an authority who will deny the diagnosis. They refuse help and hold on to their past life and values.

Stage 2 - Resistance

They state that the disease will not get them down. They are active in programs seeking cures, treatments and other patients. They are reluctant to accept help. There is an initial recognition of the change in life-orientation.

Stage 3 - Affirmation

The patients grieve for the loss of the former self. They publicly talk and explain about MS. They learn to accept help. They subjectively rearrange the priorities in their life.

Stage 4 - Integration

The patients learn to live with the disease, spending time and energy on other matters. They accept help when necessary. The patients start to integrate the disease and its symptoms and values with their life styles.

Although these phase models regarding the adaptation to chronic illness or disability are useful in setting a framework for our understanding of the process of adaptation, we need to keep the following in mind: (1) not all individuals show the same reactions when faced with illness or disability - some individuals might never manifest the reactions as described in the phase models whilst others will show many of them. For example, some individuals might never exhibit anger or depression as would be expected when considering these theories; (2) the phases described should not be seen as clearly demarcated and non-permeable entailing a specific time duration – reactions manifested in different phases of adaptation might overlap, or symptoms from one phase might be carried over to the following phases and permeate the entire adaptation process making the identification of distinct phases of specific duration very difficult; also (3) the phases do not always follow one another in a linear sequential manner - individuals might move forward skipping certain phases or regress to earlier phases in the adaptation process; and (4) the mere consideration of a final acceptance phase might be open to criticism - the question might be asked whether total or final acceptance is ever possible or even functional.

4.6. CONCLUSION

A good illustration of what the individual with MS goes through in an attempt to adapt to this chronic disease is provided by Larsen (1990) when she states that “individuals with a chronic illness are continually striving to feel normal, control physical symptoms, maintain a positive self-concept, adjust to role changes and confront their own mortality. In addition to losing physical control over their bodies, these clients may lose control over making decisions about their treatment. Their independence is threatened, and they may need to rely on others for self-care”(Larsen, 1990, p.242).

Although the most salient symptoms of MS involve aspects of the physical and cognitive functioning of patients and have therefore received the greater portion of attention both in clinical settings and research, the psychosocial aspects of having a chronic disease, if not adequately acknowledged and managed, may be even more disabling than the physical and cognitive aspects. MS does not affect the individual in isolation and the psychosocial aspects affected by MS involve a wide range of factors that in effect constitute the entire life-world of the individual.

CHAPTER 5

COGNITIVE FUNCTIONING AND MULTIPLE SCLEROSIS

5.1. INTRODUCTION

It is extremely important to identify the cognitive impairment in individuals suffering from MS, as research is increasingly showing that such impairment may have as devastating an impact on the psychosocial and vocational adjustment of these patients as the actual visible physical disability (Rao, 1990; Bagert, Camplair and Bourdette, 2002).

Ruggieri, Palermo, Vitello, Gennuso, Settapani and Piccoli (2003) found that cognitive impairment was present even before physical disability was apparent in relapsing-remitting MS. Lyon-Caen et al. (1986) also found that cognitive deficits are in fact present from the onset of MS. Furthermore, recent research as to the natural course of cognitive impairment in MS suggests that once neuropsychological impairment has developed it may remain stable over time, are not likely to improve or remit and may even progress (Bagert et al., 2002). According to Franklin, Nelson, Heaton and Filley (in Rao, 1990), cognitive symptoms, like other neurological symptoms in MS, seem to present according to the natural progression of the disease course itself. The symptoms can present with relapse and remission, relapse and progression or chronic progression. It is important to keep this fact in mind since the results obtained concerning the extent of cognitive impairment may very well be a function of the nature of the presentation of these cognitive symptoms. In other words, results regarding the level of cognitive impairment obtained at any given time during the disease course may not be an accurate representation of the level of cognitive impairment at any other given time – information that becomes very important when rehabilitative strategies are being designed.

Until recently it was believed that only a few severely disabled MS patients had cognitive deficits. Kahana, Leibowitz and Alter (1971) and Kurtzke, Beebe, Nagler, Auth, Kurland and Nefzger (1972), using only a clinical examination, indicated rates

of organic mental impairment of less than 5%. More recent studies employing neuropsychological batteries places the incidence of cognitive impairment at around 63% (Rao, Hammeke, McQuillen, Khatri & Lloyd, 1984) and 45-65% (Bagert et al., 2002). Peyser, Edwards, Poser and Filskor (1980) indicated that routine neurological examinations may overlook more than 50% of MS patients classified as cognitively impaired on neuropsychological examination. The fact that the degree of cognitive impairment may not be related to the degree of neurological disability, that patients with predominant periventricular demyelination, even with long-standing disease, may be considered mildly affected, or even silent with respect to neurobehavioural deficits and the fact that bedside mental status examination and brief standardised mental status examinations are insensitive to detecting mild to moderate neurocognitive impairment, are all possible reasons as to the enduring lack of awareness that functionally important cognitive disturbances can occur in MS (Nelson, Heaton & Filley, in Rao, 1990).

It is thus necessary to employ sensitive neuropsychological assessment, early in the disease course, to accurately determine the presence and extent of cognitive impairment in individuals suffering from MS. This will allow for early intervention and effective rehabilitative steps to be taken to combat the detrimental long-term effects that cognitive impairments might have on the effective coping and successful functioning of the individual with MS.

It is important to note that conflicting evidence exists regarding the relationship between cognitive impairment and level of neurological disability, disease course or disease duration in individual patients.

Although clinical course (chronic-progressive disease) and longer disease duration were associated with the occurrence of cognitive dysfunction in a large sample of patients (Heaton, Nelson, Thompson, Burks & Franklin, 1985), these clinical parameters are not useful predictors of cognitive dysfunction in any given patient. Bagert et al. (2002) found that several clinical variables including a progressive disease course, the level of physical disability and increasing age, were predictive of the degree of cognitive decline. This is in conflict with research done by Franklin et al. (in Rao,

1990) who found no correlation between degree of functional cognitive impairment and disease duration

Due to the nature of MS, no definite description of the course and nature of cognitive disturbances can be given that describes all sufferers of MS. The cognitive disturbances associated with MS are generally milder than those associated with other dementing conditions. They are also not as robustly evident at initial investigation as they are later in the course of the illness. Not all patients are similarly affected, or even equally severely affected, in all cases of MS. The course of these deficits is not predictable and they do not affect cognitive functions uniformly (Lezak, 1995; Rao, 1990).

5.2. SOME VARIABLES THAT AFFECT COGNITIVE FUNCTIONING IN MS

5.2.1. Lesions

There are specific relationships between white matter lesions, as depicted on MRI, and results of comprehensive neuropsychological testing in patients with MS (Rao & Hammeke, 1984). Total lesion area as seen on MRI, has been shown to be the best predictor of cognitive test performance (Rao & Hammeke, 1984). This is supported by research conducted by Zivadinov et al. (2001), that found that MRI measures of brain atrophy were found to be an independent predictor of cognitive dysfunction. Ventricular enlargement, corpus callosum atrophy or moderate to severe periventricular demyelisation may predict cognitive impairment in MS. Previous research (as reported by Franklin et al., in Rao, 1990) has shown correlations of cognitive impairment with both enlarged ventricular size and atrophy of the corpus callosum and a significant correlation was found between cerebral lesion burden attained on MRI and cognitive impairment, although the research of Bagert et al. (2002) only found weak correlations between MRI indicators of lesion burden and cognitive impairment.

Peyser, Edwards and Poser (1980) found that the areas most affected by MS, are the parieto-occipital areas of the brain followed by the frontal and temporal regions,

however frontal region lesions were the most significant predictors of cognitive impairment.

5.2.2. Duration of Illness

The duration of the illness seems to have an important negative effect on global cognitive functioning. Heaton et al. (1985, in Rao, 1990) found a significant, yet low, correlation between cognitive impairment and disease duration, a finding also supported by Ruggieri et al. (2003). Yet when considering different cognitive processes individually this might not always ring true as Peyser (1980), Rao (1990) and Ron (1991) found that cognitive impairment was related to the duration of the disease whilst when investigating memory (for example), duration of illness seemed unrelated to the severity of memory impairment (Peyser, Rao, La Rocca & Kaplan, 1990; Minden & Schiffer, 1990). On the other hand Franklin et al. (in Rao, 1990) found no correlation between degree of functional cognitive impairment and disease duration in their research.

Thus the nature of the relationship between disease duration and cognitive impairment is once again steeped in ambiguity and future research will do well to incorporate the notions of general (or global) cognitive impairment versus specific cognitive disabilities.

5.2.3. Type of Multiple Sclerosis

Patients with chronic-progressive disease tend to have more severe impairment on neuropsychological testing than those with relapsing -remitting disease. This is demonstrated by findings from research done by Rao, Leo, Haughton, St. Aubin-Faubert and Bernardin (1989) and Minden and Schiffer (1990) who found that the severely cognitively impaired patients were more frequently suffering from the chronic-progressive type of MS. Beatty, Goodkin, Hertsgaard and Monson (1990) further showed that the frequency and severity of cognitive impairment are greater among patients with the chronic-progressive disease course who suffer more severe physical disability, than amongst those less severely disabled patients with a relapsing-remitting disease course.

However even patients with the chronic-progressive type of MS may be spared from cognitive dysfunction as Heaton et al. (1985) in Rao (1990) found that 28% of these patients evidenced no cognitive impairment.

5.2.4. Degree of Physical Disability

There are contradictory results concerning the association between cognitive deficits and the degree of physical disability. Rao et al. (1991) and Bagert et al. (2002) found a significant association between these two factors while the studies of Penman (1991) and Ron (1991) showed no significant association between the degree of physical disability and cognitive impairments. Beatty et al. (1990) furthermore showed that the frequency and severity of cognitive impairment are greater among patients with the chronic-progressive disease course who suffer more severe physical disability, than amongst those less severely disabled patients with a relapsing-remitting disease course. His research did however not investigate to what extent (a) type of MS and (b) degree of physical disability contributed to the detected cognitive impairment and therefore no clear-cut conclusions can be reached.

A further problem encountered when researching the relationship between cognitive impairment and degree of physical impairment is that it is extremely difficult to determine whether the impaired performance being detected is truly representative of underlying cognitive disabilities or whether it is rather due to motor slowing (associated with increased degree of physical disability) in the absence of true cognitive inabilities. Many research studies on the subjects do not differentiate clearly enough between these two factors, whether it be apparent in their choice of assessment instruments, methodology or conclusions drawn, and it is most likely for this reason that a precise discussion of the nature of the relationship between the degree of physical disability and cognitive impairment is still lacking.

5.2.5. Influence of Comorbid Conditions

Conditions such as depression, bipolar mood and fatigue are frequently found in MS patients and might have an influence on either the accurate assessment or actual underlying etiology of cognitive impairment. An elaborate discussion of these factors is provided in chapter 4 of this document, however it is important to consider the

possible comorbid presentation of these factors whenever focus is placed on cognitive impairment in MS.

Discerning symptoms of depression from symptoms of fatigue from symptoms of cognitive impairment remains challenging to say the least. Bagert et al. (2002) states that attempts to find a causal relationship between fatigue caused by MS and cognitive impairment has yielded inconsistent results. Yet MS patients often subjectively report a decline in cognitive functioning when they feel fatigue.

It is very possible that major depressive disorder unresponsive to therapy, or bipolar disorder may herald cognitive impairment in MS. Demaree, Gaudino and De Luca (2003, p.168) found a “clear indication that depression might augment the severity of learning and processing speed deficits in MS”. Findings reported by Franklin et al. (in Rao, 1990, p.167) suggest that “affective disorder may be an organic concomitant of MS, possibly related to a substrate of cognitive dysfunction and specific patterns of subcortical demyelisation.”

Schiffer et al. (1983) reported more depressive episodes in MS patients with cerebral involvement than in those without such involvement. Depression may even precede the diagnosis of MS itself (Whitlock & Siskin, 1980). Bagert et al. (2002, p.450) state that in general “cognitive effects are minimal in patients with mild depression, whereas they are more pronounced in patients with severe depression causing psychomotor retardation.” They continue to discuss the research of Arnett et al. (1999, in Braget et al., 2002) in which it was observed that a certain ‘threshold’ of depression severity seems to be required to produce cognitive deficits and that not all cognitive tasks are affected equally.

5.3. COGNITIVE ABILITIES AFFECTED BY MS

5.3.1. Intelligence

Performance on standardised intelligence tests has been studied intensively in MS. In general, research indicates that overall intellectual functioning, as measured by means of verbal IQ, is only mildly affected in MS (Beatty, 1993). However, care should be

taken not to equate overall intelligence with any specific aspect of intelligence. No accurate conclusions concerning cognitive functioning can be made based solely on intelligence scores, as the severity of intellectual impairment could be worse than all other neurological deficits in MS, but may occasionally be missed because of the relative preservation of language functions as was found by Peyser et al. (1980).

Moreover, measures of intelligence are also sensitive to previous education, and are therefore not reliable for measuring changes in intelligence due to MS. Also the correct execution of performance on many intelligence tests requires manual dexterity and speed, which are frequently deficient in MS (Caltagirone, Carlesimo, Fadda & Roncacci, 1991).

The only conclusion that can be drawn from the above mentioned information is that intellectual and neurological deterioration seem, in most cases, to follow a parallel course (Peyser et al., 1980).

5.3.2. Attention and Information Processing Speed

Attention can be divided into focal and sustained processes. Focused attention refers to the process of the search for and localisation of target stimuli whereas sustained attention, sometimes used interchangeably with the term vigilance, refers to the monitoring of target stimuli over an extended period of time.

Heaton et al. (1985) found that chronic-progressive, but not relapsing-remitting, MS patients performed significantly poorly on measures of attention and processing speed. It thus seems that there is some evidence to suggest that MS patients have both focal and sustained attentional deficits but the relationships between these deficits and the performance on primary and secondary memory tasks are not yet clear (Grafman, Rao and Litvan, in Rao, 1990). Research reported by Bagert et al. (2002, p.449) also found that patients with MS in which cognitive impairment was present demonstrated “slowed central processing independent of deficits in sensory-motor processing speed”.

Impairments in rapid processing of information have frequently been reported in studies of MS patients as shown by the considerable deficits that are observed on tasks that require substitution of digits for symbols (and vice versa), as found by Rao et al. (1991). Greater impairments of attention and information processing speed also

occur when a written response is required and smaller but consistent deficits arise when the response is spoken (Beatty, Goodkin, Monson, Beatty & Hertsgaard, 1988; Beatty, Goodkin & Monson, 1989). Interestingly enough these findings seem to add weight to the argument (as seen in the section on intelligence and cognitive impairment discussed earlier) that verbal abilities might be greatly preserved and thus present an inaccurate picture of the true extent of cognitive impairment present. Archibald and Fisk (2000) also found that although sensory/motor processing times of MS patients weren't significantly different from normal subjects, the speed of information processing that relied on the working memory system was significantly slower. They state that the "findings suggest that slowed information processing speed may be one of the earliest cognitive manifestations of MS, but that it may be the deficits in structural and operational working memory capacity that lead to difficulties in learning new information" (Archibald & Fisk, 2000, p.698).

Existing theory states that the frontal lobes, as the functional end points of the reticular activating system, are highly involved in attention and concentration. In Swirsky-Sacchetti et al.'s (1992) study, however, it was found that effects of lesions in the right parieto-occipital region were most prominent in measures of sustained attention and visual scanning when oral output was required. Delayed recall of complex figures depended heavily on the left frontal region.

It is however very important to note that early attention deficits, which can be detected even in those patients with minimal neurological impairment, extend to involve memory and abstraction abilities as the disease advances (Peyser et al., 1980).

5.3.3. Executive Functions

Neuropsychological tests of complex cognitive functions including abstraction and conceptualisation show disturbances of shifting set, concept formation, and perseveration amongst MS patients similar to those seen in patients with frontal lobe injuries (Rao, 1986). Bagert et al. (2002) also report that deficits in executive functions and conceptual reasoning occur in MS.

In their research Foong et al. (1997) found that MS patients presented with abnormalities in verbal fluency, cognitive estimation, spatial span, spatial working memory and use of strategy and planning. They found that not all these functions

were impaired to the same extent which they view as “lending support to the hypothesis that different aspects of executive function may be subserved by different distributed systems” (Foong et al., 1997, p.23). These deficits in executive function could also not be explained as either resulting from a general intellectual decline or coexisting psychiatric symptoms or primary visual impairment. These impaired executive function scores were correlated significantly with frontal lesion load (albeit only for the more difficult levels on tasks of spatial working memory and planning) but disappeared when total lesion load was controlled for, indicating that “although frontal pathology may be crucial in causing the executive deficits, it seems unlikely to be the sole cause.” They continue to hypothesise that “it is possible that the impairment on executive tasks may be secondary to a more diffuse process affecting the general functioning of the brain or causing a disconnection between prefrontal, limbic and association cortices which has been suggested in traumatic brain injury patients” (Foong et al., 1997, p.23).

Rao et al.(1991) also found that, compared to healthy controls, MS patients were impaired on tests of problem solving. An important factor here is that the performance of MS patients on problem solving tests were qualitatively similar to that of patients with acquired lesions of the frontal lobes. Analysis of MS patients’ performance on these tasks showed patterns of perseverative responding even though negative verbal feedback was given (Rao et al., 1991). Once again the importance of the effects of the frontal lobe functions in the nature and course of MS and the problems that arise as a result thereof, is highlighted.

Conceptual reasoning skills are frequently reported to be impaired in patients with MS (Rao, 1986). Cognitive test findings suggest that MS patients have difficulties forming concepts, shifting mental sets and responding to environmental feedback (Peyser et al., 1980; Rao & Hammeke, 1984). It is not yet clear exactly what the mechanisms are that lead to impaired performance on conceptual reasoning tasks. Conceptual reasoning deficits can result from defective abstraction and concept generation skills, perseverative tendencies and defective self-monitoring. Other non-specific factors, such as inattention, low motivation, distractibility, impulsiveness, carelessness and memory disturbance may also contribute to defective performance on tasks of conceptual reasoning. There is considerable variability amongst patients in the range and severity of these deficits (Rao, 1986).

5.3.4. Visual and Auditory Processing

Rao et al. (1991) found that MS patients were mildly impaired on standard measures of visual tasks. Tasks such as judging line orientation, discriminating faces, and emotions conveyed by facial expressions, were affected. If this is considered together with the findings mentioned earlier that performance on tests of visual and auditory attention is impaired in MS patients and that slowing in information processing is also present (Peyser et al., 1980), the difficulty in determining the exact nature of these difficulties becomes apparent. To complicate the issue even further, Lezak (1995) discusses some of the sensorimotor difficulties that individuals suffering from MS experiences. These visual disturbances may include blurred vision, double vision or loss of colour perception or blindness in one or both eyes. She further states that motor symptoms are even more common with 80-90% of MS patients troubled by brief enduring episodes of limb weakness and/or spasticity, in co-ordination, and mostly some combination of these problems that show up on testing as impaired motor skills and motor slowing. Sensory alterations, including numbness and/or paresthesias, are reported by about 90% of MS patients at differing times in their disease course and for varying durations.

It is thus clear that a problem is encountered when impairments of visual or auditory processing tasks are being measured by only making use of relatively non-specific visual or auditory performance subtests of more comprehensive assessment instruments. This practice makes it impossible to determine whether the deficits that were measured arise from simple deficits in visual perception or sensorimotoric abilities or whether a higher level impairment in processing and analysing visuospatial and visuoperceptual information is present (Rao et al., 1991).

5.3.5. Memory

Memory disturbances in MS are highly variable and do not follow a distinctive progression. Longitudinal neuropsychological studies are needed to measure the rate of deterioration of memory and other cognitive functions in MS patients (Peyser et al., 1990). However some general conclusions can be reached regarding the evidence of memory deficits in patients with MS.

MS patients have been found to exhibit deficits on measures of secondary (long term) memory and verbal fluency but perform normally on measures of primary (short-term) memory, recognition memory and rate of forgetting from secondary memory. These results suggest that the memory disturbance in MS results primarily from an impaired ability to access information from secondary memory, while encoding and storage capacity is intact (Beatty, 1993). This is accordance with the results from a study done by Rao (1986) in which the researchers found that MS patients, seen as a group, started and ended with poorer recall than those of normal controls, but they were able to learn material at a rate that paralleled that of the controls. Research done by Foong et al. (1997) found that there was specific impairment of working memory as opposed to less efficient use of strategy or poor immediate recall.

Interestingly, tasks that measure implicit memory and recognition memory show normal (or near normal) performance in MS patients. Therefore, it seems that mainly processes that allow retrieved information to reach consciousness are impaired (Grafman, Rao and Litvan in Rao, 1990). Minden, Moes, Orav, Kaplan and Reich (1990) also found that the severity of the memory impairment generally reflected the severity of other cognitive deficits.

Patients with MS are known to exhibit a higher rate of depression than other patient groups with equal degree, or greater degree, of physical disability (Joffe et al., 1987; Schiffer et al., 1983; Whitlock and Siskin, 1980). These clinical observations raise the question as to what extent memory problems in MS can be attributed to depression. Grafman et al. (in Rao, 1990) discuss research (Rao et al., 1984; Fischer, 1988; Beatty et al. 1988; and Jambor, 1969) that found only a modest, if any, relationship between depression and memory performance in patients with MS. Interesting, though, is that MRI studies indicate that memory disturbance cannot entirely be caused by depression. Studies done by Franklin et al. (1988) and Rao et al. (1989) as mentioned by Grafman et al. (in Rao, 1990) found robust correlations between measures of memory performance and the total area of lesion involvement on MRI scans.

Thus, instead of the generally accepted explanation that depression produces memory dysfunction, there may be two alternative explanations for this occurrence. Firstly that depression results as a normal emotional reaction to the loss of cognitive abilities,

especially in the mildly memory impaired MS patient with intact personal insight, and secondly that both depression and memory disturbance result as a direct consequence of demyelisation lesions within the limbic system during the course of MS (Grafman et al., in Rao, 1990).

The degree of memory impairment in MS patients thus appears to be mostly unrelated to the length of the illness, the severity of disability, specific disabilities, and depression (Peyser et al., 1990; Minden et al., 1990). However, when global cognitive impairment is ignored, a significant association between poorer memory test performance and chronic progressive type of MS, lower socio-economic status and the use of anti-anxiety medication was found (Minden et al., 1990).

Rao et al. (1984) suggests that memory impairment in MS may be secondary to a frontal lobe syndrome. However Schacter (1987) is sceptical about the existence of a frontal memory disorder, expressing the view that the poor performances on memory tasks by frontal patients might well be a function of the impairment of other processes such as the integrated execution of behaviour and rule following.

The presence of memory impairment in MS patients has certain implications for patient management (Rao, 1986). Due to the nature of memory impairment in MS, clinicians are encouraged to allow sufficient time and repetition of information to facilitate maximum learning when educating MS patients on either their disease or when making use of rehabilitation strategies.

5.4. IS COGNITIVE DYSFUNCTION IN MS A SUBCORTICAL DEMENTIA?

Maier and Benson (in Rao, 1990) suggest that the cognitive dysfunction in MS is a subcortical dementia syndrome. They consider the definition of dementia (as proposed by Cummings and Benson, 1983 as cited in Rao, 1990, p.90) as “a clinical syndrome defined as an acquired, persistent loss of intellectual function affecting at least three of the following spheres of functioning: (1) memory, (2) language, (3) visuospatial skills, (4) complex cognition such as abstraction, calculation, or judgement, and (5) personality, including mood and affect.” Dementia is thus defined as a clinical syndrome and not as a specific diagnosis or single disorder. Within this syndrome, various patterns of intellectual deficits can occur, resulting from multiple etiologies.

Subcortical dementia (so called due to the involvement of predominantly subcortical pathology, especially disease of the extrapyramidal system) is characterised by:

- slowing of cognition, including difficulty with problem solving and visuospatial skills;
- memory disturbance best described as forgetfulness;
- mood changes;
- psychomotor slowing; and
- motor system abnormalities.

Language function is preserved in subcortical dementia although communication is hampered by speech disturbances such as dysarthria. In subcortical dementia, memory is affected due to problems associated with retrieval rather than with initial encoding of new information, therefore clues and recognition tasks lead to considerably improved performance in subcortical dementia. Visuospatial and cognitive skills are also disturbed and mood disturbances, personality changes and psychosis are frequent manifestations of subcortical dementia. The individual with subcortical dementia will thus appear apathetic, psychomotor-retarded, and depressed. Subcortical dementia thus involves disturbances in fundamental functions such as an arousal, timing and sequencing, motor programming, motivation, and mood. These functions are very important as they underlie the performances in many other processes.

The similarities between what Mahler and Benson (in Rao, 1990) discuss as symptoms of a subcortical dementia and what has been discussed concerning the profile of cognitive impairment of sufferers of MS in the previous sections of this chapter, now become apparent. Mahler and Benson (in Rao, 1990) argues that the neuropsychological dysfunction in MS patients, namely: memory impairment characterised by a retrieval defect and forgetfulness; disturbed concept formation, abstraction, and set shifting while language function and verbal intellectual skills are largely preserved; mood and affective disturbances such as depression and euphoria; and speech and motor system abnormalities, represent major facets of disability brought about by the disorder and lead to such an extensive dysfunction that it deserves to be considered a dementia. Lezak (1995) concurs when she states that “multiple sclerosis may qualify as a subcortical dementia on the basis of similarities in memory impairments that do not involve defective encoding or storage, in defects in what are considered to be frontal lobe functions, and in motor and/or mental slowing.....moreover, the classical cortical disorders, aphasia, agnosia, and apraxia, rarely occur” Lezak (1995, p.243-244).

Nocentia et al. (2001) also consider the pattern of cognitive impairment in MS, namely deficits of attention, memory (in particular recent and semantic memory) as evaluated by categorical verbal fluency, speed of information processing and problem-solving and abstract reasoning disturbances, as compatible with a subcortical dementia.

Yet care should be taken not to over generalise the pattern of cognitive symptoms experienced in sufferers of MS in order to fit them into a definite syndrome. As with all the other symptoms experienced by sufferers of MS, the cognitive difficulties are as individual and varied as the sufferers themselves.

5.5. THE INFLUENCE OF COGNITIVE CHANGE ON DAILY LIFE

Recent studies have demonstrated that MS patients with minimal physical disabilities may suffer cognitive impairments that are severe enough to preclude employment and cause marked disturbances in social functioning and other daily living activities (Beatty et al., 1989; Litvan et al., 1988; Rao et al., 1991).

Rao et al. (1991) studied employment and social functioning of 100 MS patients recruited randomly from a membership list of a local MS society. He found that the cognitively impaired patients were less likely to be employed, engaged in fewer social activities and required more personal assistance in activities of daily living. Reports from relatives and friends stated that the cognitively impaired patients were more often confused and less emotionally stable than the cognitively intact patients. He found that the above differences could not be attributed to levels of depression because these were comparable for both the cognitively impaired and cognitively intact patients.

Wild, Lezak, Whitham, and Bourdette (1991) studied patients that were either classified as predominantly cerebral, or predominantly spinal, based on the location of their lesions as judged by neurological examination and MRI. The spinal group was significantly more physically disabled but the cerebral group was significantly more cognitively impaired. He found that, despite their greater physical disability, the spinal patients were more likely to be employed, more likely to be currently married, less likely to have been divorced and less likely to have received psychiatric care.

5.6. CONCLUSION

Considered as a whole, research clearly demonstrates that cognitive dysfunction is relatively frequent in MS and is often serious enough to cause significant functional impairment that gives rise to tremendous social and psychological difficulties and stresses to both the patient and his/her relatives and caregivers.

It has been demonstrated that the natural history of cognitive dysfunction is as varied as the occurrence of sensorimotor deficits in MS. It is also clear that too often widely used neurological examinations may overlook these cognitive impairments to the

detriment of effective patient care. So often care and rehabilitation is regimented to focus on physical disability and relief of these symptoms, that hardly any thought is given to the cognitive impairments and the effects they have on the entire existence of the patient. It is crucial that more attention be given to this discrepancy. Cognitive dysfunction should be recognised as being just as disabling, if not more than the physical impairment associated with MS (Beatty, 1993).

However, when can medical practitioners anticipate cognitive impairments in order to refer the patient for more extensive neuropsychological evaluation? Franklin et al. (in Rao, 1990) might have an answer when they state that the clinical findings that may best predict cognitive impairment in MS are (i) gait apraxia and/or frontal release signs predominant in the lower extremities, (ii) a chronic-progressive disease course, (iii) moderate to severe periventricular demyelination, ventricular enlargement, or corpus callosum atrophy on MRI scan, and (iv) depression that appears refractory to treatment, or bipolar illness. They further state that poor predictors of cognitive impairment in individual patients are age, disease duration, and neurologic disability status. In the same vein, Bagert et al. (2002) states that cognitive impairment in individuals with MS is extremely ‘under-recognised’. They state that “affected patients often complain of trouble with memory and multitasking, but may be unaware of the full impact that such problems have on their lives. Family members, too, often fail to appreciate cognitive decline, though they may complain of problems with the patient’s daily functioning. Clinicians should be sensitive to such complaints as they may signal a cognitive decline” (Bagert et al., 2002, p.450). To assist clinicians to do this they constructed a list (see Box 5.1) of so-called ‘red flags’ that when present might alert the clinician to the possibility of the presence, or even the progression of cognitive dysfunction in the MS patient.

BOX 5.1: COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS: ‘RED FLAGS’ FOR THE CLINICIAN

- Significant cerebral magnetic resonance imaging abnormalities, particularly with signs of atrophy.
- Inability to provide coherent history.
- Frequent missed clinic visits and phone calls.
- Difficulties following directions.
- Unreasonable decisions regarding treatment.
- Unexplained difficulties at work or holding down a job.
- 'Depression' that does not respond to antidepressants.
- Patient or family members reporting cognitive difficulties.

(Bagert et al., 2002)

Due to the fact that significant cognitive impairment can occur early in the course of the disease, proper neuropsychological assessment is an important component of disease diagnosis, rehabilitation planning and overall patient care.

CHAPTER 6

METHODOLOGY

6.1. AIM OF THE PRESENT STUDY

As discussed in chapter 1 of this document, the aim of the present study was to explore the nature of the involvement of certain demographic (gender, age and education), cognitive (specifically executive functions) and psychological factors (personality changes and other psychosocial issues) in the disease process in a group of MS patients. An assessment protocol was compiled using tests that have been shown to be sensitive to these various factors and this protocol was administered to the research sample.

In this chapter the methodology of the current study will be discussed. The research sample will be described and the individual tests, that constituted the assessment protocol, will be discussed.

6.2. THE STUDY

6.2.1. Sample

The research sample consisted of 20 adults (8 male and 12 female) diagnosed with MS. Mean age was 47.65 years (mean age male = 52,38 and female = 44,50). The age range of the male and female subjects were 33-64 and 19-60 years respectively. The mean age at which the subjects were diagnosed with MS was 40,25 for the male subjects and 38,33 for the female subjects. An option would be to discard data on female participants under the age of 30 years. However given the exploratory nature of the study, where diversity is preferable to homogeneity, it was decided to include all protocols in the analyses of the data. The wide age range represented in the study served to strengthen the value of gender differences across age and the female and male sub groupings were furthermore comparable on aspects such as age at diagnosis and degree of physical impairment. Although no formal measure of degree of physical

impairment was introduced in the assessment procedures, which I consider a short coming of this study, objective observation lead me to conclude that all participants were in a similar range of physical disability. This observation was done at the time of testing as degree of physical disability could potentially impact negatively on the successful execution of some of the neuropsychological assessments measures. In this way five of the 25 individuals that responded to the invitation to take part in the study were excluded from the study due to their degree of physical impairment (one individual was excluded due to being in a comatose state at the time of testing).

A random sample was thus not possible as I was forced to include all of the remaining 20 individuals in the sample. The individuals in this sample varied in factors such as age, educational level and disease duration. Given the explorative nature of the study this presenting variety seemed desirable, as this would enhance the validity of possible statistically significant findings gained from this study. However, care was taken to collect thorough biographical data for each subject to enable accurate analysis and interpretation of the data. The subjects were all members of the South African MS Society (SAMSS) and the researcher was not able to approach individuals diagnosed with MS who were not members of the society. This fact could possibly have some effect on the research results as the SAMSS members had potential access to alternate support services such as support groups and information sharing via their membership of the MS Society. Further analyses of the sample's demographic characteristics are provided in section 7.1 in the following chapter.

The subjects were resident in the Gauteng-, Northwest-, Free State-, Northern Cape-, and Mpumalanga Provinces of South Africa. The other provinces were not included in the study as the invitations to participate in the study were sent out as an attachment to the MS newsletter of the Transvaal, Orange Free State and Northern Cape chapters of the South African MS society. It was also practically impossible for the researcher to do home visits further a field than these said provinces.

6.2.2. Procedure

I contacted the South African Multiple Sclerosis Society and arranged an interview with the society's social worker where we discussed my ideas concerning the research. I also made contact with the society's chairperson during which time the

research project was discussed further. Seeing that the society's membership lists were confidential, I could not make direct contact with potential participants. However, arrangements were made to send out letters of introduction with a newsletter from the society. A thousand letters were sent out in which I introduced myself and my proposed research and provided my contact details. A call was made for willing participants to contact me directly during which time more information would be given. Due to the difficulties that individuals, suffering from MS, experience concerning travel, I travelled to each subject's home where the interviews and assessments were conducted.

The following section discusses the procedure that was followed during the assessment protocol.

6.2.3. Assessment Procedure

The assessment period started off with an informal discussion in which the individual's experience of MS was discussed. I also explained what could be expected from the assessment period and obtained signed informed consent from each participant before proceeding with the assessment protocol. Once this was completed, the tests were administered in the order in which they appear in table 6.1. Due to the fact that patients with MS tire quickly, the time structure of the procedure was adapted slightly according to the individual subject's needs.

While the subjects completed the 16 PF, the researcher interviewed the significant other. This was done separately as the researcher was of the opinion that the significant others would speak more freely, when they were interviewed individually and separately from the patient. This interview was semi-structured and had the goal of exploring aspects such as changes regarding personality, cognitive functions, psychosocial difficulties and adaptation the sufferer had either encountered or undergone since being ill. The specific characteristics that I was interested in was aspects of cognitive impairment and personality change brought about by frontal lobe dysfunction and any psychosocial difficulties that were associated with having MS.

The information was obtained from a significant other as I was of the opinion that they would be more objective than the individual suffering from MS. It has also been

shown that patients with frontal lobe dysfunction have poor insight and therefore are limited in their ability to provide valid information aspects such as cognitive and personality changes that they might have undergone. The researcher had to rely on persons close to the patients for information concerning MS related changes and difficulties as there were no pre-morbid measures of these aspects for the individual subjects.

In lieu of the fact that no personal feedback could be provided to individual research participants and as a gesture of appreciation, I committed myself to write an article to be published in the society's quarterly newsletter as soon as the research project was completed.

6.2.4. Psychometric Measures

A comprehensive neuropsychological examination can last many hours and could stretch over more than one day. Although such extensive testing is important for thorough assessment, especially to address complicated questions concerning disability and employment issues, it was impractical within the boundaries of the present study and the typical assessment protocol had to be adopted.

A further ethical consideration was that MS patients tire quickly. Exhaustion may have grave implications because it may trigger an exacerbation of the disease. It is for these, and other practical reasons (such as the reasonable availability of the tests), that the researcher decided to use only the assessment measures as given in table 6.1. These measures were chosen for their sensitivity as measures of cognitive impairment (especially those sensitive to frontal lobe impairment) that were implicated for the methodology of the current study and the researcher makes no claims concerning the assessment protocol being a complete assessment of each subject's cognitive impairments.

TABLE 6.1: ASSESSMENT PROTOCOL

TEST	FUNCTION BEING INVESTIGATED	PREVIOUS RESEARCH USING OR ADVISING THE USE OF THESE TESTS
Open introductory discussion		
Rey Auditory-Verbal Learning Test (RAVLT)	Immediate memory span Learning Interference vulnerabilities	Minden et al. (1990) Caltagirone et al. (1991).
Controlled Oral Word Association Test (COWAT)	Verbal Fluency Organisation of thought	Peyser et al. (1990) Minden et al (1990) Rao et al (1991) Swirsky-Sacchetti et al (1992) McIntosh-Michaelis et al. (1991) Beatty et al. (1989)
Digits Forward and Backward (SAWAIS)	Working Memory Attention Tracking	Taylor (1990) Minden et al. (1990) Rao et al. (1989) Rao et al. (1991) Swirsky-Sacchetti et al. (1992) Caltagirone et al. (1991)
Block Design (SAWAIS)	Non-verbal reasoning Problem Solving Visuo-spatial Organisation	Peyser et al. (1990) Rao et al. (1991) Lezak (1995)
Trail-Making Test (TMT)	Visuo-spatial Scanning Mental Tracking Complex, sustained attention	Lezak, (1995)
Wisconsin Card Sorting Test (WCST)	Abstract/Conceptual Reasoning Mental flexibility	Minden et al (1990) Peyser et al. (1990) Rao et al. (1991) Swirsky-Sacchetti et al. (1992) McIntosh-Michaelis et al. (1991) Beatty et al. (1989) Caltagirone et al. (1991) Lezak (1995)
16 PF Questionnaire	Current Personality Dimensions	
Qualitative Interview	Demographic, psychosocial functioning, personality prior to, and after MS diagnosis.	

*SAWAIS indicates subtest of the South African Wechsler Adult Intelligence Scale

The individual tests that made up the assessment protocol will now be discussed.

6.2.4.1. Rey Auditory-Verbal Learning Test

This test consists of a list containing 15 words (list A) that is read to the subject a total of five times (trial I to V), a second list of 15 words (list B) that is presented to the subject once (trial VI), serving as a distracter trail, and an immediate recall trial (VII)

and delayed recall trial (VIII) of list A. After each trial subjects repeat as many words as they can remember and the examiner writes these words down exactly as the subjects produce them.

This test measures immediate memory span (trial I), provides a learning curve (trials I to V), reveals the presence, or absence of learning strategies (clustering of words etc.) and elicits susceptibility to interference effects (trial VI). It also measures short and long term retention (trials VII and VIII) and allows for a comparison between retrieval efficiency and encoding (recognition trial) (Lezak, 1995). Patients with frontal lobe lesions tend to demonstrate problems with the recall trials but perform normally when presented with the recognition format. This is due to the fact that patients with frontal lobe dysfunction demonstrate “impaired use of context for storage or retrieval” (Lezak, 1995, p.91). These individuals thus don’t seem to have impairment of the memory system as such, but rather have trouble organising and structuring what they learn. They also do not seem to use context to facilitate spontaneous recall, “they seem not to remember to remember” (Lezak, 1995, p.90), and this produces the pattern observed above.

6.2.4.2. Controlled Oral Word Association Test

In this test the subject is asked to reproduce as many words as possible within a one minute interval beginning with the letters F, A and S. These letters were chosen for their rate of occurrence in the English language. In Afrikaans the letters used are T, S and V. The words produced should exclude proper nouns, numbers, and words already produced just with different suffixes. The score for the test is the total of all acceptable words produced, which is then adjusted for age, sex and education.

This test measures word fluency and the patient’s ability to organise their thoughts and is thus sensitive to frontal lobe dysfunction, as frontal lobe lesions have been shown to depress word fluency scores, with left frontal lesions having a greater depressive effect than right frontal lesions (Lezak, 1995). This is because the task involves verbal or language functions which are localised to a greater extent in the left temporal and prefrontal cortex than the right prefrontal cortex. Furthermore, as shown in the section on the Rey Auditory-Verbal Learning Test, patients with frontal lobe dysfunction experience difficulties organising, contextualising and retrieving

information spontaneously which would further account for the difficulties they experience with this task.

6.2.4.3. Digits Forward and Backward (SAWAIS)

For this purpose Subtest 4: Digits Forward and Backward of the South African Wechsler Adult Intelligence Scale (SAWAIS) (obtainable from the (Human Sciences Research Council, 1983) were used. Both digits forward and backward consist of groups of random number sequences that are read aloud at the rate of one digit per second. For digits forward the subject is required to repeat the sequence in the same order. For digits backward the subject repeats the sequence in the reverse order. The tests are terminated after two subsequent incorrect responses from the subject and the score is the number of digits in the last sequence correctly reproduced.

Digits forward is influenced by attentional deficits, as digit span decreased with anxiety (Baddeley, 1986). The test furthermore measures auditory attention. In patients with frontal lobe dysfunction, attentional deficits are frequently observed. These individuals firstly find it difficult to focus their attention on a stimulus, and secondly, once they have focussed on a stimulus find it difficult to sustain and shift the focussed attention and are highly susceptible to distractions (Lezak, 1995). These deficits become more apparent as the tasks, such individuals are expected to perform, increase in difficulty.

Lezak (1995) further states that patients with diffuse damage (such as found in MS) and who experience problems with tracking, often do repeat the correct numbers but usually mix the order of these numbers. Individuals with severe impairment (especially with frontal lobe damage) may substitute sections of over learned sequences (such as 1-2-3-4 for 1-2-5) or may perseverate from previous series.

Digits backward is a complex attentional task that requires the inhibition of more automatic responses and requires double-tracking in that both the memory for the digits and the reversing operations must proceed simultaneously. This test gives an indication of working memory and is thus very sensitive to diffuse brain damage. The tracking and inhibitive abilities required for this task imply great sensitivity to frontal lobe dysfunction.

6.2.4.4. Block Design (SAWAIS)

Subtest 9: Block Design of the SAWAIS was used for this purpose. Seven designs are presented to the subject printed on cards. The subject must mentally partition the design so that it can be constructed using the blocks. The test is timed so that additional points are given for speed of responding. I followed the instructions as contained in the SAWAIS. I also obtained additional qualitative data regarding possible executive dysfunction in the following manner. In the event where the time had expired and the design had not been completed, or completed inaccurately, I enquired as to the correctness of the design. If the subjects considered the design correctly completed I urged them to have another look to double check the correctness and observed whether these individuals were able to spot their mistakes. If the subjects realised the incorrectness of the design I attempted to provide limited clues to observe whether these individuals were able to make use of the clues to correct the design.

Block design measures nonverbal reasoning, problem solving and visual-spatial organisation. Lezak furthermore states that “block design lends itself well to qualitative evaluation. The manner in which patients work at block design can reveal a great deal about their thinking processes, work habits, temperament, and attitudes toward themselves” (Lezak, 1995, p.589).

Individuals with frontal lobe damage may demonstrate impaired results on Block Design tasks due to impulsiveness, carelessness, a concrete perspective leading to random approaches to solving the problem and not seeing or correcting errors. Subjects with more severe frontal damage may show a kind of stickiness even though they say that they understand the task (Lezak, 1995). Another difficulty that individuals suffering from dementing conditions and frontal lobe dysfunction exhibit on this task is slowness in learning new response sets. In Block Design this may present as an impaired performance (failure) on approximately the first two items with a significant increased performance on each subsequent item (Lezak, 1995).

6.2.4.5. Trail-Making Test

This test of visual conceptual and visuomotor tracking is highly sensitive to brain dysfunction. In Trail A of the Trail-Making Test (TMT) the subject joins a series of numbered circles chronologically according to their numeric values (e.g. 1-2-3-4 etc.). In Trail B the subjects join the circles according to an alphanumeric sequence (e.g. 1-A-2-B-3-C etc.). On both parts of the test, the score is the time in seconds to complete the test.

Trail A measures visual scanning speed and motor speed, since numeric sequences is over learned or automatic. Trail B, however, requires mental tracking of two sets of information and switching between them. The task is therefore considered a complex attentional task requiring efficient mental tracking and flexibility.

Valuable information as to the nature of the brain impairment can be gathered when the types of errors that the subjects make (especially on trail B) are considered. According to Lezak (1995), brain trauma patients tend to make errors of both impulsivity and perseveration, which subsequently lead to the patients experiencing great difficulty in shifting between the two sets (numbers and letters) on trail B. The abilities required to successfully complete this task is reminiscent of the difficulties experienced by patients with frontal lobe damage (as discussed in chapter 3 of this document) and one might be tempted to view the TMT as a test specific of frontal lobe dysfunction. Reitan and Wolfson (1993, in Lezak, 1995) however, caution against this assumption as their research failed to demonstrate significant differences in performances on the TMT of persons with and without frontal cerebral lesions. They do however state that the TMT is generally sensitive to neuropsychological aspects of brain functions and that it provides important information concerning an individual's cognitive ability. Lezak furthermore states that "visual scanning and tracking problems that show up on this test can give the examiner a good idea of how effectively the patient responds to a visual array of any complexity, follows a sequence mentally, deals with more than one stimulus or thought at a time, or is flexible in shifting the course of an ongoing activity" Lezak (1995, p.384). It is thus, once again, a matter of considering neuropsychological tests (in this instance the TMT) rather as measurements that are sensitive, as opposed to specific, for specific loci of cerebral dysfunction.

Impairment in motor speed will adversely effect performance on the TMT, but this can be overcome by subtracting the speed for Trail A from the speed of Trail B, as suggested by Ryan (1993, in Lezak, 1995). This scoring controls for motor speed as the number of circles on both forms are the same.

6.2.4.6. Wisconsin Card Sorting Test

In this test the subject is given a pack of 60 cards with one to four symbols (cross, star, circle, and triangle) in one of four colours (yellow, red, blue, and green) printed on each card. No two cards are identical. The subject is asked to arrange these cards under four stimulus cards (one red triangle, two green stars, three yellow crosses, and four blue circles) according to principles not known to the subject. The subject is expected to deduce the principle from the pattern of the examiner's responses on the placement of the cards. The examiner changes the principle after ten successful placements by the subject. The principles according to which the cards need to be arranged can vary between colour, form and number.

In scoring the Wisconsin Card Sorting Test (WCST) two scores, namely (i) the total achieved categories and (ii) perseverative errors are especially important. The total achieved categories are the number of correct runs of ten achieved. The perseverative errors occur when the subject continues to sort according to a previous successful principle or when the subject continues to sort according to an initial wrong guess. According to Lezak "the perseverative error score is useful for documenting problems in forming concepts, profiting from correction, and conceptual flexibility" (1995, p.622). It thus becomes apparent that these scores can indicate problems concerning frontal lobe dysfunction. Research, cited in Lezak (1995), does substantiate the sensitivity of the WCST to frontal lobe dysfunction although these results should not be seen as absolute as Mountain and Snow (1993) cautions against the exclusive use of the WCST "to identify lesion sites or as a marker of frontal dysfunction" (1993, in Lezak, 1995, p.624).

6.2.4.7. 16 Personality Factor Questionnaire

The 16 Personality Factor Questionnaire (16PF) is a questionnaire for personality assessment developed by Raymond Cattell. The 16 PF scales measure an individual's

temperament; “a person’s characteristic style of thinking, perceiving, and acting over a long period of time and in a wide range of different situations” (Cattell, 1989, p.2).

The questionnaire (Form A), which was used in this study, consists of 187 items and is suitable for adults with at least grade 12 or equivalent education. The general purpose of the 16 PF is to “describe a testee’s personality and predict behaviour using a set of selected, structured items” (Prinsloo, 1991, p.2).

The fact that the Minnesota Multiphasic Personality Inventory (MMPI) is a personality questionnaire more focussed on identifying tendencies toward psychopathology would have made the use of the MMPI more appropriate in the present study. Considering the extensive literature on the effects of fatigue in the MS (as discussed in chapter 4) the length (567 items) of the MMPI questionnaire and lack of suitable norms for the South African population made the use of this questionnaire impractical. The 16 PF questionnaire provides a measure of normal dimensions of personality and would therefore provide some indication as to the personality characteristics of the research subjects.

The 16 PF was thus used as a way of describing the current personality of the MS sufferer. The semi-structured qualitative interview (with a significant other in the MS sufferer’s life), on the other hand, provided an indication of the personality changes and psychosocial difficulties encountered due to MS.

6.2.4.8. Qualitative Interview

A semi-structured interview was conducted with a significant other in the patient’s life. This significant other was a person who had known the MS sufferer for a substantial amount of time prior to the participant’s diagnosis of MS and who was still a part of the sufferer’s daily life after the diagnosis. The significant other was briefed on the purpose of the study and an informed consent form was obtained from every interviewee. I structured the interview process by guiding the discussion toward broad themes whilst allowing the interviewee the freedom to volunteer information and/or comment on anything they deemed important. The broader areas related to aspects of cognitive and personality changes and psychosocial difficulties that the interviewees had noticed regarding the day-to-day abilities and activities of the individual with MS.

These interviews were analysed qualitatively and certain themes were extracted. A second evaluator was used to ensure the validity of the themes that were extracted. The themes that were extracted are presented in table 7.3 in the next chapter.

Due to unforeseen difficulties only 14 semi-structured qualitative interviews were conducted. Two participants could not refer me to any significant other in their life that, either knew them well enough and/or knew them before their diagnosis of MS and who still had a significant presence in their life. One participant requested that I did not speak to anyone regarding their condition and another two participants' significant others withdrew their consent to participate in the research on the day the interviews were to be conducted. Another participant's significant other supplied very little information and became extremely agitated during the interview to such an extent that I needed to terminate the interview.

6.3. CONCLUSION

As can be seen from the above discussion, the assessment procedure was quite involved and lasted from 4 to 6 hours depending on the research participant's fatigability, level of motivation and physical abilities. As mentioned, the assessments were conducted in the participant's home. Although this was more convenient for the participants, it did pose unique problems concerning the timely completion of the assessment procedure, as many domestic interruptions occurred over which the researcher had little control. A discussion of this and other problems encountered during the research process, as well as a discussion of the research results and suggestions for future research will be provided in the next two chapters.

CHAPTER 7

RESULTS

7.1. INTRODUCTION

The main objective of the study was to explore the involvement of certain demographic, cognitive (especially executive functions) and psychological factors in the disease process in a group of MS patients. This chapter provides an analysis and interpretation of the data obtained from this group of MS patients during the assessment procedure.

7.2. DEMOGRAPHIC INDICATORS IN MS

The demographic variables of gender, age, and education were included in this study and their sample characteristics were analysed as follows.

7.2.1. Gender

40% of the MS patients in the sample were male ($n=8$) and 60% were female ($n=12$). This corresponds with the higher incidence of MS in the female population as reported in the literature (Multiple Sclerosis International Federation, <http://www.msif.org>; National Multiple Sclerosis Society, 2000).

7.2.2. Age

Table 7.1 shows the age distribution of the male and female subgroups of the sample. The gender subgroups (male/female) did not differ significantly in terms of their mean age scores at the time of testing ($t=1,92$; $p=0,070$), their age at diagnosis ($t=0,41$; $p=0,688$) or the years since having been diagnosed with MS ($t=1,84$; $p=0,098$). The mean age at diagnosis, namely 40,25 years for males and 38,33 years for females, is consistent with other research findings that indicate the onset of MS symptoms between the ages of 20 and 40 years (Berkow, 1977; Chipps et al., 1992; Multiple Sclerosis International Federation, 2000).

TABLE 7.1: AVERAGE AGE DISTRIBUTION

	N	Minimum	Maximum	Mean	Std. Deviation
Sample as group:					
Age at testing	20	19	64	47,65	9,58
Age at diagnosis	20	18	51	39,10	10,05
Years MS	20	1	32	8,55	6,75
Males:					
Age at testing	8	44	64	52,38	6,19
Age at diagnosis	8	18	50	40,25	10,70
Years MS	8	4	32	12,13	8,53
Females:					
Age at testing	12	19	60	44,50	10,35
Age at diagnosis	12	18	51	38,33	10,00
Years MS	12	1	13	6,17	4,11

7.2.3. Education

Seventeen of the research subjects had 12 and more years of education (of which 10 individuals received tertiary education) while only 1 individual had 11 years of formal education and 2 individuals had 10 years of education. The gender subgroups (male/female) did not differ significantly regarding their average years of education at the time of testing ($t=0,24$; $p=0,812$). Average years education for males were 13,50 ($sd = 2,62$) and for females 13,25 ($sd = 2,01$).

The number of years of education for the MS group as a whole correlated positively with certain neuropsychological variables (scores on the Block Design subtest of the SA WAIS and the RAVLT). Subjects with higher levels of education obtained higher standard scores on the block design task ($r=0,58$; $p=0,008$), were able to formulate a strategy according to which they executed this task ($r=0,58$; $p=0,008$), and needed less input from the researcher to facilitate their ultimate successful completion of this task ($r=-0,52$; $p=0,008$).

Although not statistically significant, there was a moderately strong positive correlation between the years of education for the MS group as a whole and their ability to apply learning strategies to facilitate their learning of the list of 15 words of the Rey Auditory-Verbal Learning Task ($r=0,33$; $p=0,159$). This held true for the gender sub-groups as well. For the female subgroup, the mean number of years of

education showed a moderately strong, albeit not statistically significant, correlation with the actual number of words recalled on both Trials I ($r=0,48$; $p=0,111$) and V ($r=0,41$; $p=0,189$), as well as their ability to apply a strategy for learning the list of words of the RAVLT ($r=0,38$; $p=0,229$). The relationship between the mean number of years of education and the achievement (actual number of words recalled) on both Trials I and V of the RAVLT for the male subgroup remained moderate to weak, however it appeared that as the years of education increased for the male subgroup their ability to apply a strategy for learning the list of words of the RAVLT also increased ($r=0,37$; $p=0,368$) as did their ability to self-monitor their recall responses ($r=0,69$; $p=0,061$). Although these relationships were moderately strong they were nonetheless not statistically significant. They do however warrant mentioning, as these indicators of executive functioning are a main focus of the study. Also it is important to remember that this data was collected using a very limited sized sample and further research using a larger sample might well show these relationships to be statistically significant.

An interesting finding for the female subgroup was that as the years of education increased the women showed a decreased learning curve (trial I through to trial V) ($r=-0,59$; $p=0,044$). This relationship was statistically significant and thus requires further investigation, however a possible explanation for this relationship remains elusive at this stage. It is possible that a third variable (such as disease severity or attention overload) may have interacted to produce this finding, however this requires systematic verification in a follow-up investigation.

Years of education thus seemed to exert some influence on the subjects' ability to formulate and apply strategies for attempting cognitive tasks. Later in this chapter it will be shown that the subjects showed impairment in planning and executive ability when years of education was excluded as a variable. Whereas the current correlations were moderately strong yet not statistically significant, the correlations between plan/strategy formation and application and achievement on measures of executive functioning were very strong and statistically significant. Level and quality of education thus might well play a role in either facilitating an individual's effective approach to a cognitive task or providing the individual with a better vantage point (more developed baseline of cognitive skills) from which such a task is attempted

(Nell, 1999), yet this ‘advantage’ seems to be mostly overwritten by the effects of frontal lobe pathology. This implied relationship might have some implications for rehabilitation as both the individual’s residual abilities as well as their methodological skills concerning the way they approach and manage “tasks” could be a beneficial factor towards successful rehabilitation. Only further research will tell.

7.3. COGNITIVE INDICATORS IN MS

The following discussion concerns the analysis and interpretation of the data collected from the administration of a number of neuropsychological measures. As discussed in chapter 7, these measures were chosen for their sensitivity as measures of cognitive impairment (especially of executive function) due to frontal lobe dysfunction.

Following the guidelines for analysis of the RAVLT performance proposed by Lezak (1995), the researcher considered the results obtained by the subjects on the neuropsychological measures according to the following five aspects that are closely linked to frontal lobe dysfunction and which all provide an indication of an individual’s ability to regulate their own behaviour:

- the presence or absence of a learning curve;
- the presence of learning strategies;
- self-monitoring behaviour of the individual subjects – evaluating own behaviour regarding its appropriateness/effectiveness to what is required by the situation thus involves avoiding/inhibiting responses no longer appropriate or effective);
- slowness in shifting – changing/adapting a course of thought or action according to the changing demands of the, and
- proactive inhibition - when just learned information interferes with the acquiring of new information (Lezak, 1995).

7.3.1. Rey Auditory-Verbal Learning Test (RAVLT)

Unfortunately, part of this test was presented incorrectly and therefore the data collected from this measure is sparse. Instead of presenting the distraction trial B

(consisting of list B of 15 words) only once, the researcher presented it a total of five times. Trial B thus became a new learning task instead of only having a distraction function. The increased intrusion of words from list B in the delayed recall trial and the recognition trial points to this expected effect. Nonetheless, the data that was obtained from the RAVLT yielded important information on the subjects' learning curve, learning strategies used and self-monitoring behaviour.

TABLE 7.2: RAVL TRIALS I AND V - ACTUAL NUMBER OF WORDS RECALLED

	RAVL Trial I		RAVL Trial V	
	Mean	Std. dev	Mean	Std. dev
MALE (n=8)	4,00	1,69	7,88	2,59
FEMALE (n=12)	5,67	1,50	11,17	2,62

Table 7.2 shows the average number of words actually recalled on trials I and V of the RAVL Test. The gender subgroups were statistically significantly different on the 5% level in terms of their achievement on the RAVLT, regarding the mean number of words recalled on both trial I ($t=-2,32$; $p=0,032$) and trial V ($t=-2,76$; $p=0,013$). Therefore further analysis of the data obtained from this measure was conducted separately for males and females.

The subjects' performance on the RAVLT was analysed according to the guidelines set by Lezak (1995) i.e. the following is an overview of the performance of the MS group as a whole on the RAVLT in relation to the available norms. On trial I (the initial trial where the 15 words on list A must be recalled), 25% of subjects were below normal (less than 6 words recalled) while 75% of the subjects were within the normal range (6 to 8 words recalled). On trial V (the fifth time the same list of words must be recalled and learning should have taken place), a wider distribution of results was noticed: 45% of subjects were below normal (less than 12 words recalled), 45% within the normal range (12 to 14 words recalled) and 10% above average (more than 14 words recalled).

The subjects' achievements on the first presentation of list B were the following: 35% of subjects were below normal, 60% were within the normal range and 5% were

above normal. The lower achievement of the subjects on the first recall of list B (35% within below normal range) as opposed to the first recall of list A (25% within below normal range) was especially interesting to the researcher regarding its possible indication of frontal lobe dysfunction. This could indicate a tendency towards proactive inhibition where just learned information interfered with the acquisition of new information.

Considering the achievement on trial VI (the immediate recall trial of list A after introduction of list B) one can clearly see how the incorrect presentation of list B (as learning task) influenced the results. The achievements on trial VI were as follows: 80% of individuals performed within the below normal range while 20% of individuals performed within the normal range. The same effect can be seen on trial VII (30 minute delayed recall of list A words after introduction of list B words), where 78,9% of individuals performed within the below normal range and 21,1% of individuals performed within the normal range. Thus what can be concluded is that a second learning task does in fact have a negative influence on the initial learning task. This is also demonstrated in the large percentage of individuals (89,5%) where intrusion of list B words into the recognition trial of list A was present. As well as the 50% of individuals who demonstrated intrusion of list B words on trial VI (the immediate recall of list A).

Considering the MS group as a whole regarding the presence or absence of a learning curve, 85% of subjects did demonstrate the presence of a learning curve. The 25% of individuals whose performance did not show the presence of a learning curve also did not make use of learning strategies (as would be expected) and showed slowness in shifting. These subjects' performance on the digit span were also indicative of frontal lobe dysfunction as their scores for digits forward were in the marginal to normal range and for digits reversed in the defective range as according to the guidelines proposed by Lezak (1995). This seems to indicate a difficulty regarding executive functioning due to frontal lobe dysfunction.

A further symptom that could be expected in individuals that experience frontal lobe dysfunction is a poor self-monitoring behaviour. In fact 50% of subjects did indeed show a lack in self-monitoring behaviour on the RAVLT, while 50% did not.

As mentioned earlier the gender subgroups were statistically significantly different on the 5% level in terms of their achievement on the RAVLT, regarding the mean number of words recalled on both trial I ($t=-2,32$; $p=0,032$) and trial V ($t=-2,76$; $p=0,013$) and therefore the following results regarding the correlation between different cognitive indices are discussed separately for these two subgroups.

For the female subgroup the actual number of words recalled on trial I of the RAVL was negatively correlated with the amount of perseverative errors on the WCST ($r=-0,66$; $p=0,027$). This means that as the number of words the female subjects were able to recall on trial I of the RAVLT declined so the number of perseverative errors made during the WCST increased. Another important result for the female subgroup was that the actual number of words recalled on trial V of the RAVLT was negatively correlated with the actual number of digits that were recalled on the Digit Span subtest of the WAIS ($r=-0,65$; $p=0,023$). A possible reason for this could be that these individuals manifested some impairment in recall of new information as their scores were low in both these tests for initial recall (trial I of the RAVLT and Digit Span subtest (forward)) yet as the opportunities for exercise increased, as in the increased number of repetitions of the list of words by trial V of the RAVLT, these same individuals were able to learn the required information and thus recall was facilitated.

Another interesting correlation indicative of frontal lobe involvement in the female subgroup is the positive correlation between the actual number of words recalled on trial V of the RAVLT and the use of a plan or strategy when completing the block designs of the WAIS ($r=0,60$; $p=0,038$). Thus the individuals that were not able to make use of strategies and plans to aid the completion of the block designs also did not make use of strategies to aid learning the list of words in the RAVLT and in fact this is reiterated by the positive correlation between the presence of a strategy used to learn the list of words of the RAVLT and the presence of a strategy or plan to complete the block designs of the WAIS ($r=0,77$; $p=0,003$). Another result implying frontal lobe involvement in the disease process of this female subgroup was the statistically significant correlation between the presence of a strategy for learning the list of words of the RAVLT and the number of categories achieved in the WCST ($r=0,73$; $p=0,010$). As these female subjects were able apply a strategy for learning

the list of words of the RAVLT they were also increasingly able to recognise the strategy according to which the cards were being sorted in the WCST, thus achieving more categories.

The absence of a learning curve in the RAVLT for this female subgroup was furthermore negatively correlated with the total number of words that were generated in the COWAT ($r=-0,78$; $p=0,003$) and the total number of digits recalled on the Digit Span (forward) subtest of the WAIS ($r=-0,61$; $p=0,033$) and positively correlated with the total percentage of perseverative errors made on the WCST ($r=0,61$; $p=0,048$). Furthermore the individuals who showed greater self-monitoring in the recalling of the list of words of the RAVLT also achieved more categories in the WCST ($r=0,73$; $p=0,010$).

The results for the male subgroup showed a negative correlation between the actual number of words recalled on trial I of the RAVLT and the time taken to complete Trail B of the TMT ($r=-0,73$; $p=0,039$). Thus the more words these male subjects were able to recall on the first trial of the RAVLT the less time they took to complete the B trail of the TMT. Furthermore, the more words they were able to recall on trial V of the RAVLT and as they showed the presence of a learning curve on the RAVLT, the less time they took to complete Trail B of the TMT ($r=-0,81$; $p=0,016$ and $r=-0,95$; $p=0,000$), the greater number of categories they were able to achieve on the WCST ($r=0,78$; $p=0,040$) and the less total percentage perseverative errors they made on the WCST ($r=-0,91$; $p=0,005$).

It thus seems that the above results support the frontal lobe involvement hypothesis as all these aspects namely difficulty with recall, loss of flexibility in thinking, inability to monitor own actions and responses, and the ability to formulate plans and strategies to aid learning and successful completion of tasks, support one another.

7.3.2. Controlled Oral Word Association Test (COWA)

Using the guidelines as proposed by Lezak (1995), the research subjects performed as follows on the COWA: 35% of subjects performed in the severe defective to borderline range, 55% of subjects performed in the low normal to normal range, and 10% of subjects performed in the high normal to superior range. This simplified

means that 55% of subjects performed below normal while 45% performed normal or above on this test.

The total number of words generated on the COWAT correlated positively with the percentage achieved on trial B of the TMT ($r=0,54$; $p=0,017$) and negatively with the need for clues provided by the researcher in order to complete the designs for the block design subtest of the SAWAIS ($r=-0,53$; $p=0,017$). In other words, the less words the subjects were able to generate the poorer they fared regarding trial B of the TMT and the more input they needed from the researcher to successfully complete the block design task of the SAWAIS. These correlations serve to support the involvement of executive dysfunction in MS as all three these measures are considered sensitive to frontal lobe impairment.

7.3.3. Digit Span (forward and backward) subtest of the SAWAIS

On the digits forward task, 5% of the research subjects were in the defective range, 55% in the marginal to normal range, and 40% within the normal to superior range (according to the guidelines proposed by Lezak, 1995).

On digits backward 20% of the research subjects' performances were in the defective range thus showing problems with mental tracking while 15% performed within the borderline to normal range showing a tendency towards mental tracking problems, and 65% of subjects' performances were in the normal range.

Concerning the difference between digits forward and digits backward the majority of individuals (55%) showed a difference of between 1 and 2 digits, which is considered well within the normal range, whereas 15% of research subjects showed no difference between digits forward and backward, and 30% showed a difference of more than 2 which is indicative of brain dysfunction.

The standard scores of this subtest of the SAWAIS for the MS subjects were calculated and as expected these standard scores were negatively correlated with the time taken to complete both Trails A and B of the TMT ($r=-0,52$; $p=0,021$ and $r=-0,46$; $p=0,045$ respectively). Thus as the standard scores for the digit span subtest for

the MS subjects improved so the time they took to complete both the trails of the TMT decreased and vice versa.

7.3.4. Block Design subtest of the SAWAIS

During this assessment procedure the subjects were asked to complete the block designs according to the instructions of the SAWAIS. The researcher, however, then also added instructions to investigate more quantitative data following guidelines proposed by Lezak (1995). After the amount of time was set for each task had expired, the researcher asked the subjects whether the designs they had completed with the blocks were correct or not. If they responded negatively and did not self-correct the design, the researcher proceeded to provide some clue as to where the problem might lie. This was done to assess whether the subjects needed the help in the first place and whether they could utilise the information they received. The researcher also noted whether the research subjects made use of any strategy or followed any plan to complete the block designs. These procedures thus provided qualitative data concerning possible frontal lobe dysfunction (Lezak, 1995; Stuss, 1993; Spreen & Strauss, 1998).

The majority of the research subjects (70%) seemed to follow a plan or strategy to complete the block design task, while 30% of the subjects seemed to have no strategy for completing the task. Of all the subjects completing the task, only 20% did not need a clue from the researcher and completed the task successfully on their own, while 80% of the subjects did indeed need some input from the researcher, especially concerning the more involved designs. Of the 80% of subjects that received input from the researcher, only 50% made effective use of this information while 30% could not put this information into use to successfully complete the task thus indicating some problems with frontal lobe function.

Whether the researcher gave the subjects tips regarding the completion of the block design was further also negatively correlated with the ratings of the percentiles in which the subjects' performances on both Trails A and B of the TMT fell when utilising the norms as provided by Spreen and Strauss (1998, Table 12-15, p. 541) ($r=-0,62$; $p=0,004$ and $r=-0,65$; $p=0,003$ respectively) and the total number of words generated on the COWAT ($r=-0,53$; $p=0,017$). Thus as the subjects needed increased

input from the researcher for the successful completion of the block design so their achievements on both trails A and B of the TMT and the COWAT diminished, an occurrence that was expected as all these tasks involved aspects of executive functioning. Furthermore the subjects who completed the block designs making use of a strategy or plan, required less input from the researcher for the successful completion of the task ($r=-0,69$; $p=0,001$), and required less time to successfully complete Trail A of the TMT ($r=-0,51$; $p=0,026$) and achieved higher overall standard scores on the block design subtest of the WAIS ($r=0,70$; $p=0,001$).

7.3.5. Trail Making Test (TMT)

Concerning the completion of the TMT, 78.9% of the subjects completed the tasks without errors while 21.1% of subjects did, however, make errors. According to the table proposed by Spreen and Strauss (1998), 84,2% of subjects' performances on trail A of the TMT fell below the 50th percentile for that task with only 15,8% of subjects falling between the 50th and 75th percentiles. For trail B of the TMT only 21,1% of subjects' performance fell between the 50th and 75th percentiles while 78,9% of subjects performed below the 50th percentile for this task. Considered as a whole, the group of research subjects' performance on both trails A and B of the TMT were indicative of cognitive dysfunction as the majority of subjects (84,2 for Trail A and 78,9% for Trail B) fell below the 50th percentile for performance in this test.

7.3.6. Wisconsin Card Sorting Test (WCST)

This test was administered with a single pack of 60 cards thus making it possible for an individual to achieve 6 categories after which the test was discontinued. The majority of research subjects became extremely frustrated with this task and subsequently found it difficult to sustain attention. For this reason the examiner did not use a double pack. Fatigue could also have played a role as this test was one of the last tests done during the assessment period that lasted a few hours. Of all the research subjects that completed this test, only 61,1% of subjects achieved 3 or more categories with 16,7% achieving less than 3 categories and 11,1% not being able to achieve even 1 category. Another 11,1%, however, stated the rules for achieving the categories even before the test was commenced.

The years of education for the MS group as a whole furthermore also showed a moderately strong negative, yet not statistically significant correlation with the percentages of perseverative errors made during the WCST ($r=-0,38$; $p=0,121$) i.e. the more educated the subjects were the fewer perseverative errors they made. Although these correlations are not statistically significant it is nonetheless interesting when considering the limited size of the research sample and the fact that these correlations might have been significant had a larger sample been involved - a fact that can of course only be established with further research. A relationship between these said variables makes intuitive sense, as one would expect that the level of education would exert an influence on the level of achievement on measures of cognitive function (Nell, 1999).

Perseveration errors did occur and the percentage of all cards sorted that resulted in perseveration errors showed a strong negative correlation with the number of categories achieved ($r=-0,83$; $p=0,0001$) as well as showing a strong positive correlation with the number of errors made on the TMT ($r=0,90$; $p=0,001$). The percentage of perseverative errors was statistically significantly correlated with the time taken to complete Trail B of the TMT ($r=0,57$; $p=0,017$), which seems understandable as both these measures are sensitive to perseverative type responses.

7.4. PSYCHOLOGICAL INDICATORS IN MS

7.4.1. The 16PF Questionnaire

Figure 8.1 shows the distribution of the averaged standard scores of the MS sample on the 16PF. None of the means of the standardised scores of the 16 factors of the 16PF or the second order factors were significantly different for males and females except for the mean of the factor Q2 (Group Dependency versus Self-sufficiency) ($t=2,20$; $p=0,041$). The mean for the female subgroup for factor Q2 was 5,58 ($sd=1,17$) and for the males subgroup 6,88 ($sd=1,46$). The female subgroup thus tended more towards the lower end of the scale thus towards greater Group Dependency than did the males.

The 16PF profile for the MS group as a whole seems to be in accordance with the

suggested 16PF profiles of individuals with physical illnesses (Cattell, Eber & Tatsouka, 1970). The lower scores on factor F (Desurgency versus Surgency) indicating a more sober, inhibiting, full of cares, concerned, slow and cautious character approach. Together with a lower score on factor Q3 (Low self-sentiment integration versus High strength of self-sentiment integration) indicating a lowered concern in the individual regarding his/her self-concept and social image being manifested in aspects such as self-control, persistence, foresight, consideration of others and regards for social etiquette and maybe pointing to the damaging effects the illness has on the way the individual experiences themselves as a human being. Furthermore lower scores on factor B (Low intelligence versus High intelligence) indicate low mental capacity, inability to handle abstract problems, showing poor judgement, lower morale and quitting behaviour. Interesting here is how the characteristics relating to lower Q3 and B scores relate similarly to the symptoms of executive dysfunction due to frontal lobe damage as discussed in Chapter 3. The higher score on factor Q4 (Low ergic tension versus High ergic tension) indicates a more tense, frustrated, overwrought individual. Factor Q4 also loads high on general anxiety (factor QII) an effect that can also be seen to be higher in the profile of MS subjects. Factor Q4 is furthermore the one 16PF factor with the “largest demonstrated association with clinical depression” (Cattell et al., 1970, p.109). The lower score on factor C (Emotional instability/Ego weakness versus Higher ego strength) indicates characteristics of preferential emotional reaction when frustrated, worrying, being easily perturbed and tending to give up easily finding manifestation in aspects such as being easily annoyed, being dissatisfied with the world, the restrictions of life and own health and generally feeling unable to cope with life.

Regarding the 16PF profile as a whole it is clear how this measure of ‘current personality’ reflects the underlying difficulties the MS sufferer is experiencing. The picture emerges of an individual experiencing much anxiety, frustration and self-doubt, having to cope with impairment of cognitive functions, fluctuations in emotional expression and social image.

Not surprisingly many of the personality characteristics discussed above also find reflection in the qualitative themes that were extracted from the interviews with significant others’ in the life of the MS which will be discussed next.

16PF PROFILE

	Low score description	1	2	3	4	5	6	7	8	9	10	High score description
A	Reserved				5,50 (2,14)							Outgoing
B	Less intelligent			3,25 (2,10)								More intelligent
C	Affected by feelings			3,75 (1,62)								Emotionally stable
E	Humble				4,35 (2,01)							Assertive
F	Sober			3,90 (2,25)								Happy-go-lucky
G	Expedient				4,20 (1,85)							Conscientious
H	Shy					5,05 (2,37)						Venturesome
I	Tough minded						6,55 (1,57)					Tender-minded
L	Trusting					5,55 (1,93)						Suspicious
M	Practical						6,45 (2,04)					Imaginative
N	Forthright				4,80 (2,17)							Shrewd
O	Placid						6,70 (2,70)					Apprehensive
Q1	Conservative					5,05 (2,01)						Experimenting
Q2	Group-dependent					5,58 (1,17) (F)	6,88 (1,46) (M)					Self-sufficient
Q3	Casual				4,40 (2,23)							Controlled
Q4	Relaxed						6,75 (1,97)					Tense

2nd Order factors

QI	Extraversion				4,74 (1,53)							
QII	Anxiety						6,57 (1,61)					
QIII	Tough poise				4,79 (0,82)							
QIV	Independence					5,14 (1,08)						
QVIII	Compulsivity				4,30 (1,48)							

FIGURE 7.1: 16 PF PROFILE USING THE AVERAGES OF THE STANDARDISED VALUES OF THE SAMPLE AS A WHOLE

7.4.2. Qualitative Themes

Table 7.3 contains the qualitative themes that were extracted from the semi-structured interviews (N=14) that were conducted with significant persons in the life of the MS sufferers.

TABLE 7.3: FREQUENCIES OF THEMES MENTIONED IN INTERVIEWS

THEME	% MENTIONED	% of different options of those mentioned			
		0 (Not mentioned)	1 (Less)	2 (Same)	3 (More)
Independence	100	0	71,43	28,57	0
Work Status	100	0	28,57 (Never)	0 (Working)	71,43 (Stopped due to MS)
Extraversion/Introversion	92,85	7,14	78,57 (More introverted)	14,29 (Same)	0 (More extraverted)
Depression	92,85	7,14	0	0	92,86
Memory Function	92,85	7,14	85,71 (Worse)	7,14 (Same)	0 (Better)
Self-confidence	85,71	14,29	78,57	7,14	0
Fatigue	85,71	14,29	0	0	85,71
Anxiety	78,57	21,43	0	0	78,57
Planning Abilities	78,57	21,43	50,00	21,43	7,14
Emotional Liability	78,57	21,43	0	7,14	71,43
Concentration	71,42	28,57	71,43	0	0
Aggression	64,28	35,71	7,14	0	57,14
Frustration	64,28	35,71	0	7,14	57,14
Patient Counseling Received	64,28	35,71	57,14 (None)	7,14 (Received)	NA
Motivation	64,28	35,71	64,29	0	0
Personality Change	64,28	35,71	7,14 (No)	57,14 (Yes)	NA
Other's Attitude	57,14	42,86	50,00 (Negative)	7,14 (No attitude)	NA
Insight	57,14	42,86	35,71	0	21,43
Role Change	57,14	42,86	14,29 (No)	42,86 (Yes)	NA
Accepted MS	42,85	57,14	14,29 (No)	28,57 (Yes)	NA
Inhibition	42,85	57,14	21,43	21,43	0
Future Anxiety	42,85	57,14	0	0	42,85
Religious	35,71	64,29	0	0	35,71
Stress Coping	35,71	64,29	35,71	0	0
Impulsivity	28,57	71,43	0	14,29	14,29
Guilt	28,57	71,43	0	7,14	21,43
Irrational	28,57	71,43	0	7,14	21,43
Concrete Thinking	21,42	78,70	0	0	21,43
Childish Behaviour	14,28	85,71	0	0	14,28

*Shading indicates themes where Males and Females differed significantly.

Since the aim of this study is to present a composite description, it was decided to interpret only those themes mentioned by 75% (or more) of the interviewees. Such a conservative approach to the data analysis will hopefully ensure that true main effects

are captured and that the interpretation of spurious or idiosyncratic information is minimized (Babbie, 1992). A more detailed discussion of these 10 themes follows.

7.4.2.1. Independence

This theme revolved around the degree of physical independence that the individual with MS experienced. The interviewees related this to aspects such as (i) the ability to take care of themselves, (ii) to move around (walking), and (iii) driving a vehicle. Difficulties with any of these aspects indicated difficulties with independence. Of the 100% of interviewees who commented on this 71,43 % indicated that the level of independence were negatively affected (thus the individuals with MS were less independent than what they had been prior to the onset of the disease), while 28,57% stated that the level remained the same. Independence correlated negatively with Tiredness ($r=-0,65$; $p=0,013$) which meant that as the level of Tiredness increased Independence decreased. This relationship makes intuitive sense especially keeping in mind the theory regarding the course of MS in that the more severely affected individuals show more physical as well as cognitive impairment which lead to increased levels of fatigue and mobility and thus independence.

7.4.2.2. Work status

Work status was defined as being gainfully employed. At the time of testing none of the subjects were gainfully employed. Of the 100% interviewees who mentioned work status 28,57% has never been gainfully employed (all were females) and 71,43% had to seize their occupational functions due to MS (females and males). Work status was positively correlated with gender ($r=0,63$; $p=0,015$) as MS caused all the male subjects to lose/resign gainful employment while this was the case for only 3 female subjects and all the subjects who had never been gainfully employed were female.

7.4.2.3. Extraversion/Introversion

The meaning of Extraversion/Introversion in this context is much the same as what Cattell (1989) describes as extraversion as opposed to introversion (closely matching Jung's extraversion construct according to Cattell, 1989) and one of the second order factors measured by the 16PF questionnaire. This construct indicates the individual's *'level of expressiveness and their tendencies toward being either outwardly (extravert) or inwardly (introvert) focussed'* (Cattell, 1989, p.309). Of the 92,85% of

interviewees who mentioned this theme, 78,57% reported that the individuals with MS had become less extraverted (thus becoming more introverted) since the onset of MS, whilst only 14,29% reported that this characteristic remained the same.

The theme Extraversion furthermore correlated positively with the theme Depression ($r=0,65$; $p=0,012$) thus the more the individuals became introverted (less extraverted) the more depressed they seemed to become, the theme Self-confidence ($r=0,71$; $p=0,005$) thus the less extraverted they became the less self-confident they seemed to be, and the theme Memory Function ($r=0,83$; $p=0,000$) so that the more introverted they became the worse their memory seemed to be.

7.4.2.4. Depression

The theme Depression implied a psychological meaning of the word, encompassing symptoms such as loss of enjoyment of pleasurable activities, being of negative affect, down-hearted, sad etc. This theme does not imply clinical depression as the severity of these depressive symptoms was not clinically evaluated. The construct of depression within this context should rather be seen as a negative or depressive emotional state. All of the 92,85% of interviewees who mentioned depression reported that the individual with MS were more depressed since the onset of the disease. It was however not possible to clearly distinguish how the severity of the depression that was reported varied in the course of the disease.

The theme of Depression correlated positively with the themes of Self-confidence ($r=0,56$; $p=0,036$) thus the worse the depression became the lower the individuals' self-confidence became, the theme Fatigue ($r=0,68$; $p=0,008$) so that the worse the depression became the worse the level of fatigue became and the theme Memory Function ($r=0,73$; $p=0,003$) thus the worse the depression became the worse the memory of the individual became. All these correlations are understandable when considering the symptoms of depression which include a lowering in self-confidence, tiredness, problems concentrating and memory.

7.4.2.5. Memory function

In the context of the interviews Memory Function was understood in terms of the individuals stating that the MS sufferer 'couldn't remember things' or 'forgot things'.

The cognitive construct of memory was tested during the cognitive part of the assessment and the theme of Memory Function in the context of the interview should be understood as a more casual construct. Of the 92,85% of interviewees who mentioned Memory, 85,71% reported that the memory of the MS sufferer was negatively affected (memory became worse) as opposed to 7,14% who stated the memory functions of the MS sufferer remained the same. The theme Memory was positively correlated with the theme Self-confidence ($r=0,83$; $p=0,000$) so the worse the memory of the individual with MS was the worse the individual's self-confidence was or vice versa.

7.4.2.6. Self-confidence

This theme revolved around aspects of the individual's evaluation of self, their belief in their own effectiveness in various situations especially interpersonal and in their ability to successfully do what they thought they needed to do. This is illustrated in negative self-statements uttered by the individuals with MS as reported by the interviewees like (i) 'being good for nothing', (ii) 'being a fake - having the qualifications but not the abilities', (iii) 'not being a good mother/father', (iv) 'not being wanted at work because of being useless', (v) 'not feeling sure/strong enough about myself to face people', (vi) 'doubting his own abilities' etc. Of the 85,71% of interviewees who made mention of this theme 78,57% stated that the individual with MS was markedly less self-confident while 7,14% said there was no change.

As discussed above, self-confidence was positively correlated with extraversion ($r=0,71$; $p=0,005$), depression ($r=0,56$; $p=0,036$) and memory ($r=0,83$; $p=0,000$).

7.4.2.7. Fatigue

Fatigue is a well-known symptom of MS and impacts on the sufferer's functioning both at a physical and cognitive level (see discussion of fatigue in Chapter 4). For the theme of Fatigue no differentiation was made between these two levels and interviewees most often referred to this concept as 'being to tired to.....: (i) think, (ii) get out of bed, (iii) do chores, (iv) finish what they started, (v) tiring easily, or (vi) needing to rest often in order to cope', etc. All the interviewees (85,71%) who mentioned fatigue (tiredness) indicated that the individual with MS experienced

increased levels of fatigue or became fatigued much quicker than before the onset of the disease.

The theme Fatigue was positively correlated with the theme Depression ($r=0,68$; $p=0,008$) as discussed above and the theme Anxiety ($r=0,78$; $p=0,001$). Thus, the more anxious the individual's with MS seemed to become the more fatigue they experienced or vice versa.

7.4.2.8. Anxiety

In the context of these interviews anxiety was reported as (i) 'fear of being rejected', (ii) 'fearing or feeling anxious about the future' or 'what might happen', (iii) 'feeling like something bad is about to happen'/'that something is not right', (iv) 'just being nervous', and (v) 'experiencing a lot of anxiety and fear around possible exacerbations and new symptoms or the recurrence of old symptoms'. As can be seen in the different statements regarding the theme Anxiety, this anxiety may have many causes and may concern many different aspects regarding the disease. It could relate to mechanism-like aspects of the disease such as symptoms, exacerbations, course etc. or the anxiety could be at a more psychological/philosophical level regarding future aspects, personal integrity, or negative emotional or psychosocial consequences. For the understanding of this theme the mere presence of fear or anxiety alone was considered and the myriad reasons for that fear or anxiety not brought into consideration as it could complicate the concept immensely, although could well prove a fruitful topic for further research. All of the 78,57% of interviewees who referred to anxiety reported that the individual with MS experienced increased levels of anxiety.

The theme Anxiety was positively correlated with the theme of Fatigue ($r=0,78$; $p=0,001$) as discussed above.

7.4.2.9. Planning abilities

Impaired ability to plan or structure actions and or thoughts is a known symptom of executive dysfunction. This cognitive function was assessed during the cognitive part of the assessment protocol and it is interesting that this aspect features in the qualitative themes as well. Although not as specific as the cognitive definitions, the

interviewees' references to problems with planning involved statements such as (i) 'can't think of a plan of action', (ii) 'can't solve problems and fix stuff as before', (iii) 'don't know how to do stuff he/she did before', and (iv) 'can't think around a problem to solve it'. 78,57% of interviewees referred to aspects of planning where 50,00% of these reported impaired ability to plan, 21,43% reported these abilities remained the same and 7,14% reported that the individual with MS showed increased planning abilities. On further investigation this last individual's increased 'planning abilities' related more to the day-to-day practicalities of the disease in terms of more effort going into planning the daily activities. This 'increased planning' seemed to act as a coping strategy and might have less to do with an actual impaired cognitive ability to formulate plans. This however remains speculation at this stage.

7.4.2.10. Emotional lability

Emotional lability in the context of these interviews refers to the unstableness of emotional expression. This meaning is illustrated in statements like (i) 'she cries easily', (ii) 'being like a child with his emotions', (iii) 'swinging from happy to sad to angry', (iv) 'he cries even if I just leave for work', (v) 'lacking control over his emotions' etc. Of the 78,57% of interviewees who referred to aspects of emotional lability, 71,43% reported that the individual with MS became more emotionally labile.

The theme Emotional lability was positively correlated with the theme of Frustration ($r=0,69$; $p=0,006$) and thus it seems that the more frustrated the individuals were the more emotionally labile they became, or vice versa i.e. that the more emotionally labile these individuals tended to be the more their frustration was demonstrated.

7.4.2.11. Aggression

Although only 64,28% of interviewees referred to aggression, of which 57,14% indicated that the levels of aggressiveness of the individuals with MS had increased since the onset of the disease, it is interesting to discuss the significant difference regarding this theme that was found between males and females in the sample ($t=2,98$; $p=0,011$). Of the 9 interviewees who mentioned increased levels of aggression in the MS sufferers, 2 of these subjects were female whilst 6 were male. On closer investigation it seemed this aggression referred more to 'acting out' aggressive behaviour such as cursing, shouting and aggressive behaviours than the

actual expression of feelings of aggression. It seems that females were more prone to express sadness (qualitative observation), anxiety (7 females and 4 males) and frustration (6 females and 3 males) whilst male subjects expressed aggressive acting out behaviour. Could it be that male subjects expressed frustration more through aggressive behaviour? Regarding the expression of depression however, male and female subjects seemed to manifest equally (6 males and 7 females). These differences could prove an interesting topic for further research.

7.5.CONCLUSION

The 10 selected themes comprising responses expressed by at least 75% of interviewees reflected a coherent description in line with the data obtained from the other measures. This further strengthens confidence in the reliability and interpretability of the dataset as a whole.

CHAPTER 8

CONCLUSION

8.1. OVERVIEW

In this study certain demographic (gender, age and education), cognitive (specifically executive functions) and psychological factors (personality changes and other psychosocial issues) were investigated in an attempt to gain a general and hopefully more holistic picture of the life world of the individual with MS. These factors were chosen due to their proven impact on aspects pertinent in the life of the MS sufferer. Some of these pertinent aspects affecting the life world of the MS sufferer are cognitive and physical functioning, emotional and psychological well-being, psychosocial relationships, work performance and general adaptation to the disease process. It was hoped that this explorative study would start to show those areas that were especially problematic or that seemed to underlie many of the observed difficulties MS sufferers experience and in doing so possibly generate hypotheses for further in-depth investigation.

8.2. CONCLUSIONS FROM THE DATA

8.2.1. Demographic Factors

The larger number of females (n=12) as opposed to males (n=8) in the sample reflected the findings in literature of the higher incidence of MS in the female population (Multiple Sclerosis International Federation, National Multiple Sclerosis Society, 2000).

The mean age at diagnosis 39,10 years (40,25 years for males and 38,33 years for females) of the sample is consistent with other research findings that indicate the onset of MS symptoms between the ages of 20 and 40 years (Berkow, 1977; Chipps et al., 1992; Multiple Sclerosis International Federation, 2000).

The average years of education of the sample was 13,35 ($sd=2,21$) and didn't differ significantly for the gender subgroups. Furthermore subjects with higher levels of education showed better performances on measures of planning, nonverbal reasoning, problem solving, and visual-spatial organisation as demonstrated by performances on the block design task (Lezak, 1995). However when years of education was excluded as variable even these subjects showed impairment in planning and executive abilities and it thus seems that neurological effects caused by MS such as frontal lobe impairment, overwrites the advantages of better education. This seems to support the view that frontal lobe pathology is an important contributing factor to the cognitive and behavioural difficulties that MS sufferers experience (Grigsby et al, 1993; Damasio, in Heilman and Valenstein, 1993; Lezak, 1983; Russell & Roxanas, 1990; Stuss et al., 1992).

8.2.2. Cognitive Factors

The investigation regarding the cognitive factors revolved mainly around executive functions as these factors were considered to (i) have vast effects on psychosocial functioning (Grigsby et al., 1993), (ii) might possibly be some of the earliest symptoms of MS (Mendozzi, Pugnetti, Sacconi & Motta, 1993), (iii) are linked to changes in personality and awareness (Rao et al., 1991; Stuss et al., 1992; Russell & Roxanas, 1990; Taylor, 1990) and (iv) exert an effect on other cognitive functions such as memory (Beatty et al., 1989).

Executive functions that received attention were the ability to formulate plans and strategies to aid learning and successful completion of tasks (as presented by measures of strategy formulation and effectiveness of use of these strategies), ability to monitor own actions and responses (as presented on measures of perseveration and self-monitoring), flexibility in thinking and thus adaptability of behaviour (as presented on measures of slowness in shifting and perseveration, and self-monitoring) and ability to acquire new information (as presented on measures of the presence of learning curves in the acquisition of new tasks/information, recall and the presence of proactive inhibition).

Table 8.1 contains a list of the statistically significant correlations between these various cognitive indicators.

TABLE 8.1: STATISTICALLY SIGNIFICANT CORRELATIONS BETWEEN COGNITIVE INDICATORS

Variable 1	Variable 2	r; p		
		Total Group	Females	Males
Years education	RAVLT presence of a learning curve		r=-0,59; p=0,044	
Years education	BLOCKS tips from researcher needed for completion	r=-0,52; p=0,018		
Years education	BLOCKS working according to a plan	r=0,56; p=0,010		
Years education	TMT seconds taken to complete Trail B	r=-0,49; p=0,032		r=0,88; p=0,000
Years education	TMT percentage achievement on Trail B			
Years education	BLOCKS standard scores	r=0,58; p=0,008		
Years education	BLOCKS standard scores	r=0,58; p=0,008		
RAVL actual recall on trial I	WCST perseveration errors		r=-0,66; p=0,027	
RAVL actual recall on trial V	DIGITS number of digits recalled forward		r=-0,65; p=0,023	
RAVL actual recall on trial V	BLOCKS working according to a plan		r=0,60; p=0,038	
RAVL presence of learning curve	COWAT total number of words generated		r=-0,78; p=0,003	
RAVL presence of learning curve	DIGITS number of digits recalled forward		r=-0,61; p=0,033	
RAVL presence of learning curve	WCST percentage of perseveration errors		r=0,61; p=0,048	
RAVL presence of a strategy	BLOCKS working according to a plan		r=0,77; p=0,003	
RAVT presence of self-monitoring behaviour	WCST number of categories achieved		r=0,73; p=0,010	
RAVL actual recall on trial I	TMT seconds taken to complete Trail B			r=-0,73; p=0,039
RAVL actual recall on trial I	TMT percentage achievement on Trail B			r=0,76; p=0,028
RAVL actual recall on trial V	TMT seconds taken to complete Trail B			r=-0,81; p=0,016
RAVL actual recall on trial V	TMT percentage achievement on Trail B			r=0,76; p=0,028
RAVL actual recall on trial V	WCST number of categories achieved			r=0,78; p=0,040
RAVL actual recall on trial V	WCST percentage of perseveration errors			r=-0,91; p=0,005
RAVL presence of learning curve	TMT percentage achievement on Trail B			r=0,87; p=0,005
RAVL presence of learning curve	TMT seconds taken to complete Trail B			r=-0,95; p=0,000
DIGITS standard scores	16PF factor C (adaptability to environment)	r=-0,52; p=0,020		
DIGITS standard scores	TMT percentage achievement on Trail B	r=0,46; p=0,045		
DIGITS standard scores	TMT percentage achievement on Trail A	r=0,50; p=0,030		
DIGITS standard scores	TMT seconds taken to complete Trail B	r=-0,46; p=0,045		
DIGITS standard scores	TMT seconds taken to complete Trail A	r=-0,52; p=0,021		
BLOCKS working according to a plan	BLOCKS tips from researcher needed for completion	r=-0,69; p=0,001		
BLOCKS working according to a plan	BLOCKS standard scores	r=0,70; p=0,001		
BLOCKS working according to a plan	TMT seconds taken to complete Trail A	r=-0,51; p=0,026		
BLOCKS tips from researcher needed for completion	16PF factor B (intelligence)	r=-0,51; p=0,023		

Variable 1	Variable 2	r; p		
		Total Group	Females	Males
BLOCKS tips from researcher needed for completion	TMT percentage achievement on Trail B	r=-0,65; p=0,003		
BLOCKS tips from researcher needed for completion	TMT percentage achievement on Trail A	r=-0,62; p=0,004		
BLOCKS tips from researcher needed for completion	COWAT total number of words generated	r=-0,53; p=0,017		
TMT percentage achievement on Trail B	BLOCKS standard scores	r=0,63; p=0,004		
TMT percentage achievement on Trail B	BLOCKS tips from researcher needed for completion	r=-0,65; p=0,003		
TMT percentage achievement on Trail B	COWAT total number of words generated	r=0,54; p=0,017		
TMT percentage achievement on Trail B	DIGITS number of digits recalled backward	r=0,50; p=0,028		
TMT percentage achievement on Trail B	DIGITS standard scores	r=0,46; p=0,045		
TMT percentage achievement on Trail B	WCST percentage of perseveration errors	r=-0,49; p=0,044		
TMT percentage achievement on Trail B	16PF factor B (intelligence)	r=0,48; p=0,039		
WCST percentage of perseveration errors	TMT percentage achievement on Trail B	r=-0,49; p=0,044		
WCST percentage of perseveration errors	TMT seconds taken to complete Trail B	r=0,66; p=0,107		
WCST percentage of perseveration errors	WCST number of categories achieved			r=-0,79; p=0,036

The picture that evolved from the performances on these cognitive measures were the following:

In most cases subjects weren't able to *learn* new information (as indicated by performances on the RAVLT - 25% of subjects performed in below normal range for recall on trial I and 45% of subjects in the below normal range for recall of words on trial V, digits forward subtest of the SAWAIS - 5% of subjects in the defective range and 55% of subjects in the marginal to normal range) a fact further supported by the seemingly lack of a *learning curve* when attempting these learning tasks (as indicated by performances on RAVLT - 25% of subjects did not show the presence of a learning curve). This impaired ability to acquire new information seems to have been caused by a lack of *formulating and using strategies* for learning new information (as indicated in the fact that in the RAVLT - 25% of subjects who showed no learning curve also did not seem to use strategies for mastering the learning tasks, and in the blocks subtest of the SAWAIS - 30% of subjects seemed to have no strategy for completing the task). The subjects furthermore showed a tendency toward *proactive inhibition* (as indicated by the larger difference between the first recall of list B (35% of subjects within below normal range) and the first recall of list A (25% of subjects

within below normal range) of the RAVLT). These subjects also showed *slowness in shifting* (as indicated by the below normal to borderline achievement on the digits backwards subtest of the SAWAIS, as well as the large number of subjects (55%) who showed a difference of 2 or more digits between the forward and backward tasks subtests of the SAWAIS, and the performance on the TMT where 78,9% of subjects fell below the 50th percentile for Trail B), limited *self-monitoring* behaviour (as indicated by the presence of perseverative errors on the WCST - a mean of 37,23% of perseverative errors for the subject group and the RAVLT - 50% of subjects showed perseverative type errors), difficulties with *mental tracking* (as indicated by performances on the digits backward subtest of the SAWAIS - 20% of subjects performed in the defective range and 15% of subjects in the borderline to normal range) and impaired *verbal fluency* and difficulty *organising, contextualising and retrieving information* spontaneously (as indicated by performances on the COWAT – 35% of subjects performed in the severely defective to borderline range and 55% of subjects in the low normal to normal range).

The additional qualitative indicators for executive dysfunction that were employed during the assessment process using the block design subtest of the SAWAIS, according to the guidelines proposed by Lezak (1995) and Spreen and Strauss (1998), showed that a large percentage of subjects (80% for the block design subtest of the SAWAIS) who weren't able to successfully complete the block design tasks required input from the researcher. Of the 80% of subjects that received input from the researcher regarding the block designs, only 50% made effective use of this information while 30% could not effectively employ this information to correct their designs. This clearly supports evidence for the presence of executive difficulties and thus for the involvement of frontal lobe dysfunction.

As can be seen from the correlations in table 8.1, these measures of executive dysfunction support one another across assessment instruments and thus serve to support the validity of the evidence of the involvement of frontal lobe impairment and thus executive difficulties in the disease course of MS.

The picture that emerges from the cognitive assessments seems to reflect both Walsh (1991) and Russell and Roxanas' (1990) descriptions of the symptoms that emerge

from frontal lobe damage. The data provided by the cognitive measures in this study thus serve to support the notion that frontal lobe involvement and its resulting impairment of especially the cognitive functions play an important role in the difficulties experienced by the individual with MS.

8.2.3. Psychological Factors

The profile that emerged from the 16PF questionnaire reflected results of previous research done employing the 16PF questionnaire in samples of individuals with physically illnesses (Cattell et al., 1970; Cattell, 1989). This profile shows a general loading towards the lower end of the profile. Most of the factors (12) lie within the lower section of the profile (i.e. below the graphic mean of the profile of around 5) of which factors B, C and F lie below the area for profile average of between 4 and 7. Only 4 factors (i.e. factors I, M, O, Q2) lie above the graphic mean of the profile of around 5 (all of which lie within 1 stanine above this mean) and within the area for profile average of between 4 and 7.

This profile shows an individual who is more concerned, full of cares, inhibited and cautious (low factor F), with a lowered concern for their self-concept and social image, thus possibly manifesting aspects of lowered self-control, persistence and consideration for others (low factor Q3) and with a lowered mental capacity leading to difficulties in handling abstract problems and showing poor judgement with accompanied low morale and higher incidence of quitting behaviour (low factor B). This individual furthermore seems to be experiencing high levels of frustration, is tense and generally overwrought (higher factor Q4), experiences increased levels of anxiety (factor QII) and possibly tends toward depressive emotions and emotional reactions when frustrated. In addition this individual seems worried or perturbed (low factor C) which leads to a level of dissatisfaction with the world, the restrictions of life and personal health and a general feeling of being unable to cope with life.

Once again the symptoms of frontal lobe impairment (as discussed in chapter 3) are reflected in the picture that evolves from the discussion above. This urges one to consider the influence of frontal lobe pathology on the integrity of the individual personality and seem to present support for Stuss et al.'s (1992) proposition that the primary aspect of frontal lobe pathology is a disorder of personality.

When the nature of these personality difficulties are viewed more closely it becomes clear how these personality characteristics might contribute to the difficulties and challenges faced by the person with MS.

When this picture of an individual experiencing much anxiety, frustration and self-doubt, having to cope with impairment of cognitive functions, fluctuations in emotional expression and social image that emerges from the 16PF assessment is considered, it is no surprise that many of the personality characteristics discussed above also find reflection in the qualitative themes that were extracted from the interviews with significant others' in the life of the individual with MS.

The most prevalent themes that emerged were those of loss of independence (71,43% of interviewees), having to stop working due to the effects of MS (71,43% of interviewees), becoming more introverted (78,57% of interviewees), experiencing depressive symptoms (92,86% of interviewees), impairment in memory functions (85,71% of interviewees), a decline in self-confidence (78,57% of interviewees), experiencing more fatigue (85,71% of interviewees), increased levels of anxiety (78,57% of interviewees), impairment in planning abilities (50% of interviewees), and increased emotional lability (71,43% of interviewees).

The occurrence of the above themes are in accordance with previous research findings. Research conducted by Hakim et al. (2000) found that issues of poor mobility (being able to move around), equitable to the theme of independence in this study, were shown to be a major cause of the change in work status, the withdrawal from social activities and the decrease in the number of friends of individuals with MS. Regarding the theme of work-status, their research also showed that MS played a major role in the employment status of individuals. The majority of MS patients either lost their employment or were forced to retire prematurely due to MS. Factors that were implicated in causing this change were cognitive impairment, visual disability, mobility issues (getting to work) and excessive fatigue (Hakim et al., 2000).

The study by Hakim et al. (2000) also found that depressive and anxious mood were present in a significant number of MS patients in their study (N=305). They found

that depression occurred four times more frequent in men than in women whereas anxious mood occurred equally in both genders in their sample. The current study found the reported presence of both depressive mood and anxiety but showed no significant difference in the occurrence of depressive and anxious moods between the genders.

The contents of the theme of self-confidence showed very similar properties to aspects of self-efficacy as described in Bandura's social cognitive theory as discussed by Airlie, Baker, Smith and Young (2001). In this discussion self-efficacy is defined as the individual's "belief in their ability to overcome specific challenges" and "encompasses concepts such as mastery, self-esteem and feelings of being in control of present and future events". (Airlie et al., 2001, p.260). Self-efficacy in MS has been shown to play a role in the degree of adjustment to MS and the levels of self-esteem and self-worth of MS sufferers (Airlie et al., 2001).

It is important to note how the data resulting from these various sets of assessments i.e. quantitative cognitive measures, personality profiling and qualitative psychosocial themes, support one another and in the process serve to enrich the quality of the picture that emerges. The fact that the pictures that emerge from these different measures also overlap to such an extent furthermore serves to substantiate the validity of the overall picture of the life world of the person with MS that has emerged.

8.3. LIMITATIONS OF THE STUDY AND SUGGESTIONS FOR FUTURE RESEARCH

Because of the explorative nature of this study the diversity in the sample added richness to the data and forced significant issues to become apparent. However, for a more focused study that attempts to investigate the nature of these issues in more depth, care should be taken to not only include a larger sample, but also select a sample in such a way as to control for interference variables. Aspects worth considering and which might be controlled in future research are aspects such as gender, educational level, years of MS and degree of physical impairment. Research employing a larger randomised sample will allow for increased generalisability of the

results to the general population of MS sufferers. Future research employing a larger sample size might well show many of the strong but statistically insignificant correlations found in this study to be of important statistical significance.

A further limitation of this study is the absence of formal measures of aspects such as degree of physical disability and mood state. Including measures such as these would have contributed immensely to the richness of the interpretations of the results of this study. However the assessment protocol was limited on purpose due to the practical and ethical reasons (discussed in chapter 6) and thus future research of a more focussed nature would be well advised to consider formal measures of aspects of mood and disability as this could enhance the quality of the research results.

This study produced interesting results regarding various correlations between different aspects such as demographic characteristics, indicators of cognitive impairment and psychosocial factors. However care should be taken when inferring casual relationships from these correlations, as further research employing more advanced statistical analysis would be necessary to adequately understand the precise nature of these relationships.

Another limitation of this study could be considered the ‘word of mouth’ nature of the assessment of changes that occurred as a result of MS (obtained through the semi-structured interview). However, since the goal of this study was to get an overview picture of the ‘life world’ of the MS sufferer, of which the changes constitute only part, it was considered as acceptable. Considering the richness of the data that was obtained through these interviews inclusion of this measure in the methodology of the current study seemed prudent. However, future research focussing on aspects of change in MS (e.g. the role of frontal lobe pathology on personality change in MS) would require a longitudinal research methodology as this kind of research would have to include both pre and post morbid assessments.

During the execution of this study, two major voids regarding the research literature and management of MS came to the fore. The first of these is the role that patient education and counselling (regarding aspects such as the disease course, realistic expectations and uncertainties) has in effecting successful adaptation to and

management of MS. Many participants in this study expressed the notion that if adequate patient education were present at the time of diagnosis it would most likely have served to allay many of the fears and uncertainties with which they grappled in trying to adapt to the disease. Future research regarding this topic could centre on the effects that informative and timely patient education and counselling, aimed at the patient, their loved ones and caregivers, has on the degree of successful adaptation to and overall management of MS.

The second of these voids involve aspects to be considered when designing and implementing rehabilitative strategies. Many aspects that were touched on in this study (factors such as patient demographics, patient educational level, degree of cognitive impairment, residual abilities and skills, neurological involvement and various psychosocial factors) might have very important implications for the type and effectiveness of different rehabilitative strategies. Future research centred on these influences and success rates will add value to the body of knowledge regarding MS.

8.4. CONCLUSION

Although this study attempted to paint a general picture of the MS sufferer it is by no means that the researcher is of the opinion that all MS sufferers are the same and the fact that the nature of the MS disease course is difficult to predict due to its uncertain course as well as its very individualistic manifestations in every MS patient's life is reiterated. However, a fair number of common symptoms are also evident. The future refinement of our understanding of these commonalities will not only benefit diagnostic procedures and rehabilitative interventions, but will also lead to an enhanced quality of life for MS sufferers.

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