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**The Effects of Multiple Sclerosis:  
Exploring Executive Dysfunction and its Links  
with other Cognitive Impairment**

A thesis  
submitted in partial fulfillment  
of the requirements for the Degree  
of  
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by  
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## **ABSTRACT**

Multiple Sclerosis (MS) is one of the most common chronic diseases of the central nervous system, and in New Zealand an estimated 4,000 people are currently affected. Although the physical manifestations of the disease are well known, and memory impairments have been comparatively well researched, those cognitive abilities known collectively as executive functions, and their relationship with other cognitive processes, have seldom been examined.

To fill this research gap, the present study examined the extent and nature of executive dysfunction and other cognitive impairments in a community based sample of participants with MS, and explored any links between executive dysfunction and other cognitive processes. Due to the well known heterogeneous nature of the effects of MS, impairment was assessed not only for the sample as a whole, but more informatively, and in contrast to much of the previous research on MS, within smaller more homogeneous groups formed on the basis of the extent and nature of the cognitive impairment of the participants. As the behavioural characteristics of executive dysfunction may have an influence on the ability to function appropriately on a daily basis in the community at large, evidence of typical 'dysexecutive' behaviour was also examined.

Ninety five participants with MS were assessed on general ability (WAIS-III), memory (WMS-III), executive functioning (D.KEFS), information processing speed and simple attentional processes. While the extent of impairment remained low on general ability measures, some impairment became evident in over half of the participants with MS on the memory measures. Five categories of executive functioning were used to assess the extent and nature of executive dysfunction; Inhibition, Shifting, Reasoning,

Planning and Fluency. Working memory was not included as an executive category, as the primary scores obtained from the D.KEFS assessment did not enable this process to be isolated. Working memory was however evaluated as part of the memory assessment (WMS – III). Over half the participants were found to be impaired in at least one category of executive dysfunction, and the most commonly impaired categories were fluency and reasoning. Although sixteen different profiles of executive dysfunction were evident amongst the participants, the majority of those impaired were assessed with only one category of impairment. Surprisingly, no impairment in information processing speed was evident, but some participants were impaired in relation to simple attentional processes.

The participants with MS were subsequently divided into four groups based on the nature of their impairment, that is, depending on whether the participant had no impairment, memory impairment only, memory impairment and executive dysfunction or executive dysfunction only. The index scores for visual memory were found to be consistently lower than those for auditory memory for all the ‘impairment type’ groups, but little difference was found between long-term and short-term memory performance. Working memory was found to be the only cognitive process which differentiated between those groups with executive dysfunction and those without, and at all levels of performance, proved to be a reliable predictor of the degree of executive dysfunction. Working memory was also found to have a differing relationship with each of the other five specific categories of executive functioning.

When the everyday behavioural characteristics of executive dysfunction, such as inhibition, intentionality, executive memory and positive and negative affect were assessed with the Dysexecutive Questionnaire, there was little evidence of any self

reported problems. In particular, levels of insight were shown not to be compromised, therefore it seemed that if any behavioural difficulties did arise for the participants, they would have been able to recognize and subsequently address them. Thus, it appeared for this sample of participants with MS that although some executive dysfunction was more prevalent than had previously been suggested in the literature on MS, generally the living arrangements of these participants seemed appropriate in relation to their ability to function independently.

Overall, it was recommended that for the initial cognitive assessment of those with MS, a comprehensive evaluation of working memory integrity should be included. This would provide valuable information regarding the likelihood of other executive dysfunction and would allow a more targeted assessment approach by limiting the more extensive testing of executive functions to only those people whose comparatively lower working memory performance indicated that further problems may exist.

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## LIST OF ABBREVIATIONS

ACI	Attention Concentration Index
ACT	Attentional Capacity Test
ACT – R	Adaptive Character of Thought – Revised Model
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
ANCOVA	Analysis of CoVariance
BADS	Behavioural Assessment of Dysexecutive Syndrome
CCST	California Card Sorting Test
CMDI	Chicago Multiscale Depression Inventory
CNS	Central Nervous System
DEX	Dysexecutive Questionnaire
D.KEFS	Delis Kaplan Executive Function System
EDSS	Expanded Disability Scale
FSIQ	Full Scale IQ
HSD	Honestly Significant Difference
IQ	Intelligence Quotient
LTM	Long Term Memory
M	Mean
MANOVA	Multivariate Analysis of Variance
MMPI	Multiphasic Personality Inventory
MS	Multiple Sclerosis
PASAT	Paced Auditory Serial Addition Test

PIQ	Performance IQ
SD	Standard Deviation
VIQ	Verbal IQ
WAIS	Wechsler Adult Intelligence Scales
WAIS-R	Wechsler Adult Intelligence Scales Revised
WAIS-III	Wechsler Adult Intelligence Scales Third Edition
WCST	Wisconsin Card Sorting Test
WMS	Wechsler Memory Scales
WMS-R	Wechsler Memory Scales Revised
WMS-III	Wechsler Memory Scales Third Edition
WTAR	Wechsler Test of Adult Reading

## Chapter 1

### LITERATURE REVIEW

#### **General**

Imagine trying to do a responsible job in the workplace or run a household whilst having increasing difficulty adhering to a schedule which enables a task to be completed in an orderly manner. It is obvious this would result in many tasks being started and few, if any, being completed. Imagine also the confusion that would arise if you began to have difficulty understanding more complex concepts and were unable to solve problems, or plan ahead. Imagine the consequences of being in an unfamiliar situation and having no idea how to behave, or make reasoned decisions about an appropriate course of action. Then, when common sense would indicate caution, your behaviour instead becomes more impulsive. Imagine also, the dangers of driving a car when your judgement is impaired, and lack of 'insight' reduces the ability to see the implications of a course of action and thus avoid dangerous situations. Surprisingly, people with these or similar 'executive' problems can do well on many standard neuropsychological tests, and therefore these 'executive' problems, which can be very wide ranging, often escape detection, and have not been extensively examined in those people with Multiple Sclerosis (MS).

The implications of undetected executive dysfunction in those with MS, especially for those who live alone, are potentially of a very serious nature. For example, many with MS are on medication which usually requires an exact administration of the medication at prerequisite times; a task that could be very difficult for someone who can not plan ahead, or make accurate temporal judgements. Limited mobility could also be exacerbated for someone with an

inaccurate perception of their own abilities or who has difficulty judging distances (spatial processing). For these people, their limitations, which may also include planning difficulties, would often necessitate many mid-course corrections during a task as simple as negotiating oneself onto an unfamiliar chair. These additional manoeuvres would tax their problem solving abilities and place further demands on an already compromised balancing and motor system.

It is, therefore, very important to be aware of these types of problems, not only in order to ensure the safety of the person concerned, but because of the contribution of executive functions to nearly all areas of successful daily functioning. In the first instance, compromised executive functioning would severely limit ones ability to maintain employment, unless the work was largely routine and required little self motivation. Also, the lack of ability to self initiate activity would result in problems at home where everyday tasks such as preparing a meal or doing laundry would often be neglected. Social interaction, an important part of our lives, would most likely become very limited due to a loss of social awareness which then manifests in socially inappropriate behaviour. To compound these issues, the person concerned, in most cases is unaware of their limitations, and unfortunately for those affected, this is difficult for others to understand, often resulting in further alienation.

Executive dysfunction also has important implications well beyond day to day functioning. Compromised reasoning skills combined with an inability to assess the consequences of an action or decision, could call into question the bigger issue of legal competence. It is quite probable that someone with these problems should not be making important financial or other decisions which may have a significant impact on their lives. However, because executive dysfunction is often undetected by a clinician, those affected remain free to do just that, often with dire repercussions.

Because of the nature of executive functions, the sometimes-used analogy with the executive of a company is quite apt. They are both involved in setting goals and determining the most efficient strategies by which to achieve them. These skills also require the ability to prioritise and keep track of several things at once, whilst being sufficiently flexible to be able to adapt to changing situations. A successful executive is one who is able to accurately assess outcomes, but good social skills are also an important requirement.

For many reasons then, executive functions play an important role in our ability to function appropriately both as an independent individual and as a member of society. Thus it is the examination of the integrity of these various executive functions in people with MS, along with the nature of their substrates, which this research will address.

## **Executive Functions**

Although it is primarily the integrity of our executive functions that enables us to negotiate the most economical path through the many unstructured and novel situations we encounter on a daily basis, they remain one of the unsolved mysteries of the human brain. That they are an important cognitive domain, involving higher order or 'metacognitive' processes is not in doubt. However, the problems in understanding them do begin at a very fundamental level, as it is difficult, in the first instance, to find an exact definition of these functions. A complicating factor is that the term is often used synonymously with frontal lobe functions, and as such, throughout the range of literature, it could be assumed that they encompass almost the entire range of cognitive processes (Reitan & Wolfson, 1994; Tranel, Anderson, & Benton, 1994).

## ***Definitions***

Lezak (1995) defines executive functions as “those capabilities that enable a person to engage successfully in independent, purposive, self-serving behaviour...” (p. 42). A definition that does not point immediately to any specific factor or factors that could be systematically examined. It is, however, a definition whose general meaning is echoed by Stern and Prohaska (1996), who define executive functions as “those abilities that allow one to carry out social and instrumental activities successfully ...” (p. 243). These broad definitions, of necessity, then go on to describe the range of processes that could contribute to those abilities.

Because of the seeming difficulty in being specific, some authors choose not to attempt a definition but rather rely on a description of the most typical processes that the term implies. Burgess (1997) suggests that executive functions “describe a range of poorly defined processes which are putatively involved in activities such as problem solving, planning, initiation of activity, cognitive estimation and prospective memory” (p. 81). He also acknowledges, however, that impairment to these processes is typical of those problems observed after frontal lobe damage, so the frontal lobe/executive boundaries have in this case been blurred.

The difficulty of providing a precise definition to incorporate the many abilities that have been ascribed to the term executive function is perhaps best summed up by Banich (1997) who states that “executive function is a term that covers many abilities and, as such, is a concept for which providing a precise definition is difficult” (p. 369). A sentiment repeated by Tranel, Anderson, and Benton (1994) who opt not to “attempt a precise definition of the term...” (p. 125).

More concise definitions can be found in those cases where single factor theories lie behind the interpretations. These would include such succinct examples as “Executive functions are control processes” (Denckla, 1996, p. 265), an idea expanded in the definition given by Miyake who describes executive functions as “general purpose control mechanisms that modulate the operation of various cognitive subprocesses....” (Miyake, Friedman, Emerson, Witzki, & Howerter, 2000, p. 50). Although these more succinct definitions may imply a greater specificity, further reading of the authors suggests that this is not the case.

One of the problems behind the lack of consensus over a precise definition is quite probably the frequent interchange of the terms ‘frontal’ and ‘executive’. Whilst executive functioning, or dysfunction, is inextricably linked with the frontal lobes, its origin can be seated in any of a number of areas of the brain (Foong et al., 1997). Frontal lobe pathology on the other hand relates specifically to the frontal lobes and may or may not result in executive dysfunction. Whilst neuropsychological, and more recently, neuroimaging studies suggest that there is some (often considerable) overlap between frontal lobe activity and executive functions (Reitan & Wolfson, 1994; Stern & Prohaska, 1996; Stuss & Alexander, 2000; Tranel et al., 1994; Van Der Linden, Meulemans, Marczewski, & Collette, 2000) there is no doubt that many of these functions draw on both posterior association cortices and subcortical structures for many elements of their execution (Beatty, 1993; Collette & Van Der Linden, 2002; Mecklinger, Weber, Gunter, & Engle, 2003; Sylvester et al., 2003). This is highlighted by the mixed results (in terms of identifying subjects with frontal lesions) found on many ‘executive function’ tests which are used erroneously to identify frontal lobe damage (Reitan & Wolfson, 1994; Tranel et al., 1994). Weinberger, Berman and Daniel (1991) cite an example of people with

Schizophrenia and people with Huntington's disease who both performed poorly on the Wisconsin Card Sorting Test (WCST). Whilst those with Schizophrenia were shown to exhibit reduced activity in the frontal lobes, this was not the case for the people with Huntington's who instead were determined to suffer from caudate atrophy. It is therefore apparent, that an inability to perform adequately on these 'executive function' tests can not be automatically attributed to frontal lobe pathology. Modern imaging techniques have now left little doubt that although frontal lobe damage is responsible for many cases of executive impairment, damage to any of the many interrelated subsystems could result in a similar manifestation of impairment due to reduced transfer of information between the participating areas (Dagher, Owen, Boecker, & Brooks, 2001).

Areas which do have significant neural interaction with the prefrontal cortex include the dedicated processing modules of the posterior cortex, the limbic structures, output from the striatum, and the ascending monoaminergic and cholinergic systems from subcortical regions (Cummings, 1993; Mega & Cummings, 1994; Robbins, 1996). The resulting complex neural networking also makes clear the need to make a distinction between anatomical and functional concepts (Baddeley, Della Sala, Gray, Papagno, & Spinnler, 1997) and, especially in the case of executive functions, to resist the temptation to use neuropsychological tests to make neuroanatomical assumptions.

Those authors that do discuss executive functions as a concept in their own right, generally agree that they incorporate such factors as planning/temporal ordering, decision making/reasoning, and judgement/concept formation, on the complex level and establishing, maintaining and shifting mental set, inhibition, and working memory on a more primary level along with an awareness of self that

enables self monitoring and utilization of feedback (Spreeen & Strauss, 1998; Stern & Prohaska, 1996; Tranel et al., 1994). Lezak (1995) uses the broader concepts of volition, planning, purposive action and effective performance to define executive functions, and discusses these separately from concept formation and reasoning.

Which ever set of definitions is adopted it is obvious the concept of 'executive functions' is multidimensional, with generally accepted broad interrelated characteristics, but certainly not explicitly defined.

### *Theories*

Just as the definitions of executive functions become intertwined with characteristics of frontal lobe functioning, many of the theories of executive functions are in fact models of the operations of the frontal lobe. An early differentiation between executive and non executive behaviours related to the concept of controlled and automatic behaviour (Rabbitt, 1997). This idea was based on the work of Shiffren and Schneider (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). Their model of information processing proposed a qualitative differential between automatic processing at one end of a continuum and controlled processing at the other.

Automatic processes, considered to equate to non-executive behaviour, were defined as those which elicit an automatic attention response. They involve a relatively permanent set of associations in long term memory, require considerable training to develop and are therefore difficult to suppress or alter. These processes make very few demands on memory capacity but are extremely task specific with the most minor change in parameters necessitating reversion to some degree of control.

Controlled processing at the other end of the continuum was considered to characterise executive behaviours. In contrast to automatic processes, controlled processing involves a temporary activation of nodes in a sequence that has not been learned. It requires some attentional and memory capacity and can be limited by these capacities. This theory proposes that these controlled processes are able to be set up and applied in novel situations, with the obvious similarity to the nature of executive functioning. Complex behaviours can, however, be made up of both automatic subsystems and the controlled processes which build on them, and in its general form, this theory, which lacks any quantitative differential of tasks seems to fall short of an adequate explanation of executive functioning.

More recent theorists have however used this concept of control and applied it to more specific theories. One of these theories (Duncan, Emslie, Williams, Johnson, & Freer, 1996) suggests that the concept of Spearman's 'g' incorporates the control factor which underlies executive functioning. Spearman's 'g' is that abstract 'general intelligence' element that is responsible for the reasonably consistent performance of any one person on a variety of ability tests. By this theory Spearman's 'g' is a measure of the underlying 'control' functions of the frontal lobe and is also highly correlated with 'goal neglect'. Goal neglect, which involves the disregard of some of the requirements of a task, is a phenomenon that is displayed in novel or high demand situations where the total requirements of the task require greater levels of controlled processing (Duncan et al., 1996; Duncan, Johnson, Swales, & Freer, 1997). Along with a strong link to the degrees of goal neglect, Spearman's 'g' also correlates highly with tests that reflect less the crystallised, knowledge based intelligence, but more the fluid intelligence which is said to facilitate problem solving and other goal directed behaviour thought to be

characteristic of executive functioning. It is therefore this control factor, which Duncan et al. (1996, 1997) believe is fundamental to 'g' which underlies the operations of executive processes.

It has been shown however, using animal problem solving studies, children with Attention Deficit Hyperactivity Disorder (ADHD) and adults with executive function deficits that executive functions are in fact something other than general intelligence whether measured as psychometric IQ or fluid 'g' (Crinella & Yu, 2000). For the animal studies, very little overlap was found between those brain structures that are utilised for general intelligence tasks and those that are utilised in problem solving tasks. For both the adults and the ADHD participants with executive dysfunction, IQ scores, which were considered an estimate of g, were not impaired.

Norman and Shallice 1980 (cited in Shallice & Burgess, 1991) also developed a model, based on control processes, in an attempt to explain neuropsychological findings in people with frontal lobe pathology. Their model consists of a lower order control mechanism, the contention scheduler, and a higher order control mechanism, the supervisory attentional system. The contention scheduler operates when relatively routine action or thought procedures are sufficient to achieve a goal. At this level a finite set of schemas can be activated, and if there is competition between them, the lateral inhibitory mechanisms of the contention scheduler can prevent two competing schemas being selected. If the problem is more complex (non-routine), the supervisory system takes over and operates by modulating the activation levels of the competing schemas. This control mechanism (originally considered a unitary process), was thought to represent anterior brain systems which were required to operate in up to five different situations. However, a more recent review of this mechanism by Shallice and Burgess, resulted in these five situations being

summarised into two; when unmodulated contention scheduling would result in an incorrect response, or when no routine procedure is available to produce the required response (Shallice & Burgess, 1991). Since its original concept this model has undergone further refinement in an attempt to explain the different subsystems operating within the supervisory process (Shallice & Burgess, 1996). The Mark II supervisory system model incorporates processes which enable the generation of an appropriate schema (strategy) for novel situations, along with its implementation and monitoring.

Another theory based on cognitive control but using the different aspects of attention as the focus is that developed by Stuss (Robbins, 1996; Stuss, Shallice, Alexander, & Picton, 1995). This theory is a more detailed explanation of the supervisory processes originally outlined by Norman and Shallice, and suggests five processes which are considered to be operational during various attentional tasks. The five anterior processes suggested by this model are; Energisation of a schemata, Inhibition of schemata, Adjustments to contention scheduling, Monitoring schemata, and Controlling the 'if-then' logical processes. In this model these control processes are shown to operate in varying degrees of importance in seven types of tasks, namely, sustaining, concentrating, sharing, suppressing, switching, preparing and setting, all of which can be required in attentional processes.

Although the concept of control can have very broad implications, a recent review of the neurophysiological, neurobiological and neuroimaging studies which have been carried out in an attempt to determine the primary role of the prefrontal cortex, suggests that various control mechanisms do operate over the many interconnected brain structures. This review therefore, does tend to lend weight to

those theories which suggest that control processes of one kind or another are central to executive functioning (Miller & Cohen, 2001).

A further multi-process theory, is one based on the perception-action cycle. This theory suggests that the role of the prefrontal cortex is to integrate perception, action and cognition over time in the process of working toward the achievement of a goal. This is achieved through the processes of selective attention, working memory (providing retrospective integration), preparatory set (the basis of prospective integration) and the monitoring of the success or otherwise of the responses (Fuster, 2002). This theory is hierarchical in nature, with the relevant processes contributing to the highest ranking function of the prefrontal cortex which is considered to be the temporal organisation of behaviour (Fuster, 2001). Integral to this theory are the many interconnecting networks throughout the brain which contribute to the end result, but whose input is directed, organised and integrated across time by the prefrontal cortex to facilitate the attainment of goals. In general terms these processes could also be seen as control functions, but in this theory temporal organisation is the focus.

There are also theories that consider the single process of working memory to underlie executive functioning. Goldman - Rakic (1995) suggest that working memory functions are evident in several areas of the dorsolateral prefrontal cortex but whilst they share a common process the domain of processing differs. Thus by this theory, the processes which substantially support executive functioning, namely the registering, maintaining and processing of information, are duplicated throughout several locations each with a designated type of information to be processed. The studies which support this theory however, are based on the more limited concept of working memory which includes maintenance and updating of information but not

manipulation (Goldman - Rakic & Leung, 2002). Another theory of working memory is that of Petrides (1994; 2000), who suggests that working memory does not reside in one particular area of the brain but rather the lateral prefrontal cortex acts upon information received from posterior association areas and thus executive processing is carried out in working memory in two stages. The ventrolateral prefrontal cortex, guided by intended plans and actions, operates on information made available by various posterior cortical areas, thereby carrying out such executive processes as selection of information (retrieval), comparisons and judgements regarding the relevance of the stimuli. The mid-dorsolateral prefrontal cortex on the other hand is responsible for the higher level executive processes of active monitoring and manipulation of information being held on line. It is this area that is also necessary for the ordering of actions (planning) required in the attainment of a goal.

These theories of working memory have some support in the workings of a computer model (adaptive character of thought model - ACT - R) whose procedures were designed to enable them to simulate performance on four different executive function tasks (Kimberg & Farah, 1993). The model consisted of logically identical production designs, made up of procedural knowledge and representations of declarative knowledge, and their operations. When the associations between the representations and their operations (simulating the role of working memory) were weakened, performance on all four tasks deteriorated. This suggested to the authors that working memory provided the common underlying factor of executive functioning. However, this model would require multiple information specific working memory systems to account for the dissociations of results often seen between executive tasks.

One model which has been widely adopted is the multicomponent concept of working memory developed by Baddeley and Hitch. This model comprises a phonological loop, a visuospatial scratch pad and more recently an integrative episodic buffer (Baddeley, 2000), all of which are considered 'slave' systems to the central executive. This central executive bears many similarities to the original supervisory system of Norman and Shallice, and at this stage still exists more as a concept than an anatomical reality. It is therefore generally depicted as functioning as a whole, but it is acknowledged that it is probable that it is modular and fractionable (Baddeley, 1998). The function of the central executive in this model is the control and allocation of resources, functions which are closely allied with executive processes. This link has led to an attempt to further define the nature of the central executive and determine whether it is a unified system with many functions or a collection of independent, interacting control processes (Baddeley, 1996). Evidence pointing to a differentiable system was obtained (Baddeley, 1996), but treated with caution by the author who concluded with some doubt whether further analysis would leave us "with a single coordinated system that serves multiple functions, a true executive, or a cluster of largely autonomous control processes – an executive committee .." (p. 26).

Thus, although there is not as yet a single, universally accepted, all explanatory model of executive functioning, a factor which is common to many models is the concept of control. This concept can take many forms, for example, selection, switching or inhibition and operate at many levels (Robbins, 1996; Stuss et al., 1995) but it does appear to be a key element of executive functioning.

## *Unity or Diversity?*

Along with the various theories of executive functioning is the question of whether executive functions are the result of a single underlying process or many interrelated processes. Which ever model proves to be the best representation of executive functioning, there can be no doubt that the frontal lobes do play an important role in those processes, and their structure suggests that some differentiation is possible. At a purely superficial level there are dominant gyri (precentral, superior frontal, middle frontal, inferior frontal, orbital frontal and cingulate) and sulci (central, precentral, superior frontal, inferior frontal and cingulate), which provide distinct anatomical landmarks. There are also well accepted cytoarchitectural divisions within the frontal lobes, again suggesting some degree of differentiation of function. These differentiations are based primarily on Brodman's maps, which include Areas 4, 6, 44, 45, 47, 8, 9, 10, 32, 11, 12, 24, 25 and 46 (Damasio, 1991; Kolb & Whishaw, 1995). Myeloarchitectonic variations also exist, with higher architectonically organised areas (e.g., Area 8) containing a higher myelin content than the less organised areas. The more differentiated areas also seem to have fewer interconnections in comparison to the less well differentiated areas which have a wider network of incoming and outgoing connections (Barbas & Pandya, 1991).

At a functional level, there are a number of studies which support the possibility of differentiability of executive functions (Barbas, 2000; Miyake et al., 2000; Robbins, 1996; Stuss & Alexander, 2000; Van Der Linden et al., 2000). Cognition, memory and emotion in primates was the focus of the study by Barbas (2000) who reached the conclusion that whilst there were functionally distinct 'frontal' areas, many of these areas were utilised in a variety of tasks suggesting

differing patterns of connections for different cognitive processes. This conclusion was reiterated in the review of recent data on the relationship between executive functions and memory processes by Van Der Linden et al. (2000). Stuss and Alexander (2000) summarised studies where they had demonstrated differential impairment on various memory, attention and fluency tasks, the nature of which depended on the location of the lesion within the frontal area. Robbins (1996) based his study on people with frontal lobe lesions, and examined factors commonly considered to be part of the range of executive functions. Planning ability, working memory, response control and attentional shifting, were shown to reflect dissociable aspects of executive functioning. In addition to low correlations between the individual test measures, the neuropsychological testing and neuroimaging results confirmed that the prefrontal cortex plays an important role in response selection processes at several functionally dissociable levels. Updating of working memory, inhibition and shifting were shown again to be related but separable in the study by Miyake et al. (2000). In this study structural equation modeling also suggested that each of these comparatively 'lower level' functions contributed differentially to the more complex tasks of Tower of Hanoi, Wisconsin Card Sorting Test, Random Number Generation and Operation Span providing further evidence that executive functions are not homogeneous.

This view is not without its challengers (Duncan et al., 1997; Hanes, Andrewes, Smith, & Pantelis, 1996). However, in the study by Duncan et al. (1997), although low correlations between the executive function tests were found, an argument was made for a common underlying factor, namely Spearman's 'g'. This is a very broad concept and it would be hard to imagine that it could preclude selective areas of impairment. The second study (Hanes et al., 1996) found differentiable

patterns of results on executive function tests between those diagnosed with Huntington's, Parkinson's and Schizophrenia but then combined their results to correlate the tests used. It is therefore possible, that by amalgamating the different patterns of results, the scores could have been evened out, which would then produce the correlations that were found.

The notion of functional distinction but overlapping networks has been clarified to a greater extent more recently with the advancement of neuroimaging techniques (Collette & Van Der Linden, 2002; Duncan & Owen, 2000; Nyberg et al., 2003; Ruff, Knauff, Fangmeier, & Spreer, 2003; Smith & Jonides, 1999; Stuss, Alexander, Floden et al., 2002). The common areas of recruitment within the frontal cortex, seem to be the dorsal anterior cingulate, mid-dorsolateral and mid-ventrolateral (Duncan & Owen, 2000), however when examined in more detail different cognitive demands do result in different patterns of activation within these areas (Mecklinger et al., 2003; Owen, 2000; Smith & Jonides, 1999; Stuss, Alexander, Floden et al., 2002). It also seems that it may not only be brain 'areas' that are commonly recruited for many different tasks but differential activity at neuronal level has been found (Duncan & Miller, 2002; Miller & Cohen, 2001). Studies are cited which indicate that many neurons behave in an adaptive manner, responding differentially according to the relevance of a particular stimuli to the current task.

These findings indicate that it is not different areas of the frontal cortex that are dedicated to specific functions but rather it seems it is different networks within similar areas which are recruited depending on the particular cognitive processes engaged. This could prove to extend to an even finer level in that differential neuronal activity within a network could separate some tasks.

On a behavioural level, Stern and Prohaska (1996) cited evidence for three distinct behavioural syndromes arising out of damage to either the orbitofrontal system, the mesial frontal system or the dorsolateral prefrontal system. Orbitofrontal system damage can result in impulsive, socially unacceptable behaviour which is often stimulus driven, along with irritability and personality changes. The mesial system involves the ‘emotional’ circuits and damage to this network can result in a general apathy accompanied by a lack of motivation and reduced spontaneity. The dorsolateral system supports executive functioning and when compromised can manifest in such ways as poor organisation and planning, inability to maintain, prioritise or shift a behavioural set, impaired mental flexibility and reasoning/problem solving skills and generally result in a lack of purpose or structure to behaviour (Duffy & Campbell, 1994; Saint-Cyr, Bronstein, & Cummings, 2002; Stern & Prohaska, 1996). These behavioural syndromes are supported neuroanatomically, by three subcortical circuits, originating in the dorsolateral, lateral-orbitofrontal and anterior cingulate areas of the prefrontal cortex, all involving the same structures (frontal lobe, striatum, globus pallidus, substantia nigra and thalamus), however, their relative location is preserved at each site (Mega & Cummings, 1994).

Collectively the above behavioural syndromes have been described as the ‘dysexecutive syndrome’ by Burgess, Alderman, Wilson, Evans, and Emslie (1996); cited in Burgess, Alderman, Evans, Emslie and Wilson (1998). Burgess et al. (1998) concluded that these behavioural characteristics of executive dysfunction could be fractionated into five distinct categories. With the exception of the two categories that related to the participant’s affect, the remaining three closely correspond to the differentiation proposed by Miyake et al. (2000). Whilst the ‘updating and

'inhibition' categories of Miyake et al. (2000), correspond almost exactly with Burgess et al.'s (1998) 'inhibition' and 'executive memory', the later's 'intentionality' factor, which includes planning problems, poor decision making, distractability, lack of insight and a knowing/doing dissociation, is somewhat different to Miyake et al.'s (2000) 'shifting' category which relates to one's ability to shift mental sets. The difference possibly occurs as Miyake et al. (2000) chose to focus on primary or lower level executive functions which could be more easily operationally defined, whereas the 'intentionality' factor clearly relates to rather more complex elements of executive function.

Current evidence strongly suggests that executive functions are differentiable. However, the complex underlying neural networks which involve posterior as well as frontal cortical areas are interlinked, indicating that any accurate assessment of executive functions needs to be comprehensive.

### ***Executive Functions and Memory***

There is now agreement that executive dysfunction is not related to the types of amnesic problems that characterise dementia (Shimamura, 1991; Stuss, Eskes, & Foster, 1994). Therefore, whilst many people with executive dysfunction perform within normal limits on batteries such as the Wechsler Memory Scales (WMS), variable results have been found on span tests, free recall, working memory (Owen, Morris, Sahakian, Polkey, & Robbins, 1996; Shimamura, 1991; Stuss et al., 1994) and recognition (Stuss & Alexander, 2000). Other areas which have been shown to be affected are frequency and recency judgements, and proactive interference effects (Shimamura, 1991; Stuss et al., 1994).

When the processes underlying these problems are analysed it seems they arise primarily when organisational strategies are required (Owen et al., 1996; Shimamura, 1991; Stuss & Alexander, 2000; Stuss et al., 1994) and this can occur over a range of tasks and affect a variety of processes. That executive functioning can impact on memory processes is not surprising when the underlying neural networks are considered. It seems all memory processes involve networks which include both posterior and prefrontal areas, however the more posterior areas (medial temporal and diencephalic structures) generally serve a more passive storage role (Fletcher & Henson, 2001). In long term memory processes it has been generally considered that the left frontal cortex subserves encoding strategies whilst the right frontal cortex is involved in retrieval and monitoring tasks (Stuss & Alexander, 2000; Van Der Linden et al., 2000), though this is certainly not universal as there are material and difficulty related exceptions to this rule. Recent neuroimaging studies carried out during working memory tasks suggest that mid dorsolateral areas are active during the encoding phase, especially in more complex tasks, and if manipulation or monitoring processes are required. More ventro-lateral areas operate when information is to be held on line, thereby performing more of a maintenance function, though this area can also be involved at the encoding stage of a task (D'Esposito & Postle, 2002; D'Esposito, Postle, & Rypma, 2000; Owen, 2000; Rypma & D'Esposito, 1999; Van Der Linden et al., 2000). These areas along with the frontopolar and anterior cingulate cortex have been shown to be common to both working memory and long term episodic and semantic memory (Nyberg et al., 2003; Ranganath, Johnson, & D'Esposito, 2003; Van Der Linden et al., 2000), thereby providing considerable common ground for these functions. Their relation to executive tasks is illustrated in reviews of studies of people with frontal lesions or

where brain imaging has accompanied the execution of executive function tests (Christoff & Gabrieli, 2000; Fletcher & Henson, 2001; Stuss, Alexander, Floden et al., 2002). It has been shown that those 'frontal' areas, which are critical to memory processes, also form part of the networks engaged in performing 'higher order' operations such as those required for the, Tower of London, Wisconsin Card Sorting Test, Raven's Matrices, Dual task and Fluency tests. Therefore, it seems there are areas of the brain that can be recruited for many different cognitive operations. Thus, in so far as executive functioning is dependant on these areas in the frontal cortex, it seems likely that executive dysfunction would impact on, or be related to, measures of memory. The exact nature of this relationship, however, has not yet been established.

### ***Measurement and Categorisation***

***Measurement:*** Although the processes underlying executive functioning are slowly being revealed there is still no doubt that measuring these complex cognitive operations does have its difficulties. In the first instance the ecological validity of executive function tests is often called into question as many of the individual tests do not have a high degree of sensitivity or specificity (Stuss, Alexander, & Benson, 1997). This means there is often a marked discrepancy between test performance and real world ability (Cripe, 1996; Tranel et al., 1994).

One of the key factors which necessitates the recruitment of executive ability is novelty or the unstructured elements of a situation. In many instances this type of condition is difficult to reproduce in an assessment setting thereby possibly minimizing the executive requirements of a test (Cripe, 1996; Lezak, 1995). On the other hand most executive function tests do have a 'novel' quality to them and

require effortful processing, though the degree of novelty will of course vary between individuals (Burgess, 1997; Phillips, 1997).

Burgess (1997) outlines four problems that he sees with the assessment of executive functions. The first is that executive tasks are complex, made up of several different processes. It is therefore often difficult to determine whether a poor test score reflects impaired executive functioning or the failure of an underlying process. This problem can be minimised if the primary underlying processes can also be examined. However, this would require both the identification and isolation of these processes, an exercise that is not always possible. The second problem also relates to the underlying processes, in that there is a lack of a direct correspondence between the behaviour and the processes that precede it. This, Burgess points out, means that any observed dissociation of behaviour does not necessarily point to a dissociation of any particular underlying process which may in fact be common to a number of situations. Likewise a lack of dissociation of behaviours does not automatically imply a complete correspondence of underlying processes. The third related problem results from the fact that interdependent sequences of behaviour make up any complex behaviour. Thus the chain of behaviours can fail at any number of points with a range of possible flow on effects making a comparison between executive functions difficult unless the different stages can be monitored.

A fourth point is based on the assumption that executive behaviour operates in an adaptive manner. If this is so, no matter how similarly structured any two tasks are they can never be exactly the same. This is also why an executive function test when repeated does not have the same diagnostic power a second time, and provides some explanation for the low level of reliability many executive function tests exhibit.

These points all indicate that attempting to assess the integrity of an individual's executive functions cannot be based on the single score of a single, or even a small few tests (Cripe, 1996). Rather a comprehensive battery should be used (Stuss et al., 1994), where, if possible, the primary processes which contribute to the executive test can be separated out.

***Categorisation:*** Based on the previously mentioned characteristics of executive dysfunction (Spreeen & Strauss, 1998; Stern & Prohaska, 1996; Tranel et al., 1994), five main categories have been identified (shifting, working memory, inhibition, planning, reasoning) which it has been shown can be analysed separately. These five categories are the characteristics most commonly associated with the dorsolateral prefrontal system. Problems relating to affect can, however, also be a part of the 'dysexecutive syndrome' and will be addressed in the discussion of the Dysexecutive (DEX) questionnaire in Chapters Three and Eight. To these five most commonly accepted categories of executive functioning, another sixth category, I suggest, should be added. Described by Kolb and Wishaw (1995) as 'behavioural spontaneity', this executive behaviour, when compromised, manifests in the reduced verbal and/or non-verbal (figural) fluency which has been shown to be characteristic of, but not limited to, frontal lobe pathology (Cohen & Stanczak, 2000).

### 1. Shifting

As defined by Miyake et al. (2000) this category involves the ability to shift back and forth between multiple tasks, operations or mental sets, an operation that incurs a temporal cost (Vandierendonck, 2000), especially when the switch is internally driven. This process involves the ability both to disengage from a no

longer relevant task and actively engage in the relevant task. It may also require the ability to overcome proactive interference or negative priming which could occur due to activation of the previous task set.

Banich (1997) suggested that those experiencing frontal lobe related executive dysfunction have more of a problem with extradimensional shifts, that is, shifting between rather than within concepts, indicating an underlying problem of generalising rules across task boundaries, an ability which is linked to the concept of flexible thinking. It is also worth noting in terms of the interrelatedness of the concepts that make up executive functions, that any goal directed behaviour becomes difficult if 'switching' is a problem as most tasks are made up of a hierarchy of sub-tasks which must be executed in succession to achieve the ultimate goal.

It is also obvious that in many tasks, it would be difficult to separate out the logical precursor to this ability to 'shift', that is, the ability to initiate behaviour in the first place. Impairments in ability to initiate behaviour manifest as the 'psychological inertia' that can characterise patients with dysexecutive syndrome (Banich, 1997). In those cases where 'inertia' exists, it can often be coupled with a difficulty in stopping the behaviour once it has been initiated, which then results in perseveration of the response, another related characteristic of executive dysfunction.

Although, initiation, maintaining, shifting and perseveration have been characterised as distinctive executive or frontal problems by Lezak (1995); Fuster; cited in Tranel et al. (1994); Tranel et al. (1994); and Kolb and Wishaw (1995), by adhering primarily to the Miyake et al.'s (2000) concept of shifting, it is also more practical, in terms of measurement, to combine them into one category.

## 2. Working Memory

It is in this category that the interrelatedness of the executive functions is particularly evident, and some would argue that working memory is in fact the foundation of all executive functioning (Goldman-Rakic, 1995; Petrides, 1994). The previously mentioned ACT - R model developed by Kimberg and Farah (1993) was set up to represent working memory processes. When the associations between the representations and their operations were weakened, representative of a failed working memory system, performance on four executive function tasks was impaired. This illustrated the possibility that damage to this one underlying process (working memory), could result in impaired behaviour in a range of executive functions. However, the requirement of this model, that multiple, information specific working memory systems (productions) existed to account for dissociation of performance that is sometimes evidenced on different but logically similar tasks, seems unlikely due to the vast numbers of systems this would require.

Tranel et al. (1994) also suggest that working memory is a crucial part of virtually all operations and behaviours that make up the domain of executive functions. The ability to bring on line and adapt, manipulate or update relevant facts and features of a situation are crucial to the selection of an optimal response, and applies equally to situations involving social conduct through to complex decision making.

Although working memory resources are recruited in many cognitive operations, this category is in fact separable from other categories of executive functioning. This was demonstrated in the results obtained by Lehto (1996) who compared a variety of working memory tests, covering the range from simple span to dual task and updating exercises, with three executive function tests (WCST, Tower

of Hanoi and Goal Search). His results indicated that working memory functions were in fact separable from other executive functions, and therefore it is possible to assess working memory operations and integrity separately.

Miyake et al. (2000) define this category, or concept of working memory, as the monitoring and coding of incoming information for relevance to the task at hand, along with appropriate revision of the items held in working memory. This results in the replacement of no longer relevant information with newer more relevant data. These authors acknowledge that the process may also involve temporal tagging of information to keep track of which is old and which is new information, but regardless, the process is one that involves more than passive maintenance of information, but rather involves some active manipulation. This updating function can be expected to be involved in all situations where appropriate behaviour requires the utilisation of feedback and/or a degree of self monitoring, both of which are important in maintaining goal directed behaviour.

Because this category has such wide reaching influence, in that the successful performance of many tasks requires at a basic level the ability to hold and manipulate or update the contents of working memory, its integrity is not always possible to separate from the behaviour it contributes to. However, if the appropriate tests are used, it is possible to assess this function independently.

### 3. Inhibition

This category refers to the ability to inhibit dominant automatic or prepotent responses. As such it involves an internally generated act of control, which Kimberg and Farah (1993) point out could involve actively boosting weaker to-be-selected pathways rather than necessarily suppressing the dominant prepotent response.

Impairment of this function can be seen when a person knows how they should be acting but fails to do so, indicating perhaps a disconnection between thought and action (Banich 1997). In its extreme, it manifests in what is known as 'environmental dependency syndrome' where behaviour is entirely governed by environmental cues suggesting complete lack of internal control over behaviour (Banich 1997).

#### 4. Planning

The ability to organise behaviour toward a goal is multi-faceted. It requires the ability to sequence both in the future and in relation to past events. That is, one needs to be able to generate sequential behaviour but also to keep track of the sequence of events, or what has been done previously. Although this attribute undoubtedly requires working memory resources, the temporal tagging requirement in this instance is a primary requirement and enables a separate analysis.

Successful planning also involves the ability to formulate a strategy that is most likely to achieve one's goal in the most efficient manner. Tranel et al. (1994) suggests this requires the ability to be able to make an accurate assessment of where one is, where one wishes to be and the best means of getting there. This necessitates the ability to make choices between both sequential alternatives and hierarchical alternatives in order to direct behaviour toward goal achievement along the most efficient path (Lezak, 1995). The inability to form strategies is thought to underlie not only the comparatively complex formulation of plans but also some memory retrieval impairments. Some studies, (Mangels, 1997; Troyer, Fisk, Archibald, Ritvo, & Murray, 1996) suggest that verbal recall and recall of temporal order respectively, break down due to a deficiency in retrieval strategy.

Weaknesses in the attributes required for the successful formulation of plans manifest in an inability to make reasonable judgements about both ones own abilities and/or about the world at large. Judgements of the frequency of events can also be impaired, and if one is not able to accurately assess an event probability as being high or low it is unlikely that an optimal plan of action can be chosen. Obviously an ability to utilise feedback to assess the success or otherwise of the formulated plan, and if necessary the ability to ‘switch’ behaviour are also necessary components of the successful conclusion of a plan, but will be assessed under their separate categories.

## 5. Problem Solving

This category involves the abilities of abstraction and conceptual thinking, along with logic and deductive processes. These processes also require cognitive flexibility at all levels, which in turn make possible multiple interpretations and responses; an attribute that is essential when one encounters a novel situation. Lezak, cited in Tranel (1994) refers to a deficit in this category as a ‘concrete attitude’ which she describes as an inability to understand the abstract supraordinate nature of stimuli and situations. There are two types of flexibility which are relevant to this category (Banich, 1997). The first is reactive flexibility, where environmental stimuli are reacted to in a different manner from that used on previous occasions. The second is spontaneous flexibility, which involves the generation of multiple ideas required when the environment provides little guidance as to the appropriate response. This type is also sometimes referred to as ‘ideational fluency’ and involves the ability to break old associations and develop or create new ones. Both types of flexibility are able to be assessed independently.

## 6. Fluency

Although aphasia, amnesia and reduced motor speed have all been suggested as reasons for fluency deficits, Ruff, Evans, and Marshall (1986), suggest that successful performance on fluency tasks depends primarily on the ability to utilise different performance strategies. This conclusion was supported by Elfgrén and Risberg (1998), who acknowledged, however, that as well as an ability to plan, some internal monitoring and ability to follow rules was required to achieve well on these measures. It may seem, therefore, that the primary mediators of performance on fluency tasks are those factors already covered in the previous ‘planning’ or ‘working memory’ categories. However it is possible to measure fluency separately and more specifically than would be possible within the more complex categories, thus it seems appropriate to consider ‘fluency’ as a sixth separate executive category. This decision is supported in part by the factor analytic results of Cohen and Stanczak (2000) which suggested that fluency measures relate to something different, at least, to the Trails test, generally regarded as a test of ‘shifting’, and the Stroop test used as an indication of ‘inhibition’.

In conclusion, it could be said that executive functions encapsulate the complexities of the human species and it is therefore not surprising that they remain somewhat of an enigma. However, advances in technology and science are helping to provide an increasing number of answers to the questions that have surrounded these complex functions. Although definitions remain somewhat imprecise, it now seems certain that executive functions are differentiable, and that executive dysfunction constitutes an increasingly well recognised set of behavioural characteristics. It is also apparent, however, that the assessment of executive functioning should not be

limited to one characteristic or one test, as it is not possible to make assumptions about overall executive integrity on the basis of a limited assessment.

## **Multiple Sclerosis**

To this day Multiple Sclerosis (MS) remains, to a large extent, an enigmatic disease. Research to date has clarified some issues but there appear to be many questions that remain unanswered. Explanations for the disease range between environmental; being seen primarily in the temperate zones, viral; appearing in the MS free Faeroese Islands after occupation by British troops, genetic; with greater risk for relatives and twins, and racial; several races seem largely immune (Beatty, 1996; Brassington & Marsh, 1998; Knight, 1992). These explanations vary in their credibility and the definitive answer remains illusive. A recent study of the association between socio-demographic, lifestyle and medical history and MS in 200 people newly diagnosed with MS in Canada, found a strong association (twice the risk) between cigarette smoking and the development of MS (Ghadirian, Dadgostar, Azani, & Maisonneuve, 2001). This then adds yet another possibility to the list of suggested causes. The disease does effect women more than men and most patients with MS are aged between 15 – 50 years with the average age for initial symptoms being 29 – 30 years (Sibley, 1990).

## ***Pathology***

Historically MS was described in the literature as a purely demyelinating disorder (Brassington & Marsh, 1998; Knight, 1992; Raine, 1990; Rao, 1986; White, Nyenhuis, & Sax, 1992). It is now accepted, however, that whilst demyelination remains the primary hallmark of the disease, inflammation, gliosis and axonal

pathology are common coexisting features (Ransohoff & Karpus, 2003). Where some axonal degeneration occurs, it is suggested that molecular remodelling in the affected axons (the apparent acquiring of a greater than normal number of sodium channels), can explain the relapsing remitting course of MS, in that remission occurs as the damage is counterbalanced, but it cannot explain the progressive forms (Waxman, 2000). Studies are cited that indicate that it is the crossing of a certain threshold of axonal loss that is responsible for any permanent neurological disability that occurs in MS (Waxman, 2000; Wujek et al., 2002). Where remyelination occurs, the regenerated myelin is, somewhat different to the original. Typically the internode distance is shorter and the myelin thickness often bears no relationship to the thickness of the nerve fibre. Consequently, the resulting conduction efficiency is at best variable, though there is still much to be learnt about this process (Herndon, 2003).

Modern imaging techniques have now also differentiated four different types of lesions. Type 1 and type 2 involve T-cell mediated myelin loss but type 2 is characterised by the addition of antibody activity. In contrast, the 3<sup>rd</sup> and 4<sup>th</sup> types of lesion involve pathologically distinct types of degeneration of the oligodendrocytes (Simon, 2003). Again there is still much to learn about the implications of these differences.

### ***Symptoms***

Demyelination does remain the most prevalent characteristic of the disease and the resulting lesions can occur throughout the central nervous system (Beatty, 1996). Possible lesion sites have been listed as: cerebral hemispheres, optic nerves, brain stem, cerebellum and spinal cord (White et al., 1992), indicating “no region of

the neuraxis is spared” (Raine, 1990, p. 21). Accordingly, symptoms are varied but it seems common that early symptoms involve weakness of limbs, and/or optic neuritis, which results from disturbance of the optic nerve. Other possible symptoms include incontinence, vertigo, affective changes, ataxia, facial paralysis and/or pain, seizures, deafness, diplopia, aphasia, fatigue, cognitive difficulties and paraesthesiae (Brassington & Marsh, 1998; Knight, 1992; White et al.,1992).

### ***Classification***

As with most aspects of MS, the course of the disease also varies widely among sufferers. Historically individual cases were classified as either relapsing/remitting or chronic/progressive, however these categories were too broad to be of much clinical use. Beatty (1996) and Brassington and Marsh (1998) indicate five disease course categories that were defined by a group of international professionals, but commonly four types of disease course are currently recognised. These are: relapsing remitting, secondary progressive, primary progressive and progressive relapsing (Tselis & Khan, 2001). The relapsing/remitting course is characterised by a series of relapses, each followed by a full or near full recovery, the secondary/progressive course begins with a relapsing/remitting profile but is followed by a steady progression of the disease, with or without remissions. Primary/progressive cases display a continual disease progression from the outset, whilst the progressive/relapsing course shows a continual progressive decline punctuated with acute relapses (Brassington & Marsh, 1998; Beatty, 1996). The international body was not able to reach a definitional consensus on the relapsing progressive category, therefore this category is not currently recognised.

## *Assessment*

Because of the diversity of possible manifestations, MS can be extremely difficult to diagnose. It seems common criteria are those outlined by Poser and colleagues (Poser et al., 1983). These criteria require evidence of two separate lesions by way of two separate and characteristically different attacks, each lasting at least 24 hours and separated by at least a month, to warrant a clinically definite diagnosis. A clinically probable diagnosis is based on the occurrence of either two attacks, with one able to be attributed to a lesion, or one attack with evidence of two separate lesions.

More recently an update of the Poser diagnostic criteria has been undertaken, in part, to take into account the more exact diagnostic tools now available (McDonald et al., 2001). Four primary points were made; the first emphasised the necessity of obtaining objective evidence for the temporally separate and characteristically different attacks. The second suggests that historical evidence is not sufficient in itself for a diagnosis of MS. The third includes the possibility of using MRI, CSF or visual evoked potentials as a diagnostic aid, and the fourth indicates that the diagnostic outcomes would be “having MS”, “not having MS” or “possible MS” where the evaluation is not complete. In line with the variability of the disease it is interesting to note that there is also a recommendation that “there must be *no better explanation* for the clinical and paraclinical abnormalities” (McDonald et al., 2001, p. 125).

Several studies comparing the two sets of diagnostic criteria have been undertaken and it seems that the McDonald criteria, with the use of imaging techniques allows an earlier “MS definite” diagnosis than the Poser criteria, though

some concerns regarding standardisation of protocol have been raised (Barkhof, 2003).

The overall disability rating scale that is commonly used to assess the degree of disability in those with MS is the Expanded Disability Status Scale (Kurtzke, 1983). This scale ranges from 0 (no disability) to 10 (death). The ratings between 0 and 5 are appropriate for those who are still ambulatory, and scores from 5.5 to 10 are derived in conjunction with an assessment of eight functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, mental and other) which together cover the range of possible manifestations of Multiple Sclerosis lesions. One of the primary disadvantages of this rating scale is that it gives very little weight to the cognitive impairment that may also accompany MS.

### *Affective Consequences*

One of the main affective disorders associated with MS is depression which has been estimated to affect 47 – 54% at some stage of their lives (Fischer et al., 1994). It is possible however, that this figure may overestimate the problem as the most frequently used measures, the Beck Depression Inventory and the Minnesota Multiphasic Personality Inventory (MMPI) include neurovegetative symptoms of depression which overlap with symptoms of MS (Arnett, 2000). Regardless of the accuracy of the percentages, however, there is no doubt that depression can often be an issue for those with MS along with other affective disorders including euphoria, apathy and irritability (Rao, 1986).

## *Cognitive Consequences*

Cognitive difficulties in those with MS were recognised as early as 1877 when Charcot reported that his MS patients exhibited “marked enfeeblement of memory: conceptions are formed slowly; the intellectual and emotional faculties are blunted in their entirety” (cited in Beatty, 1996). However it is not until relatively recently that cognitive impairment in those with MS has been examined in detail. Rao’s neuropsychological review (1986) noted that while broad neuropsychological testing batteries were being used in the 1960s and 1970s it was not until the 1980s that testing of discrete cognitive functions began. It is now thought that 40% to 60% of those with MS are cognitively impaired, especially in relation to learning and memory (Rao, Grafman et al., 1993). Although memory has been the most extensively examined cognitive domain, it is becoming increasingly evident, that because there is a wide variability in the distribution of lesions throughout the central nervous system, almost all cognitive domains can be affected. As a consequence, there is a multiplicity of possible cognitive profiles amongst those with MS, which can be extremely diverse. It is also apparent that the impairment is not usually global but rather tends to be related to specific domains and can therefore often go undetected (Fischer, 2001).

**General Ability:** While there has been considerable variability in the results obtained from research into the effects of MS on the various memory domains, there is greater consensus in regard to the effects on general ability as measured by the WAIS battery of tests. The most common findings in people with MS are summed up by White et al. (1992) “...the most common WAIS-R IQ pattern is that of a discrepancy between Verbal and Performance IQs, with Verbal IQ being higher” (p.

188). This observation is echoed by Rao (1996) who suggests that “On the Wechsler scales, the Performance IQ is typically 7-10 points less than the Verbal IQ” (p. 252).

To illustrate this point, Rao (1986) published the results of 7 studies where all 11 subtests of the Wechsler scales were administered. In accordance with the predictions the difference between the Verbal IQ score and the Performance IQ score ranged from 7 to 14 with the Performance subtest of Digit Symbol generally scoring the lowest followed by Picture Arrangement and Object Assembly, both also part of the Performance IQ. With the exception of two of the studies, the lowest scoring of the Verbal IQ subtests was Digit Span, but for the two exceptions the lowest score was in Arithmetic which in both cases was followed by Digit Span.

Individual studies which have produced similar results include Klonoff, Clark, Oger, Paty and Li (1991) where their sample of 86 participants with MS performed significantly below the controls in the digit symbol and object assembly subtests as well as the similarities verbal subtest. This result could also be an indicator of some level of executive dysfunction, a factor which is endorsed in part by a significantly poorer performance by their MS sample in word fluency and trails but not in the Halstead category score. A slightly different result was found in the study by Ryan, Clark, Klonoff, and Paty (1993) where their sample of 119 with MS performed significantly more poorly on digit symbol and object assembly and also the block design and picture arrangement performance subtests whilst no verbal subtests were affected. This result was closely mirrored in the results of a 9 subtest version of the WAIS-R that was administered by Andrade et al. to 25 participants with MS (Andrade et al., 1999).

The general nature of these results is also supported by the meta analytic study of Zakzanis (2000), where the largest effect size was for the Performance IQ, ( $d = -$

0.59), though the differences between those with MS and controls for the General Intelligence measures were not large.

It is also important to note that it is not possible from these results to conclude that visuospatial functions are likely to be compromised in those with MS as many of the Performance subtests rely on a degree of motor dexterity that is often compromised in this population. Because of the ambiguity of the Performance IQ results some studies choose to use only the Verbal IQ subtests as measures of general intelligence (McIntosh - Michaelis et al., 1991; Rao, Leo, Bernardin, & Unverzagt, 1991). These studies however produced conflicting results, as Rao, Leo, Bernardin et al. (1991) found significant differences between controls and MS participants in all subtests, while McIntosh-Michaelis et al. (1991) found no significant difference in Verbal IQ between those with MS and their controls and that all the age scaled subtest means were within the 'normal' range.

Based on these previous studies it seems likely that there would be some impairment in processing speed which requires considerable manual dexterity. This would tend to lower the scores on the Processing Speed Index and may subsequently effect the aggregate WAIS-III indices. It is also possible that some impairment may be evident in visuospatial skills which would result in lower scores for the Perceptual Organisation Index.

**Memory:** Rao (1996) suggests some degree of cognitive dysfunction can be found in 43% to 65% of patients, with severe cognitive dysfunction affecting some 20% to 30%, indicating that a relatively large number of those with MS could be expected to exhibit some form of memory impairment. Whilst these estimations have

been shown to paint a reasonably accurate picture of the prevalence of impairment, classifying the nature of memory impairment in those with MS is far from simple.

MS is often characterised cognitively as a subcortical dementia and in terms of memory ability, this typically implies an impairment on memory recall, an impairment which can however be improved by cuing. Recognition abilities generally remain in tact and by inference so, therefore, do encoding and storage abilities.

Whilst using the 'subcortical dementia' umbrella to describe MS many authors when describing the neuropsychological symptoms of the disease, do however point out that the cognitive symptom profile can be extremely diverse (Fennell & Smith, 1990; Mohr & Cox, 2001; White et al., 1992). Consequently, when looking at individual studies a variety of results surface:

In a sample of 37 participants with MS, Rao, Leo and St. Aubin-Faubert (1989) found deficits in long term memory but performances similar to controls on short term measures, recognition and rate of forgetting. This result was largely duplicated (in terms of memory) by Rao, Leo, Bernardin et al. (1991), when a larger sample of 100 participants was used. In 1993, Rao, Grafman et al. also found a word length effect in a working memory task along with a deficit in long term free recall but again intact recognition and encoding abilities. In contrast, Minden, Moes, Orav, Kaplan, and Reich (1990) concluded that their group of 50 participants with MS was impaired on tests of immediate recall, both verbal and visual, and at the .05 level of significance were also impaired on delayed recall, cued recall and recognition measures, though no learning difficulties were indicated.

In the examination of learning difficulties, DeLuca, Barbieri-Berger, and Johnson (1994) did find that impaired verbal learning accounted for any verbal recall or recognition difficulties, a result closely replicated again by DeLuca, Gaudino,

Diamond, Christodoulou, and Engel (1998). This later study however, also determined that while verbal recall and recognition were unimpaired when they were adjusted for the impaired rate of verbal learning, visual learning, recall and recognition were all impaired. In testing a similar learning hypothesis Demaree, Gaudino, DeLuca, and Ricker (2000) also found a learning impairment in both verbal and visual modalities however when this was accounted for, this study found no impairment in either verbal or visual recall.

On finding both short and long term deficits on the Selective Reminding Test, Beatty et al. (1996) performed a cluster analysis on the data from their sample of 99, in an attempt to clarify the results. They found the sample could be divided into three distinct clusters. The first (24%), performed as well or better than controls on most measures, the second, (22%) exhibited severe impairment on both encoding and retrieval measures, in both the short and long term, while the third cluster, (54%) were similar to the controls on short term measures but were mildly deficient in long term storage and retrieval.

A similar grouping of results was found in a sample of 45 participants with MS who were divided into a cognitively preserved group and a group of those assessed as showing mild cognitive decline. The preserved group performed similarly to a control group while those with mild cognitive decline were significantly worse on all measures of immediate and delayed recall of verbal and non verbal materials and learning scores (Kujala, Portin, & Ruutiainen, 1996).

Disease type has also been used in an effort to create more homogeneous groups which would then enable more meaningful conclusions to be drawn from assessment results (Andrade et al., 1999; Beatty, Goodkin, Monson, Beatty, & Hertsgaard, 1988). Beatty et al. (1988) limited their study to a group of 38 patients

with chronic progressive MS and found that they were impaired on measures of both anterograde and long term memory tests as well as recall (short and long term) and recognition measures, with more than 45% scoring below the 10<sup>th</sup> percentile. In contrast Andrade et al. (1999) tested a group of 25 participants with Relapsing Remitting MS and found no short term deficits but impaired learning, visual and verbal long term memory

The meta analysis of Thornton and Raz (1997) was conducted in an attempt to provide some cohesion to this disparate array of results. It included 36 studies which had compared the memory performance of those with MS to a group of healthy controls. On measures of short term memory, working memory and long term memory the MS population was shown to be impaired, though short term deficits were not as extreme as the other two measures. Cued recall and recognition impairment was also indicated with the effect size for recognition being less than that for cued recall, whose effect size did not differ significantly from that of free recall. These effects remained when examined over separate domains, however the effect size of verbal free recall, exceeded non verbal free recall, but the reverse applied for cued recall and recognition (i.e., non verbal effect size was greater than verbal). Similar results were found in the meta analytic study carried out by Wishart and Sharpe (1997), where visual and verbal learning, immediate and delayed recall and recognition were all significantly different from the results of controls.

Zakzanis (2000), however, whilst providing evidence from a third meta analytic study concludes somewhat differently that although both verbal and non verbal recall tasks show impairment, recognition remains largely intact.

It is therefore not surprising when an extensive neuropsychological description of MS is undertaken (Rao, 1986, Brassington & Marsh, 1998), studies

(sometimes contradictory) are cited which can point to impairment (or otherwise) in all memory related domains.

Given this variability of results it would be very difficult to predict what pattern of results could be expected in any particular community based sample of people with MS. A predictive starting point could however be made by looking at the results from other research where the Wechsler Memory Scale has been used. One such study where the WMS was used was conducted by Rao, Hammeke, McQuillen, Khatri, and Lloyd in 1984 and cited in Knight (1992). Although the various Index scores are different from the current version of the WMS, it is interesting to note that the overall Memory Quotient, though lower than the control group was, at 100.5, in the normal range. Information, Digit Span and Associative Learning (Immediate) did not differ from the controls. Orientation, Mental Control and Associative Learning (Delayed) were statistically significantly different from the control group, but the biggest differences appeared in Immediate and Delayed Logical Memory and Visual Reproduction.

A more recent study of memory impairment in a population of those with MS was carried out by Fischer (1988) using the WMS-R battery. Compared to a group of matched controls only the Digit Span (forwards and backwards) subtest of the ACI Index was significantly different, a result contrary to Rao et al. (1984), whereas for the General Memory and Delayed Recall Indices, all subtests proved to be significantly different. Examination of retention percentages and learning rates also revealed significant difficulties in the MS group, though no significant modality difference was found in any of the subtests. Fischer further submitted her results to a cluster analysis and like Beatty et al. (1996) found evidence of three distinct clusters. The first cluster was impaired on all indices, retention and learning measures and did

show greater visual than verbal impairment. The second cluster performed in a similar manner to the controls and the third cluster showed a comparatively unimpaired Attention and Concentration Index, with problems in the General Memory and Delayed Recall Index. These cluster characteristics are similar to those identified by Beatty et al. (1996). It should be noted that the scores of the control group used in Fischer's study were higher than those for the age matched standardization sample which provides the basis of the Index scores for the WMS-R battery. This would have the effect of possibly increasing the numbers showing as being impaired compared to what would have been indicated if the comparison had been based on the WMS-R standardisation sample. However, regardless of the numbers involved that there are at least three differentiable patterns of memory impairment within the MS population.

A more direct means of prediction can be found in the technical manual of the most current WMS-III test. Amongst the data collected in the compilation of this manual are the results from a sample of 25 participants with MS. These results indicate impairment (at 1 SD below the mean) in only the visual immediate and visual delayed subtests with all other subtest results and aggregated indices being above this level. The SDs for all measures however ranged from 14.3 to 19.1 indicating some considerable variability in the scores. Whilst the overall results of the Fischer (1998) study indicated no modality differential when compared with the control group, it should be noted that when the results were compared to the WMS standardisation sample a modality difference was apparent.

The median percentiles for single-trial learning, learning slope, retention and retrieval all indicated a lack of impairment, however the ranges varied from 1% - 98% (learning slope) to 5% - 88% (retrieval) again suggesting a wide range of

individual abilities. Some of these percentiles however, taken in isolation, provide very little informative detail. For example a low learning slope score could be the result of a high initial retrieval performance which would then leave very little room for improvement.

Based on the above studies, it is evident that cognitive impairment, and especially memory impairment is, for many, a consequence of MS. Although there is no specific cognitive deficit or aspect of memory that is reliably associated with the disease. Therefore, if practical, it would be wise to make any cognitive assessment as broad as possible. It does seem, however, that Recognition would be most likely to be spared and Visual Memory possibly more affected than Verbal.

***Executive Functions:*** Early studies of MS, considered that the disease displayed the characteristics of the type of subcortical dementia seen in Parkinson's and Huntington's disease (Mahler & Benson, 1990; Rao, 1986; White et al., 1992). As well as memory retrieval failure, accompanied by relatively intact encoding and storage capacity, other characteristics include impaired conceptual/reasoning skills, slowed information processing speed, personality disturbance (apathy, depression or euphoria) along with intact intellect (as measured by such instruments as the Wechsler Intelligence Scales) and in the absence of aphasia (Rao, 1986). This generalization seemed to influence much of then current research into executive functioning. Consequently, many early studies which included the examination of executive functions, limited their testing to the Halstead Category Test (Peyser, Edwards, Poser, & Filskov, 1980) revealing mixed results (Rao, 1986). This test purportedly measures the ability to form abstract concepts but has been found to correlate highly with age and the Wechsler Intelligence Scales. It also gives only a

single score, making analysis of underlying problems impossible (Lezak, 1995; Tranel et al., 1994).

To date studies of executive functioning in subjects with MS have yielded little in the way of detailed information. This is primarily because the executive functions per se have not been studied systematically in a manner which covers the range of possible characteristics, nor have they been related to behavioural characteristics. Tests which are considered to measure executive functions, are often used as part of a broader neuropsychological battery in an attempt to assess cognitive impairment generally (Amato et al., 1995; Amato, Ponziani, Siracusa, & Sorbi, 2001; Andrade et al., 1999; Klonoff et al., 1991; McIntosh - Michaelis et al., 1991; Ryan et al., 1993). The efficacy of this approach is further undermined by the lack of consistency in the tests used to assess this aspect of cognitive functioning. For example, Ryan et al. (1993) and Klonoff et al. (1991) used the Fluency, Categories and Trail tests, McIntosh-Michealis et al. (1991) used WCST and Fluency tests, Amato et al. (1995, 2001) used the SET test and Ravens Progressive Matrices, and Andrade et al. (1999) used the Stroop and Fluency tests as part of their extensive cognitive battery which was administered in an attempt to assess the extent of cognitive dysfunction in the MS population of Brazil.

With brain imaging techniques that are now available, executive function test results are also increasingly used in studies examining the possible correlates of particular brain pathology (Arnett et al., 1994; Benedict et al., 2002; Edwards, Liu, & Blumhardt, 2001; Leocani et al., 2000; Sperling et al., 2001). Again, however there is little consistency in the particular tests that are used. Edwards et al. (2001) used a fluency test, the WCST and Butters Five Question task in combination with other tests to derive a cognitive index score which was then compared (along with the

individual tests) with white matter volume. Sperling et al. (2001) used a fluency test as part of a battery, the results of which were compared to total lesion volume. Leocani et al. (2000) used WCST and Fluency tests as part of a broader battery to differentiate 'impaired' from 'unimpaired' and related this status to the integrity of cortico-cortical connections and brain lesion load. Arnett et al. (1994) examined the correlation between performance on the WCST and frontal lesion load, and more generally Benedict et al. (2002) used the WCST as part of a larger battery whose results were related to the degree of cortical atrophy. Two studies did use an extensive range of tests (Verbal Fluency, Cognitive Estimates, Stroop, Spatial Working Memory & Tower of London), in an attempt to relate executive functioning to the NAA/Cr ratio in the frontal lobes (Foong, Rozewicz, Davie, & Thompson, 1999), and to lesion load (Foong et al., 1997).

In studies of cognitive dysfunction in participants with MS, memory has been examined in more detail than other domains, and some studies have used executive function tests to help clarify the nature of general memory impairment. Verbal fluency was used to help determine the nature of memory disturbance in subjects with MS (Rao, Leo et al., 1989), the WCST was chosen to determine the role of conceptual reasoning in verbal recall (Troyer et al., 1996), and DeLuca et al. (1998) used the WCST and Fluency tests as measures of executive functioning which was examined in relation to measures of verbal and visual learning and memory.

Working memory, considered by some to be the primary facilitator of executive functioning, but at the very least is accepted as one aspect of executive functioning, has also been examined in relation to information processing efficiency, (Archibald & Fisk, 2000) and in relation to depression scores, (Arnett, Higginson, Voss, Bender & Wurst, 1999). Ruchkin et al. (1994) related Event Related Potential

(ERP) results to tests of verbal working memory. It has also been found to correlate with subjective complaints and verbal fluency (Matotek, Saling, Gates, & Sedal, 2001).

There are only a very few studies which have attempted to examine executive functions and their relationship to other areas of cognitive functioning (Beatty, Goodkin, Beatty, & Monson, 1989; D'Esposito et al., 1996). Beatty et al. (1989) used the WCST and Fluency tests to examine the relationship between encoding ability and recognition, recall memory and frontal lobe dysfunction, and D'Esposito et al. (1996) used working memory measures in conjunction with WCST and phonemic and semantic fluency tests as possible executive function correlates of measures of information processing speed, memory and visuospatial function. The first study was, however, limited to those with chronic progressive MS, and whilst they were impaired compared to controls on all measures except recognition, no relationship between encoding ability, executive tests or memory measures was found. Similarly D'Esposito et al. found that inefficiencies in a dual task condition (working memory), were related, in certain instances, only to information processing speed.

Other areas of Executive Functioning that have been examined, largely in isolation, but sometimes as part of a broader analysis, include, reasoning (Halligan, Reznikoff, Friedman, & La Rocca, 1988), attentional deficits (Beatty, Hames, Blanco, Paul, & Wilbanks, 1995; Kujala, Portin, Revonsuo, & Ruutinen, 1995); metamemory, (Beatty & Monson, 1991; Scarrabelotti & Carroll, 1999); ability to use imagery mnemonics (Canellopoulou & Richardson, 1998); hypothesis testing (Rao & Hammeke, 1984); and picture and motor sequencing (Beatty & Monson, 1994). Beatty and Monson (1996) used the WCST and the CCST to examine problem solving abilities in subjects with MS, and the same two tests along with the Shipley

institute of living scale were used by Beatty et al. (1995) to investigate verbal versus non-verbal reasoning skills. Temporal ordering, semantic encoding and planning were studied by Arnett et al. (1997), in a professed attempt to extend the examination of executive functions.

Mendozzi, Pugnetti, Saccani and Motta (1993) were one of the few researchers to use an extensive Executive Function test battery in an attempt to examine 'frontal cognitive functions'. Their primary interest was, however, in the relationship of those results with age at onset of the disease. Unfortunately, also, they chose a battery which is seldom used in MS research (Luria-Nebraska Neuropsychological battery), so future comparisons will be difficult.

Although the above is not an exhaustive account of the research into the integrity of executive functions in those with MS, it seems sufficient to indicate that no single study exists of the systematic examination of a broad range of executive functions and their possible underlying constructs. In general terms, a description of the areas of 'executive processes' which may be compromised in the MS population have been listed as; attention, information processing speed and conceptual reasoning (Rao, Leo, Bernardin et al., 1991). An itemisation of what is 'known' and what is 'believed' in relation to MS, included deficits in complex attention, slowed information processing speed and impaired executive functions such as problem solving as part of the 'known' (Fischer et al., 1994). In keeping with the broad definitions and almost piecemeal analysis in the area of executive functioning, group deficits have been found on many of the tests used to assess executive functioning. For example; Fluency and WCST (Beatty et al., 1989; Beatty et al., 1995; Beatty & Monson, 1996; Caltagirone, Carlesimo, Fadda, & Roncacci, 1991), planning measures (Arnett et al., 1997) and on all measures of a broader battery (Foong et al.,

1999; Foong et al., 1997). In most cases, it is also acknowledged that there is a large amount of variability in the results, and in some studies no deficit is found (Jennekens-Schinkel, van der Velde, Sanders, & Lanser, 1989; Troyer et al., 1996). Consequently in this population knowledge of the nature of executive dysfunction is largely limited to the broad concept.

To provide accurate information regarding the nature of cognitive impairment in those with MS, the patterns of impairment should be analysed on the basis of small homogeneous groups differentiated on the basis of the nature of their impairment. If we are to obtain an accurate picture of the problems of those with MS, then a number of tests, covering a wide range of these differentiable functions should be used. Executive functions are important because of what they represent, but because of the interconnections of the primary underlying brain structure (the frontal lobes), with other brain areas, the origin of a deficit can only be assessed by looking at an even broader range of tests which assess both executive functions and other cognitive domains, and then closely analysing the patterns of deficit that are present.

### ***Methodological Issues***

Regardless of the disease course, most literature on the characteristics of MS acknowledges that there seems to be a considerable amount of variety in the nature of neuropsychological dysfunction. Because the manifestations of MS are so diverse, the research into cognitive dysfunction has often revealed conflicting results. This makes evident the need to break down the samples of those with MS, into cognitively homogeneous groups to enable more precise examination of the nature of the deficits.

Some authors have instead applied a meta-analytic technique to numbers of these smaller studies in an attempt to clarify the nature of cognitive impairment in

people with MS (Thornton & Raz, 1997; Wishart & Sharpe, 1997; Zakzanis, 2000). Thornton and Raz (1997), for example, looked exclusively at the nature of memory impairment and contrary to the findings of many studies (DeLuca et al., 1998; D'Esposito et al., 1996; Landro, Sletvold, & Celius, 2000; Rao, 1986; Rao, Grafman et al., 1993), found memory impairment to exist across all areas studied. These included short term memory and recognition memory, areas previously thought to be spared. They also concluded that a retrieval based account of memory dysfunction was not supported. This analysis, by increasing the number of participants, has simply identified the fact that the overriding characteristic of MS is that, potentially, no area governed by the CNS is spared.

One of the questions Zakzanis (2000) specifically addressed was whether there were patterns of neurocognitive deficit that were characteristic of the disease courses. He concluded that there was not only a difference in the magnitude of deficits but that the two main subtypes of disease course were in fact characterised by different patterns of impairment. His findings showed a greater tendency for frontal lobe related impairment in the chronic progressive group with more memory related problems predominating the relapsing remitting group.

The meta analysis conducted by Wishart and Sharpe (1997) divided the research into nine neuropsychological domains of cognitive functioning, and whilst differential degrees of effect size were revealed, again, all domains reached statistical significance at the  $p < .05$  level, confirming the fact that those with MS, can potentially, exhibit degrees of impairment in all areas of cognitive functioning. One interesting outcome of this study was, contrary to Zakzanis' (2000) findings, no significant statistical difference between the two main disease courses, relapsing remitting and chronic progressive, was found in any of the domains studied.

Zakzanis (2000) also reached a different conclusion on the nature of memory impairment to that of Thornton and Raz (1997), in that Zakzanis' results suggested that recognition was relatively preserved, and a retrieval based account of long term memory dysfunction was supported. Zakzanis suggested this discrepancy could be explained by the fact that his meta analysis was made up of a comparatively narrower range of more recent studies (fourteen years compared to twenty nine years). He argued that these more recent studies may have been more consistent in their interpretation of memory impairment than some of the older studies included in the meta analysis of Thornton and Raz. This perhaps could also explain the discrepancies between his findings and those of Wishart and Sharp (1997) whose studies spanned the twenty years from 1974 to 1994. However, it is also probable that aggregated results are going to depend just as much on the particular samples used as on any statistical or methodological difference.

In keeping with Zakzanis' (2000) differentiation between the MS subgroups, many individual studies have attempted to minimise the variability in their results by analysing separately the two original disease subtypes (relapsing remitting and chronic progressive). For example, when the Sternberg test was used to analyse information processing speed in the disease subtype groups separately, no significant group difference was found between the relapsing remitting and control groups for the sensory/motor reaction time. There was, however a significant difference between the chronic progressive group and the control group on this measure and both groups were found to have reduced information processing speed compared to the control group (Archibald & Fisk, 2000). In contrast, when the same paradigm was used with only two groups (MS and control), a significant difference between the groups in both

the sensory/motor reaction time and the speed of information processing was found (Rao, St. Aubin-Faubert, & Leo, 1989).

Other areas where different impairment characteristics between disease courses have been found include; measures of information processing speed (Snyder, Cappelleri, Archibald, & Fisk, 2001); temporal ordering, semantic encoding and planning task (Arnett et al., 1997). Assessments using the WAIS and Halstead Reitan Battery (Heaton, Nelson, Thompson, Burks, & Franklin, 1985); and the Wisconsin Card Sorting Test (WCST) (Rao, Hammeke, & Speech, 1987), have also highlighted differences between those with different disease courses. It should be noted, however, that this apparent distinction between the two original disease course groups does not always hold, another testimony to the variable nature of the disease (Beatty, Goodkin, Hertsgaard, & Monson, 1990; Sperling et al., 2001).

In their attempt to improve on broad group analysis, Kujala, Portin, Revonsuo and Ruutiainen (1994) differentiated three stages of information processing (automatic, controlled and motor programming) and three groups of participants. The sample was divided on the basis of a cognitive deterioration score into 'impaired MS', 'unimpaired MS', and control, to enable the analysis of the data to be based on cognitively homogeneous groups. The results showed the 'impaired MS' group, as a group, to be impaired on all tests, whilst the 'unimpaired MS' group showed only minor selective deficits. The same group differentiation was used to examine attentional deficits in participants with MS (Kujala et al., 1995). A similar pattern of results were found except the 'impaired MS' group in this study was not uniformly impaired but rather contained a number of individuals with only selective impairment patterns.

Cluster analysis has also been used in an attempt to provide a more detailed analysis of the MS population (Fischer, 1988; Richardson, 1996; Ryan, Clark, Klonoff, Li, & Paty, 1996). Ryan et al. (1996) used cluster analysis on the results of five tests, each of which represented a different area of cognitive ability. They were able to identify different patterns of impairment between two groups which were classified as cognitively impaired or unimpaired. They revealed six definite profiles of test results for the impaired group and ten for the unimpaired. Given that the sample consisted only of those with relapsing remitting MS who had an Expanded Disability Status Scale (EDSS) score of less than six (ambulation without assistance), the six profiles are probably only a small percentage of possibilities throughout the 'impaired' MS population.

Fisher (1988) also used cluster analysis on scores from the Attention Concentration Index, the General Memory Index and the Delayed Recall Index from the Wechsler Memory Scale - Revised (WMS-R). This enabled the identification of three quantitatively and qualitatively different patterns of memory impairment in those with MS, who as a group demonstrated global impairment. This result was duplicated by (Beatty et al., 1996), when they re-examined group results which had suggested widespread retrieval based memory deficits.

Richardson (1996) used the same method of analysis in a more qualitative study using the reports of everyday memory impairment made by both the participants with MS and their relative. This attempt to identify qualitatively different patterns of memory problems revealed only two clusters, impaired and unimpaired which applied equally to both the participants and the relatives' reports. However, on more detailed analysis it was revealed that although the numbers that made up each cluster were similar for both the participants and the controls, the items

that differentiated each cluster were entirely different between the groups. In this study this highlighted the difference between self perceived problems, and problems that others see, an important result which may have been overlooked if the different clusters had not been isolated.

Other studies that have broken down their units of analysis to reveal more informative information include Foong et al. (1999), who initially found no significant correlation between executive function test scores (which on the basis of the group average, proved significantly lower than a control group) and a chemical ratio (NAA/Cr), present in the frontal brain of the participants with MS. However, when the group of those with MS was subdivided into three on the basis of their (normal to low) NAA/Cr ratios, significant differences in particular test results were found in relation to the various NAA/Cr levels.

Similar detailed analysis by Beatty and Monson (1991) revealed that only those participants with MS who were impaired on both the WCST test and recognition memory tests, had significant problems with metamemory. This domain of interest was also found to be minimally but differentially impaired in those who had difficulty with only one of the tests. This indicated that not only was metamemory a multidimensional concept, but also that the component parts revealed in this study could be impaired in isolation. A broad group analysis would have resulted in a less informative conclusion about the nature of metamemory and a presumption regarding the integrity of metamemory skills in those with MS that depended entirely on the make up of the sample in terms of their relative abilities on the WCST and the recognition memory tests.

Illness duration has also been used as a discriminating factor in analysis of cognitive dysfunction in an MS sample (Halligan et al., 1988). However the irregular

deterioration they observed prompted them to comment that “Idiographic screening procedures ... should be refined further” (p. 547). When levels of depression were the differentiating criteria significant differences between the groups (depressed MS, non-depressed MS and controls), were found on measures of working memory (Arnett et al., 1999). This result was in contradiction to the findings of others who suggest there is no relationship between levels of depression and cognitive impairment (Archibald & Fisk, 2000; Demaree et al., 2000; D'Esposito et al., 1996; Landro et al., 2000).

Although it seems evident that using the mean score obtained from a sample of participants with MS in its entirety, would provide little in the way of meaningful information, this does not always appear to be the case (Ryan et al., 1993). A specific deficit model, a subgroup deficit model, a dissociation syndrome model and a global dissociation model were compared to determine which model of cognitive deficit best represented their MS sample. In spite of the evidence above, that analysis of subgroups, or specific patterns of impairment provide a more detailed picture of any difficulties, these authors concluded that minimising variability did not result in better prediction of cognitive impairment in their particular sample than group means. Whilst they did acknowledge some considerable variability in the scores, they concluded that the specific deficit model proved to be the best fit. In their study, greater variability was commonly associated with lower group means, though this sample consisted of only mildly impaired, relapsing remitting participants.

Although there are obviously exceptions to every rule one study which clearly shows the advantage of detailed analysis is that of Grossman et al. (1994). Using a comprehensive battery of neuropsychological tests along with measures of mood and fatigue, they demonstrated in detail the varying patterns of cognitive

impairment in a sample of participants with MS. Initially, the analysis was carried out on a disease course differentiated group basis (relapsing remitting, chronic progressive and control) and a significant main effect of group was found along with a significant group by task interaction effect, revealing task specific differences of impairment between the groups. The analysis was then broken down to an individual level, where individual patterns of impairment, not evident in the broader analysis, were revealed. It was also determined that although a greater proportion of participants in the chronic progressive group were considered 'demented', a result consistent with the group analysis, many individuals in the relapsing remitting group also had specific areas of impairment not previously revealed in the group analysis.

Although the sample size in the above study was small, it highlights the evidence of the other previously cited examples, which acknowledge considerable individual differences within their group of interest. With the possible exception of the study by Ryan et al. (1993) which used only mildly impaired participants, it is evident that more meaningful information about an individual's difficulties, can only come from studies that incorporate a micro approach, rather than a broad-based group approach, to the examination of cognitive impairment. Therefore to obtain meaningful information about the nature of cognitive impairment in such a heterogeneous group as those with MS, it is especially important that the individual groups used in the analysis are as homogeneous as possible to ensure that valuable information is not lost or diluted.

In contrast, because of the many possible manifestations of executive dysfunction, the examination of this construct requires a broader based approach than has previously been undertaken. For this measure, to ensure multiple executive weaknesses are assessed, a comprehensive battery would provide a more appropriate

tool than any individual test. That there is a need for such a detailed examination of executive functioning, along with any possible underlying constructs, has been acknowledged – “further research is needed to examine the interrelationships between executive functions (planning, decision making, social judgement, temporal sequencing, reasoning) and memory, and to identify the various subtypes of memory impairment observed in the heterogeneous MS population.” (Rao, Reingold, Ron, Lyon-Caen, & Comi, 1993, p. 659). Although that comment was made ten years ago the need for this type of assessment still remains.

Therefore, based on the literature discussed above, it can be seen that MS is a disease with a variable number of comparatively well-recognised physical symptoms. It has also become evident that in many cases the physical disabilities are accompanied by an equally heterogeneous, but not so well recognised set of cognitive impairments. The nature and extent of executive dysfunction in particular, requires more research in those with MS, as this has not been examined nearly as extensively as memory functioning in this group of people. Although most studies that have examined cognitive impairment in those with MS have also established that there is little if any relationship between the nature or degree of cognitive impairment and the level of physical disability, the relationships between the various cognitive constructs have not been well researched. This is especially true of the relationships between executive functions and other cognitive abilities, therefore, this issue will be a focus of this study.

## **Chapter 2**

### **PRESENT STUDY**

#### **Rationale**

In the first instance, it was noticeable in the literature review that most of the cited previous studies, which examined the effects of Multiple Sclerosis (MS) on cognitive functioning, used participants that were associated with a clinical facility. However, many of those in New Zealand that have MS live independently, often with only limited, if any, access to a specialist clinic. For the current study, it was therefore considered important to use a comprehensive community based sample that was more representative of the New Zealand MS population, in order to examine the issues that this research addresses.

To provide a detailed account of the characteristics of the research sample that was selected, not only was demographic data obtained but three pre-assessments were conducted. These included the Chicago Multiscale Depression Inventory (CMDI) measure of depression, which not only enabled an assessment of the levels of depression, but also enabled the influence of disease characteristics on this measure to be taken into account. The Expanded Disability Status Scale (EDSS) measure provided detail regarding of the levels of physical disability in this sample, and the Wechsler Test of Adult Reading (WTAR) assessment of premorbid intelligence levels was also included as a pre-assessment measure as the main assessments in this research did not include a control group. The scores from the WTAR therefore enabled conclusions to be made regarding the effects of MS on cognitive ability.

The fact that a considerable number of those with MS in New Zealand do live alone, or have minimal support, is also the reason that a primary focus of the current study was to determine the extent of executive dysfunction in this particular population. Gathering more information on the prevalence of executive dysfunction in those people with MS was of primary importance due to the severe impact that executive dysfunction can have on a person's ability to function competently on a day to day basis.

As reviewed, previous research has most often assessed executive functioning (and other cognitive functions) on a broad group basis, where typically the average scores obtained from a sample of those with MS were compared with the average scores of a control group. However, as the literature revealed, the cognitive profiles of those with MS seemed to be extremely diverse (and most studies acknowledge sizeable measures of variability in the MS scores), results from such a research approach may not provide an accurate picture of the problems that do exist within that particular MS sample. Therefore to overcome this problem and to better provide a more detailed picture of the extent of executive dysfunction in the sample that was selected, the numbers of participants impaired on any category or combination of categories of executive function was reported. This enabled the actual prevalence of executive dysfunction to be obtained, rather than just a general indication of whether the sample on average was impaired on any one measure.

The literature review has also indicated that previous assessments of executive dysfunction have very often been limited to one or two tests, often as part of a broad neuropsychological battery used to determine cognitive impairment generally. This has made it difficult to ascertain just what executive dysfunction characteristics may be present amongst those with MS. That one or two executive

function tests may not cover all possible manifestations of executive dysfunction has been demonstrated by many of those who have assessed participants with frontal lobe pathology (e.g., Tranel et al., 1994). These studies have often found inconsistent results on many of the tests, suggesting that even when frontal lobe damage was a given, the outcomes on any particular executive function test could not be predicted.

Some research involving participants with MS have used executive function tests specifically, in particular the Wisconsin Card Sorting Test (WCST), to examine any correlate between executive dysfunction and particular brain pathology, and some studies have focused on specific executive functions such as reasoning, metamemory or fluency. However, there were a very few studies (e.g., Mendozzi et al., 1993) that have used a sufficiently comprehensive assessment of executive functions to enable a conclusion to be drawn regarding the full nature of executive dysfunction in those with MS. Therefore, this study used a broad battery of executive function tests which together covered most of the six executive dysfunction categories that were described in the literature review, thus enabling an account of each individual profile of executive dysfunction and thereby providing a detailed picture of the full nature of executive dysfunction in the sample that was selected. The assessment battery that was used is the new Delis-Kaplan Executive Function System (D.KEFS), that was published in 2001, which is made up of nine separate tests whose primary scores, along with contrast and error scores, provided measures which can be attributed to one of at least five of the six executive dysfunction categories discussed in the previous section. Unfortunately it was not possible within this battery to obtain an accurate measure that relates specifically to working memory functions, therefore this category was measured more specifically by the Working Memory Indices of the Wechsler Memory Scale - III (WMS-III).

Of neurological interest, is the issue of which (if any) other cognitive impairment is consistently related to executive dysfunction. Within the general population, the literature review suggested that general ability and executive functioning have very little in common (e.g., Crinella & Yu, 2000), and while some of those with memory impairment have been shown to also have some executive dysfunction, no clear relationship between a particular aspect of memory and either a particular executive function category or even executive dysfunction in general has been established. This question has not previously been addressed in relation to those with MS, and as reviewed previously, was considered by Rao, Reingold et al. in 1993 to be an outstanding issue in relation to the MS research which had been carried out to that date. The current study explored such relationships comprehensively by using test scores of well established batteries of general ability (WAIS-III) and memory (WMS-III), each covering a broad range of cognitive functions.

Additionally, the literature suggested that the cognitive functions of attention and information processing speed may be linked with executive functioning, and both functions seemed to be often impaired in people with MS (e.g., Brassington & Marsh, 1998; Fischer et al., 1994). The current study also therefore included measures of these functions to further explore their links with executive functioning in the selected sample. This is particularly important as slowed information processing speed was considered a characteristic of the subcortical dementia that was thought to characterise those with MS, and some authors (e.g., Mohr & Cox, 2001) consider this process to underlie other cognitive impairment in those with MS. Similarly, complex attention in particular was also considered to be a common impairment in those with MS (e.g., Arnett, 2000), therefore it was of interest to

measure this construct to determine whether there is any link between an ability to pay attention and the presence of executive dysfunction in the selected sample.

To make any relationship between other cognitive functions and executive functioning as specific as possible, it was considered important to compare the underlying cognitive profiles of groups of participants who share the same executive dysfunction profile. That is, if the number of different executive dysfunction profiles (combinations of categories executive dysfunction) were not too numerous then any other cognitive impairment within each group would have been compared to provide information as to whether certain other cognitive impairments are specific to certain profiles of executive dysfunction. However, based on the literature, it was probable that the number of profiles would have been quite considerable and comparisons between broader 'impairment type' groups needed to be considered.

Given the differing views on the role of working memory in executive functioning, that is, whether it forms the basis of executive functioning or whether it is one of a number of separable categories, it was of particular interest from a neuropsychological point of view to ascertain in the current study just what relationship working memory does have with the other categories of executive functioning. If it was, as some suggest, the basis of all other executive dysfunction (e.g., Goldman-Rakic, 1995), one could expect to see all those people with MS that have executive dysfunction to also be impaired on measures of working memory. If however it was one of several differentiable executive functions it would only be impaired in a limited number of those with executive dysfunction.

Because there is very little indication to date regarding which (if any) other cognitive functions may be related to executive functioning in those with MS, it was useful to further explore the nature of any relationship between other cognitive

functions and executive functioning that was indicated by this study. That is, it was of interest to know whether the relationship held only for those cases with impaired executive functions or whether it remained regardless of the type of impairment and for the sample as a whole.

Finally, given the importance of executive functioning in facilitating competent and safe daily behaviour, it was considered important to discover not only the extent and nature of executive dysfunction in this community based sample which was selected, but also which behavioural characteristics were associated with the assessed impairment. This provided some indication as to whether or not those in this sample should in fact be left to care for themselves (if that is the case) and whether they should be free to make important decisions which may impact on their future welfare. To examine this issue, the DEX questionnaire, which addresses the most common behavioural characteristics associated with executive dysfunction, was used.

Thus, the four questions that were addressed in this research are as follows:

## Research Questions

1. What is the extent and nature of executive dysfunction and other cognitive impairments in a community based sample of people with Multiple Sclerosis?
2. Are there any links between executive dysfunction and other cognitive impairments?
3. What is the relationship between working memory and executive functioning?
4. Does executive dysfunction impact on daily functioning in this community based sample of participants with Multiple Sclerosis?

## Research Considerations

### *Participants*

The participants for this research will be recruited from the wider community rather than from a clinical setting and this does have some implications. First, this approach should ensure that a wide variety of Multiple Sclerosis manifestations are included in the research, excluding only those who are severely disabled and who would have considerable difficulty completing the assessments. Secondly, the categorization of disease type will be based on the participants' self reporting of their symptoms and not verified by a medical practitioner. This means that the accuracy of this information cannot be guaranteed, however it was not the intention, in this research, to base any analysis on disease type. The third issue relates to medication. As one of the aims of this study was to assess behavioural characteristics, with a view to determining whether existing levels of independence were appropriate, it was felt that any necessary medication should form an integral part of this assessment. Accordingly, no participant will be excluded on the basis of any MS related medication.

### *Pre-Assessments*

***Depression:*** Although depression is not a focus of this research, it is a recognized symptom of MS, and a factor that can affect cognitive functioning. It was therefore decided that a measure of depression should be taken as this illness could prove to be a confound to cognitive results. The *Chicago Multiscale Depression Inventory*, (CMDI) developed and standardised by Nyenhuis, Luchetta, Yamamoto, Terrien, Bernardin, Rao, & Garron, (1998), was especially developed for medical patients where symptoms of depression, such as fatigue, are also symptoms

attributable to the medical condition. This makes it an especially suitable instrument for use with a Multiple Sclerosis population and will be the assessment that will be used in this study.

***Level of Disability:*** In keeping with other MS research, the *Kurtzke Expanded Disability Status Scale* (EDSS; Kurtzke, 1983) will be used to assess the overall level of disability for each participant. Limited instruction from a neuropsychologist was obtained in regard to this assessment, and the score will be assessed in conjunction with the participant. Therefore, apart from the few who will have been assessed on this measure by their own neurologist, the scores obtained for this research can only be approximate.

***Premorbid Intelligence:*** As it is possible that a community based sample of individuals with MS may not reach clinical levels of cognitive impairment, it was felt that a measure of premorbid intelligence would be useful in order to determine any cognitive deterioration attributable to MS. The *Wechsler Test of Adult Reading* (WTAR; Wechsler, 2001) was chosen due to its affiliation with the Wechsler General Ability and Memory batteries, which will make up a major part of the primary assessments undertaken in this study. It has also been established by an Australian based study that for the Australian population this test was a satisfactory predictor of intellectual functioning, but the US norms were a more accurate predictor than those from the UK (Mathias, Barrett-Woodbridge, & Bowden, 2004). This study also found that, on average, the WTAR tended to under estimate the actual results, suggesting that predicted figures may be conservative. It seems,

therefore, that this measure should provide a satisfactory, if somewhat conservative measure of premorbid intelligence for the New Zealand population.

### ***Main Assessments***

***General Ability and Memory:*** The assessments chosen to examine these measures were the *Wechsler Adult Intelligence Scales – III* (WAIS-III; Wechsler, 1997a), and the *Wechsler Memory Scales – III* (WMS-III; Wechsler, 1997b). They were chosen not only because they are extensive, but because they also include normative data that is based on a substantial standardization sample. It was considered optimal for this study to use the available normative data as the comparative benchmark, rather than a separate control group, as this would enable the numbers of MS participants to be maximized. This was considered to be the preferred option as MS samples are notoriously heterogeneous, and if any patterns of impairment were to be identified, the numbers of participants needed to be as extensive as possible. Recent research (Bowden, Lissner, McCarthy, Weiss, & Holdnack, 2004), has also indicated that measurement models comparing Australia and the U.S. in relation to the latent and manifest variables of the WAIS - III are essentially equivalent. In so far as Australia and New Zealand are similar, this suggests therefore, that the WAIS - III normative data is appropriate for use in a New Zealand setting.

***Executive Functions:*** In accordance with the literature, the categories of executive functioning that will be examined in this study are five of the six which were outlined in the introduction section. These are shifting, inhibition, planning, reasoning and fluency. The most appropriate means of conducting such a broad based

assessment will be to use the Delis-Kaplan Executive Function System (D.KEFS), which does not, however, include a sufficiently specific measure of working memory to enable the inclusion of this category in the assessment of executive dysfunction. Assessment of working memory integrity will instead be based primarily on the Working Memory Index of the WMS - III but some subtests from the Working Memory Index of the WAIS – III will also be used.

The D.KEFS does however have at least two advantages over the use of a collection of independent tests. The first is that the tests that make up this assessment battery include normative data that has been compiled from a substantial standardization sample that is comparable to that of the WAIS - III and the WMS - III. This again reduces the need for a separate control group and keeps the comparisons used for each assessment as consistent as possible. The second advantage arises from the range of tests in this battery, which between them cover the above categories of interest. One disadvantage, which would also apply to other individual tests, is that there is not always a one to one mapping of specific test scores to specific executive categories. Further details regarding the classification of executive function impairment will be made in the following data analysis section

### ***Other Cognitive Assessments***

***Attention:*** Because some authors maintain that aspects of attention whether selective, focused or sustained, are an integral part of executive functioning (Barkley, 1996; Manly & Robertson, 1997; Passingham & Rowe, 2002; Stuss et al., 1995) it was considered that a measure of attention should be included in this study. It was decided, however, that the measure should be a simple measure of attention and should minimize any calculating processes that characterize those more complex

measures of attention. The *Attentional Capacity Test* (ACT) designed by Weber (1988), was chosen for this study, as the requirements of this assessment are limited to recognizing predetermined targets, which become progressively more complex.

***Information Processing Speed:*** Another factor which some consider to influence cognitive impairment including executive functioning ability, and which has been shown to be affected in MS populations is information processing speed (Archibald & Fisk, 2000; Rao, St. Aubin-Faubert et al., 1989). It was therefore considered necessary to include a measure of this process in the current study as a possible indicator of executive dysfunction. One measure which has previously demonstrated an ability to discriminate between levels of processing speed in the Multiple Sclerosis population is that based on the Sternberg paradigm (Archibald & Fisk, 2000; Janculjak et al., 1999; Rao, St. Aubin-Faubert et al., 1989). Accordingly, this is the measure of processing speed that will be used for this research.

***Everyday Behavioural Problems:*** The behavioural characteristics considered to represent the 'dysexecutive syndrome' have been analysed and put together for assessment use in the form of the *Dysexecutive Questionnaire* (DEX) by Burgess, Alderman, Wilson, Evans and Emslie (1996); cited in Burgess et al. (1998). Not only does this assessment provide behavioural ratings on five factors (inhibition, intentionality, executive memory, positive affect and negative affect) shown by a Varimax rotational factor analysis to be dissociable, but it also provides a measure of 'insight'. This insight score, obtained by comparing the behavioural ratings of the participant with the behavioural ratings of a person who knows them well, gives a measure of a participant's level of self-awareness in regard to the range of

behavioural characteristics covered by the questionnaire. Because of the nature of the behaviours covered by the DEX, this insight measure could provide a useful guide as to whether the level of independence experienced by the participant in their daily lives is appropriate, and will therefore be used for this study.

***Temporal Judgment:*** It was also considered necessary to incorporate some measure of temporal judgment accuracy. This was due to the importance, in terms of everyday behaviour in numerous contexts, of being able to assess frequency and/or duration of time, reasonably accurately. The only formal assessment of these measures known to the researcher were the temporal questions which form part of the Behavioural Assessment of Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie, & Evans, 1996) assessment (BADs). However, some questions that may have had non-specific answers in their country of origin were considered to have unsuitably specific answers, which many participants in a New Zealand context would have known. Therefore a series of five questions were constructed which were modelled on, but were not the same as those used in the BADs assessment.

## **Chapter 3**

### **METHOD**

#### **Participants**

##### ***Recruitment***

Members of the Waikato Multiple Sclerosis (MS) society were sent Information Sheet 1) with a covering letter (see Appendices A and B), which explained the purpose of this research and described what would be required of each participant. An incentive was offered to potential participants in that they were advised they would all go into a draw and two participants would win a massage or the equivalent value in book or music vouchers. Those that were interested in participating were invited to contact the researcher to arrange suitable times for the assessments. Forty-nine members contacted the researcher and agreed to take part in this research. In the Whakatane, Thames and Tauranga districts, copies of the same two documents were sent to the regional field officers who spoke to their members and passed on to me the names of those willing to participate. A total of 98 participants were originally recruited but one was excluded from the analysis due to an aneurysm and another had epilepsy. One participant was suspected of malingering and was also excluded, which left 95 participants who made up this research sample. All participants recruited someone who knew them well, who will be referred to from now on as 'other', to complete the behavioral questionnaire and 75 of these also agreed to participate as a control for the Attentional Capacity Test (ACT) test of attention and 74 acted as a control for the information processing speed assessment.

## Demographics

The participants were aged between 17 and 78 years. The average age was 52.6 years (Standard Deviation SD = 11.4), and the majority fell between 40 and 60 years (see Figure 3.1).

### Frequency Stem & Leaf

2	Extremes	(= $\leq$ 21)
2	2.	79
4	3.	0559
25	4.	01222333344445555556667799
35	5.	01122334444455555556666666777778999
18	6.	0000122333344555579
6	7.	023568

Stem width: 10  
Each leaf: 1 case

Figure 3.1. Frequency Distribution of Participants' Ages to the Nearest Half Year<sup>1</sup>

The average number of years of education was 12.8 (SD = 3.3 years), and although the range was from 2 years to 27 years, the majority did fall within the more narrow range of 10 to 12 years (see Figure 3.2).

The average number of years since the participant detected the first symptoms of MS was 24.2 years (SD = 13.0 years), reflective of an extensive range, which was from 2 years to 61 years, with the majority falling within the relatively wide time frame of 10 to 38 years. In contrast to the number of years since first symptom detection, the average number of years since MS was first diagnosed was only 11.8 years. The standard deviation was 10.4 again reflecting the wide range of 0.5 years to 48 years.

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<sup>1</sup> To read Stem & Leaf plots, multiply each stem value by the stem width and add leaf values to get actual data values. For example, in Figure 3.1 the stem width is 10 therefore there are two scores in the 20s (27 & 29), four in the 30s (30, 35, 35, & 39) etc.

Frequency Stem & Leaf

1	Extremes	(= $\leq$ 2.0)
2	9.	00
19	10.	000000000000000000
16	11.	0000000000000000
16	12.	0000000000000000
9	13.	000000000
7	14.	0000000
7	15.	0000000
6	16.	000000
3	17.	000
2	18.	00
4	Extremes	( $\geq$ 19.0)

Stem width: 1  
 Each leaf: 1 case

*Figure 3.2. Frequency Distribution of the Years of Education*

Of the 95 participants, 20 (21.1%) were male and 75 (78.9%) were female. Although this sample was typical of the overrepresentation of females that present with this disease, it was a slightly disproportionate representation of the incidence for each gender in the MS population, which is approximately 2:1 in favour of females. In terms of employment category, as suggested by the average age, a large portion, 31 (32.6%), classified themselves as retired, 25 (26.3%) were in paid employment, 20 (21.1%) were sickness beneficiaries, 15 (15.8%) classified themselves as homemakers, and 2 (2.1%) were unemployed and the same number were students. Approximately one third, 31 (32.6%) did not take any medication but the majority, 64 (67.4%) were taking some form of medication. For this study no participant was excluded on the basis of their medication. Because one of the aims of this study was to determine whether levels of independence were appropriate in relation to the participant’s ability to cope, it was considered that prescribed medication formed an integral part of this dynamic.

The classification of disease course showed a predictable split. The majority 47 (49.5%) indicated they had the relapsing-remitting form of MS, 30 (31.6%) had acute or secondary progressive, with only 15 (15.8%) indicating they were chronic progressive and very few 3, (3.2%) indicating the benign form.

## **Materials**

### ***Pre-assessments***

These included the *Chicago Multiscale Depression Inventory*, (CMDI) developed and standardised by Nyenhuis et al. (1998). In developing this assessment, Principle Component analysis, followed by confirmatory factor analysis resulted in the formation of three subscales. The first scale is described as a mood scale and includes such items as 'sad', 'glum' and 'low', the second scale, or evaluative scale, includes such items as 'punished' and 'resented', and the third, vegetative scale, addresses such issues as fatigue and ability to concentrate, and includes such items as 'unable to pay attention' 'exhausted' and 'sluggish'. There is also a composite score. The scoring is based on a Likert scale of 1 (which represents 'not at all') to 5 (which equates to extremely'), and the participants were required to indicate which number best describes them during the past week in relation to each of 50 items. The standardised scaled scores were derived from a sample of 420 adults, demographically matched to the 1980 U.S. census figures, and have a mean of 50 and a standard deviation of 10.

The normative data for this test showed high internal consistency, (Alpha coefficients range from 0.77 to 0.91), but slightly lower split-half reliability for the individual Vegetative (0.61) and Evaluative scales (0.72). Convergent validity was demonstrated in significant correlations with the Beck Depression Inventory (BDI),

Profile of Mood States (POMS) and Geriatric Depression Scale (GDS), while discriminant validity was evidenced in the lower correlations with non-depression POMS scales.

The most commonly used indicator of the degree of physical disability in the MS population is the *EDSS* (Kurtzke Expanded Disability Status Scale) score (Kurtzke, 1983). This scale ranges from 0 (normal), and progresses in 0.5 increments, to 10, which is death. Ratings between 0 and 5.0 relate to those who are fully ambulatory, while ratings from 5.5 upwards relate to the ability to ambulate, with accompanying guidelines as to the usual functional system scores that relate to each level. The accompanying assessment comprises eight functional systems, namely Pyramidal, Cerebellar, Brainstem, Sensory, Bowel and Bladder, Visual, Mental and Other. Each of these is scored on a scale from 0 (normal) to either 5 or 6 (extreme impairment) and are neuroanatomically mutually exclusive, but together make up the range of possible manifestations of multiple sclerosis lesions.

Premorbid intelligence was assessed using the *Wechsler Test of Adult Reading* (WTAR). It requires the participant to read aloud, 50 words which were presented on a card. Age adjusted standard scores are available based on either a U.S. standardization sample of 1134 adults, or a U.K. standardization sample of 331 adults. Internal consistency was high with reliability coefficients for each age group ranging from  $r = .90$  to  $r = .97$  (U.S. sample) and  $r = 0.87$  to  $r = 0.95$  (U.K. sample). Test-retest reliability coefficients were also in the .90's. Concurrent validity was assessed by correlations with other measures of reading recognition, intellectual functioning, and memory measures. There was a strong relationship with reading measures, ranging from  $r = .73$  (WRAT-R Reading) to  $r = .90$  (AMNART), and Verbal Intelligence ( $r = .75$  VIQ). Relationships were weaker between the WTAR

and PIQ ( $r = .59$ ) and Memory Indices ( $r = .47$ , Immediate Memory,  $r = .49$  General Memory and  $r = .51$ , Working Memory). The WTAR manual (Wechsler, 2001) indicated that combining demographic data and WTAR performance enhances the predictive power for intellectual functioning, with verbal intellectual ability being more accurately predicted than visual-perceptual skills or memory.

### ***Main Assessment Measures***

These included the *Wechsler Adult Intelligence Scales – III* (WAIS-III; Wechsler, 1997a), the battery used to assess general ability. This battery provides standardized age appropriate scaled scores for each of the subtests which are summed to form four Index scales; Verbal Comprehension Index, Perceptual Organisation Index, Working Memory Index and Processing Speed Index, which in turn provide the data for the Verbal IQ, Performance IQ and Full Scale IQ. Internal consistency and test-retest reliability has been shown to be high with reliability coefficients ranging from the .70s to the .90s. Likewise concurrent (criterion) validity was established through similarly high correlations with WAIS – R, and the Wechsler Individual Achievement test (WIAT). High inter correlations amongst most subtests, along with a two factor hierarchical model separating the performance from the verbal subtests provided evidence of both convergent and divergent construct validity.

Memory functions were assessed using the related *Wechsler Memory Scales - III* (WMS-III; Wechsler, 1997b) which also had standardized age adjusted scaled scores for each subtest, which are added to form five Index scales; Auditory Immediate, Visual Immediate, Auditory Delayed, Visual Delayed and Auditory Recognition. These scales then provide the data for the Immediate Memory, General

Memory and Working Memory scores. Reliability coefficients for internal consistency were similar to the WAIS - III, however test – retest reliability coefficients were somewhat lower with most falling in the .60s or .70s. Concurrent validity coefficients relating the WMS - III to the WMS - R, and the Wechsler Individual Achievement Test (WIAT) were variable but provided evidence, especially in the relationships with the CMS, for convergent and divergent validity. Convergent and divergent validity was also demonstrated by the inter-test correlation coefficients which ranged from low to high and the confirmatory factor analysis solution which optimally supported the immediate and delayed memory differentiation along with a separate working memory factor.

The *Delis Kaplan Executive Function System* (D.KEFS) was used to assess executive functioning. This battery consists of nine tests, which are adaptations of tests currently used for assessing executive functions. These tests are, Trail Making, Verbal Fluency, Design Fluency, Colour-Word Interference, Card Sorting test, Twenty Questions, Word Context, Tower test and Proverbs. The Trail Making test is comprised of five parts, visual scanning, number sequencing, letter sequencing, number-letter sequencing and motor speed, each preceded by a short practice exercise. Each part (except motor speed) has a selection of randomly placed encircled numbers and letters distributed over a double page. For the visual scanning part the participant was required to make a line through all the '3s', for number sequencing, pencil lines were drawn to connect sixteen consecutive numbers, and for letter sequencing the lines were drawn to connect sixteen consecutive letters. Number – letter sequencing requires the encircled numbers and letters to be connected consecutively in alternating order. For each part the participant was instructed to complete the task as quickly as possible. The motor speed part consists

of blank circles covering a double page which are connected with a broken line, for this exercise the participant was required to trace the path of the broken line as quickly as possible. Each part generates its own primary scaled score and for this test six comparative scores and a switching error score were also obtained.

For the Verbal Fluency assessment the participants were first required to generate as many words as possible beginning with the letters F, then A, and then S. This was followed by a category fluency assessment where the participants were required to produce animal names and then boys' names. The final part of this assessment requires the participant to alternate between the names of fruit and the names of furniture. Each condition has a time limit of sixty seconds, and a scaled score was obtained for letter fluency, category fluency, category switching and switching accuracy. Contrast and error scores were also recorded.

Design Fluency consists of three parts each preceded by a brief practice exercise. For all conditions the page is divided into thirty five squares each of which includes an identical arrangement of dots. For the first part of this test each square includes five black dots, and using a continuous pencil line to connect the dots the participant must draw as many different designs comprising four straight lines, as they can in sixty seconds. The squares for the second part include both black and white dots and this time the designs were drawn connecting only the white dots. The third condition also includes black and white dots but for this exercise the connections must alternate between black and white dots. This test generates a total correct scaled score, along with a combined score, a contrast score and error scores.

The Colour-Word Interference test has four parts. Each part is on a separate page containing first a short practice section of two rows each with five items, then the main section of five rows each with ten items. For the first part the items on the

page are randomly sequenced patches of blue, green or red colour, and the participant was required to name the colours in order along the rows as quickly as they could. For the second part, the items are randomized colour names printed in black type which the participant was required to read. The items in part three are colour names printed in incongruent colours and the participant in this exercise was required to name the colour of the ink, thereby ignoring the word. The final part also has colour names printed in incongruent colours but for this part half of these words are contained in rectangles. For this exercise the participant named the colour of the ink for those names not enclosed in a rectangle, but read the word if it is enclosed in a rectangle. There is a scaled score for each part, as well as combination, contrast and error scores.

The Card Sorting test was administered using two sets of six irregular shaped cards. Every card displays various perceptual features and has a stimulus word printed on it. For each set the participant was first required to sort the six cards into two groups of three in as many ways as possible so that the three cards in each group are similar in some way. The sorting can be based on a variety of categorization rules or conceptual factors including colour, shape, meaning of the word, size, or print style, and after each sort the participant was asked to describe the concept that was used to generate the sort, that is, how the three cards in each set are similar. For the second part, the examiner sorted each set of cards into each of the eight target sorts and for each arrangement the participant was asked to identify the categorization rule or concept that was used as the basis of the sort. This test provides four primary scores, and a number of contrast, repetition, initiation and error type scores.

The Twenty Questions test consists of a page of thirty coloured illustrations of common items which can be broadly classified as animal, vegetable or mineral. The participant was instructed that they must try to guess the item that the examiner has selected by asking the examiner questions. The questions must be able to be answered with a yes or no and the participant must use the fewest number of questions they can. The most effective strategy is to ask questions based on broad categories so as to eliminate a maximum number of items. If the item has not been identified after 20 questions have been asked, that item is discontinued, and the process begins again with the next item. There are a total of four items selected and three primary scores are obtained from this test.

The Word Context test requires the participant to identify the meaning of ten made up words, each of which is included in a series of five clue sentences. For each word the five sentences are presented consecutively and after the presentation of each sentence the participant was asked to guess what the word may mean. As each sentence gives an additional clue as to the meaning of the target word, by incorporating the information given about the word in each preceding sentence, the possible meanings are subsequently narrowed. This test has one primary score and two error scores.

The Tower test consists of nine items of increasing difficulty. The tools for this test consist of a board with three pegs of equal height and five circular blocks with graded diameters, each with a central hole so they can be placed on the pegs. For each item the examiner arranged a number of blocks on the pegs in a start position and the participant was shown a picture of the end position of the same number of blocks. The participant was then instructed to create the arrangement in the picture by moving the blocks one at a time between the pegs without placing a

larger disc on top of a smaller disc. The participants were also instructed to complete the arrangement as quickly and in as few moves as possible. This test provides one primary score and five subsidiary scores.

The final test in this assessment battery is the Proverbs test. For this assessment the participant was first required to explain the meaning of eight proverbs. The first four proverbs are common, and the last four are less well known. The second part of this assessment requires the participant to choose the most accurate meaning of each of the proverbs from a choice of four alternative answers presented on a page of the administration booklet. One overall scaled score is obtained as well as separate scaled scores for the common and uncommon proverbs, accuracy and abstraction.

For this assessment battery, the standardised, age adjusted scaled scores which are provided for all tests, are based on normative data from a large sample (N = 1750) which is representative of the United States population. Internal consistency measures for the tests ranged from moderate to high but test – retest reliability was low to moderate, possibly an artifact of the nature of the tests.

Validity for the tests that closely resembled existing tests (Stroop, Trail Making, Fluency, Towers, Twenty Questions and Proverbs), was considered by the authors to have been proven over the years by the demonstrated “sensitivity of these tests to the detection of brain damage, particularly frontal lobe dysfunction” (Delis, Kaplan & Kramer, 2001, Examiners’ Manual, p. 47). Several studies were cited which demonstrated the validity of the card sorting test in its ability to distinguish between the various processes involved in concept formation.

## ***Other Cognitive Tests***

These included the *Attentional Capacity Test* (Weber, 1988), which was chosen to assess attention as it excludes the confounding effects of calculating ability that is included in other measures such as the Paced Auditory Serial Addition Test (PASAT). It does however correlate significantly with the PASAT (+.49) and in the normative study, scores achieved by brain damaged patients correlated highly with staff ratings of attentional capacity (Lezak, 1995). For this research the test was administered on a Compaq Presario laptop and consists of eight progressively more difficult levels each with three trials. Each trial was preceded by a double-buzz signal and the completion of a trial for levels 2 to 8 was indicated by a single buzz. The first level consisted of the auditory presentation of a randomly chosen single letter which the respondent was required to identify. The requirements of the subsequent levels are as follows:

Level 2: Count the number of ee's in a sequence of ee's

Level 3: Count the number of 8's in a sequence of 8's.

Level 4: Count the number of 8's in a series of random numbers

Level 5: Count the number of 8's and 5's (one total) in a series of randomly generated numbers.

Level 6: Count the number of 4's, 5's, 7's and 8's in a randomly generated sequence of numbers (one total).

Level 7: Count the number of sequential 4 – 7's and 5 – 8's (one total) in a randomly generated sequence of numbers.

Level 8: Count the number of 5 - (any number) – 8 sequences in a randomly generated sequence of numbers.

For levels 2 to 8 the total number of targets for each trial was between 1 and 9 and the total number of targets for each level was 20. The total number of numbers generated for each trial for levels 4 to 6 was 20 and for levels 7 and 8 there were 30 numbers in each trial. The numbers were presented at the rate of one every second and the response was made in the participants own time – each trial beginning when the participant indicated they were ready. Levels 2 to 6 were regenerated random numbers for each administration, however for levels 7 and 8 the same three sequences were repeated at each presentation.

To minimize any memory confounds, participants were advised that it was acceptable to use their fingers to keep track of their stimuli count if they felt more confident doing so. As these same instructions were given to both those with MS and the controls it was not considered that this would affect the reliability of the results.

A version of the *Sternberg Paradigm* (Sternberg, 1967), was administered to provide a measure of information processing speed. This test was also administered on a Compaq Presario laptop computer. The stimuli consisted of single digits and for each trial the participant was required to memorise a set of 1, 2 or 4 digits which were presented together in the center of the computer screen. There was a maximum time of 2 minutes for this ‘memorisation’ stage however the trial could be started when the participant indicated they were ready. For each trial, a semi-random set of 15 digits were presented, one at a time, in the center of the screen. The subject was asked to press the left internal mouse key if the digit on screen was a member of the ‘positive’ set (i.e., one of the numbers that had been remembered), or press the right internal mouse key if the number was in the ‘negative’ set. There were a total of 12 trials, four for each number set size, presented in random order. The ‘to be remembered’ numbers were different for each trial and there were four positive

responses on each trial. The test was preceded by two practice trials each of which contained a memory set of 3 digits. After each key press response, visual feedback of “correct” or “incorrect” appeared on the screen for 0.5 seconds followed by a ‘+’ sign which remained in the center of the screen for 1 second prior to the presentation of the next digit.

The *Dysexecutive Questionnaire* (DEX) was developed by Burgess et al. (1996) cited in (Burgess et al., 1998), as part of the Behavioral Assessment of the Dysexecutive syndrome. It is a 20 item questionnaire requiring a rating of how frequently certain behaviors, thought to be characteristic of dysexecutive syndrome, are experienced. The scoring is on a Likert scale of 0 (never) to 4 (very often) and separate, but identical, questionnaires are completed by both the MS participant (who answered in relation to themselves) and some one (‘other’) who knows them well (who answered in relation to how they perceived the participant). Scores of ‘others’ were shown to correlate with executive function test results of the clinical participant, and factor analysis of these independent rater’s scores produced a five factor solution. These five factors were described as inhibition, intentionality, executive memory, positive affect and negative affect and indicated a dissociation of dysexecutive characteristics. The inhibition factor includes items which address issues such as poor abstract thinking, impulsivity, social disinhibition, lack of concern, restlessness, inability to inhibit responses and lack of concern for social rules. The item which addresses impulsivity, for example, says ‘I act without thinking, doing the first thing that comes to mind’. The intentionality factor addresses planning, lack of insight, distractibility and poor decision making, and an example of an item which relates to decision making says ‘I have trouble making decisions or deciding what I want to do’. The third factor relates to executive

memory and includes such issues as confabulation, poor temporal sequencing and perseveration. An example of an item from this factor is 'I get events mixed up with each other, and get confused about the correct order of events'. The positive affect factor addresses the affective issues of euphoria, variable motivation and aggression, and an example from this factor says 'I loose my temper at the slightest thing'. The fifth factor relates to negative affect and covers apathy and shallow affect and includes such items as 'I have difficulty showing emotion'.

A comparison of the participants' scores and the scores of the 'other' also provided a measure of 'insight'. If the scores are similar, it can be assumed that the participant is able to judge their own behavioural characteristics and difficulties accurately. If however, there is a considerable discrepancy between the two scores (typically with the other's scores being higher), then it could be considered that the participant is not aware of the extent to which they exhibit that particular behavioural characteristic, or any problems that behaviour may incur. Thus the difference between the two scores, or level of insight, should be a good indicator of potential problems in relation to competent daily functioning. For this research, 5 temporal judgment questions were also presented (see Appendix C). They were modeled on the temporal judgement questions that form part of the Behavioural Assessment of the Dysexecutive Syndrome assessment (BADS; Wilson et al., 1996). Two examples are as follows: "How long do you think it would take to blow up a standard party balloon?" and "How many times do you think the 13<sup>th</sup> fell on a Friday over the last three years?"

## Procedure

Ethical approval for this research was obtained from the Psychology Research and Ethics Committee at the University of Waikato. Appointments were made with the participants on dates and at times that best suited them. The assessments were carried out over two, three hour sessions. The first session began with a reiteration of a brief overview of my research and an explanation of the assessments that would be carried out. Once any questions had been answered the consent form was signed (see Appendix D) and the WMS - III was administered. Following this assessment there was a break during which time the demographic data was collected by way of a semi-structured interview (see Appendix E), an Expanded Disability Status Scale (EDSS) rating estimated, and the Wechsler Test of Adult Reading (WTAR) and Chicago Multiscale Depression Inventory (CMDI) were completed. The time taken for this 'break' varied for each participant, but whatever time was needed was given. The WAIS - III was then administered.

The second session began with the Attentional Capacity Test (ACT), followed by the information processing speed assessment. Instructions for each level of the ACT test were given prior to the commencement of that level. The information processing test was preceded by an explanation of the procedure along with the instruction to respond as quickly, but as accurately as possible. If the person selected by the participant as the 'other' was present and had agreed to participate in those assessments, they often completed their assessments at this time, after a semi structured interview similar to that conducted with the participant was completed (see Appendix F). This also enabled the MS participants to have a break from testing. Following the completion of these assessments the D.KEFS battery was administered and this session was completed with the completion of the DEX

questionnaire and temporal judgment questions. On occasion the 'other' person completed the questionnaire and the assessments (if relevant) at the completion of the assessment of the MS participant. For those 'others' who were not available at the time of assessing the MS participant, a separate appointment was made at another address. The WMS - III, WAIS - III and the D.KEFS were all administered in the manner set out in their respective administration manuals.

The time between the first and second sessions also varied but the minimum intervening time was two days and the maximum was two months. When all assessments were completed the reference numbers went into a draw and two numbers were drawn out. The relevant participants were then given a choice of a massage, \$75 worth of book vouchers or the same value in music vouchers. When the complete data set had been collated a summary was sent to all participants with MS.

## **Data Analysis**

Demographic data, EDSS ratings, and all standardized scores from the CMDI, WTAR, WAIS - III, WMS - III, and the D.KEFS were recorded in spreadsheet form using SPSS for Windows (SPSS Inc, 2001).

As one standard deviation below the standardized sample mean has been shown to optimize the balance between sensitivity and specificity of factor scores of the WAIS - III and WMS - III (Taylor & Heaton, 2001), this was the criterion chosen to determine impairment on these measures. Likewise, as it was of interest to capture those more subtle cases of executive dysfunction, this criterion was also applied to the D.KEFS results. As well as maintaining a consistent criterion, it was suggested in the D.KEFS examiner's manual (Delis et al., 2001), in support of this

stance, that psychologists use this scoring level and below as an indication of deficient performance (p. 30). Therefore, executive function impairment in general was determined primarily by examining any scores throughout the battery which fell below that chosen criterion. However a supplementary set of results using 1.64 standard deviations below the standardised mean as the cut-off criteria can be seen in Appendix G. Categorization of executive dysfunction was based on the five categories outlined previously, namely: Shifting, Inhibition, Planning, Reasoning/Problem Solving and Fluency.

Because there is often no one to one mapping between specific test scores and one or other of the five categories of executive functioning, it was sometimes necessary to take into account the overall performance of the participant, as well as the specific scores, to enable an assessment regarding the category of problem(s). This approach was supported by the results of a recent attempt to isolate the relevant components of several executive function tests (Testa & Bennett, 2004). A factor analysis of four 'planning' tests, revealed seven different factors that showed no significant inter-correlation. The authors therefore observed that many executive tests are multi faceted, thus some qualitative assessment of the problem is required.

Some tests, however, were more specific in what they measured than others, and the primary considerations for each category of impairment were as follows:

The Shifting category was assessed primarily by the Number-Letter Switching score on the Trails test, but performance on the California Card Sorting test, in particular the Repeated Descriptions score, along with the Switching measures of the Verbal and Design Fluency tests were also considered. The primary measures of inhibition were the Inhibition and the Inhibition/Switching scores of the Stroop test, however the Accuracy Ratio and Rule Violation scores of the Tower test

along with general behaviour of the participant also provided information in regard to this concept. Planning impairment was judged primarily by the Total Achievement score of the Towers test though procedures used to eliminate items in the 20 Questions test were also informative in relation to this category. Although reasoning/problem solving difficulties were most apparent in the five primary scores of the California Card Sorting test, the Abstraction and Uncommon Proverb Achievement scores of the Proverbs test, the three primary scores of the 20 Questions tests and the Total Consecutively correct score from the Word Context test also contributed to the assessment. The Letter Fluency, Category Fluency and Switching scores from the Verbal Fluency test along with the Primary Measures of the Design Fluency test were used to assess the Fluency category as these tests are designed specifically for this purpose. Although Working Memory is also considered an executive function, it forms an inseparable part of all of the D.KEFS tests, and was therefore not be assessed as a separable executive category but was more directly measured in the WMS - III and the WAIS - III batteries.

For all these categories, although the relevant scaled scores provided the primary information, the various contrast scores, which compare results on the underlying contributing functions to the primary result, were also taken into account. For example in the Trails test the time taken to sequence numbers alone and letters alone was considered when making a judgment on the time taken when the sequencing involved switching from numbers to letters. In some cases, accuracy or error scores also provided relevant information. For example a satisfactory time score on the Stroop test would not have been indicative of a satisfactory performance if the error score was unacceptably low (indicating a high number of errors).

The Attentional Capacity Test (ACT) generated a data file for each individual, recording each response as correct (1) or incorrect (0). The correct responses from each file were added to give a total attention score which was then added to an SPSS data spread sheet. Similarly, the Sternberg paradigm generated a data file for each participant, but in this case the information from these files was entered into an Excel spreadsheet where initial response time (intercept) and information processing speed (slope) values for each individual were calculated. This information, along with the 'error' scores was then transferred to SPSS for further analysis.

In those cases where two factors within the same group were compared, paired sample t-tests were used, and if two separate groups were compared independent samples t-tests were the method of comparison. To reduce the number of participants into smaller more homogeneous groups the average linkage between groups method of cluster analysis was employed followed by a multiple discriminant analysis (MDA) to determine the optimum number of clusters. If one variable was compared across several groups, a one-way between groups analysis of variance (ANOVA) was used in conjunction with a Tukey's honestly significant difference post hoc comparison. Where several variables had similar contributing numbers, and were compared across the same groups, a multivariate analysis of variance (MANOVA) was conducted using the Bonferroni adjusted method of post-hoc comparison. In those cases where the data did not meet the requirements for parametric testing Kruskal-Wallis or Mann Whitney analyses were conducted depending whether the comparisons were between two groups (Mann-Whitney) or several groups (Kruskal-Wallis).

## **Order of Presentation of Results**

### ***Chapter 4: Pre-Assessments***

*CMDI*: Means; Standard Deviations; Frequency Distribution.

*EDSS*: Means; Standard Deviations; Frequency Distribution.

*WTAR*: Means; Standard Deviations; Frequency Distribution.

### ***Chapter 5: Research Question One – What is the extent and nature of executive dysfunction and other cognitive impairments in a community based sample of participants with Multiple Sclerosis?***

*General Ability*: Means; Standard Deviations; Cluster Analysis; Individual Impairment (% and numbers impaired).

*Memory*: Means; Standard Deviations; Cluster Analysis; Individual Impairment (% and numbers impaired).

*Executive Functions*: Numbers Impaired; Frequency and nature of individual profiles; Degree of executive dysfunction; Frequency of impairment of each executive function category.

*Attention*: Means; Standard Deviations; ANOVA (group x age).

*Information Processing Speed*: MANOVA (group x age x information processing variables).

### ***Chapter 6: Research Question Two – Are there any links between executive dysfunction and other cognitive impairments?***

Comparisons were made between four 'Impairment Type' groups (No Impairment, Memory Impairment Only, Memory Impairment and Executive Dysfunction, Executive Dysfunction Only) in relation to the following:

*Demographic data*: MANOVA

*General Ability scores*: ANOVA

*Memory scores: MANOVA*

*Clusters based on WMS-III Index scores: Line graphs*

*Working Memory subtest scores: MANOVA*

*Attention scores: ANOVA*

*Information Processing Speed: MANOVA*

***Chapter 7: Research Question Three – What is the relationship between working memory and executive functioning?***

*The sample as a whole: Correlation between working memory and the degree of executive dysfunction.*

*Impaired working memory: Correlation as above.*

*Unimpaired working memory: Correlation as above.*

Comparison between working memory impaired and working memory unimpaired in relation to the numbers impaired in each executive function category.

***Chapter 8: Research Question Four – Does executive dysfunction impact on daily functioning in this community based sample of participants with Multiple Sclerosis?***

Analysis of Dysexecutive Questionnaire (DEX) and Temporal questions.

## **Chapter 4**

### **PRE-ASSESSMENTS**

The demographic data for the participants were presented in Chapter 3. The pre-assessments were conducted, in part, to provide a more detailed account of the characteristics of the selected sample. More specifically, the Chicago Multiscale Depression Inventory (CMDI) measure of depression comprising three subscales (Mood, Evaluative and Vegetative, see section on Materials for more details) was used to enable an assessment of the levels of depression in this sample, a factor which could have had some influence on the cognitive measures. It was also used, however, to verify whether obtained depression scores were indicative of levels of depression per se or whether they were the result of other disease symptoms. Similarly, the Expanded Disability Status Scale (EDSS) measure of the levels of physical disability was obtained for all participants, in order to more fully describe the characteristics of the participants in the selected sample. The Wechsler Test of Adult Reading (WTAR) assessment of premorbid intelligence levels was also included as a pre-assessment measure. The primary intelligence assessments in this research did not include a control group, therefore to enable any conclusions to be made regarding the effects of MS on levels of intelligence, it was necessary to incorporate this measure of premorbid intelligence levels as an alternative benchmark.

### **Results**

The mean score for the Mood Subscale of the Chicago Multiscale Depression Inventory (CMDI) was 50.9 (Standard Deviation SD = 11.9), with a relatively large

range from 39.8 to 92.3 The distribution was positively skewed indicating a predominance of lower scores and therefore little impairment of the participants on this subscale (see Figure 4.1).

Frequency	Stem & Leaf
21	3. 99999999999999999999
17	4. 111111133333333333
14	4. 555555777777778
13	5. 0002222244444
11	5. 66666677799
2	6. 13
4	6. 5568
6	7. 002444
2	7. 66
2 Extremes	(>=87)

Stem width: 10  
 Each leaf: 1 case

*Figure 4.1.* Frequency Distribution of the Mood Subscale Scores of the Chicago Multiscale Depression Inventory (CMDI)

The Evaluative Subscale mean was 52.0 (SD = 12.8), with scores ranging from 44.0 to 112.0. Similar to the Mood subscale, the Evaluative subscale scores were also positively skewed again indicating a predominance of lower scores and little evidence of depression in this sample (see Figure 4.2). The Vegetative subscale had a slightly higher mean of 58.7 (SD = 13.2) but also exhibited an extensive range of scores from 33.8 to 91.8. In contrast to the other two scales however, the mean score of the Vegetative subscale was higher than the other two subscales and the scores were clustered around the 50s and 60s thereby causing the somewhat higher mean and indicating some level of depression (see Figure 4.3).



of full activity or require minimal assistance; ..... able to walk without aid or rest some 300 metres.’ and level 5.0 – ‘Ambulatory without aid or rest for about 200 metres; disability severe enough to impair full day activities (e.g. to work a full day without special provisions)’ (see scoring guidelines, Kurtze, 1983). The standard deviation for this measure was 2.0 and the range was from 1.0 to 8.0, which does not really reflect the distribution which was of a bimodal nature peaking at both level 3.0 and then again at level 6.0 (see Figure 4.4).

Frequency	Stem & Leaf
3	1. 055
10	2. 0000000555
25	3. 0000000000555555555555555555
6	4. 000005
9	5. 000555555
19	6. 00000000555555555555
13	7. 0000000555555
7	8. 0000000

Stem width: 1  
 Each leaf: 1 case

*Figure 4.4.* Frequency Distribution of the Kurtzke Expanded Disability Status Scale (EDSS) Scores

The mean Wechsler Test of Adult Reading (WTAR) score for this sample was 106.0 (SD = 11.6) and again there was a relatively wide range of scores, which varied from 68 to 123. For this measure the scores were somewhat negatively skewed, distributed around the higher 100s and 110s supporting the mean which indicated an above average level of premorbid intelligence for many participants this sample. (see Figure 4.5).

Frequency Stem & Leaf

1	Extremes	(= $\leq$ 68)
1	7.	7
7	8.	0016699
17	9.	02225566667889999
26	10.	1112244455556777777788889
32	11.	000001111133334444666677799999999
8	12.	00223333

Stem width: 10  
Each leaf: 1 case

Figure 4.5. Frequency Distribution of the Wechsler Test of Adult Reading (WTAR) Scores

### Summary and Discussion

Overall, these pre-assessments have shown that this sample as a whole has not indicated depressive tendencies. In terms of physical disability it would seem that two groups have emerged, one with minimal disability and another whose disabilities extended to the upper end of the scale, which together provided an extensive range of levels of physical impairment. Finally, the Wechsler Test of Adult Reading (WTAR) results suggested that levels of premorbid intelligence were above average for this sample.

Although all three subscales of the Chicago Multiscale Depression Inventory (CMDI) included a wide range of scores, it was only the more normally distributed Vegetative subscale, which addresses such issues as fatigue and ability to concentrate, whose scores indicated some impairment in the sample. As these issues are common symptoms of MS, the scores on this subscale were more readily attributable to MS than depression per se, thus the above average composite CMDI mean score which was influenced primarily by the Vegetative subscale, was not a true reflection of the levels of depression in this sample. Therefore, contrary to some

findings, which suggest that depressive tendencies are a common accompaniment to MS (e.g., Arnett et al., 1999; Landro et al., 2000; Minden et al., 1990) this sample overall did not demonstrate depressive tendencies.

Many studies which concluded that their samples had a tendency to depression (e.g., Andrade et al., 1999) used such measures as the Beck Depression Inventory where all symptoms of depression were combined into the one score. In contrast, the current study illustrated the advantage of using the CMDI multiscale depression assessment for this, and similar, clinical populations, as it made clearer whether the obtained depression scores were indicative of a level of depression per se or whether they were, as in this study, primarily the result of other disease symptoms. Therefore using the selected sample in this study, it was not expected that any depression scores would significantly influence any cognitive measures.

The bimodal nature of the distribution of Expanded Disability Status Scale (EDSS) scores, indicated that although approximately half the sample had only minimal levels of physical disability, there was an almost equally large number whose physical disabilities were more severe. This may therefore have had some influence on the scores obtained in any assessment that required a certain degree of manual dexterity, and this needed to be taken into consideration in the further analysis of cognitive functions in this sample.

In relation to the Wechsler Test of Adult Reading (WTAR) measure of premorbid intelligence, the mean score for this assessment suggested that this sample, on average, had a level of general intelligence prior to their MS that was somewhat above average. The scores for this measure, which have also indicated a tendency to underrate predicted levels of intelligence (Mathias et al., 2004), was also an accurate reflection of the author's perception during the assessment procedure that

this MS sample generally had an above average level of 'intelligence'. It was obvious that a large number of participants in this sample were highly functioning individuals before they were diagnosed with MS, therefore, in so far as this sample was representative of the MS population, these results raise the question of just how typical the above average level of premorbid intelligence found in the current study is amongst this clinical population.

## **Chapter 5**

### **RESEARCH QUESTION ONE**

***What is the extent and nature of executive dysfunction and other cognitive impairments in a community based sample of people with Multiple Sclerosis?***

The answer to the first research question will finalise a comprehensive picture of the demographic and cognitive characteristics of the selected community based sample of participants with Multiple Sclerosis (MS). In particular, detailed information will now be obtained regarding the extent and nature of their executive dysfunction and their cognitive abilities in relation to general intelligence, memory, attention and information processing speed. The goal was to provide extensive executive dysfunction profiles of those in this sample as well as a comprehensive analysis of other cognitive impairment whose relationship with executive functioning will be explored in the following section (Chapter 6).

Research question one was answered by analysing the participants performance on the general ability assessment (Wechsler Adult Intelligence Scales – III), the memory assessment (Wechsler Memory Scales – III), the executive functioning assessment (Delis-Kaplan Executive Function System) and the assessment of attention (Attentional Capacity Test), along with a version of the Sternberg paradigm, which measures information processing speed.

As outlined earlier, no control group was selected for the three main assessments (general ability, memory and executive functioning). This was in order to maximize the number of participants with MS in this research and thereby

facilitate the identification of common patterns of impairment. Thus it was decided to utilize the normative data available with these three main assessment batteries and use this as the comparative benchmark. A control group was used, however, to assess the attention scores and the information processing speed data from the Sternberg paradigm.

To determine any impairment in the sample of participants with MS for general ability and memory, and to follow the lead of previous research on MS that has used a broad group based approach, first the sample means for all the indices were compared with the normative data of the respective test batteries. Any mean that fell below 85 (one standard deviation (SD) below the mean of the standardized data) was considered to indicate some impairment on that particular measure. However, as discussed in the literature review, because the those individuals with MS have been shown to be extremely heterogeneous in relation to both the extent and the nature of their cognitive impairments, the results from this broad sample analysis were not expected to reveal a sufficiently accurate picture of the cognitive characteristics of those within this sample.

Therefore secondly, in line with some previous studies, the sample was clustered on the basis of the composite index scores for general ability and memory in order to isolate smaller more homogeneous groups of participants. This enabled the identification of subgroups of participants who had similar patterns of scores on each of these measures so that a clearer picture of the extent and nature of cognitive impairment that existed within this sample could be obtained.

Thirdly, to identify on an individual basis, the extent of impairment that existed within this sample, the number of participants who scored less than 85 on each of the general ability and memory indices was reported. Thus providing a

detailed account of both the numbers impaired on each index (extent of impairment) and of the areas of cognitive functioning that were most commonly impaired (nature of impairment). It was then of interest to compare those numbers of individuals impaired with the levels of impairment that were indicated by the broader preceding analyses. Within the memory assessment, modality differences (visual versus auditory) and temporal differences (immediate versus delayed) were also examined at all three levels of analysis.

Also, there may have been some participants who have experienced significant deterioration in their general ability and/or memory performance but have not yet reached the threshold (<85) that would classify them as impaired. Therefore the Wechsler Test of Adult Reading (WTAR) scores were used to determine their predicted premorbid performance levels. Comparing these scores with their actual general ability scores revealed any significant decline in the participant's performance irrespective of whether this had reached the level of 'impairment'. This potentially provided additional information regarding cognitive decline in those with MS.

In order to assess executive functioning in the selected sample of participants with MS, primary scores that were more than one standard deviation below the age related standardized means of the normative sample, were examined across the entire Delis-Kaplan Executive Function System (D.KEFS) battery along with the contrast and error scores, as a means of assessing the existence of any executive dysfunction, thus enabling the extent of executive dysfunction to be determined.

The nature of any executive dysfunction was then be determined in the first instance by a count of the number of participants exhibiting each of the profiles of single or combined categories of executive dysfunction. The participants were also

categorized on the basis of the number of impaired categories (degree) of executive dysfunction they were assessed with. A further count of the incidence of each executive function category gave an indication of the overall prevalence of that category of executive dysfunction, and any relationship between the impaired categories was also examined. That is, it was made evident whether a particular category was impaired predominantly in isolation or more commonly in conjunction with one or more other categories.

Finally, attention and information processing speed data for the whole sample with MS was compared with the control group.

## **Results**

### ***General Ability***

In keeping with much of the previous research on cognitive impairment in those with MS, the performance levels of the sample as a whole was first examined. Because of the physical limitations that characterised some of the participants with MS, not all participants were able to complete the full compliment of subtests which make up the Performance IQ measure. However, it should be noted that for all but one participant sufficient subtests were completed to enable a Performance IQ score to be prorated using the tables in the Wechsler Adult Intelligence Scales – III (WAIS-III) Administration and Scoring manual. The means and standard deviations for the various WAIS - III indices are illustrated in Figure 5.1, which shows that the scores of this sample were distributed around the standardized mean (100) for most of the seven indices that make up the general ability assessment. The one exception was the Processing Speed Index whose mean score was somewhat lower than the other indices.

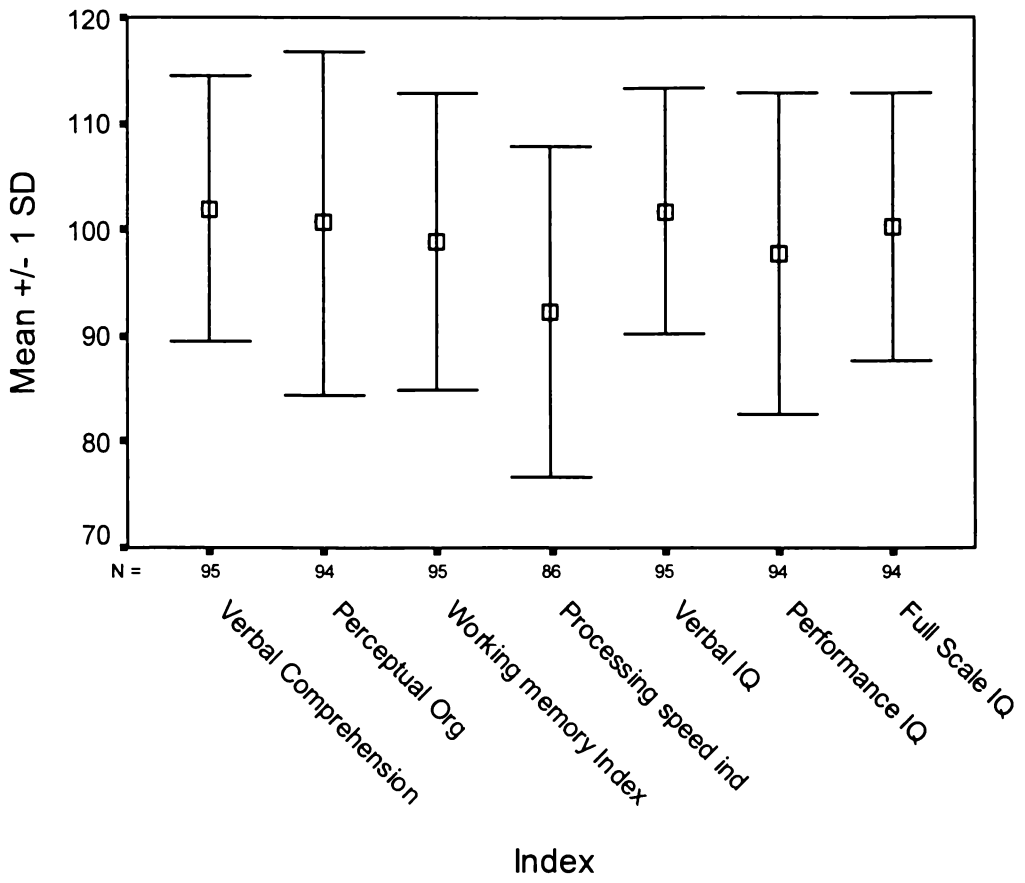


Figure 5.1. Means and Standard Deviations of the WAIS-III Indices including the IQ Measures

The detailed numerical values (means, standard deviations and number impaired) can be seen in Appendix H.

Figure 5.1, supported by the table in Appendix H suggests there was no impairment in general ability in this sample of participants. The mean Full Scale IQ of 100.22 was very close to the mean premorbid IQ prediction of the Wechsler Test of Adult Reading (WTAR), which was 106.0. Therefore, when the detrimental impact of possible physical limitations on the Performance indices of the WAIS - III was considered, the mean premorbid IQ prediction suggested, in support of the group results, that there has been very little decline in general intelligence in this sample.

However, when the Wechsler Test of Adult Reading (WTAR) predicted score was compared with the actual score of each participant, 45 (47.37%) participants exhibited WTAR predicted Verbal IQ, Performance IQ, and/or Full Scale IQ scores which were significantly higher than their actual score. Of these 45 participants, 15 (33.33%) scored significantly lower than predicted on all three indices, the majority, 22 (48.89%) scored significantly lower on the Performance IQ or both Performance IQ and Full Scale IQ, and only 8 (17.78%) scored significantly lower on their Verbal IQ or both Verbal IQ and Full Scale IQ. In contrast to the Wechsler Adult Intelligence Scales scores, these data suggest that there has in fact been some significant decline in general ability performance of the participants in this sample, though based on the sample results it would seem that this did not generally extend to clinical levels.

Cluster analysis was then conducted in an attempt to isolate smaller more homogeneous groups of participants with similar patterns of impairments. Because the Processing Speed Index was so dependent on well functioning motor skills, and for this reason there were a number of missing data on this measure, it seemed

prudent to exclude this index from the cluster analysis. Therefore, based on the Verbal Comprehension Index, the Perceptual Organisation Index and the Working Memory Index, two main clusters were found that correctly grouped 95.8% of the participants (see Figure 5.2).

Although the scores obtained for the Processing Speed Index did not form part of the cluster analysis, they were included in Figure 5.2. This figure shows that cluster one contained 37 (39%) of the participants, and had mean scores which were all lower than the mean scores of cluster two and were also, on average, all below the standardized mean of 100. It was, however, only the Processing Speed Index of this cluster which had a mean score in the 'impaired' range (<85). Figure 5.2 also illustrates that it was the comparatively higher score of the Verbal Comprehension Index which was primarily responsible for the greater differential between the lower Perceptual Organization Index and the higher Verbal Comprehension Index seen in this cluster in comparison to cluster two. The mean Working Memory Index score for this group was also comparatively lower, more in line with the performance scores (Perceptual Organisation & Processing Speed) than the higher Verbal Comprehension Index score.

Thus, it would seem that even the lower scoring subgroup within this sample did not, on average, show signs of clinical impairment. However, of the 37 participants that made up this cluster with the lower means, 30 or 81%, had index scores that were significantly lower than the score that had been predicted by the Wechsler Test of Adult Reading. Fourteen (38% of the cluster) were significantly lower on all indices, eleven (30% of the cluster) were significantly lower on the Performance IQ or both the Performance IQ and Full Scale IQ and only five (13% of the cluster) had lower Verbal IQ or VIQ and Full Scale IQ scores.

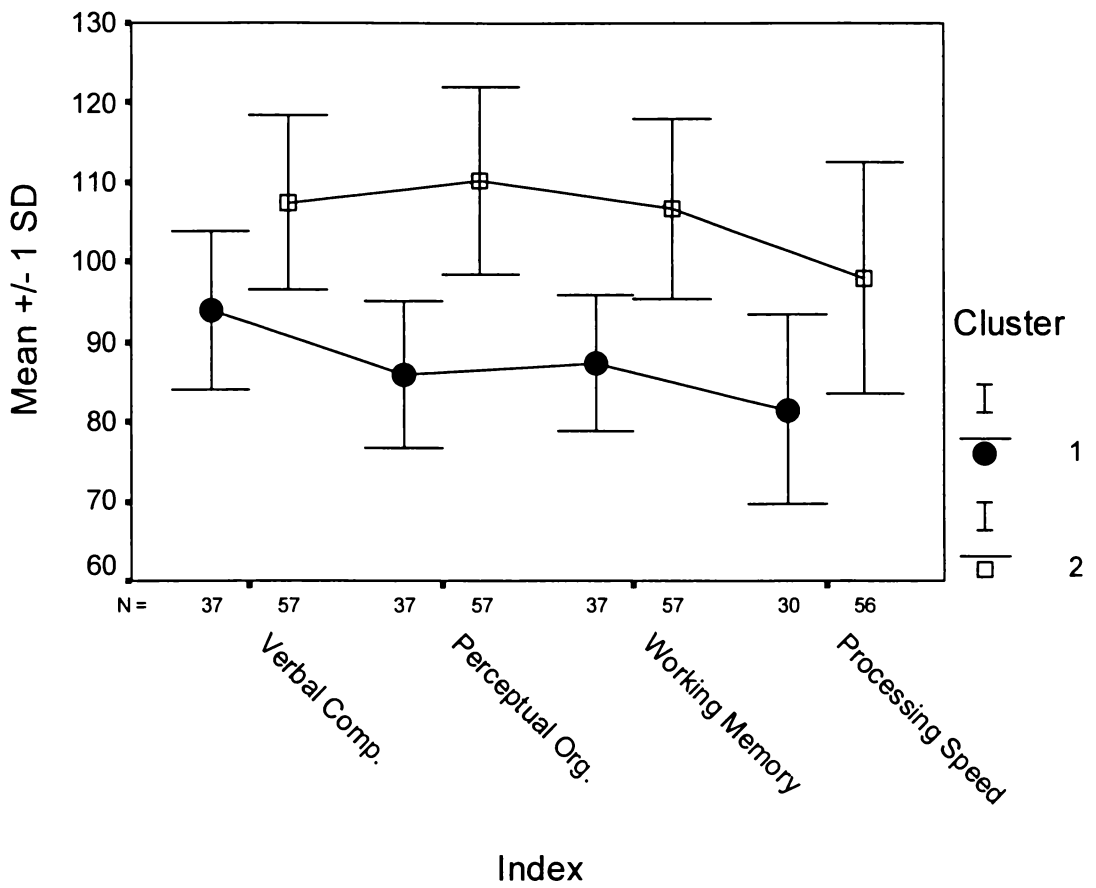


Figure 5.2. Clusters of Participants based on the Verbal Comprehension Index the Perceptual Organisation Index and the Working Memory Index of the WAIS-III

This suggests that a large proportion of this lower performing cluster had experienced some decline in their performance on general ability measures, though for some this decline was limited to performance measures and could have been the result of compromised motor skills rather than intellectual decline.

Cluster two included the remaining 57 participants (61% of the sample), and had mean index scores which were well above the standardized mean of 100. In contrast to cluster one, this cluster showed very little variability between the index scores, a pattern which usually suggests little, if any, cognitive deterioration. Also in contrast to the first cluster the Perceptual Organisation Index mean of this cluster was higher than the Verbal Comprehension Index mean, although similar to cluster one, the Processing Speed Index mean was again lower than the means of the other indices. This could suggest that for those in cluster two, where there is some performance deterioration it is primarily related to motor skills rather than intellectual functioning.

Although this cluster was characterized by scores that were well above the standardized mean, it did include 15 participants (26%), whose IQ scores were significantly lower than predicted by the Wechsler Test of Adult Reading. As suggested by the cluster pattern, the majority of these, (10, 18% of the cluster) scored significantly lower on Performance IQ or Performance IQ and Full Scale IQ, in comparison to only 3 (5% of the cluster), which had significantly lower Verbal IQ or Verbal IQ and Full Scale IQ scores. However, the most notable difference for this cluster (compared to cluster one) was that only 2 participants (4% of the cluster) were significantly lower on all measures. It is also worthy of note, that of these 15 participants only six had a Full Scale IQ score lower than 100 and these were all in the 90s, indicating that their achievement levels were still comparatively high and not

in the impaired range. In contrast, within the group of participants in the smaller cluster (cluster one) only one participant had a Full Scale IQ score that was above 100.

Although the clusters provided more detail regarding the cognitive profiles of the two subgroups that were shown to exist within this sample, clusters were again represented by mean index scores of the participants. Therefore, it seemed feasible to assume that the level of impairment indicated by the clusters could still be an oversimplification of the true extent and nature of cognitive functioning with this sample of MS participants. Thus the actual number of participants impaired (more than one standard deviation below the mean of the Wechsler Adult Intelligence Scales - III standardized data) for each index and IQ measure making up the WAIS-III are shown in Table 5.1.

It can be seen from Table 5.1 that in line with the results obtained from the cluster analysis, the actual number of participants 'impaired' on each index were generally low and in several instances did not exceed the 16% that would be expected to perform below this level in a 'normal' population. The one exception was the Processing Speed Index (PSI), which for this sample may not have been an accurate measure of what it purported to assess, as a good performance on this index required a high level of manual dexterity. As outlined earlier, it was for this reason, that the Processing Speed Index was excluded from the cluster analysis.

Overall, these results suggested that the majority of participants with MS in this sample were functioning at above average levels on the Wechsler Adult Intelligence Scales - III measure of general ability. Where some decline was indicated it was often not at a clinical level of impairment, and it was predominantly on the Performance measures which in this sample may not relate to intellectual decline.

Table 5.1

*Number and Percentage of Participants Impaired on each WAIS - III Index and IQ Measure*

WAIS - III Index	Number Impaired	Percentage Impaired	Sample Size
Verbal Comprehension	7	7%	95
Perceptual Organisation	15	16%	94
Working Memory	17	18%	95
Processing Speed	32	37%	86
IQ Measures			
Verbal IQ	6	6%	95
Performance IQ	19	20%	94
Full Scale IQ	12	13%	94

*Note.* Verbal IQ is made up of the Verbal Comprehension Index and the Working Memory Index. Performance IQ is made up of the Perceptual Organisation Index and the Processing Speed Index. Full Scale IQ is the aggregate of the Performance IQ and the Verbal IQ.

**Memory**

This analysis followed the same order as the preceding analysis of general ability. The sample means and standard deviations for the various Wechsler Memory Scales – III (WMS-III) indices are shown in Figure 5.3. Detailed numerical values (means, standard deviations and number impaired) for each index can be seen in Appendix I.

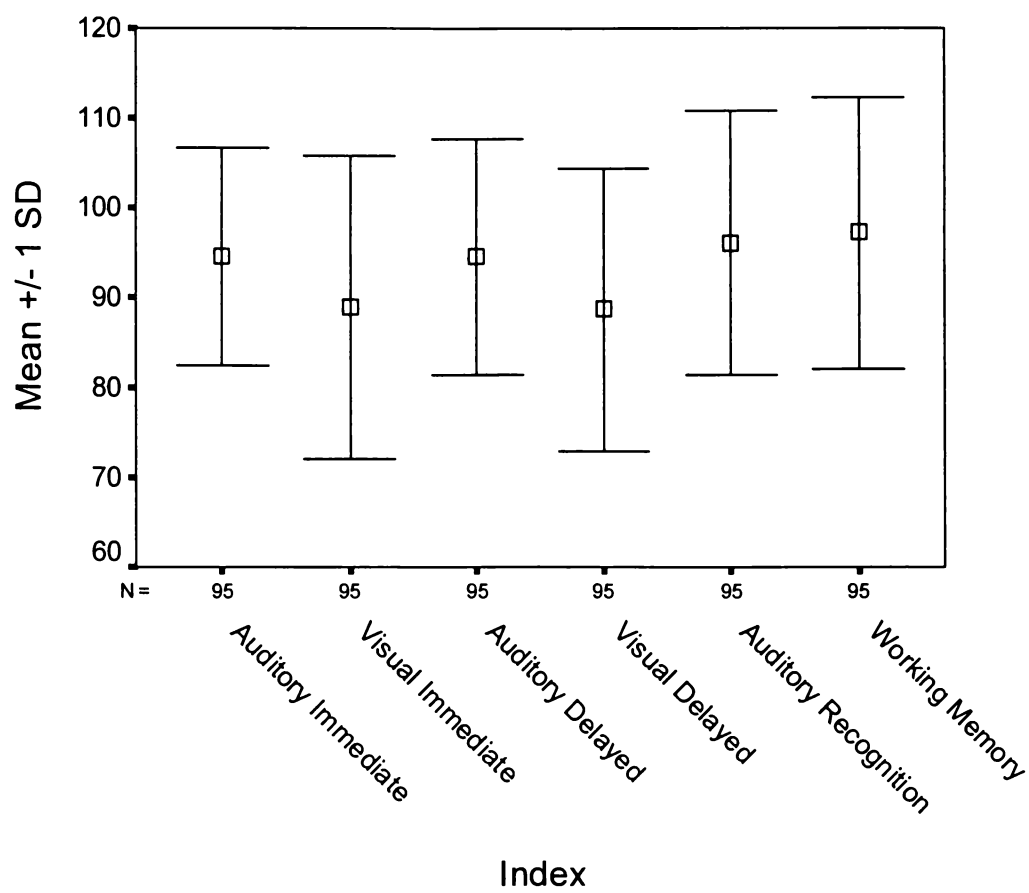


Figure 5.3. Means and Standard Deviations of the WMS-III Index Scores

Figure 5.3 shows that for this sample of participants with MS overall, no memory impairment was indicated, as none of the index means were lower than one standard deviation below the mean of the standardized data. It was however evident that the mean visual scores, both Immediate ( $M = 89.03$ ) and Delayed ( $M = 88.68$ ), were lower than the comparable auditory scores (Immediate  $M = 94.55$  and Delayed  $M = 94.62$ ), and a relatively greater variability within the visual indices (Visual Immediate  $SD = 16.89$  and Visual Delayed  $SD = 15.72$ ) is also illustrated in Figure 5.3.

Paired sample t-tests indicated statistically significant modality differences (visual versus auditory), for both Immediate Memory,  $t(94) = 4.098, p < .001$  and Delayed Memory,  $t(94) = 5.022, p < .001$ . No statistically significant temporal differences (Immediate versus Delayed Memory) were found in either modality. Therefore, again group results would indicate that the extent of impairment in this sample of MS participants on the WMS - III measures was very limited, but it seems that visual memory scores were significantly lower than auditory memory scores.

Cluster analysis was again conducted in order to isolate smaller more homogeneous groups of participants with similar patterns of memory scores. The indices used as the basis for the hierarchical cluster analysis were the composite Immediate Memory (Auditory Immediate & Visual Immediate), General Memory (Auditory Delayed, Visual Delayed & Recognition) and Working Memory Indices. Both the three and four cluster solutions produced a 95.8% correct classification of participants, however one cluster in the four cluster solution had only four members therefore the three cluster solution was considered optimal (Figure 5.4 shows the three clusters with all six indices that make up the three composite scores).

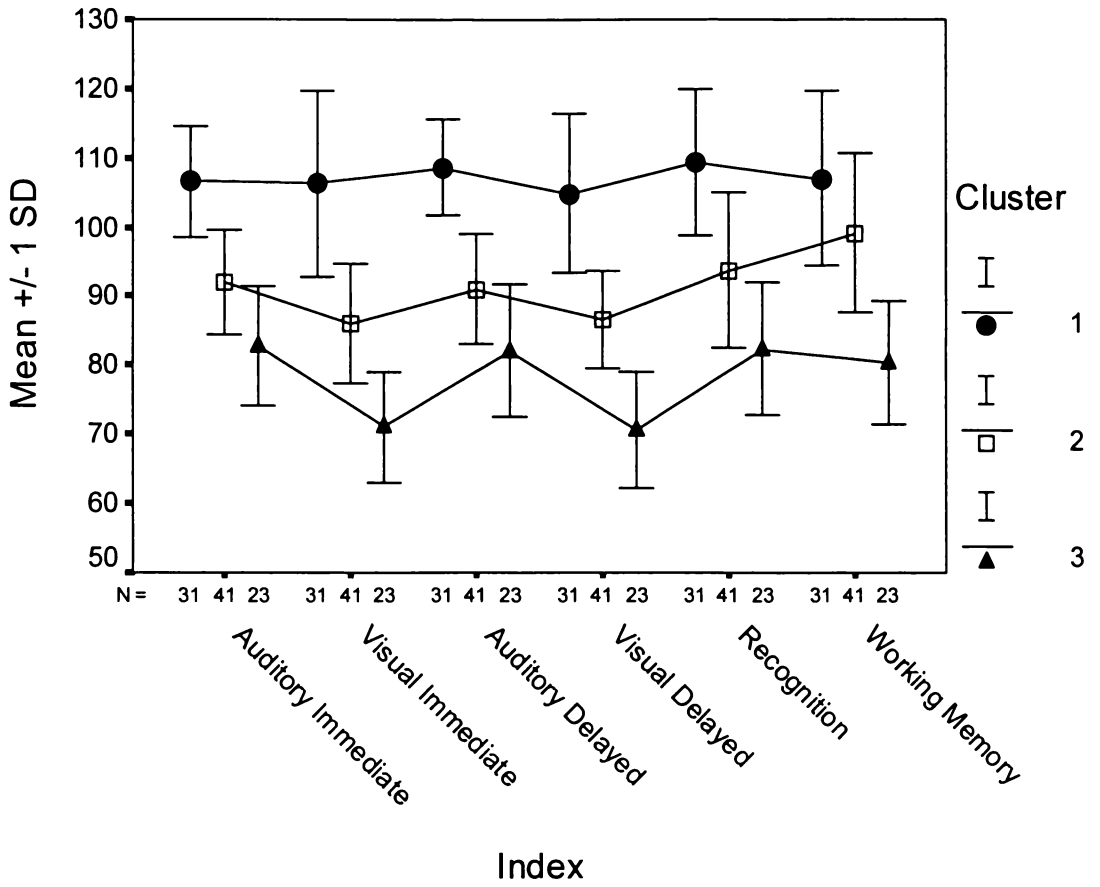


Figure 5.4. Clusters of Participants based on the Immediate Memory, General Memory and Working Memory Indices of the WMS-III

Figure 5.4 shows cluster one (n = 31), containing 32.6% of the total MS sample, with mean memory index scores all well above the standardised mean of 100. This cluster contained only seven participants (23% of the cluster) who had WAIS - III scores significantly lower than their WTAR predicted scores, with the majority of these (5) coming from the WAIS - III cluster with the highest scores. This indicated that for the majority of this cluster their performance level was above average, and the few who were performing significantly below predicted levels were still able to achieve above average scores for both the WAIS - III and the WMS - III

Cluster two (n = 41), 43% of the total MS sample, had mean index scores that were lower than those of cluster one but which were not below the one standard deviation cut off criterion, and were therefore not in the impaired range. This group, however, was also characterized by somewhat lower visual than auditory memory scores, and contained 19 participants (46% of this cluster) whose WAIS - III scores were significantly lower than their WTAR predicted scores. Unlike cluster one, these nineteen participants came almost equally from the two WAIS - III clusters, with 11 coming from the cluster with the lower average scores and 8 from the cluster with the higher scores.

Thus cluster two revealed a group of participants who not only have indicated a lower level of performance than the participants in cluster one, but of the 46% of participants in this cluster who performed at below predicted levels for the Wechsler Adult Intelligence Scales - III many also performed at the lower of the two levels revealed on that measure. This cluster has also shown more indication of the visual versus auditory differentiation that was revealed in the group analysis.

Cluster three (n = 23), 24.2% of the total MS sample, had mean memory index scores that were all lower than one standard deviation below the standardized

mean, indicating impairment on all memory measures. For this cluster, the visual indices relating to both short and long term memory were significantly lower than the comparable auditory indices, and it contained 19 participants (83% of this third cluster) with WAIS - III scores significantly lower than their WTAR predicted scores. For this cluster, however, the majority (17) of those whose WAIS scores were significantly lower than their predicted scores came from the WAIS cluster with the lower scores. In comparison to the memory measures however, these lower levels of performance were not in the impaired range for the general ability measures.

Therefore in contrast to the results obtained for the sample as a whole, which suggested that there was no memory impairment, cluster analysis revealed that, in relation to their memory performance, this sample consisted of three distinct subgroups. The first group had, on average, scores that were well above the standardized mean on all indices and showed little evidence of any difference between visual memory and auditory memory. The second group, which had lower scores on all indices, also remained above the level of impairment for all indices, but it was in this cluster that evidence emerged of visual memory scores that were lower than auditory memory scores. The third group of participants in this sample was the only group to show evidence of memory impairment. For this cluster all memory index means were in the impaired range and there was evidence of a substantial difference between the lower visual memory scores and the higher auditory memory scores. There remained however, no evidence of a differential between Immediate Memory and Delayed Memory in any of these subgroups.

To provide further detail regarding the extent and the nature of memory impairment in this sample, the scores for each index were examined for each participant, and the numbers of individuals that were assessed as 'impaired' (more

than one standard deviation below the WMS-III standardised mean) are shown in

Table 5.2.

Table 5.2

*Number and Percentage of Participants Impaired on each WMS-III Index*

WMS-III Index	Number Impaired	Percentage Impaired	Sample Size
Auditory Immediate	19	20%	95
Visual Immediate	49	52%	95
Immediate Memory	39	41%	95
Auditory Delayed	23	24%	95
Visual Delayed	43	45%	95
Recognition	19	20%	95
General Memory	38	40%	95
Working Memory	24	25%	95

Table 5.2 shows that rather than approximately 24% being impaired, (the number of participants in cluster 3), the percentages range from 20% for the Auditory Immediate and Recognition Indices to as high as 52% for the Visual Immediate Index. This indicates that the extent of memory impairment in this sample was not only considerably greater than was suggested by the results of the overall sample

analysis, but was also greater than the extent of impairment that was revealed by the smaller subgroups. This more detailed analysis did however support the group results regarding the nature of memory impairment, in that it is quite evident that approximately twice as many participants had impaired visual memory than had auditory memory impairment, but the numbers impaired on Immediate Memory and General Memory (Delayed Memory) were similar (41% and 40% respectively).

### ***Executive Functions***

The range, means and standard deviations for twenty of the Delis-Kaplan Executive Function System (D.KEFS) primary scores can be seen in Appendix J, along with an indication of the category that each score contributed to. The twenty scores which have been reported are as follows: Trails (number-letter switching); Letter Fluency; Category Fluency; Category Switching; Design Fluency (total correct); Stroop Inhibition; Stroop Switching; Card Sorting (correct sorts); Card Sorting (free description); Card Sorting (recognition); 20 Questions (abstraction); 20 Questions (total questions); 20 Questions (total); Word Context (total); Tower Test (total); Proverbs (total); Proverbs (common proverbs); Proverbs (uncommon proverbs) Proverbs (accuracy); Proverbs (abstraction). Each age adjusted score had a range from 0 to 20 with a mean of 10 and a SD of 3.

Although in isolation these scores provided only limited information, it seems that Stroop Inhibition and Switching along with Fluency Switching and Trails Number-Letter Switching had the scores with the lowest means. In contrast the Proverbs and the 20 Questions Abstraction had the scores with the highest means. This suggests that for this sample overall, the participants had more difficulty with

inhibition and shifting or flexibility than they did with tasks requiring abstraction abilities.

Based on the assessment methods outlined in Chapter 3 (data analysis section), 53.7% (n = 51) of the participants were assessed with executive dysfunction in at least one of the five categories (inhibition, shifting, reasoning, planning and fluency), leaving 46.3% (n = 44) of this sample who were not impaired in any category. Therefore the extent of executive dysfunction in this sample was considerably greater than had been previously suggested.

The frequency and nature of the individual profiles of dysfunction that were identified are shown in Figure 5.5.

This Figure shows that the most commonly occurring profiles were those where verbal fluency (n = 7) or reasoning impairment (n = 8) occurred in isolation. The frequency of these two profiles was closely followed by the frequency of inhibition impairment (n = 6) also occurring in isolation. The most commonly occurring combination of categories of impairment was the combination of fluency and reasoning, which was evident in 5 participants. There were also 7 different combinations of categories of impairment, which were seen in only one or two participants.

The analysis of executive dysfunction profiles in this sample would have been more comprehensive if it had been possible to include working memory as a category within the Delis-Kaplan Executive Function System (D.KEFS) assessment. However, as this was not possible it was considered that the information regarding the different executive dysfunction profiles would be more complete if those impaired on the Working Memory Index of the Wechsler Memory Scales - III were incorporated with

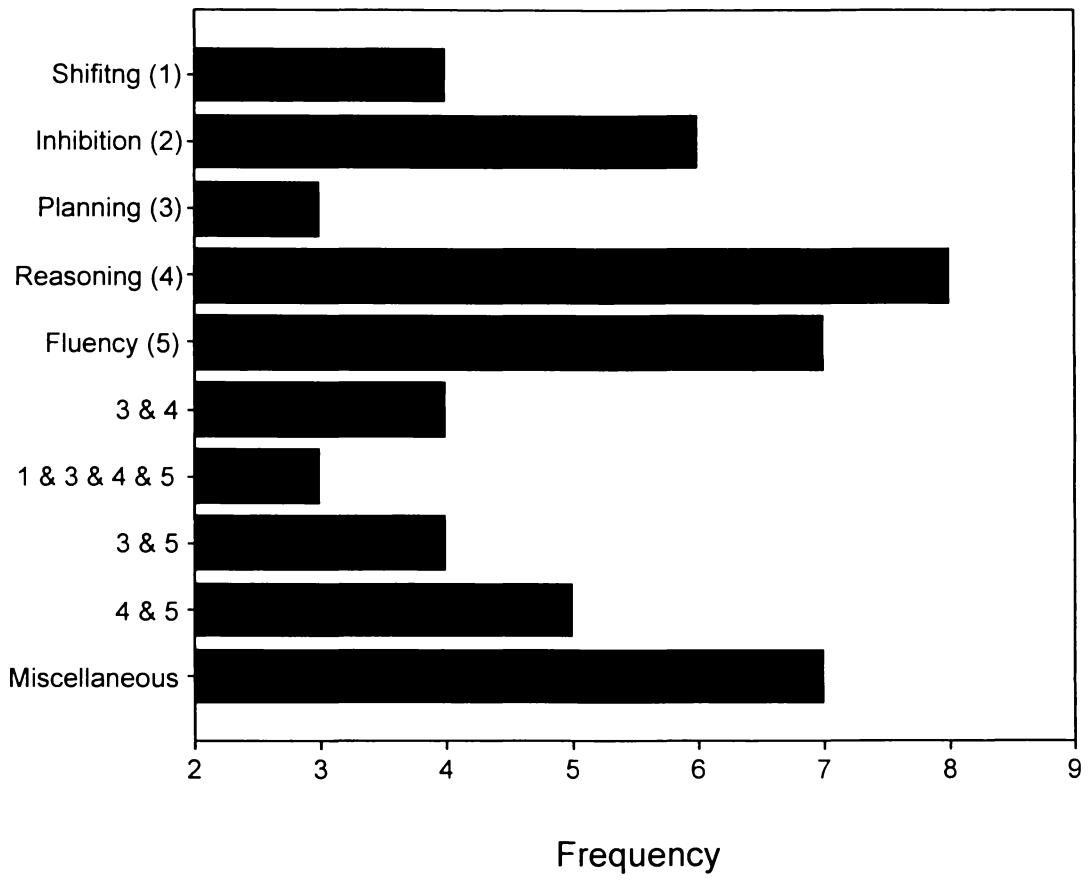


Figure 5.5. Frequency of Executive Function Profiles

the profiles resulting from the D.KEFS assessment. The resulting profiles can be seen in Figure 5.6.

This Figure indicates that although working memory impairment occurred in isolation in only 3 participants, there were in fact 21 participants whose executive dysfunction profile included working memory impairment. Although fluency, reasoning and inhibition, in isolation, still remained the most commonly occurring profiles, the inclusion of working memory as a sixth category had the effect of further increasing the number of different profiles of executive dysfunction present within this sample.

The percentage of participants in this sample with one, two, and three or more categories (degree) of executive dysfunction, is shown in Figure 5.7. It indicates that the majority,  $n = 28$  (54.9%), of those with executive dysfunction, were assessed as having only one category of impairment, and only 8 (15.7%) were assessed as having three or more categories of executive impairment.

An examination of the frequency of occurrence of the five designated categories, either in isolation or in conjunction with another category, indicated that verbal fluency and reasoning problems were the most prevalent, each occurring in a total of 25 of the participants. The next most commonly affected category was the planning category, which was found to be impaired in 16 participants, followed by inhibition and shifting which affected 10 and 9 participants respectively.

The relationships between the various categories of executive dysfunction are shown in Table 5.3. It shows first the numbers of participants with impairment in each particular category either in isolation, with one other category or with two or more other categories, and secondly, in italics, the proportion of times, as a percentage, each category occurred in isolation, with one other category or with two

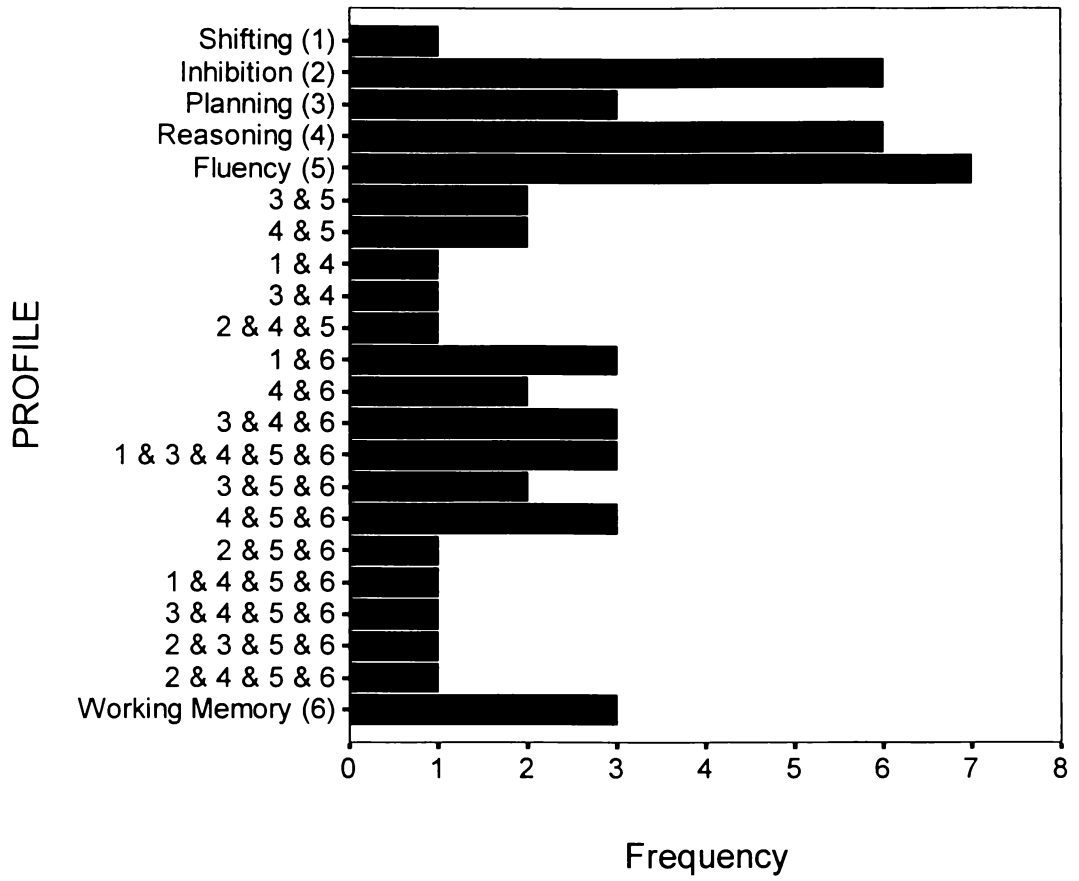
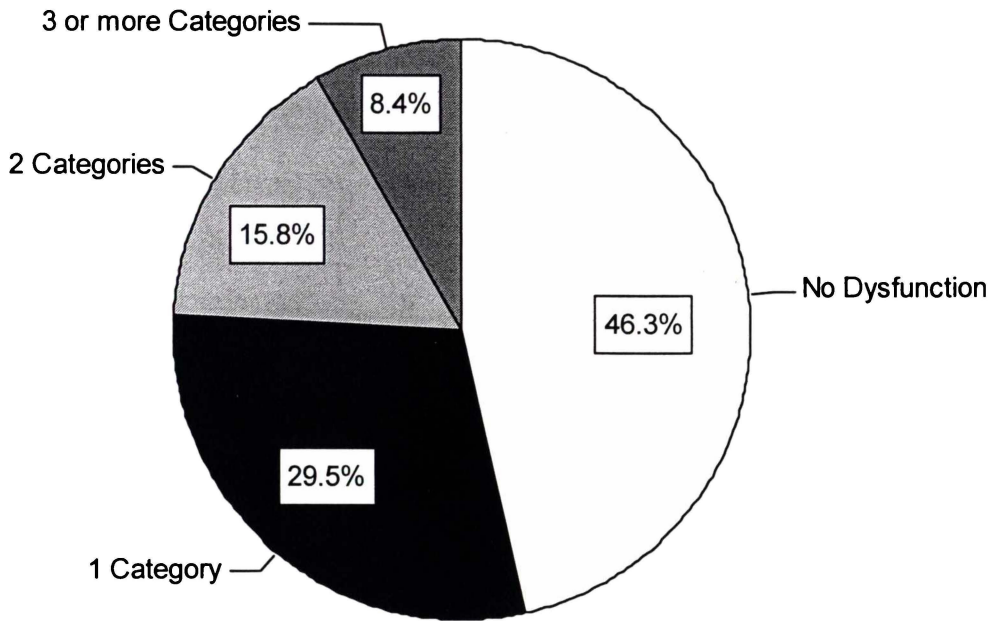


Figure 5.6. Frequency of Executive Dysfunction Profiles including Working Memory



*Figure 5.7.* The Percentage of Participants with Various Numbers of Categories of Executive Dysfunction

or more other categories.

Table 5.3

*The Frequency of Occurrence of Impairment for each Category of Executive Functioning in Relation to the other Categories*

Category	In Isolation	With one other	With two or more
Shifting	4 (44%)	1 (12%)	4 (44%)
Inhibition	6 (60%)	1 (10%)	3 (30%)
Planning	3 (19%)	8 (50%)	5 (31%)
Reasoning	8 (32%)	10 (40%)	7 (28%)
Fluency	7 (28%)	10 (40%)	8 (32%)

*Note.* N = 95

In general terms it seemed that the majority of categories of executive dysfunction were present most often in conjunction with one or more other categories. The one notable exception to this was the inhibition category, which in this sample occurred most often in isolation. Although it was not possible to include working memory as a category within the Delis-Kaplan Executive Function System (D.KEFS) assessment it can be seen from Figure 5.6 that working memory impairment as measured by the Wechsler memory Scales - III occurred in isolation in only 3 (12.5%) of cases and with two or more other categories in 16 (66.7%) of cases. This suggested that working memory was also a category of executive dysfunction that most commonly occurred in conjunction with one or more other categories of executive dysfunction.

## *Attention*

Because age may have been a factor that influenced attentional ability, the participants with MS (N = 95) and the control group (N = 75) were initially divided into age based groups which substantially reflected the age divisions of the standardized data for the primary assessments of general intelligence, memory and executive functioning. However, because of the limited number of participants at either end of the age scale in this sample, it was necessary to make the first age group (30 years or less) and fifth age group (65 years and over) combinations of several separate categories that existed within the previous assessments. The means and standard deviations for the Attentional Capacity Test (ACT) assessment for both the participants and the control group in each age group are shown in Figure 5.8.

The maximum possible score for ACT measure of attention was 24 and the overall mean for the participants with MS was 18.68 (SD = 3.21), and the overall mean for the control group was 20.44 (SD = 2.53).

A 2 x 5 ANOVA was conducted to evaluate the effect of MS (participants vs controls) and age (5 age groups: < 30 years, 30 – 44 years, 45 – 54 years, 55 – 64 years and >64 years) on the ACT scores. There was a significant main effect for MS,  $F(1, 160) = 9.73, p < .01$ , and age,  $F(4, 160) = 2.54, p < .05$ , as well as a significant interaction between MS and age,  $F(4, 160) = 2.62, p < .05$ . This indicated that there was a difference between the participants with MS and the controls on the ACT measure of attention, and there was also a difference in the ACT scores between the age groups. Figure 5.8 suggested, however, that the significant interaction effect was the result of a strong age effect (declining scores with increasing age) in the participants with MS, which was not visible in the control group.

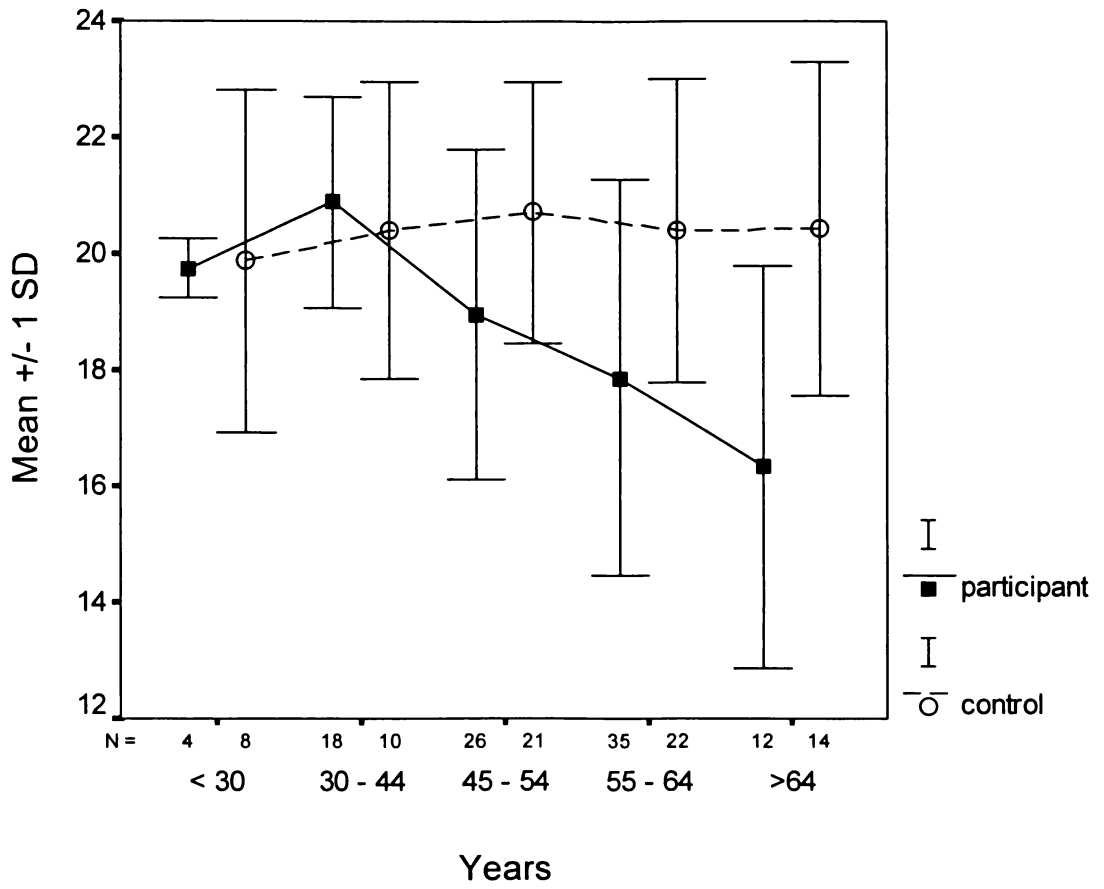


Figure 5.8. Means and Standard Deviations of the Attentional Capacity Test Scores for Participants and Controls for each Age Group

To support this indication, using one standard deviation below the mean of the control group as the cut off criterion, it was found that no participants in the younger groups 1 and 2 were impaired, however, 8 (31%) of group 3, 13 (37%) of group 4 and 7 (58%) of group 5 were impaired.

As an age effect was not evident in the control group it seemed likely that there would be factors other than age that would explain the result obtained for the participants with MS. Age was therefore correlated with other demographic and disease variables and significant correlations were found for the participants with MS between age and years since first MS symptoms,  $r(93) = .522$ ,  $p < .001$ , the Expanded Disability Status Scale scores,  $r(93) = .274$ ,  $p < .01$ , and the Chicago Multiscale Depression Inventory scales; Vegetative,  $r(92) = -.283$ ,  $p < .01$ , Evaluative,  $r(92) = -.272$ ,  $p < .01$  and Mood,  $r(92) = -.235$ ,  $p < .05$ . This suggests that although scores on the Attentional Capacity Test (ACT) were significantly lower for those with MS than they were for the control group, this was especially true for those in the older age groups. However, it seemed that it was not age per se that influenced attentional performance but more probably it was some factor(s) relating to MS such as years with MS, extent of physical disability or level of depression which influenced attentional ability.

### ***Information Processing Speed***

For this assessment participants were required to press a left mouse key if the stimulus presented on the screen was one they had been asked to remember ('yes' response) or the right mouse key if the stimulus on the screen was not one they had been asked to remember ('no' response). (see the Materials section of Chapter 3 for further detail regarding the procedure for this assessment). The most important

measure obtained from the Sternberg assessment was the slope which was derived from the progression of time taken to respond to the one, two and four stimulus conditions. This provided the measure of information processing speed for each participant. The Sternberg assessment also provided an 'intercept' value which was taken as a measure of initial response speed. This related to the speed of 'initiating' responses which were separate from the memory scanning processes which contributed to processing speed. The number correct out of 60 responses for the one, two and four stimulus conditions was also recorded.

Because many of the participants were unfamiliar with computers and were not always aware of the implications of the continuous timing mechanism operating during the testing, some data did not seem to be representative of memory scanning (information processing) speed. For example, there often occurred a time-taking response to a recognized mistake, or a lapse in concentration where the 'to be remembered' stimuli were reconfirmed. Because these types of incidents would have incorrectly inflated the time taken to respond, extreme outliers, identified as per SPSS guidelines (SPSS Inc, 2001) were replaced with the average of the remaining times for that particular group of 15 responses.

Initially, to determine whether it was possible to combine the 'yes' response time data with the 'no' response time data, paired sample t-tests were carried out on the control group data ( $N = 74$ ), between the times for the 'yes' and 'no' responses for each of the one, two and four stimulus conditions. The response times were not significantly different for the one and two stimuli conditions, but the times for the 'yes' and 'no' responses for the four stimuli condition were significantly different at the .05 level of significance,  $t(73) = -2.06$ ,  $p = .042$ . The effect size, however, was not considered sufficiently powerful ( $d = .24$ ), especially in view of the results of the

other two conditions, to maintain two separate data sets. This decision was also in keeping with other studies, none of whom had found significant differences between the two types of response (Sternberg, 1966; Archibald & Fisk, 2000; Rao, St. Aubin-Faubert et al., 1989).

The groups were initially divided into the same age groups as those used in the Attentional Capacity Test (see previous section) and a 2 x 5 multivariate analysis of variance (MANOVA) was conducted to determine the effect of age (5 age groups) and MS (participants vs controls) on processing speed (slope), initial response times (intercept) and the number correct out of 60 for the one, two and four stimulus conditions. Significant multivariate effects were found for age,  $F(20, 498) = 2.43, p < .001$ , and MS,  $F(5, 150) = 4.94, p < .001$ . There was no significant interaction effect, which meant that the difference between the two groups (participants and controls) on the information processing variables did not depend on age. Subsequent ANOVAs were conducted using the Bonferroni method of adjustment and a significant effect of age on the initial response time was found,  $F(4, 154) = 7.77, p < .001$ . Post-hoc comparisons indicated that age groups 4 and 5 both had significantly slower initial response times than age group 2. No other variables were significantly different between the age groups.

The post hoc ANOVAs also indicated that the participants with MS had a significantly slower mean initial response time than the control group,  $F(1, 154) = 21.81, p < .001$  (Mean control  $M = 0.57s$ , Mean MS  $M = 0.75s$ ), and made significantly more errors on the two stimulus condition,  $F(1, 154) = 1.28, p < .05$  (Mean control  $M = 59.35$ , Mean MS  $M = 58.96$ ). Neither the information processing speed nor the number of errors on the one and four stimuli conditions were significantly different between the two groups.

Although a non-significant age x MS interaction indicated that both the participants with MS and the controls contributed equally to the age effects that were evident in relation to the initial response time, a significant effect of MS on the initial response time was demonstrated which suggested that it was the MS participants who showed a greater deterioration of response speed with age than the control group.

Therefore for the MS participants in this sample, it seems that their information processing speed was not significantly slower than the information processing speed of the control group. Their initial response times were however significantly slower and although there was also a significant difference in the number correct for the two stimulus condition the difference was less than one full point.

## **Summary and Discussion**

### ***General Ability***

As a whole this particular sample of participants with MS did not show any indication of impairment on the general ability measures. Indications of impairment remained low when the sample was broken into two sub groups, and again when the actual number of participants who were impaired was examined. When the predicted premorbid scores were compared with the actual scores it did become apparent however, that a considerable number of participants were performing at a level significantly below that which was predicted for them.

Similar to the results of previous studies (e.g., Zakanis, 2000) the levels of performance on the Wechsler Adult Intelligence Scales - III for this sample of MS participants overall were close to the standardized mean. As predicted, the one exception was the Processing Speed Index whose mean score was somewhat lower

than the others. This index score is however influenced by the integrity of the participant's motor skills, and therefore in this clinical sample is not a completely reliable indication of the processing speed it purports to measure. Even with this confounding issue the Performance IQ score of this sample was only approximately four points lower than the Verbal IQ, rather less than the seven to ten point difference that was suggested in previous studies (Rao, 1986). In keeping with the results of previous research however (e.g., Klonoff et al., 1991 & Ryan et al., 1993), it was evident that some number in this sample did have greater difficulty with the Performance assessments than they did with the Verbal assessments, as the individual indices making up the Performance IQ (Perceptual Organisation and Processing Speed), and as a consequence, the aggregate Performance IQ, did show a greater variability of contributing scores than the other indices.

Although it is impossible to make comparisons with other research regarding the nature of the two clusters that were formed when the sample was broken down into more homogeneous subgroups, it was not inconsistent with previous results to find that although one group performed at levels consistently lower than the other, it was only the Processing Speed Index of this lower scoring group that was in the 'impaired range'. Also in keeping with the suggestion that the level of impairment in this sample of participants with MS was minimal, when the actual number impaired on each general ability index was examined it was revealed that for all but the Processing Speed Index, Working Memory Index and the Performance IQ that the numbers impaired did not exceed the 16% of a normal population that would be expected to perform at those levels.

This more detailed analysis did reveal however, that the difference between the number impaired on the Performance IQ and the number impaired on the Verbal

IQ was considerably greater than was previously indicated. It was also evident that it was the Processing Speed Index, with its motor skill requirements, which contributed substantially to this difference, making it difficult to draw conclusions regarding the relative levels of impairment in these two areas of general ability. However, whilst 'numbers impaired' is different to average scores, when the influence of the Processing Speed Index was removed a differential more in line with predictions was seen between the Perceptual Organisation Index and the Verbal Comprehension Index. As this lesser differential is probably a more realistic indication of the relative prevalence of impairment in the perceptual versus verbal domains in this sample, this suggested that the results for this study were consistent with previous findings in relation to the nature of general intellectual abilities in those with MS.

It could be argued that by using normative data of the Wechsler Adult Intelligence Scales - III (WAIS-III) rather than a demographically equivalent control group little can be said about the effect of Multiple Sclerosis on the general intelligence of this group. This argument would be based on the fact that the standardization sample does not exactly match the clinical sample on such factors as age, gender and years of education, all of which may influence performance on WAIS-III measures, thereby limiting the value of the normative data as a benchmark for this and other specific clinical samples. However, while this may or may not be the case, the inclusion of the Wechsler Test of Adult Reading (WTAR) assessment in this study enabled some conclusions to be drawn. Although the mean score from the WTAR for the whole sample indicated little deterioration in Full Scale IQ scores, closer examination of each participant's actual scores compared to their WTAR predicted scores, showed that while most participants were still performing within

normal limits, almost half of the participants in this sample had experienced some decline in their intellectual functioning.

Although the majority of these were in the cluster with the lower scores, a small number were also in the larger second cluster which had higher mean index scores. Of those who were performing significantly below their predicted level in this larger cluster however, the majority were performing below predicted levels on performance measures. This suggested that compromised motor skills rather than intellectual decline may be responsible for the discrepancy between actual and predicted scores for these participants.

Thus although the results for both the group as a whole, and the sub groups identified by cluster analysis, showed a general lack of impairment on the Wechsler Adult Intelligence Scales - III measures, the differing result patterns of each of the two clusters highlighted the variability that was present in this sample of participants with MS. Comparisons with predicted premorbid scores suggested that in many cases performance levels have deteriorated, and where overall achievement levels were still high, this deterioration seemed to be most often a selective decline in the predicted area of perceptual and performance skills rather than verbal abilities. Where overall achievement levels were lower, however, the decrease in performance was more likely to be across the board, with a bias again toward performance deterioration in the minority of cases where the effect was selective.

### ***Memory***

Similar to the general ability results, the overall mean scores for each of the memory indices indicated that there was no memory impairment in this sample. There was however, a significant difference between the visual memory scores and

the auditory memory scores in relation to both Immediate Memory and Delayed Memory, but no overall difference between Immediate and Delayed memory was found. Cluster analysis on the WMS - III scores did however reveal a rather different story, in that the mean scores of one of the three clusters (24% of the sample) were in the impaired range for all the memory indices. Again, when the number of individuals actually impaired on each index were also examined, yet another picture emerged. It then became evident that there was an even greater level of individual impairment (up to 52%) in this sample than previous group means had indicated.

Although group results on any measure can hide many individual stories, this is especially true of memory assessments in samples of people with Multiple Sclerosis. For this sample, the group results of the Wechsler Memory Scales - III did not indicate a deficit in any of the indices, but the predicted visual versus auditory domain differential was evident to some degree.

Cluster analysis of the data from the entire sample based on the composite indices (Immediate Memory, General Memory and Working Memory), followed the pattern of previous research (e.g., Beatty et al., 1996; Fischer, 1988), in that three distinct clusters emerged. Two of these, the first with generally high scores and minimal modality (visual versus verbal) differential, and the third with generally low scores and an exaggerated modality differential were also in keeping with the results of the Beatty and Fischer studies. The second cluster, however, in previous research, had been characterized by delayed but not immediate memory impairment, whereas in this research the second cluster showed evidence of a modality, but not temporal differentiation. An interesting point of similarity to note is that this second cluster makes up approximately 50% of the participants in all studies. The study by Beatty et al. 1996 used the Selective Reminding test to assess memory impairment, making

comparisons with this study a little more difficult. However a closer comparison can be made with the Fischer (1988) study where a previous version of the Wechsler Memory Scales was used. In that study the sample size was 45 and for that group as a whole, the mean for the Visual Index was lower than that of the Verbal Index, but the mean for the Delayed Memory Index was also lower than the mean for the Immediate Memory Index. When one standard deviation below the mean of the Wechsler Memory Scales - R normative sample was used as the cut off criteria, these same differentials in percent 'impaired' remained. However, when both one and two standard deviations below the mean of a demographically matched control group (N = 25) were used as the cut off criteria, the percent impaired for the Visual Index and the Verbal Index became similar, but the immediate and delayed differential remained. Therefore, for each of the three comparative criteria a selective impairment in long-term versus short-term memory was evident. This difference also remained evident in two of the three resulting clusters and only disappeared in the cluster whose mean scores were all in the impaired range.

This difference between immediate and delayed memory was not evident in the data from this current study at this level of analysis, however one similarity was the non-difference seen in the cluster with the lowest scores. One possible explanation for this discrepancy could be the greater sample size in this research, which, even when broken down into smaller clusters would tend to conceal any variability in the results. In all likelihood, however, this difference between the Fischer study and the current study relating to conclusions regarding the relative impairment of immediate and delayed memory, is purely a consequence of the difference between the two separate samples taken from this very heterogeneous group of people.

The other contradictory result was that of a modality difference, which was evident in the current study both within the sample as a whole and to varying degrees in all three clusters, but apparently was not evident in the Fischer study. In this instance, however, it seems that the comparative criterion does hold the key to the different conclusions. The normative sample for the Wechsler Memory Scales - III is much more extensive than the 25 participants used as the benchmark in Fischer's study and would therefore provide a more generally representative comparison. Apart from which, when the means of the two indices (visual and verbal), were examined for each of the three clusters in the Fischer study, it was evident that the Verbal Index was either two, seven or 17 points higher than the Visual Index depending on the cluster. These differences closely approximated the differences between the means of the visual and verbal indices in the current study, although they did not always apply to the same cluster.

Thus it would seem, in relation to the issue of modality difference, the overall results of the two studies are similar, though the Fischer study concluded that there was no evidence of a significant modality difference. Although a significant modality difference was found within the cluster with the lowest scores in the Fischer study, her overall conclusions in relation to any modality differential were based on a non-significant group x modality interaction which arose due to the similarly lower visual memory scores of her control group.

Looking at the similarities and differences between the two studies at this level of analysis, it seems that 50% of the participants with Multiple Sclerosis can be divided into two groups, one characterized by high achievement on all measures and another similarly sized group which has significantly lower achievement scores on all measures. The other 50% apparently produce more variable results. However, when

the index means of this cluster in the Fischer study are compared with the WMS normative sample, none are below the one standard deviation cut off point, making those results similar to this study, at least in terms of impairment. Unlike the results of this study, however, there was evidence in Fischer's study, of lower scores for long term compared with short term memory measures and apparently, evidence against a domain differential.

When the actual number impaired on each index of the Wechsler Memory Scales - III was examined, it was not unexpected to see that the number impaired was considerably greater than had been suggested by the cluster patterns. It was also apparent that almost twice as many were impaired on the visual indices than were impaired on the auditory indices, but the number impaired on short term (Immediate) and long term (General) measures were about equal. This discrepancy between actual numbers impaired and the levels of impairment indicated by broader analyses, supports the need to use a more refined level of analysis than group results, if a realistic picture of the extent and the nature of impairment is to be obtained. This is especially true with a clinical group such as those with Multiple Sclerosis whose impairment patterns are known to be extremely heterogeneous.

### ***Executive Functions***

Approximately 50% of this sample was assessed with executive dysfunction in at least one of the designated categories, but the majority of those impaired displayed only the relatively mild symptoms of one category of impairment. It was also evident, however, that 'impairment' in virtually all possible combinations of the five designated categories of executive functioning was demonstrated, with fluency and reasoning being the most commonly impaired categories. With the exception of

the inhibition category, the other executive categories were also most commonly impaired in conjunction with at least one other category.

The advantage of using the broad Delis-Kaplan Executive Function System (D-KEFS) battery of executive function tests has been highlighted in the data obtained in the current study. Contrary to the 15% to 20% estimated to be affected with executive dysfunction (Fischer, 2001; Fischer et al., 1994; Rao, Leo, Bernardin et al., 1991), the results of this study suggest that the figure was closer to 50%. However, the two categories most commonly used as an indicator of executive integrity in the Multiple Sclerosis population, namely verbal fluency and reasoning or problem solving, were the most common problems found in this study, and one or both of these categories of impairment were found in 75% of those participants with executive dysfunction.

It should also not be surprising, when the vast number of interconnecting neural networks which include the frontal lobes are considered, that the percentage of those experiencing some executive decrement closely resembles the upper level of those affected on the individual memory indices. This number (approximately 50%) is also reflective of the numbers the Wechsler Test of Adult Reading (WTAR) indicated as performing significantly below predicted levels in general cognitive functioning, though this decrement was most often not at a clinical level. A closer look at the individuals involved does, however show that there is not a complete overlap of these groups. Seventeen (25%) of those with some impairment did not exhibit any executive dysfunction and 13 (29%) of those who scored significantly lower than the WTAR predicted were also not assessed with executive dysfunction. This does however leave the vast majority (70 – 75%) who's actual or predicted problems include executive dysfunction. These numbers lend support to the

perception of the 'fragile' characteristic of the frontal lobes, which led Goldberg (2001) to observe that the "frontal lobes have an exceptionally low 'functional breakdown threshold'," and that they "are more vulnerable and are affected in a broader range of brain disorders .... than any other part of the brain" (p. 115).

Although not all deterioration of function in the current study included measurable impairment of executive functioning, it seems that the higher than predicted number of those with some executive dysfunction should not come as a surprise if the frontal lobes are as sensitive to any breakdown in brain functioning as Goldberg suggests.

The multiplicity of executive dysfunction profiles observed in this sample, especially when working memory impairment was included, reinforced previous accounts of the variability of results found on individual tests of executive dysfunction exhibited by those with frontal lobe pathology (e.g., Tranel et al., 1994). They also illustrated the need for the use of a broad range of assessments wherever possible, as it is evident that the executive dysfunction profile of any individual would be impossible to predict.

In so far as the number of categories impaired reflected the degree of executive dysfunction assessed for each participant, this was easier to establish than the nature of the executive dysfunction. It was also interesting that the 45% of those 'impaired' that had two, or three or more categories of impairment, equated to 24% of the whole sample. It could be proposed, therefore, based on the numbers previously reported as being impaired in executive functioning (15% - 20%), that only the 8.4% of this entire sample who were impaired in three or more categories, plus a number of those with two impaired categories, that is, essentially the few 'worst' cases would be the only ones typically identified as having executive problems.

While the individual 'executive' profiles were shown to be extremely diverse, the relationships between the various individual categories of impairment did, however, seem to have some neurological explanation. Although the picture was far from definitive, it was interesting to note that planning, and to a lesser extent fluency and reasoning were isolated problems in only a small percentage of the cases in which that category was assessed as impaired. The shifting category was more evenly distributed occurring equally frequently with two or more other categories and in isolation (each in 44% of cases). Inhibition on the other hand showed the reverse trend, occurring in isolation in 60% of cases where it was identified as a problem. This pattern loosely supports the growing volume of neuroimaging and lesion study data which is working toward isolating the cortical regions involved in various executive tasks (Bench et al., 1993; Dagher, Owen, Boecker, & Brooks, 1999; D'Esposito et al., 2000; Elfgren & Risberg, 1998; Owen, 2000; Stuss, Alexander, Floden et al., 2002; Stuss, Bisschop, Alexander, Katz, & Izukawa, 2001; Troyer, Moscovitch, Winocur, Alexander, & Stuss, 1998).

In keeping with the pattern of relationships this study has shown between the various categories of executive functioning, fluency, planning (as measured by the Tower of London) and reasoning (measured by the California Card Sorting Test) all seem to involve both the superior medial areas and, in common with working memory the dorsolateral areas. In contrast, the Stroop test (a measure of inhibition) seems to activate the right anterior and medial frontal cortex (Bench et al., 1993), with the incongruent condition preferentially activating the right superior posteromedial region. Stuss, Alexander, Floden et al. (2002), noted however, that many with frontal lobe lesions do in fact perform normally on this task, indicating both some differentiation of process and that other areas of the brain may also play an

important role. The Trails test as a measure of shifting, has been found to discriminate those with dorsolateral prefrontal lesions but only on error (not time) measures. However, the degree of differentiation on the number of errors between dorsolateral, inferior medial, or anterior cingulate pathology was not significant, indicating more widespread involvement of several prefrontal regions and explaining the more evenly distributed relationship of the 'shifting' category in relation to the other categories.

It does seem that many executive functions do, in broad terms, commonly recruit the dorsolateral prefrontal cortex, however, there are sufficient differences in either the specific areas recruited, or the processes involved, or both, for some functions (e.g., inhibition and shifting) to produce a different pattern of relationships with other categories. It is also noteworthy that in working memory tasks it has been shown, that both the ventro and dorsolateral prefrontal cortex (DLPFC) are recruited at various stages of the process (i.e., encoding, maintenance and manipulation) with increased dorsolateral activation observed when manipulation of information is required. When an element of inhibition is required to overcome proactive interference, a slightly more superior postero ventral area is activated, similar to that recruited in the incongruent condition of the Stroop task. As suggested above, these cortical regions are also implicated in other executive functioning, therefore it would be reasonable to expect some relationship between working memory and the other executive categories. This was in fact shown to be the case when working memory impairment was incorporated into the Delis-Kaplan Executive Function System categories, as it was evident that working memory was most often impaired in conjunction with other categories.

It is, however, impossible to surmise that these categories of executive dysfunction originate in these particular frontal areas. It could be that the differing individual profiles reflect differing points of pathological origin. However, regardless of the importance of the origin of a particular profile of impairment, the relationship between the categories shown in the results did tend to support the idea that although there is some differentiation between frontal areas recruited for the various tasks, it seems that certain broad areas are likely to be commonly involved in the execution of many different tasks. This makes the numbers of different profiles of executive dysfunction interesting. To the extent that any specific area of the frontal cortex is a primary contributor to successful performance on a variety of tasks, the possibility arises that exploring differentiation of function within the frontal lobes should go beyond the identification of the cortical region involved. The literature suggested that differing networks or processes do operate within a common area, but there is also the possibility of multiple properties for individual neurons. These neurons may then be selectively and differentially impaired. To some degree this has been shown to be the case (Duncan & Miller, 2002).

### ***Attention***

The participants with MS in this sample were shown to have significantly lower scores on the Attentional Capacity Test (ACT) of attention than the control group. Although a decrease in the mean score along with an indication of an increasing range of scores occurred with increasing age for the participants with MS, this 'age' effect was, however, subsequently shown to be more likely a consequence of disease duration and severity of physical disability, along with depressive issues, rather than age per se.

The results from the ACT attention measure were somewhat surprising. The particular test of attention that was used in this study was chosen to measure the less complex aspects of attention such as the sustained or focused attention and selective attention, which is required simply to recognise the nominated stimuli. For this exercise the 'inhibitory' aspects of, for example, the Stroop test, which is sometimes seen as a measure of attention, were not required. Neither were other more 'executive' aspects of attention such as switching or dividing attention, nor were any calculations required.

It is difficult to make comparisons with other research on this measure, as commentaries on the nature of cognitive dysfunction in those with MS often discuss attention in conjunction with executive functioning (White et al., 1992), or with information processing speed (Arnett, 2000; Rao, Leo, Bernardin et al., 1991). Another comparative problem arises when considering the assessments used, which have included Digit Span (forwards and backwards), and Paced Auditory Serial Addition Task (PASAT), verbal or visual, all of which make more extensive demands on working memory abilities, and have shown mixed results with this clinical group. One exception to the use of more demanding attention tasks was a study by Comi et al. (1995) who used a simpler cancellation task to measure this domain, and in this case found 10% of their sample to be impaired.

A common conclusion in relation to attention in those with MS is, however, that it is the more complex speeded tasks that are more likely to be impaired, but the ability to 'pay attention' or immediate rote attention is largely unaffected (Arnett, 2000; Paul, Beatty, Schneider, Blanco, & Hames, 1998; White et al., 1992). As the latter aspect of attention was what was assessed in this research, minimal, if any impairment could have been expected. There was, however, a significant difference

found in the ACT scores between the control group and the participants with MS, but unlike the controls the impairment seemed to increase with age. There was no significant difference in the scores of participants compared to the scores of the controls for those 44 years or younger, but approximately 30% of those aged between 45 and 64 years were classified as impaired in comparison to their control group and this rose to almost 60% of those aged over 65 years. These percentages are both higher than the 16% of a 'normal' population that would be expected to score within this range. As age effects were not evident in the control group it was, initially, a little difficult to explain this trend. However subsequent analysis suggested that disease variables such as disease duration, and to a lesser extent severity of physical disability, along with levels of depression in all scales were the more likely contributors to this result, indicating that even the relatively simple ability to 'pay attention' can be influenced by MS.

The 28 participants (30%) from this sample that were 'impaired' in comparison to the control group, was also a substantially higher proportion than those assessed as impaired in the study by Comi et al., (1995). However, Comi et al. used two standard deviations below the mean of a control group as an indication of impairment. When that criteria was applied to the data in this sample a more comparable 6% were impaired. Considering, however, that there were substantially more than 16% of this sample that fell below the less conservative criteria, and the fact that this sample tended on average to perform at levels above those of a normal distribution on other cognitive measures, it seems that 6% would considerably underestimate the numbers of this sample whose levels of attention, as measured by ACT, were compromised.

## *Information Processing Speed*

Somewhat surprisingly, there was no significant difference in information processing speed between the participants with MS and the control group. A significantly slower initial response time was however indicated for the participants, and although there was also a significant difference found between the participants with MS and the control group in the number correct for the two stimuli condition, the difference in the mean number correct between the participants and the controls was less than one full point for all stimulus conditions.

Some authors list reduced processing speed as one factor in the cognitive profile of those with MS, e.g. (Arnett, 2000; Beatty, 1996; Fischer et al., 1994; Rao, 1995, 1996). Others go so far as to suggest that reduced processing speed is a key factor which possibly underlies other cognitive impairment (Brassington & Marsh, 1998; Demaree, DeLuca, Gaudino, & Diamond, 1999; Mohr & Cox, 2001). Again, however different assessment tools and definitions tend to make direct comparisons of results difficult, but in the case of information processing speed there are some studies that have used versions of the Sternberg paradigm to assess this construct. Two of these, (Archibald & Fisk, 2000; Rao, St. Aubin-Faubert et al., 1989), obtained results in keeping with the literature, but were contrary to the results of this study. One possible explanation of the different outcomes may be in the 'trade off' that can occur between accuracy and speed. Regardless of the assessment used, it has generally been reported that accuracy, in those with MS, is not impaired (Beatty, 1998; De Sonneville et al., 2002; Demaree et al., 1999). In the study by Archibald and Fisk (2000), which found information processing speed to be impaired, only correct responses were used in the calculations of response speed across memory set size, and there was no indication of the level of error. Rao, St. Aubin-Faubert et al.

1989, reported an error rate of 0.9% for the controls and 1.9% for the participants with MS, with no indication of whether this difference was significant. In contrast the average error rates in this study were 1.51% for the control group and 2.33% for the participants with MS, both higher than those reported by Rao et al. and significantly different from each other. It could be then, that for the current study, contrary to the instructions given at the commencement of the assessment, there was in fact some compromising of accuracy, especially by the participants with MS, which would have resulted in a faster scanning rate than that which would have been seen if accuracy had been higher.

Another possible reason for the different processing speed outcomes is the proportion of 'yes' and 'no' responses in the assessments. Previous studies have tended to construct the stimuli so that the number of 'yes' responses is equal to the number of 'no' responses. In this assessment the stimuli were formulated as per Sternberg (1967), where only 4 of the 15 stimuli in any one trial were positive. This could have resulted in some degree of 'automatic' responding, thereby explaining the higher error rate and faster than predicted scanning speed. However if this had been the case, a significant 'yes' / 'no' response time differential would have been expected in those cases where there was no error, due to the additional time required to change from an automatic to a controlled response. This difference was not evident in the control data, and although there was some evidence of a 'yes'/'no' differential for the participants it was the fewer 'yes' responses which recorded the faster times.

It should also be noted, in support of the results in the current study, that a study by Litvan (1988), cited in Brassington and Marsh (1998), using both the Sternberg paradigm and the Paced Auditory Serial Addition Task (PASAT), found a deficit in the two fastest levels of the PASAT and in the motor response time

(intercept) for the Sternberg test, but not in the memory scanning rate. A similar result was also obtained in the study by Janculjak et al. (1999), where again a significantly slower initial response time was found, but no significant decrement in scanning rate. In the latter study the positive set sizes ranged from one number to six numbers and a trend toward more errors was evident in stimuli set sizes greater than four. These conditions would have required additional working memory resources but would have had little influence on the overall scanning rate.

As indicated by the above mentioned studies, a slower initial response time for those with MS is a common finding which was supported by the results of this study. The initial response time is a factor that would include motor speed, stimulus recognition time and other initiating responses that remain constant regardless of the number of stimuli to be processed. It therefore involves processes that are separate from the memory scanning processes that contribute to the information processing speed measurement. There were also indications in this study, however, that this initial response speed became slower with age in this MS sample, and therefore, similar to the findings in relation to attention, it is probable that it is disease variables rather than age per se which was responsible for this trend.

Thus, in relation to the first research question, the overall results indicated, that within this MS sample, the extent of impairment in general ability was shown to be minimal at all levels of analysis, but performance measures were more likely to be compromised than verbal measures. Where predicted scores for general ability measures were significantly higher than actual scores, this deterioration did not often reach clinical levels.

While group measures again indicated little impairment on memory measures, the more detailed cluster analysis and the examination of performances on each individual memory index revealed that the extent of impairment was as high as 50% on some measures. Although some impairment was evident on all aspects of memory, visual memory was compromised to a significantly greater extent than auditory memory, but there was no difference seen between immediate and delayed memory.

The extent of executive dysfunction was also shown to be considerably greater than predicted, and almost all possible combinations of impairment of the five executive functioning categories were represented in the individual profiles, although fluency and reasoning were the most commonly impaired categories. The ability to 'pay attention' was compromised in some, and although initial reaction times were shown to be slower, and some error rates higher in comparison to the control group, information processing speed was not significantly reduced in this sample.

## Chapter 6

### RESEARCH QUESTION TWO

#### ***Are there any links between executive dysfunction and other cognitive impairments?***

A further aim of this study was to determine which (if any) other cognitive impairments were indicative of executive dysfunction in this sample. In particular, a closer examination of the relationship between the various types of memory impairment and executive dysfunction was made, as to date little exploration of these relationships has been found in the literature on MS (see Chapter 1). Furthermore, any links between attention as well as information processing speed and executive functioning were also examined as information regarding the relationship between these processes and executive functioning has also been limited.

To examine these links, simply dividing the sample into participants with executive dysfunction and those without executive dysfunction would not have provided the answer to the research question. This was because a large proportion of those with executive dysfunction in this sample also had memory impairment and it would therefore have been impossible to link other cognitive processes exclusively to executive dysfunction. However, as there were a number of participants who had only executive dysfunction, the links between executive dysfunction and other cognitive processes were explored by breaking the sample into smaller groups of participants with similar cognitive profiles. If it had been feasible to examine the patterns of cognitive impairment in groups of participants with the same executive

dysfunction profile this would have been done. That is, if all of the participants with executive dysfunction had fallen into a small number of groups each with different categories of impairment, whether it was one category, for example fluency, or a combination of categories, for example fluency and reasoning, then the underlying cognitive profiles of these different groups could have been compared in order to examine what other cognitive impairment characterized each group. However, as the previous results showed there were more than 16 different profiles of executive dysfunction (and more when working memory was included), with many combinations of the categories (shifting, inhibition, planning, reasoning & fluency) applying to only one or two participants, broader 'type of impairment' groups were formed.

After much consideration, it was decided to divide the sample into four groups, which were formed on the basis of whether the participants had no impairment, some memory impairment and/or some executive dysfunction. For this analysis the WMS - III memory assessment (Auditory Immediate, Visual Immediate, Auditory Delayed, Visual Delayed, Working Memory & Recognition Indices) and the D.KEFS executive function assessment, reported in the previous chapter determined group membership. The groups were:

*Group 1 - No (No impairment)*

Members in this group had no memory impairment or executive dysfunction.

*Group 2 - Memory (Memory impairment only)*

Members in this group had some memory impairment (at least one index score of the memory assessment that was more than one standard

deviation below the standardized mean, that is, less than 85), but no executive dysfunction.

*Group 3 - Both* (Both memory impairment and executive dysfunction)

Members in this group had some memory impairment, and were also assessed with at least one category of executive dysfunction.

*Group 4 - Executive* (Executive dysfunction only)

Members in this group had no memory impairment but had at least one category of executive dysfunction.

Groups 3 and 4 facilitated the identification of any cognitive processes that may uniquely characterize those groups with executive dysfunction. It was considered that any cognitive assessment scores that were similar for these two groups could indicate a link between the processes represented by these scores and executive functioning. Or on the other hand, for example, if the two groups with memory impairment *Group 3 - Both* and *Group 2 - Memory* had similar cognitive assessment scores, then performance levels on those cognitive processes were likely to be related to memory impairment. These comparisons became more informative when the relative scores of all three groups with impairment were considered. If, for example *Group 2 - Memory* had similar cognitive assessment scores to *Group 4 - Executive* and at the same time the scores for *Group 1 - No* were higher and the scores of *Group 3 - Both* were lower, this would have suggested that the extent of cognitive impairment generally rather than its nature had influenced the performance level on these particular cognitive constructs. Likewise, a link to executive

functioning would only have been suggested if the cognitive assessment scores for *Group 3 - Both* and *Group 4 - Executive* were similar but different from *Group 1 - No* and *Group 2 - Memory* which in themselves may or may not have been similar. It was of course expected that *Group 1 - No* would have had the highest mean scores on all cognitive measures as they were the only participants who were not impaired on any measure.

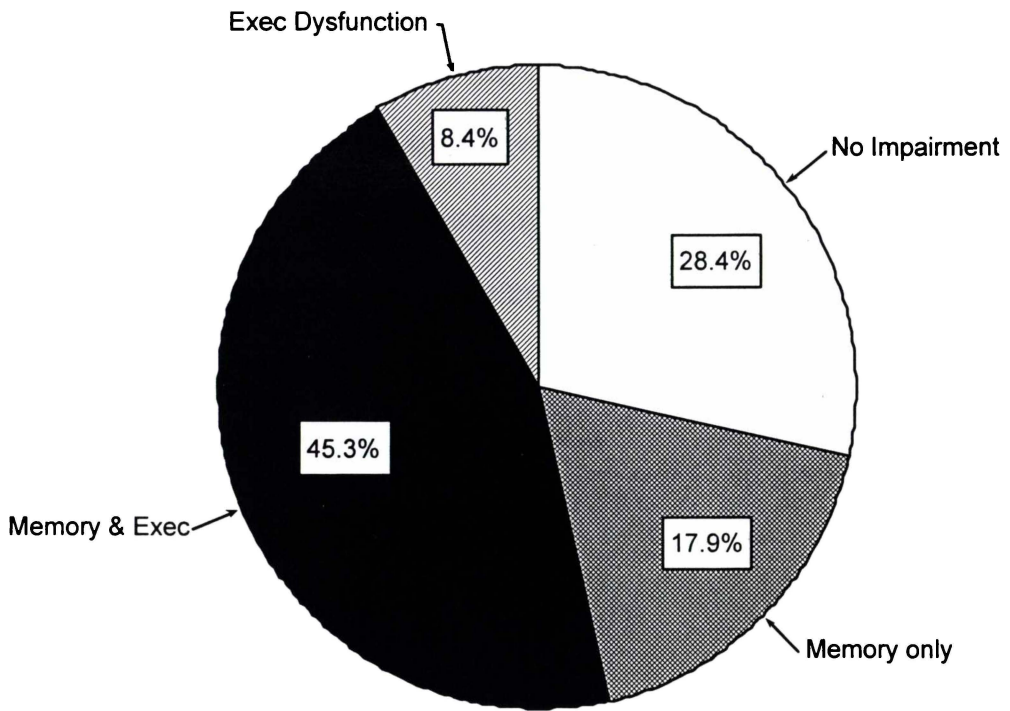
First, differences between the four groups were evaluated in relation to those demographic characteristics and pre-assessment data that could have affected cognitive performance and therefore confounded the data of interest. Secondly, although very little clinical impairment was revealed on the general ability measures in the previous Chapter, their index scores were compared across the four groups. Thirdly the memory index scores were statistically compared across the four groups, but they were also examined in more detail using cluster analyses within each of the four groups to explore more specific patterns of impairment.

Finally, the scores for attention and information processing speed were also compared across these same four 'impairment type' groups.

## **Results**

Using the grouping criteria outlined above, each of the 95 participants was assigned to one of the four 'impairment type' groups. The percentage of participants in each of the four groups is illustrated in Figure 6.1.

This Figure shows that *Group 3 - Both* (memory impairment and executive dysfunction) with 43 participants was considerably larger than the other three groups.



*Figure 6.1.* Percentage of Participants in each 'Impairment Type' Group

As expected the smallest group with only eight participants was *Group 4 - Executive* (executive dysfunction only).

### ***Demographic and Pre-Assessment Data***

Demographic details and data for two of the pre-assessments for each of the four ‘impairment type’ groups are shown in Table 6.1 and Table 6.2 respectively. The corresponding data for the Wechsler Test of Adult Reading will be reported later.

Table 6.1

*Means (and Standard Deviations) of the Demographic Data for the four ‘Impairment Type’ Groups*

	‘Impairment Type’ Groups			
	1. No	2. Memory	3. Both	4. Executive
Age	49.5 (9.3)	54.4 (11.3)	53.9 (12.0)	52.5 (14.3)
Years Education	13.1 (3.1)	12.5 (2.5)	12.8 (3.8)	12.5 (2.6)
Years since First Symptoms	22.9 (11.0)	25.5 (15.0)	23.8 (13.5)	27.9 (16.3)

*Note.* No = No Impairment (n = 27), Memory = Memory Only (n = 17), Both = Memory Impairment and Executive Dysfunction (n = 43), Executive = Executive Dysfunction Only (n = 8).

Table 6.1 shows that the groups were similar in relation to the demographic mean scores and no clear difference between the groups was evident. Additionally data regarding the disease course and number of participants taking medication were also compared across the four groups but not shown in the table. There were no

significant differences between the groups in any disease course prevalence, nor was there any relationship between group membership and being on medication.

Table 6.2

*Means (and Standard Deviations) of the Pre - Assessments for the four 'Impairment Type' Groups*

	'Impairment Type' Groups			
	1. No	2. Memory	3 Both	4. Executive
CMDI				
Mood	49.3 (13.1)	50.8 (10.6)	51.7 (10.8)	51.8 (16.9)
Evaluative	48.8 (10.1)	55.8 (15.9)	52.5 (12.7)	51.6 (13.9)
Vegetative	63.2 (13.5)	59.7 (12.0)	56.8 (12.7)	52.5 (15.0)
Total	53.6 (12.4)	56.6 (12.9)	55.2 (13.3)	52.1 (16.6)
EDSS	4.2 (1.9)	4.2 (1.4)	5.5 (2.1)	4.6 (2.2)

*Note.* CMDI = Chicago Multi Scale Depression Inventory. EDSS = Expanded Disability Status Scale. There was one set of incomplete data for the CMDI, therefore the number of participants for that assessment was 94. No = No Impairment (n = 27), Memory = Memory Only (n = 17), Both = Memory Impairment and Executive Dysfunction (n = 43), Executive = Executive Dysfunction Only (n = 8).

In regard to the Chicago Multiscale Depression Inventory (CMDI), it can be seen from Table 6.2 that *Group 1 - No* (no impairment) had the highest mean Vegetative scale score and this was largely responsible for the above average Total score (>50) seen for this group. Table 6.2 also shows that *Group 3 - Both* (memory impairment and executive dysfunction) had an Expanded Disability Status Scale (EDSS) score that was somewhat higher than the other three groups whose EDSS scores were very similar.

A one-way multivariate analysis (MANOVA) was conducted to determine the effect of 'impairment type' on each of the above demographic (age, years education, years since first MS symptoms) or the two pre-assessment measures (CMDI scales, EDSS scores). Significant differences were found among the four groups on the dependant measures,  $F(24, 241) = 1.63, p = <.05$ . Post-hoc analyses of variance (ANOVAs) were conducted on each of the demographic and pre assessment measures using the Bonferroni method of adjustment, and none of the ANOVAs proved to be significant. This suggests that although the mean score of 5.5 (representing 'Ambulatory without aid or rest for about 100 meters, disability severe enough to preclude full daily activities' - see scoring guidelines, Kurtzke, 1983) on the EDSS measure for participants in the *Both* group represented a greater level of physical impairment than for those participants in the other three groups, this difference was not significant.

As previously reported (Chapter 5), 45 of the participants in this sample (approximately 50%) performed significantly lower than predicted on the general ability measures as revealed by the Wechsler Test of Adult Reading, thus indicating a possible decline in their intellectual functioning, though this seldom reached clinical levels. It was therefore of interest to determine how these participants were distributed amongst the four groups: Eight participants had no assessed problems, (30% of *Group 1 - No*), five had only memory impairment, (29% of *Group 2 - Memory*), the majority of 29 were in the group with both memory and executive dysfunction (67% of *Group 3 - Both*) and 3 were assessed with executive dysfunction only (38% of *Group 4 - Executive*). Therefore, approximately one third of those estimated to be performing below premorbid levels on measures of general ability ( $n = 16$ ) have shown either no, or only limited clinical impairment on other measures,

but the remaining two thirds (n = 29) had impairment in both memory and executive functioning as well as their assessed deterioration in general ability.

### ***General Ability***

In this section, the four ‘impairment type’ groups were compared in relation to the means of the index scores (Verbal Comprehension Index, Perceptual Organisation Index, Working Memory Index & Processing Speed Index) and IQ measures (Verbal IQ, Performance IQ & Full Scale IQ) that were obtained from the Wechsler Adult Intelligence Scales - III (WAIS-III). These comparisons indicated whether there was a similarity between the two groups with executive dysfunction (*Group 3 - Both* and *Group 4 - Executive*) on any of the general ability measures, thereby suggesting that those measures may be associated with executive functioning.

The data in relation to the WAIS - III indices and IQ measures for the four groups are shown in Table 6.3. This table shows that the scores for *Group 3 - Both* were lower than the other three groups on all measures. It was also apparent that for *Group 4 - Executive* the Working Memory Index was one of the lowest scores in that group, and *Group 4 - Executive* and *Group 3 - Both* each had Working Memory Index scores that were lower than the scores of the other two groups whose scores on that index were similar.

As the contributing cell sizes were unequal, separate one-way analyses of variance (ANOVAs) were conducted to evaluate the effect of ‘impairment type’ on the general intelligence measures. The ANOVAs were all significant ( $p < .001$ ), and Tukey’s HSD post-hoc results showed, not surprisingly, that scores for *Group 3 - Both* were significantly lower than *Group 1 - No* on all indices, and were also significantly lower than the scores for *Group 2 - Memory* on all indices except the

Perceptual Organisation Index. Similarly, *Group 4 - Executive* had significantly higher scores than *Group 3 - Both* on all but the Verbal Comprehension Index, the Working Memory Index and the Verbal IQ. No other group comparisons were statistically significant.

Table 6.3

*Means (and Standard Deviations) of the General Intelligence Indices and the IQ Measures for the four 'Impairment Type' Groups*

WAIS-III Indices	'Impairment Type' Groups			
	1. No	2. Memory	3. Both	4. Executive
VCI <sup>a</sup>	107.7 (12.4)	105.2 (10.4)	96.0 (11.9)	107.4 (5.9)
POI <sup>b</sup>	111.6 (12.3)	101.2 (11.3)	92.3 (16.0)	106.5 (13.4)
WMI <sup>a</sup>	104.9 (12.0)	104.8 (14.1)	92.5 (13.5)	100.8 (9.3)
PSI <sup>c</sup>	103.6 (12.4)	96.8 (11.6)	80.5 (11.5)	97.1 (15.2)
IQ Measures				
VIQ <sup>a</sup>	107.6 (11.4)	105.8 (8.7)	95.7 (10.9)	105.6 (5.7)
PIQ <sup>b</sup>	109.9 (11.6)	99.5 (10.4)	88.5 (13.4)	102.5 (12.4)
FSIQ <sup>b</sup>	109.3 (10.3)	103.4 (8.5)	92.2 (11.4)	104.9 (7.1)

*Note.* VCI = Verbal Comprehension Index; POI = Perceptual Organisation Index; WMI = Working Memory Index; PSI = Processing Speed Index; VIQ = Verbal IQ; PIQ = Performance IQ; FSIQ = Full Scale IQ. No = No Impairment, Memory = Memory Only, Both = Memory Impairment and Executive Dysfunction, Executive = Executive Dysfunction Only.

<sup>a</sup>N= 95, <sup>b</sup>N= 94, <sup>c</sup>N= 86,

Thus this analysis indicated that there were significant differences in general ability between the four ‘impairment type’ groups. Although it was not surprising that the scores of *Group 3 - Both* (memory and executive dysfunction) were lower than the scores of the other 3 groups, it was interesting that the Working Memory Index score of *Group 4 - Executive* (executive dysfunction only) was closer than any of its other index scores to *Group 3 - Both*. This result along with the comparatively higher and similar Working Memory Index scores of *Group 1 - No* (no impairment) and *Group 2 - Memory* (memory only), provided further evidence that working memory was more closely associated with executive functioning than other memory functions were. The next section will examine the differences between the four groups on the measures obtained from the memory assessments.

### ***Memory***

Because the scores on the Wechsler Memory Scale - III (WMS-III) were part of the basis of the group divisions, it was expected that there would be some similarity on the memory measures between *Group 2 - Memory* and *Group 3 - Both*. That is, both groups would have some memory scores that were less than 85. Likewise however, some similarity on the memory measures was also expected between those in *Group 1 - No* and those in *Group 4 - Executive* as neither group included any impaired memory index score (<85). What was of greater interest however was whether *Group 4 - Executive* showed a similarity with *Group 3 - Both* on any of these measures. Such a similarity would have been counter to the expectation that the scores of *Group 4 - Executive* would be similar to *Group 1 - No*, unless there was some link with executive dysfunction,

For this analysis the mean scores of the six indices obtained from the WMS - III memory assessment (Auditory Immediate, Visual Immediate, Auditory Delayed, Visual Delayed, Recognition & Working Memory) were compared across the four 'impairment type' groups to determine whether any of these measures showed any relationship between the two groups with executive dysfunction.

The means (and standard deviations) of the WMS-III indices for each of the four groups are shown in Table 6.4.

Table 6.4

*Means (and Standard Deviations) of the WMS - III Index scores for the four 'Impairment Type' Groups*

WMS-III Index	'Impairment Type' Groups			
	1. No	2. Memory	3. Both	4. Executive
<b>Immediate</b>				
Auditory	104.0 (9.1)	93.1 (10.6)	87.1 (9.4)	105.6 (7.1)
Visual	107.2 (11.8)	81.7 (7.4)	77.6 (10.1)	104.9 (8.6)
<b>Delayed</b>				
Auditory	106.4 (8.5)	90.8 (11.4)	86.3 (9.4)	108.0 (5.1)
Visual	104.9 (9.8)	81.2 (8.4)	78.6 (10.3)	103.9 (11.0)
Recognition	106.9 (12.3)	93.5 (11.6)	89.0 (13.4)	103.8 (10.9)
Working Memory	105.4 (12.7)	101.2 (14.3)	90.1 (14.9)	98.9 (9.1)

*Note.* No = No Impairment, Memory = Memory Only, Both = Memory Impairment and Executive Dysfunction, Executive = Executive Dysfunction Only

Table 6.4 indicated that the modality (visual versus auditory) differences, which were demonstrated in Chapter 5, were most apparent in *Group 2 - Memory* (memory only) and *Group 3 - Both* (memory impairment and executive dysfunction). This confirmed again a possible modality bias in memory deterioration in this sample, that is, for those with MS who had some memory impairment there was either a selective impairment in visual rather than auditory memory or a more severe impairment in visual memory compared to auditory memory. Table 6.4 also illustrates, as predicted, the similarity in most scores between *Group 2 - Memory* and *Group 3 - Both*, as well as between *Group 1 - No* and *Group 4 - Executive*.

For the Wechsler Memory Scale - III indices, the cell sizes contributing to each index were equal therefore a one-way multivariate analysis of variance (MANOVA) was conducted to determine the effect of 'impairment type' on each of the six WMS - III measures. Significant differences were found among the four groups on the WMS - III measures,  $F(18, 244) = 8.22, p < .01$ , and subsequent post-hoc analyses of variance (ANOVAs), conducted on each WMS - III measure using the Bonferroni method of adjustment, showed that all indices were significantly different between at least two groups ( $p < .001$ ). For these measures the results of the post-hoc comparisons indicated that the scores of *Group 3 - Both* were significantly lower than the scores of *Group 1 - No* for all measures, and the scores of *Group 2 - Memory* were also significantly lower than *Group 1 - No* for all except the Recognition Index.

The *Group 4 - Executive* had significantly higher scores than *Group 3 - Both* on all measures except the Working Memory Index, and significantly higher scores than *Group 2 - Memory* on all except the Working Memory Index and the Recognition Index. Apart from a significant difference between the higher Working

Memory Index score of *Group 2 - Memory* and the lower Working Memory Index score of *Group 3 - Both*, no other comparisons were significant.

Thus the one exception to the general pattern of scores illustrated in Table 6.4 was the Working Memory Index score, which for *Group 2 - Memory* (memory only) was higher than the other index scores, and unlike the other index scores of this group it was significantly different from *Group 3 - Both* (memory impairment and executive dysfunction). Interestingly, for *Group 4 - Executive* (executive dysfunction only), the Working Memory Index score was lower than the other index scores of that group and was not significantly different from either *Group 3 - Both* (memory impairment and executive dysfunction) or *Group 2 - Memory* (memory impairment only). Thus the Working Memory Index scores of the two groups with executive dysfunction were both lower than the Working Memory Index scores of *Group 1 - No* and *Group 2 - Memory*. These results, together with results of the group comparisons on the general ability measures (see previous section), suggested that working memory may have some relationship with executive functioning.

Given these general group differences, a more detailed cluster analysis of the memory scores within each of the four groups will now be conducted to provide more information regarding the nature of any differences there may be between the groups.

As previously outlined, in order to create smaller more homogeneous subgroups and provide a more detailed picture of the patterns of impairment within each of the four groups a hierarchical cluster analysis was performed on the Wechsler Memory Scales - III (WMS-III) scores within each group. The clusters were derived on the basis of three composite indices from the WMS - III battery of tests. That is, the Immediate Memory Index (a scaled score composite of the Auditory and Visual Immediate Indices), the General Memory Index (a scaled score

composite of the Visual and Auditory Delayed Indices and Recognition), and the Working Memory Index. The resulting cluster patterns within each of the four groups were then visually compared, in an attempt to identify any characteristic that may be unique to those groups with executive dysfunction.

For *Group 1 - No*, a four cluster solution seemed optimal as sufficient differences between the clusters remained, to justify no further collapsing of the data (see Figure 6.2).

Although the cluster analysis was conducted using the composite scores, Figure 6.2 shows the mean scores within each cluster for each of the individual indices (Auditory Immediate and Delayed, Visual Immediate and Delayed, Recognition and Working Memory). This provided a clearer picture of the pattern of scores within each cluster and showed that cluster 1 ( $n = 5$ ) was the cluster with the lowest scores, and cluster 4 ( $n = 3$ ) was the cluster with the highest scores in this group. Cluster 1 and cluster 2 ( $n = 10$ ) each showed a similar pattern of scores for all indices, with the mean scores for cluster 2 being consistently higher. Cluster 3 ( $n = 9$ ) similar to cluster 4 had slightly higher scores for the Visual Immediate Index than the Auditory Immediate Index, but although these two clusters followed parallel paths for both visual and auditory indices the Recognition score for cluster 3 became comparatively higher and the Working Memory Index comparatively lower than cluster 4 which showed the reverse pattern with its Recognition score being comparatively lower and its Working Memory Index score comparatively higher than cluster 3. Within this group working memory did not help to separate the clusters as, with the exception of cluster 4 (lowest scores), there was little relationship between working memory scores and other memory measures.

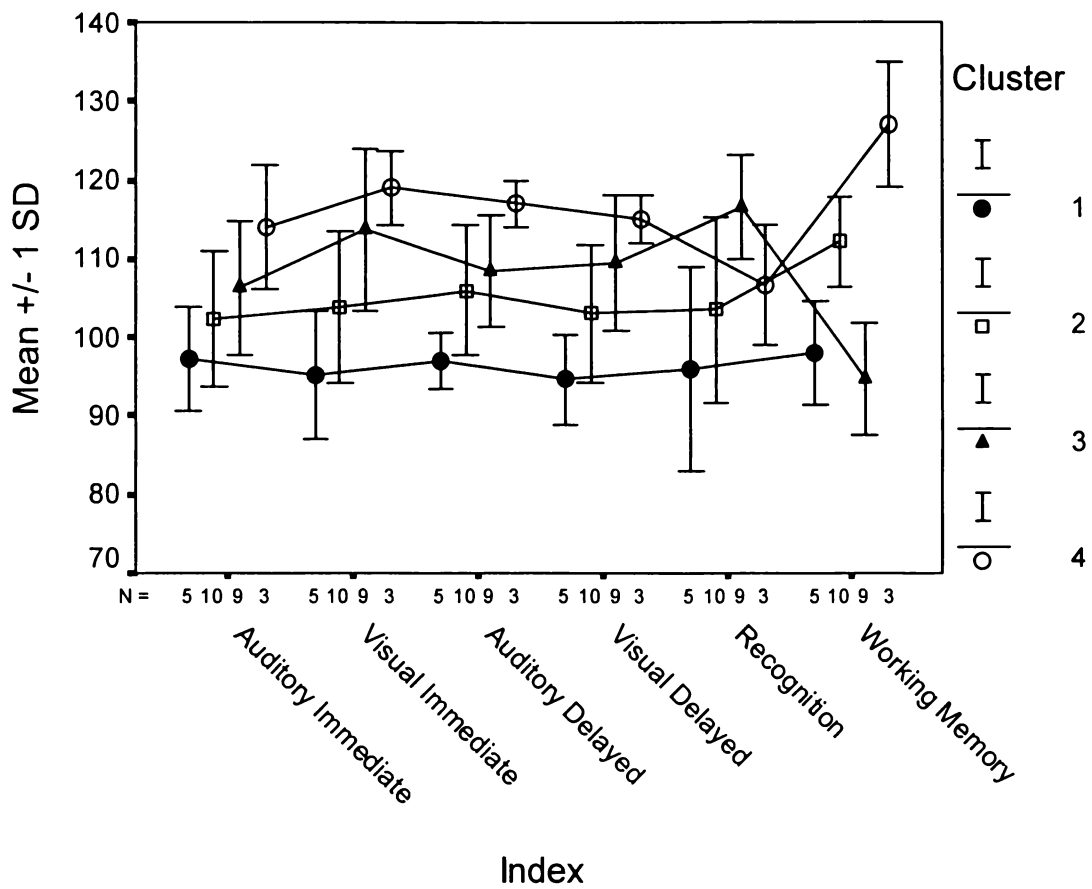


Figure 6.2. Clusters based on the Immediate Memory, General Memory and Working Memory Indices of the WMS-III for the Group with No Impairment (Group 1 – No)

In *Group 2 - Memory*, a three cluster solution yielded one cluster with only a single member, and as further Multiple Discriminant Analysis suggested little was lost in collapsing that data, a final solution of two clusters was reached (see Figure 6.3). It can be seen from Figure 6.3 that both clusters have a consistently higher auditory versus visual score, with the differences being most marked in cluster 2 (n = 7), which also has a markedly higher Working Memory Index score.

For *Group 3 - Both* a three cluster solution was most appropriate (see Figure 6.4), and again a consistently higher auditory (compared with visual) score was evident in all clusters. Figure 6.4 also indicated that for cluster 2 (n = 14) with the highest scores, and cluster 3 (n = 4) with the lowest scores the Working Memory Index score was higher than the scores of the other indices in the same cluster. For cluster 1 (n = 25), however, the mean index scores were between the other two clusters but the Working Memory Index score was one of the lowest scores of this cluster.

The smallest *Group 4 - Executive*, required a two cluster solution (see Figure 6.5), and for both of these clusters the Working Memory Index was either lower than the other indices (cluster 2, n = 5) or was one of the lowest (cluster 1, n = 3). Figure 6.5 also showed that for cluster 2, all index scores apart from working memory, were very similar, a trend that followed for the Visual and Auditory Immediate and Auditory Delayed Index of cluster 1. However for cluster 1 the remaining index scores (Visual Delayed, Recognition and Working Memory) were somewhat lower.

Overall, there was a strong similarity of pattern over the visual and auditory indices for all clusters. That is, for the majority of the clusters the Auditory Immediate Index score was higher than the Visual Immediate Index score and the Auditory Delayed Index score was higher than the Visual Delayed Index score.

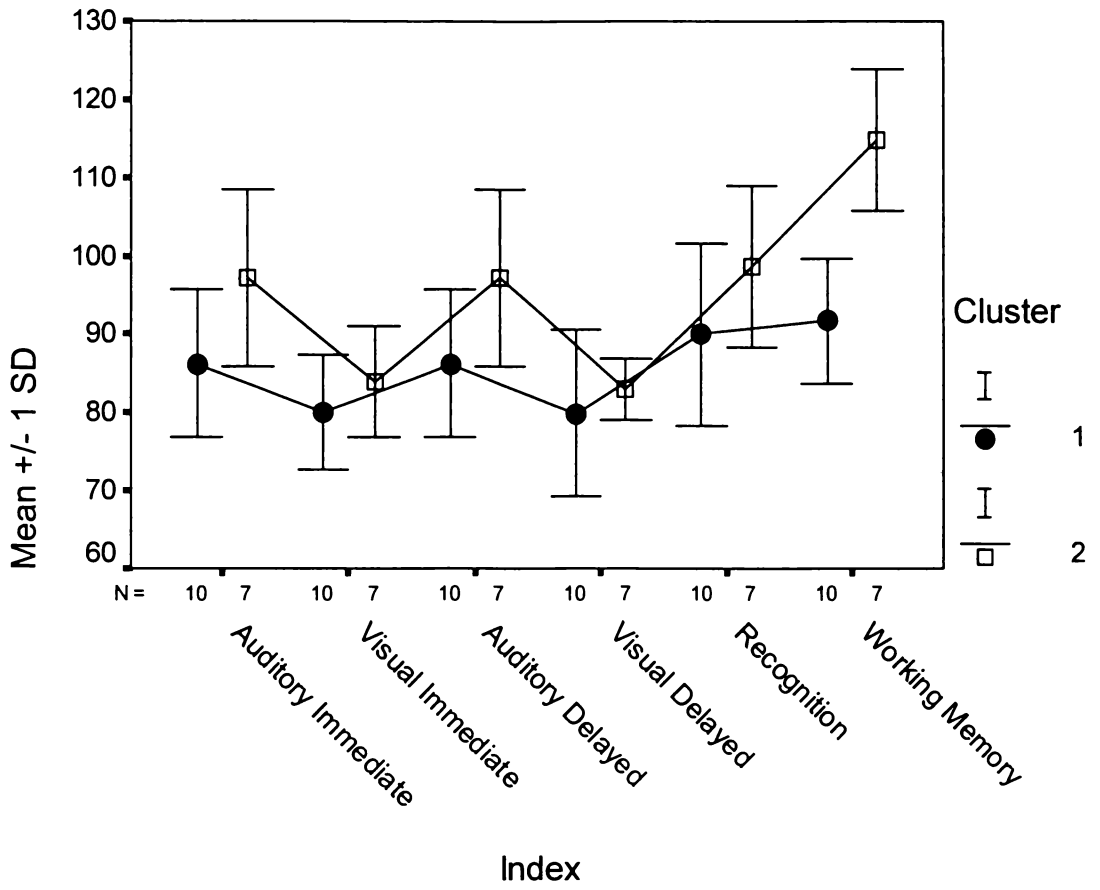


Figure 6.3. Clusters based on the Immediate Memory, General Memory and Working Memory Indices of the WMS-III for Group with Memory Impairment Only (Group 2 – Memory)

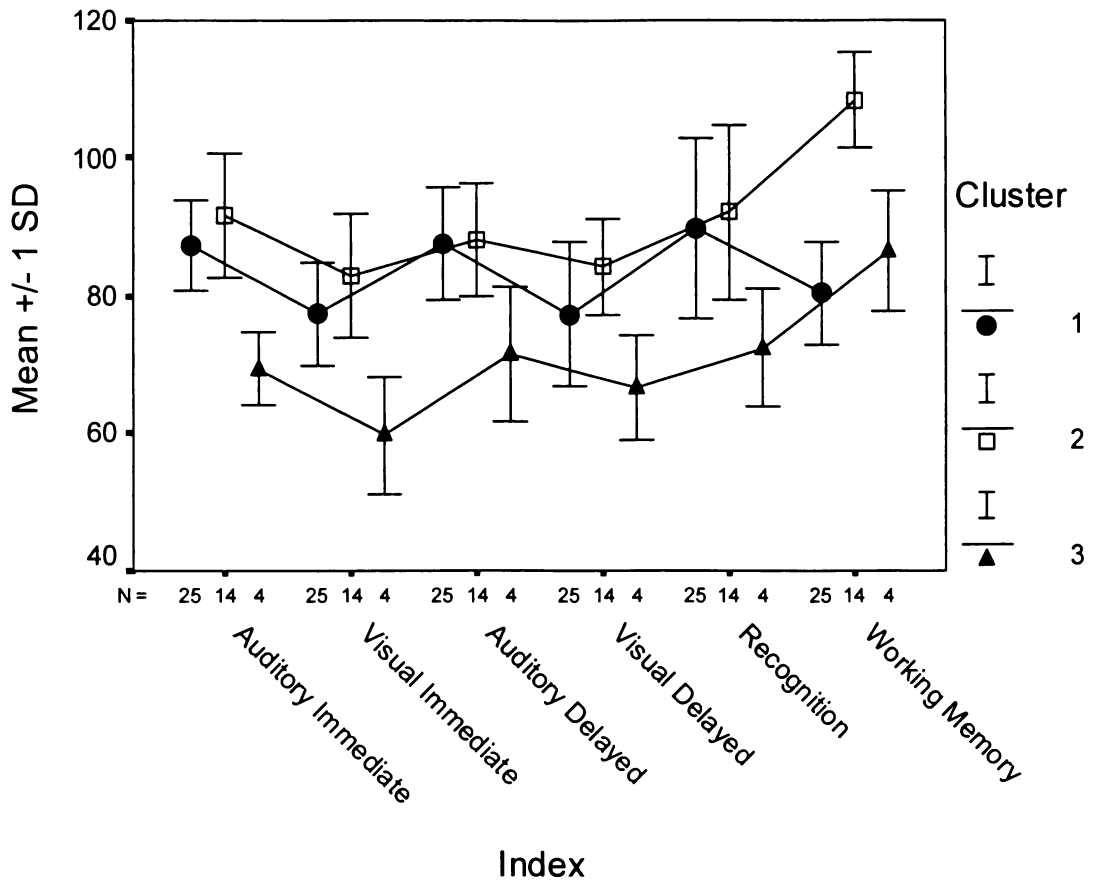


Figure 6.4. Clusters based on the Immediate Memory, General Memory and Working Memory Indices of the WMS-III for the Group with both Memory Impairment and Executive Dysfunction (*Group 3 – Both*)

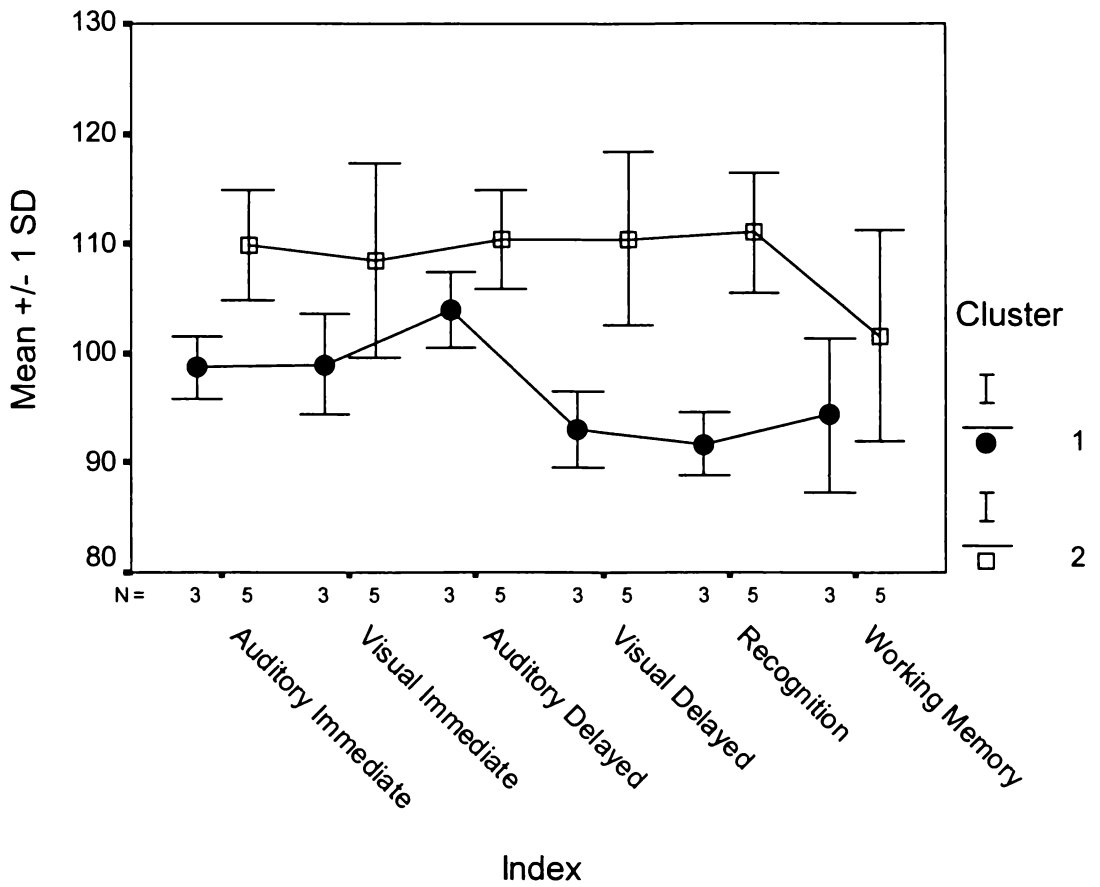


Figure 6.5. Clusters based on the Immediate Memory, General Memory and Working Memory Indices of the WMS-III for the Group with Executive Dysfunction Only (Group 4 – Executive)

This pattern was least evident in the two groups with no memory impairment (*Group 1 - No* and *Group 4 - Executive*).

The similarity between the Immediate and Delayed Index scores for both the Visual and Auditory modalities was however even more consistent within each of the clusters. Recognition followed a reasonably similar trend across the groups, generally staying very much in line with the ‘average’ of any one cluster, however the Working Memory Index score seemed to be much more variable both within and across groups, and was therefore worthy of closer attention. Of particular note was the comparison between those in *Group 2 - Memory*, where the Working Memory Index score was higher than the other index scores for both clusters, and *Group 4 - Executive* where the Working Memory Index score was either comparatively lower, as in one cluster, or was one of the lower index scores as in the other cluster. The *Group 3 - Both* included both these patterns, but the majority of this group was in the cluster whose Working Memory Index score was lower than the other index scores. This suggested that a lower working memory score may be associated with other executive dysfunction.

Therefore, in order to examine in more detail this link between working memory and other executive functioning, the analysis was extended to explore any differences between the four ‘impairment type’ groups in the patterns of scores for the individual subtests that make up the Working Memory Indices of both the general ability assessment (WAIS-III) and the memory assessment (WMS-III). This indicated whether any particular aspect of working memory, as assessed by the various subtests, was more closely associated with executive dysfunction than another.

The means and standard deviations of each of the six working memory subtests (Arithmetic, Letter-Number Sequencing, Digits Forwards, Digits Backwards,

Spatial Span Forward, Spatial Span Backwards) for each of the four ‘impairment type’ groups are shown in Table 6.5.

Table 6.5

*Means (and Standard Deviations) of the Working Memory Sub-Test Scores for the four ‘Impairment Type’ Groups*

Sub-Tests	‘Impairment Type’ Groups			
	1. No	2. Memory	3. Both	4. Executive
Arithmetic	10.3 (2.9) <sub>b</sub>	10.4 (3.0) <sub>a</sub>	8.0 (3.2)	9.4 (2.7)
Letter-Number Sequencing	11.6 (2.9) <sub>b</sub>	11.4 (2.8) <sub>a</sub>	8.7 (3.4)	10.9 (2.0)
Digits Forward	6.6 (1.6)	6.5 (1.4)	6.3 (1.1)	6.7 (1.3)
Digits Backward	4.2 (1.7)	4.3 (1.5)	3.5 (1.5)	3.6 (0.8)
Spatial Span Forward	9.4 (2.7) <sub>a</sub>	8.6 (3.4)	7.3 (2.8)	8.4 (3.3)
Spatial Span Backward	11.3 (2.3) <sub>b</sub>	9.8 (2.5)	8.8 (2.6)	10.4 (3.0)

*Note.* No = No Impairment, Memory = Memory Only, Both = Memory Impairment and Executive Dysfunction, Executive = Executive Dysfunction Only. <sub>a</sub> = Significantly different from the Memory and Executive Dysfunction group at  $p < .05$  using the Bonferroni adjusted method of comparison. <sub>b</sub> = Significantly different from the Memory and Executive Dysfunction group at  $p < .01$  using the Bonferroni adjusted method of comparison.

To enable the differentiation of age adjusted Digits Forward and Backwards, the raw scores of each were taken as a percentage of the age adjusted overall index score. Although it may seem unlikely that age would contribute equally to the decline of both the forwards and backwards exercise, it has been shown that this does seem to be the case. (Gregoire & Van Der Linden, 1997; Myerson, Emery, White, & Hale, 2003).

Table 6.5 shows that for *Group 3 - Both*, all scores (except Digits Forward and Digits Backwards) were lower than the scores for *Group 1 - No*, and the means for the Arithmetic and Letter-Number Sequencing tests were also lower than for *Group 2 - Memory*. Table 6.5 also illustrates that for the Arithmetic, Letter-Number Sequencing and Digits Backwards tests the means for *Group 3 - Both* and the means of *Group 4 - Executive* are both lower than the means of *Group 1 - No* and *Group 2 - Memory*, which are in turn very similar.

A one way multivariate analysis of variance (MANOVA) was conducted to determine the effect of ‘impairment type’ on the six individual tests that make up the working memory indices of both the WAIS - III (Arithmetic) and the WMS-III (Letter-Number Sequencing, Digits Forward and Backwards, and Spatial Span Forwards and Backwards). The MANOVA was significant,  $F(18, 244) = 1.91, p < .05$ , and post-hoc analyses of variance (ANOVAs) were conducted on each subtest using the Bonferroni method of adjustment. The ANOVAs on the Arithmetic,  $F(3, 91) = 4.58, p < .01$ , Letter-Number Sequencing,  $F(3, 91) = 6.34, p < .001$ , and Spatial Span Backwards,  $F(3, 91) = 5.20, p < .01$  subtests were significant, indicating some differences between the groups on these measures. Post-hoc comparisons revealed significant differences between the lower scores of *Group 3 - Both* and the higher scores of *Group 1 - No* where all scores (except Digits Forward and Digits Backwards) were significantly different. The lower scores of *Group 3 - Both* were also significantly different from the higher scores of *Group 2 - Memory* for the Arithmetic and Letter-Number Sequencing tests. No other comparisons were significant.

Although previous results had indicated that the four ‘impairment type’ groups were not significantly different on any demographic or pre-assessment

measures, an additional analysis was performed to confirm that working memory scores were not disproportionately influenced by other factors in any of the four groups. A one-way analysis of covariance (ANCOVA) was conducted with the Working Memory Index as the dependent variable and years of education and the CMDI scores as the covariates. None of the covariates contributed more than .01% to the variance of working memory between the four 'impairment type' groups, nor were they significantly related to working memory, therefore the original results remained unchanged.

Thus it seems that it was more particularly the Arithmetic, Letter –Number Sequencing and Digits Backwards scores that were similarly lower for the two groups with executive dysfunction. This suggested it was not the passive rehearsal but rather the more active manipulation aspects of working memory that were also common to executive functioning.

### ***Attention***

This section will now explore any differences between the four 'impairment type' groups on the Attentional Capacity Test (ACT) of attention to determine whether this measure of attention shows any similarity of scores between the two groups with executive dysfunction. If the two groups with executive dysfunction have ACT scores which are more similar than any of the other group comparisons, this would then indicate some link between this measure of attention and executive functioning.

The ACT assessment had a maximum possible score of 24 (100%), and the mean and standard deviation for each of the four groups (no impairment, memory

impairment only, memory and executive dysfunction and executive dysfunction only) are shown in Table 6.6.

Table 6.6

*Means (and Standard Deviations) of the Attentional Capacity Test scores for the four 'Impairment Type' Groups*

	'Impairment Type' Groups			
	1. No	2. Memory	3. Both	4. Executive
ACT	20.5 (2.4)	19.5 (2.3)	16.9 (3.2)	19.8 (2.4)

*Note.* No = No Impairment (n = 27), Memory = Memory Only (n = 17), Both = Memory Impairment and Executive Dysfunction (n = 43), Executive = Executive Dysfunction Only (n = 8).

Table 6.6 illustrates that *Group 3 - Both* had the lowest mean score and that there was a close similarity between *Group 2 - Memory* and *Group 4 - Executive* for this measure. Also, not surprisingly, *Group 1 - No* had the highest mean score.

A one-way analysis of variance (ANOVA) was conducted to evaluate the effect of 'impairment type' on the ACT scores. The ANOVA was significant,  $F(3, 91) = 10.38, p < .001$ , and Tukey's HSD post-hoc comparisons showed that the scores for *Group 3 - Both* were significantly lower than *Group 1 - No* ( $p < .001$ ), *Group 2 - Memory* ( $p < .01$ ) and *Group 4 - Executive* ( $p < .05$ ). No other post-hoc comparisons were significantly different.

The similarity of scores between *Group 2 - Memory* and *Group 4 - Executive*, together with the lower scores for *Group 3 - Both* and higher scores for *Group 1 - No*, suggests that it was the extent of the cognitive impairment rather than its nature that influenced the level of performance on this assessment of attention. This also

suggested that executive functioning integrity had no particular influence on ACT scores.

### ***Information Processing Speed***

As it is possible that information processing speed is affected by cognitive impairment, or as was discussed previously (see Discussion, Chapter 5), reduced information processing speed underlies other cognitive impairment in those with MS, the following section will now compare each of the four ‘impairment type’ groups on the information processing measures to determine whether any of the scores indicate a similarity between the two groups with executive dysfunction.

A one-way multivariate analysis of variance (MANOVA) was conducted to determine the effect of ‘impairment type’ on the information processing measures. That is, information processing speed (slope) initial response time (intercept) and the number correct for the one, two and four stimulus conditions. The MANOVA was significant,  $F(15, 227) = 2.07, p < .05$ , and subsequent ANOVAs which were conducted on each of the information processing variables using the Bonferroni method of adjustment, indicated no significant difference between the four groups in relation to information processing speed, but there were significant differences between the groups on the other variables: Intercept,  $F(3, 86) = 6.13, p < .001$ ; Error 1,  $F(3, 86) = 11.91, p < .01$ ; Error 2,  $F(3, 86) = 4.62, p < .01$ ; and Error 4,  $F(3, 86) = 4.04, p < .01$ . Post-hoc analysis indicated, not surprisingly, that *Group 1 - No* had a significantly faster initial response speed and a higher number correct on all stimulus conditions than *Group 3 - Both*, and *Group 2 - Memory* had more correct in the one stimulus condition than *Group 3 - Both* but no other post-hoc comparisons were statistically significant for these measures.

Therefore it seemed that there were no differences in the mean information processing speed between the four groups. Although *Group 3 - Both* (memory impairment and executive dysfunction, Mean processing speed  $M = .082$ ) and *Group 4 - Executive* (executive dysfunction only, Mean processing speed  $M = .073$ ) had mean processing speeds (slope values) that were both comparatively slower than *Group 2 - Memory* (memory impairment only, Mean processing speed  $M = .064$ ) and *Group 1 - No* (no impairment, Mean processing speed  $M = .068$ ) these differences were not significant.

## **Summary and Discussion**

Overall, there was shown to be a relatively similar representation of the demographic characteristics and pre-assessment variables within each of the four ‘impairment type’ groups, although there were some differences in the number of participants in each of the four groups. For the measures of general ability and memory, not surprisingly, the lowest scores were most commonly found in the group with both memory and executive dysfunction and the highest scores found in the group with no impairment. Working memory performances, however, appeared to show a somewhat different pattern to the other measures, and together with the cluster analysis suggested that a poorer working memory performance was associated with other executive dysfunction. Attentional ability seemed to be primarily related to the level of other cognitive impairment rather than its nature, and there was no difference seen between the groups in relation to information processing speed.

It was evident from the statistical comparisons between the four groups that the majority of demographic characteristics and pre-assessment scores were similar for each of the four ‘impairment type’ groups. It was also evident however that the

small group with executive dysfunction only had on average a somewhat greater number of years since first MS symptoms than the other three groups. For this measure it may have been expected that the group with the most widespread cognitive impairment (memory impairment and executive dysfunction) would also have had MS for the longest period of time. It seemed however, that this was not the case and reinforced the mixed results obtained from previous studies which have suggested that cognitive impairment and MS do not have a consistent or predictable relationship.

The data for the depression assessment were also relatively consistent between the four groups, suggesting that no one group would have been unduly influenced by a higher (or lower) level of depression. It was evident that the group with both memory impairment and executive dysfunction was made up of participants who had, on average, a higher level of physical disability than the other three groups, which in turn were all similar on this measure. Although physical disability can influence performance on those tasks requiring manual dexterity, most studies which have looked at cognitive impairment in those with MS have concluded that levels of cognitive impairment are not related to levels of physical disability (e.g., Amato et al., 1995; Grossman et al., 1994). Therefore it was not expected that the group differences seen in this sample on the measure of physical ability, had any influence on the cognitive scores, and overall, the similarity between the groups on these demographic and pre-assessment measures ensured also that no other of these measures would have disproportionately influenced the cognitive scores of any of the four groups.

Participants whose IQ appeared to have deteriorated were found in all four of the 'impairment type' groups. However, by far the greatest proportion of these

participants appeared in the group with both memory impairment and executive dysfunction. For the remaining three groups such participants made up approximately one third of the group, but for the memory and executive dysfunction group, two thirds were performing significantly below predicted levels. This suggested that there were a number of participants in this sample whose impairment included not only memory and executive functioning, but also some deterioration in general ability, making the cognitive deterioration for these participants somewhat widespread. As previous studies have suggested that pervasive cognitive impairment affects from only 5% (Arnett, 2000) to less than 10% (Rao, 1996) it seemed therefore in this study, that the majority of those with indications of widespread deterioration had not reached a level of impairment which could be classified as severe.

In keeping with this evidence of cognitive deterioration in some participants, it was apparent that there was some considerable difference in the cognitive performances of the participants in each of the four groups. As expected, the 27 participants (28% of the sample) with no impairment performed at a higher level on almost all measures than those in the other three groups. In line with their high levels of performance on general ability measures, and contrary to the predictions of Rao, (1986), who suggested that Verbal IQ was typically seven to ten points higher than Performance IQ in those with MS, the mean difference between these measures within this group was only two points. In addition, and in support of the results of the study by Fischer (1988), this group did not display any significant modality differences in their memory assessment.

For the participants with only memory impairment, the performance level on the general ability measures was lower than for those with no impairment, but showed some similarity with the group with only executive dysfunction. However,

one notable difference between these two groups was the considerably lower level of achievement of the group with memory impairment only on the Perceptual Organisation Index. This suggested that for those with memory impairment only, their six-point difference between Verbal IQ and Performance IQ was not the result of compromised motor skills that can affect the processing speed measure that also contributed to Performance IQ. Rather it seemed that it may be the visuo-spatial skills that were assessed in the Perceptual Organisation Index, which were compromised to some extent in this group. Previous studies (e.g., Ryan et al., 1993) have indicated that these skills may be impaired, although it is the slower processing speed that was more commonly shown to be responsible for the Performance IQ being typically lower than the Verbal IQ for those with MS. The second difference of note was the relatively higher working memory performance of the group with memory impairment only compared to the group with executive dysfunction only. It was also evident however, that performance on this measure was not considerably higher than performance on the other measures within this group. Therefore rather than the difference between these two groups in relation to working memory being reflective of a higher level of working memory performance for those with only memory impairment, it was the consequence of a comparatively lower working memory performance for those with only executive dysfunction.

Not surprisingly, this group with memory impairment only performed at a similar level to those in the *Group 3 - Both* group for all memory measures except working memory, and unlike the conclusions of some studies (e.g., Fischer 1988) a significant difference between lower visual memory scores and higher auditory memory scores was also illustrated. Although the working memory performance that was part of the general ability assessment was only one of the higher scores within

that assessment, it was evident that working memory performance was the highest of all the memory measures within this group. However, taken together, working memory performances for both the general ability and memory assessments indicated that for those whose memory abilities are compromised, this deterioration did not necessarily extend to performance on working memory measures.

As would have been expected, the *Group 3 - Both* group (memory impairment and executive dysfunction) performed most poorly on all measures, and came closest to Rao's predictions that for those with MS, performances on Verbal IQ would exceed performances on Performance IQ by seven to ten points (Rao, 1986). It was also noticeable in the general ability assessment that for this group it was the Processing Speed Index whose performance average was the lowest. As this group also had the highest level of physical impairment (as indicated by the physical rating scales), this seemed to reinforce the important influence of motor skills in levels of performance on this measure. It was also apparent therefore that this measure of processing speed was not particularly appropriate for many of those with MS.

For the memory assessment there was some similarity between this group and the *Group 2 - Memory* group, but on the whole, the performance level of those with both memory impairment and executive dysfunction was the lower of the two. It was notable however, that although performance in relation to the Working Memory Index was lower than for the other three groups, it was the highest of the memory measures for this group, again suggesting some differentiation of process between the other memory measures and working memory. Although the modality differences found in this group were not supported by the Fischer study (Fischer, 1988), the twenty-five people with MS that were assessed on the Wechsler Memory Scales - III to provide data for its manual, were found to be impaired only on the visual indices,

therefore that group did support the modality differences found in this study. As is usual with those with MS as a group, however, the variability of scores was considerable.

As it is most commonly deficits in complex attention that are thought to characterize those with MS (e.g., Fischer et al., 1994), it was somewhat surprising to find that this sample overall performed significantly more poorly than the control group on the comparatively simple Attentional Capacity Test. Because the participants with both memory impairment and executive dysfunction performed more poorly than the other three groups on this measure, it could be expected that it was the participants in that group which contributed substantially to the poorer performance of the MS sample overall compared to the performance of the control group. The levels of performance across the four 'impairment type' groups also suggested that the extent of cognitive impairment generally had some influence on performance in the simple attentional task. It was also the case that this group with both memory impairment and executive dysfunction had the slowest information processing speed when measured by the Sternberg paradigm. Therefore, when it was considered that two thirds of this group had also shown some deterioration in Full Scale IQ scores, it did seem that some evidence of global cognitive deterioration within this group existed.

The fourth *Executive* group (executive dysfunction only) indicated a slightly lower level of performance on general ability measures than the group with no impairment but performances were generally higher than for those in the group with only memory impairment. Two exceptions were first the considerably slower processing speed, which was only marginally faster than the processing speed of the group with only memory impairment, and secondly, the comparatively lower level of

working memory performance. Most notably, the levels working memory ability of this group and the group with memory impairment and executive dysfunction were both lower than the levels of working memory ability of the other two groups.

As could have been expected, the memory assessment performance levels for this group were closer to and sometimes exceeded those with no impairment. Again the exception was the considerably lower working memory performance, which together with the working memory performance of those with both memory impairment and executive dysfunction, were again both lower than the scores for the other two groups. It was also noticeable that the selective deficit found by some (e.g., Rao, Leo et al., 1989, Rao, Leo, Bernardin et al., 1991) in long-term but not short-term memory was not replicated in any group in this study.

The comparative similarity of working memory performance between the group with only executive dysfunction and the group with both memory impairment and executive dysfunction, along with the difference between this measure and other memory measures was reinforced in the cluster analysis. For each of the three groups with impairment it was evident that a contrast existed between the comparatively higher levels of working memory performance for the participants in those clusters in the group with only memory impairment, compared to the comparatively lower level of working memory performance for the participants in the clusters in the group with only executive dysfunction. In keeping with this trend the majority of those in the group with both memory impairment and executive dysfunction also had comparatively lower levels of working memory performance.

Most theories or models of working memory support the differential between working memory and other memory indices that has been found in this study. Unfortunately, however, working memory as a concept, similar to executive

functioning generally, also suffers from a lack of a universally accepted definition, and therefore a consistent means of assessment. However when the definitions from ten different contributors to a collection of models of working memory were combined into one definition, which encapsulated the common properties from all theorists, several factors emerged. This definition asserted that “Working memory is those mechanisms or processes that are involved in the control, regulation, and active maintenance of task relevant information in the service of complex cognition, including novel as well as familiar, skilled tasks.....Working memory is closely linked to LTM, and its contents consist primarily of currently activated LTM representations, but can also extend to LTM memory representations, that are closely linked to activated retrieval cues and, hence, can be quickly reactivated.” (Miyake & Shah, 1999, p. 450)

This definition highlights the uniqueness of working memory while making clear its relationship with other memory functions. Specific theories of working memory which can be related to the results of this study and which describe in greater detail the elements which make up the process of working memory, include the embedded process model of Cowan (1999). This model is a hierarchical model with increasingly specialized functions forming smaller subsets of long-term memory. In this model, as in others, general (long-term and short-term) memory is a crucial element of the process, in that relevant information needs to be accessible, but it also progressively needs to be activated and according to this model, then become the focus of attention. This focusing of attention is controlled by processes which are very similar to those of the ‘central executive’ which is a crucial element of the Baddeley and Hitch model of working memory, and arguably also similar to the more detailed processes outlined by Stuss et al. (1995). Cowan (1999) describes these

control processes as “effort-demanding processes directed by the central executive (defined operationally as the collection of mental processes that can be modified by instructions or incentives)” (p. 65). As well as directing attention toward relevant stimuli or away from irrelevant stimuli, the central executive of Cowan’s model also controls ongoing voluntary processing.

Although this model of working memory included both memory and ‘executive’ (control) functions, Cowan also pointed out that while working memory makes the information relevant to a complex task readily available through these processes, it remains distinct from the level of performance on any given task.

A clearer demonstration of the relationship between memory, working memory and executive functioning is given by way of a critical path model (Engle, Kane, & Tuholski, 1999). These authors, like Cowan, considered that working memory consists of activated portions of long-term memory (STM), along with controlled attention. They also postulated however, that individual differences in the controlled processing aspect of working memory, may represent the differences found in general fluid intelligence, and that these processes are mediated by the dorsolateral prefrontal cortex and its associated structures. To demonstrate their theory, Engle et al. used three ‘span’ tasks, which each included two operations, as working memory measures, and three simpler (single operation) span tasks were used as short term memory measures. It was hypothesized by Engle et al. that the shared variance would reflect the ‘memory’ component and any residual variance would equate to the controlled processing element of working memory, which they proposed is required to resolve conflict and overcome distraction and interference. It was also proposed that this working memory residual, but not the STM residual, would correlate with measures of general fluid intelligence. Their critical path model did demonstrate that,

in spite of a significant correlation between working memory and short-term memory, they were separable. This was illustrated by the significant correlation that was shown to exist between the working memory residual and measures of fluid intelligence, a relationship that was not evident in relation to the short-term memory residual. This model also illustrated that the 'common' factor, which represented the 'memory' component, was not related to the measures of fluid intelligence, a finding supported in this current study by the lack of relationship evident between general memory indices and executive functioning.

Engle et al. (1999), considered that the working memory residual relates to the controlled attention component of working memory, a similar concept to the focused attention processes in Cowan's model. They also considered that it is this controlled attention that is important to higher order functioning. The measures of fluid intelligence that were used in this analysis were Ravens Progressive Matrices, and the Cattell Culture Fair test. The Ravens has been used in the past as a test of executive functioning, and although it has weaknesses (especially in terms of isolating the source of a problem), it does tap reasoning processes considered to be part of the suite of executive functions. Therefore to the extent that the general fluid intelligence in this model was representative of executive functioning, it seems to have illustrated the relationship between working memory and both memory and executive functioning.

Although this current study does not appear to support the close link between working memory and other memory measures which was demonstrated in the above critical path model, a link between working memory and other executive functions has been suggested, not only in this current study, but also in a more recent study (Anderson & Knight, 2004). The Anderson and Knight study is based on the

Baddeley and Hitch model of working memory, and adds further support to the proposed relationship between working memory and other executive functioning. A dual task exercise, simultaneously activating the two primary memory components of the Baddeley and Hitch model, and therefore requiring the involvement of the central executive, was shown to be the most sensitive measure of executive dysfunction in a group with traumatic brain injury. Whilst there was a significant decrement in each task from the single task condition to the dual task condition for the clinical group, there was no corresponding decrement evident in the control group. There was also either no significant difference or a lesser significant difference indicated between the two groups on other more traditional measures of executive dysfunction such as the Controlled Word Association Task (COWAT), FAS Word Fluency test, the Trails test and the Wisconsin Card Sorting test (WCST). Therefore it seems that working memory, especially when its resources are taxed, is a good indicator of other executive dysfunction.

That the nature of the particular working memory test does influence the strength of its relationship with other executive functions was illustrated by the differing levels of performance seen on each of the working memory sub-tests within each of the four 'impairment type' groups. It was evident that those tests that required more active mental manipulation and arguably made greater demands on the control processes, for example, Letter Number Sequencing, Arithmetic and Digits Backwards, were the tests that showed the greatest similarity of scores between the two groups with executive dysfunction.

Not surprisingly, this further supports those models of working memory which suggest that it is the more complex working memory processes that are most closely linked with other executive functions. The relationship between these working

memory processes and other executive functioning will therefore be explored in more detail in the following section.

## Chapter 7

### RESEARCH QUESTION THREE

#### ***What is the relationship between working memory and executive functioning?***

The results of the previous chapter provided some evidence that working memory functioning appeared to be related to executive functioning. The unique pattern of the working memory scores within and across the four ‘impairment type’ groups suggested that this measure was different from other general ability measures and different from other memory measures. It also seemed to indicate that a lower working memory performance maybe associated with other executive dysfunction. In addition, it was subsequently established that it was those working memory subtests which utilized the more complex or ‘executive’ working memory processes that were most closely linked with executive functioning. This finding supported the critical path model of Engle et al. (1999), which demonstrated a link between working memory and executive processes, a link that did not apply to other memory processes.

On the basis of these results, the following analyses examined in more detail the nature of the relationship between working memory and other executive functioning. It was of particular interest, to determine whether working memory formed the basis of all other categories of executive functioning as was suggested by the Adaptive Character of Thought model (Kimberg & Farah, 1993), or whether it was a related but separable executive function as suggested by Miyake et al. (2000). If working memory was a related but separable function, then it was also of interest to

determine the strength of its relationship with each of the other executive function categories.

First, it was determined in general terms (for the whole sample) whether increasingly lower working memory scores were associated with an increasing degree of executive dysfunction. Based on the five categories of executive functioning, namely, fluency, shifting, planning, inhibition, and reasoning, the D.KEFS assessment was recorded as 0, 1, 2 or 3 depending on whether the assessment had been no impairment, impairment in one category, two categories or three or more categories. Thus for this analysis, this then provided the degree of executive dysfunction for each participant. These scores were then correlated with the working memory scores of the whole sample.

Following this, the relationship between working memory scores and the degree of executive dysfunction for those whose working memory was impaired was compared to the same relationship for those whose working memory was not impaired. This analysis indicated whether any relationship between the level of working memory scores and the degree of executive dysfunction was equally strong regardless of the integrity of working memory. To facilitate this analysis the sample was divided into two subgroups based on their Working Memory Index scores.

*Group A - Impaired, (n = 24)*

The participants in this group had Working Memory Index scores that were less than 85.

*Group B - Unimpaired, (n = 71)*

The participants in this group had Working Memory Index scores that were equal to or greater than 85.

Finally, the issue of whether working memory formed the basis of all other executive functioning or whether it was a separable function was addressed. For this analysis the frequency of impairment for each of the five categories of executive dysfunction was calculated within each of the two working memory based subgroups (*A - Impaired and B - Unimpaired*) and the resulting category frequencies for each group were then compared. For those categories most often impaired when working memory was also impaired, it was determined that these executive functions were more closely linked with working memory processes than those whose frequency of impairment was more evenly distributed between the two working memory based subgroups. From this analysis it was also possible to determine which executive categories were impaired in the absence of working memory impairment, suggesting in those cases some differentiation of process.

For the following analysis only the Working Memory Index score from the Wechsler Memory Scales - III was used as the aggregate measure. If however the working memory subtests were included in the analysis then the Arithmetic subtest from the Wechsler Adult Intelligence Scales - III was also included, as this subtest was additional to those included in the WMS - III assessment and seemed to show some relationship with executive functioning, see Chapter 6.

## **Results**

### ***Working Memory and the Degree of Executive Dysfunction***

As outlined above, correlations between the Working Memory Index score, the working memory subtest scores and the degree of executive dysfunction were first conducted for the whole sample to determine the extent to which lower working memory scores were related to a greater number of categories impaired (degree of

executive dysfunction). The subtest scores were included in this analysis to determine whether any one aspect of working memory was more strongly related to the degree of executive dysfunction than another.

From the WMS - III all correlations were significant; Working Memory Index,  $r(93) = -.56, p < .001$ ; Letter Number Sequencing,  $r(93) = -.47, p < .001$ ; Digit Span Backwards,  $r(93) = -.36, p < .001$ ; Spatial Span Forward,  $r(93) = -.44, p < .001$ ; Spatial Span Backwards,  $r(93) = -.46, p < .001$ ; except Digit Span Forward,  $r(93) = -.12, p = .121$ . From the WAIS - III, the correlation between the Arithmetic subtest and the degree of executive dysfunction was also significant,  $r(93) = -.42, p < .001$ .

This suggests that for the sample as a whole, the relationship between increasing degrees of executive dysfunction and decreasing scores for both the Wechsler Memory Scale - III (WMS-III) Working Memory Index and the majority of the contributing subtests was robust.

To determine whether lower working memory scores were related to a greater degree of executive dysfunction both for those whose working memory was impaired and those whose working memory was not impaired, correlations between the degree of executive dysfunction and working memory scores were conducted within each of the two working memory based subgroups (*Group A - Impaired and Group B - Unimpaired*).

For *Group A - Impaired*, only the correlation for the Working Memory Index was significant,  $r(22) = -.411, p < .05$ , with none of the subtests reaching significance. This suggests that whilst a greater degree of executive dysfunction was strongly related to lower Working Memory Index scores, the relationship between the degree of executive dysfunction and any of the individual working memory subtests scores, was at best inconsistent for those whose working memory was impaired.

The same correlations in *Group B - Unimpaired*, reached significance for the Working Memory Index,  $r(69) = -.225$ ,  $p < .05$  and also Spatial Span Forwards,  $r(69) = -.266$ ,  $p < .05$  and Arithmetic,  $r(69) = -.268$ ,  $p < .05$ . No other relationships were significant, but it seems that the relationship between the Working Memory Index scores and the degree of executive dysfunction also applies when working memory is not impaired. For this group it also seemed that the relationships between the degree of executive dysfunction and the various subtests was slightly less inconsistent than for those whose working memory was impaired. However, it can be seen that the effect size for the *Group A* analysis ( $r = -.411$ ) was greater than that for *Group B* ( $r = .225$ ), and this would suggest that in fact the likelihood of lower working memory scores being associated with a greater degree of executive dysfunction was greater when working memory was impaired. It is also the case however that the range of Working Memory Index scores was more limited in *Group A - Impaired*, therefore it is possible that the strength of that correlation may be somewhat overstated.

To reinforce previous results which indicated that lower working memory scores were associated with a greater degree of executive dysfunction, the frequency of each degree of executive dysfunction within each of the two working memory based subgroups was compared, that is *Group A - Impaired*, was compared with *Group B - Unimpaired*. Of those participants in *Group B*, 58% had no executive dysfunction and only 10% had more than one category of executive dysfunction. In contrast only 12.5% of those in *Group A* had no executive dysfunction and 67% had more than one category of dysfunction, indicating a substantial difference between the two groups in the relative frequency of each degree of executive dysfunction. This suggests that although there was shown to be a relationship between working memory scores and the degree of executive dysfunction within both *Group A* and *Group B*, for

those participants whose working memory is impaired there is in fact a greater likelihood of that impairment being associated with other executive dysfunction.

### ***Working Memory and other Executive Function Categories***

To examine any relationship between working memory performance and impairment in each of the five categories of executive functioning, the frequency of impairment for each category was calculated. That is, the numbers of participants who were assessed as being impaired in each of the shifting, inhibition, planning, reasoning or fluency categories, either in isolation or in combination with other categories were summed. This gave the frequency for each category, with any participant who had been assessed with more than one category of executive dysfunction, contributing to the numbers for each category of their assessed impairment. A comparison of the numbers impaired on each category of executive functioning was then made between those in *Group A - Impaired*, and those in *Group B - Unimpaired* (see Table 7.1). This Table shows first the number of participants in each particular category of executive dysfunction for each of the two groups. The percentage of the total number of participants in that group that this number represents is in brackets, realizing that many of the participants in each group will be represented in more than one category. To further clarify the relative prevalence of any one category in either group, the percentage in italics represents the proportional incidence within each group (or in total) that each category represents. This was calculated for each group (and in total), by summing the numbers of participants across the five categories of impairment, and then calculating the percentage of that total that each category represented.

Table 7.1

*Number (and Percentage) of Participants Impaired and Percentage Prevalence of each Category of Executive Dysfunction for Participants with MS within each of the two Working Memory Subgroups*

Executive Category	Working Memory Sub Group		Total
	Group A Impaired (n = 24)	Group B Unimpaired (n = 71)	
1. Fluency <i>% Prevalence</i>	13 (61.9%) <i>27.6%</i>	12 (40%) <i>31.6%</i>	25 ( <i>29.4%</i> )
2. Shifting <i>% Prevalence</i>	7 (33.3%) <i>14.9%</i>	2 (6.7%) <i>5.3%</i>	9 ( <i>10.6%</i> )
3. Inhibition <i>% Prevalence</i>	3 (14.3%) <i>6.4%</i>	7 (23.3%) <i>18.4%</i>	10 ( <i>11.8%</i> )
4. Planning <i>% Prevalence</i>	10 (47.6%) <i>21.3%</i>	6 (20%) <i>15.8%</i>	16 ( <i>18.3%</i> )
5. Reasoning <i>% Prevalence</i>	14 (66.7%) <i>29.8%</i>	11 (36.7%) <i>28.9%</i>	25 ( <i>29.4%</i> )

*Note.* Group A - Impaired = Working Memory Index score < 85 (Impaired) Group B - Unimpaired = Working Memory Index score >= 85 (Unimpaired). Numbers represent the count of participants impaired in each category. Percentages in brackets represent the percentage of participants in any one group with each category of impairment.

Percentages in italics represent the relative incidence of each category in each group (and in total).

The pattern of frequencies shown in Table 7.1 illustrates some differences between the two groups. Shifting, planning and reasoning were impaired in a greater number of participants and made up a greater percentage of the total executive dysfunction in those whose working memory was impaired. The differences between the two groups were not however as great for the reasoning category as they were for the other two categories. A greater number of participants in the group whose working memory was impaired were also impaired on the fluency category, but this

category made up a greater percentage of the total impairment in those whose working memory was not impaired. Similar to the reasoning category, the differences between the two groups on the fluency category were not substantial. In contrast, the inhibition category was impaired in both a greater percentage of participants and made up a greater proportion of the impairment in those whose working memory was not impaired.

Therefore in general terms it seems that working memory processes did not underlie all other executive categories equally. While shifting and planning impairment were most often associated with lower working memory ability, fluency and reasoning were impaired almost equally often whether working memory was impaired or not. In contrast impairment in the category of inhibition seemed to be most common in those whose working memory integrity was not compromised. This suggests a somewhat variable contribution of working memory to other executive functions.

## **Summary and Discussion**

This analysis has revealed that lower working memory scores were shown to be associated with a greater degree of executive dysfunction within the sample as a whole, but seemed to be weaker within the two subgroups formed on the basis of the working memory scores.

Compared to those whose working memory was not impaired, a greater number of those with an impaired working memory score were assessed with a greater degree of executive dysfunction, and some differences between the frequencies of impairment for each of the five executive categories were also evident between the two working memory based subgroups.

A broad relationship between lower working memory scores and a greater degree of other executive dysfunction was shown to exist in relation to the whole sample, as the scores of all working memory measures (except Digit Span Forward) were related to the degree of executive dysfunction. This suggested that overall this relationship was relatively robust and applied to all but one aspect of working memory. The different result for the Digit Span Forward test supported the model proposed by Engel et al. (1999), which suggested that short term memory has a more limited role to play in 'executive' processes.

Because the relationship over the whole sample seemed strong, the slightly weaker relationships between working memory scores and the degree of executive dysfunction that were demonstrated within each of the two working memory based subgroups were surprising. In particular, it seemed initially that the relationship was more consistent within the group whose working memory was not impaired. It was also the case however, that although there were considerably fewer participants in the group whose working memory was impaired (24 versus 71), the effect size of the relationship between the Working Memory Index and the degree of executive dysfunction within that group was considerably greater than for the group whose working memory was not impaired. Although this suggested that there was in fact a stronger link between Working Memory Index scores and the degree of executive dysfunction for those whose working memory was impaired compared to those whose working memory was not compromised, the more limited range of scores in the group whose working memory was impaired may have resulted in an artificially high effect size. It was therefore difficult to determine which (if either) of the two groups had the stronger relationship, but more importantly it was evident that some relationship

between working memory scores and the degree of executive dysfunction existed regardless of the integrity of working memory.

Although the weaker relationships between the degree of executive dysfunction and the various working memory subtests within the two working memory based subgroups was initially somewhat surprising when compared with the relationship within the whole sample, Engle et al.'s (1999) model of working memory may provide some explanation. Engle et al. suggested that it is the more complex working memory tasks that related most closely to other executive functioning. As the aggregate index is made up of all the aspects of working memory that are assessed by the subtests, this could be consistent with the fact that for those whose working memory was impaired it was only this aggregate index, which incorporates all elements of working memory, which was related to the degree of executive dysfunction. This possibility becomes more likely when it is considered that each working memory subtest addresses different working memory processes and any of these may have been both selectively impaired and have a differing degree of relationship with other executive functioning. Thus it was possibly not so surprising that for those with some impairment in working memory it was only the overall Working Memory Index that was shown to be significantly related to the degree of other executive dysfunction. Furthermore, it must also be considered that working memory (especially its executive processes) is not the only factor that underlies the successful completion of other executive tasks (Cohen, 1999). Thus for those whose working memory is impaired, these other factors may take on a more predominant role. Therefore in conjunction with the possible differential impairment of the various working memory processes this provides an additional reason why the correlation

between individual working memory subtests and other executive dysfunction may not be strong in those participants whose working memory was impaired.

For those whose working memory was not compromised however, individual differences in performance level and the strategies used, which are separate from the integrity of working memory, could explain the reduced relationship. It could also be, however, that for this group, the 'executive' elements of working memory were not required to any great degree in order to carry out the working memory tests, thus limiting the relationship between working memory and other executive functioning.

In general terms, however, a link between decreasing working memory scores and increasing degrees of executive dysfunction was demonstrated, although this relationship was stronger within the sample as a whole and may have been more robust for those whose working memory was impaired. Comparisons between the two groups formed on the basis of their working memory scores, also confirmed that lower working memory scores were associated with a greater degree of executive dysfunction.

The relationship between working memory and other specific categories of executive functioning was rather less clear. However, the trends suggested that fluency skills and reasoning abilities were the executive functions that were most often compromised, and this impairment could occur with or without associated working memory impairment. This is consistent with previous research which has suggested that in common with working memory, both reasoning (measured by the California Card Sorting Test) and fluency skills, utilise the dorsolateral prefrontal cortex, but these processes also involve other cortical regions which are not common to working memory (e.g., Elfgrin, 1998). Therefore, as these executive functions do not rely exclusively on the working memory network a dissociation of function would

be possible. This current study has also suggested that impaired planning and shifting abilities were more closely linked with a lower working memory. The neuroanatomical link between planning and working memory networks has been described previously (Dagher et al., 1999) and a similar, but not closer, association with working memory networks to that of fluency and reasoning was suggested. In contrast shifting, as measured by the Trails test (Stuss et al., 2001) showed an increased number of errors for those who had dorsolateral frontal lesions, but the same differentiation of lesion locality was not evident for the time measures on this test. In so far as working memory processes utilize the dorsolateral prefrontal cortex, this would suggest, contrary to the indications from this study, that the relationship between shifting and working memory should not be particularly strong.

Impairment in the inhibition category seemed to be most prevalent when working memory was not impaired, supporting indications that the Stroop test, used to measure inhibition, does rely on cortical areas or networks that are somewhat different to those activated by working memory tasks (e.g., Bench et al., 1993). These patterns of relationships between the executive categories followed, in general terms, the relationships between the categories that were discussed previously (see Chapter 5). In the previous analysis it was those categories most commonly impaired with some other category, in particular fluency, planning and reasoning, which are now also predominantly associated with working memory impairment. The one possible exception is the shifting category, which in this analysis seemed to be more strongly associated with working memory impairment than was previously suggested by the nature of its association with other executive categories. Together these two sets of results suggest that for those categories most commonly impaired in conjunction with

some other executive category (including working memory), they must share at least some part of their neural processing network.

Alternatively, the lack of any clear relationship between working memory and any other specific executive category is quite probably due to both the varying degree of overlap of cortical areas (e.g., Barbas, 2000) and processes (e.g., Stuss et al., 2002) involved in the different executive functions, and the variable importance of working memory in the other executive tasks. Along with these factors, there would also be a variety of other issues relating to the individual participant and how they perform each task, which could have a differential influence on performance on the other executive function tests.

Thus, it seems that an association has been established between working memory generally and more specifically those subtests where some mental manipulation is required and other executive functioning. Generally, lower working memory scores were linked with a greater degree of executive impairment, but there was some suggestion that these relationships maybe weaker when working memory was not compromised. More specifically working memory impairment seemed to be most closely related to impairment in the categories of shifting and planning. It is also evident, as proposed by Miyake et al. (2000), that working memory is a separable executive function that does however contribute to a varying extent to other executive function processes.

The following section will now examine how the extent and nature of executive dysfunction evident in this sample of participants with MS affects these same participants in their everyday lives.

## Chapter 8

### RESEARCH QUESTION FOUR

#### ***Does executive dysfunction impact on daily functioning in this community based sample of participants with Multiple Sclerosis?***

This final section will examine how executive dysfunction impacts on this sample of participants with MS in their daily lives. The measure that was used to assess everyday behaviour related primarily to those behaviours that characterize executive dysfunction. These were considered to be the most important as the above average general intelligence levels that characterized this sample of participants could be expected to help compensate for any difficulties associated with memory impairment. That is, unless memory impairment had reached dementia levels (beyond the levels indicated by most in this sample) the general intelligence levels required to initiate the use of memory aids were generally far exceeded by the participants in this sample. Unfortunately, if the impairment extended to executive dysfunction then the same ability to 'self help' could not be guaranteed. This is because one serious aspect of the behaviour that characterizes executive dysfunction is the inability of the person to recognize their problems, that is, their level of insight is considerably reduced.

Although the analyses conducted in the previous sections indicated that approximately 50% of this sample had some level of executive dysfunction, the majority of these participants were assessed with only one category of executive dysfunction. This suggested that the degree of executive dysfunction in this sample was generally not severe, however, there were a small number (8) who were

assessed with three or more categories of executive dysfunction. Therefore because there may be some number of participants in this community based sample who are unable to initiate self-help measures and, as discussed previously, because of the many other possible adverse consequences of such undetected behaviours as for example, impulsiveness and reduced reasoning skills, those behaviours characteristic of executive dysfunction were the focus of the following section.

This final research question was addressed first by way of analysis of the data from the Dysexecutive Questionnaire (DEX) and secondly by an assessment of the accuracy of the participants estimates of either frequency or time. The five behavioural factors which were considered to characterize executive dysfunction and were therefore addressed by the DEX, were established from the data obtained by Burgess et al., (1998). These were described as inhibition, intentionality, executive memory, positive affect, and negative affect, (described in more detail in Chapter 3) with higher scores suggesting a more frequent occurrence of that characteristic. These factors relate to everyday behaviours such as, for example, impulsivity, planning, temporal sequencing, euphoria and apathy, any or all of which can characterize those people with executive dysfunction. This analysis was therefore conducted to determine whether any behaviour characteristic of the dysexecutive syndrome was evident to the extent of impairing effective daily functioning in this sample, and which, if any, group of participants were most affected. It also enabled an assessment of the extent to which the participant was aware of any problems they may have.

The estimates that related to frequency or time were obtained from the answers given to five temporal questions that were outlined in the Method section (Chapter 3), and the estimates of the participants were compared with the estimates

of the 'others'. This enabled an assessment of how accurately the participant was able to judge frequency and time, an issue which could be important for those taking medication or even when organizing tasks that need to be completed in any one day.

## **DEX Questionnaire**

The scores for the DEX questionnaire were analysed on the basis of the five factors outlined above. As well as the levels of scoring on each factor, another important measure described as 'insight' was obtained from this questionnaire. This measure was obtained by comparing the participant's rating of their behaviour with the rating of the 'other' (a person who knows the participant well). This provided a good general indication of the extent to which the participant was aware of any undesirable behaviour resulting from executive dysfunction that they may have exhibited.

First, the scoring on each of the five factors was obtained for the sample as a whole, both for the participants and the 'others'. This enabled a comparison of the scoring levels of the factors in relation to one other and therefore the relative prevalence of the behavioural characteristics addressed by each of the factors.

The insight measure for each factor was then examined for the sample as a whole, and to determine whether a particular 'impairment type' group demonstrated more or less insight than any other group this measure was also examined within each of the four 'impairment type' groups that were described in Chapter 6, (*Group 1 – No, Group 2 – Memory, Group 3 – Both and Group 4 – Executive*). In keeping with previous analysis, and to determine whether working memory integrity affected the level of insight, the insight measure was also examined both within and between

each of the two working memory based subgroups that were described in Chapter 7, (*Group A – Impaired and Group B – Unimpaired*).

Finally, for the whole sample an overall ‘difference’ score between the participants and ‘others’ for each question was obtained to enable a comparison of the levels of ‘insight’ in relation to the particular behaviour that each of the questions addressed.

## **Results**

The means and standard deviations for the each of the five factors, for both the participants and the ‘others’ are shown in Table 8.1. Because there were a different number of questions that made up each factor, the means represent the mean score of the questions that make up the factor. The scoring scale for each question ranged from 0 to 4, with 0 representing no evidence of the particular behaviour addressed by the question, and 4 representing a significant problem with that particular behaviour.

Table 8.1

*Means (and Standard Deviations) of the scoring on each DEX Factor for the Participants with MS and ‘Others’*

Factors	MS	‘Others’
1. Inhibition	1.1 (0.5)	1.1 (0.8)
2. Intentionality	1.2 (0.7)	1.2 (0.9)
3. Executive Memory	0.8 (0.6)	0.8 (0.9)
4. Positive Affect	1.0 (0.6)	1.1 (0.8)
5. Negative Affect	1.2 (0.8)	1.2 (1.0)

Table 8.1 indicated that the scoring levels within each factor were equally low for both the participants and the 'others', although the variance was marginally greater for the 'others'. Interestingly it seemed to be the Executive Memory factor which scored the lowest of all the factors, suggesting that problems associated with the behaviours that characterized this factor were negligible.

As the scoring of the participants was the same as that of the 'others' for all but one factor, and the differences in the variance not substantial, it was not considered necessary to include a measure of insight in the following analysis. It was evident from Table 8.1 that lack of insight was not a significant issue, and that for the sample as a whole the self evaluation of behaviour by the participant was similar to the evaluation by the 'other'.

A one way multivariate analysis (MANOVA) was conducted to determine the effect of factor characteristics on the scoring levels for both the participants and the 'others'. That is, to determine whether the level of scoring of the participants and the 'others' was similar for each of the factors or whether there was some difference between the factors in the levels of scoring. A significant effect of factor characteristic was found,  $F(8, 938) = 4.24, p < .05$ , indicating some differences in the scoring levels of the factors. Analyses of variance (ANOVAs) were conducted on the factor scores for each of the two groups (participants and 'others') using the Bonferroni method of adjustment. Both were significant,  $F(4, 470) = 7.1, p < .001$  and  $F(4, 470) = 3.1, p < .05$  for the participants with MS and 'others' respectively, indicating some difference in the scoring levels of the factors for both groups. Post-hoc comparisons indicated that for the participants with MS, factors 1(Intentionality), 2 (Inhibition) and 5 (Negative Affect) were all scored significantly higher than factor 3 (Executive Memory) but no other comparisons were significantly different. For the

'others', only factor 5 (Negative Affect) was scored significantly higher than factor 3 (Executive Memory) and no other comparisons were significant.

Therefore, although the Executive Memory factor was scored significantly lower than the other factors by both the MS participants and 'others', suggesting almost no evidence of any of the behaviours that characterize Executive Memory, overall it seemed that behavioural problems were minimal and lack of insight was not an issue for the participants in this sample.

As earlier analyses have suggested however, it was possible that within smaller 'impairment type' sub groups a different picture may emerge, and this was now explored. The means and standard deviations for each factor for both the participants and 'others' in the four 'impairment type' groups are shown in Table 8.2.

This Table showed that for each group the mean score for the questions in each factor remained low, with the Executive Memory factor again scoring the lowest of the factors. This reinforced the indications from the data of the whole sample that there were minimal behavioural problems for the participants in this study. This table also indicated that for every group except *Group 3 - Both* there were some factors whose questions were scored more highly by the participants. In particular the 'others' rating ( $M = 0.4$ ) for the negative affect factor in *Group 4 - Executive* was considerably lower than the participants rating ( $M = 1.1$ ). This difference could have suggested a lack of 'insight' in relation to that factor, however in this instance it seemed that the participants were more concerned about those behaviours that characterized the negative affect factor than the 'others' were.

This pattern of scoring is not typical of those with executive dysfunction, and was not evident in *Group 3 -Both*. For this group the participant's scores were lower

than the 'others' scores for all five factors, suggesting some lack of insight for the participants in this group.

Table 8.2

*Means (and Standard Deviations) of the scoring on each DEX factor for the Participants with MS and 'Others' in the four 'Impairment Type' Groups*

	'Impairment Type' Groups							
	1. No		2. Memory		3. Both		4. Executive	
	MS	'Others'	MS	'Others'	MS	'Others'	MS	'Others'
1.	1.1 (.5)	1.1 (.7)	1.2 (.4)	1.0 (.6)	1.1 (.6)	1.2 (.9)	1.0 (.3)	0.9 (.7)
2.	1.2 (.6)	1.0 (1.0)	1.0 (.5)	1.1 (.8)	1.2 (.7)	1.4 (1.0)	1.3 (.8)	1.0 (.6)
3.	0.8 (.5)	0.7 (.7)	0.8 (.5)	0.5 (.7)	0.9 (.6)	1.1 (1.0)	0.7 (.7)	0.5 (.5)
4.	1.1 (.5)	1.3 (1.0)	1.0 (.6)	0.8 (.6)	0.9 (.6)	1.1 (.8)	1.0 (.6)	1.0 (.7)
5.	1.3 (.7)	1.1 (.9)	1.3 (.8)	1.5 (1.1)	1.2 (.8)	1.4 (1.0)	1.1 (.7)	0.4 (.4)

*Note.* 1= Inhibition, 2 = Intentionality, 3 = Executive Memory, 4 = Positive Affect, 5 = Negative Affect. No = No Impairment, Memory = Memory Impairment Only, Both = Memory Impairment and Executive Dysfunction, Executive = Executive Dysfunction Only

Within each of the four groups a one-way multivariate analysis of variance (MANOVA) was conducted to determine the effect of MS (MS and 'others') on the scoring on each of the five factors. None of these analyses came close to significance ( $F < 1.07, p > .41$ ), indicating that there was no evidence of a significant lack of insight for the participants with MS in any of the four 'impairment type' groups.

In keeping with previous analysis the scoring within each of the two working memory based subgroups, that is *Group A - Impaired*, and *Group B - Unimpaired*, was also examined to determine whether working memory integrity had any influence on the extent of any behavioural problem or the level of insight. The means and standard deviations for the scoring on each factor for both the participants and ‘others’ within *Group A* and *Group B* are shown in Table 8.3.

Table 8.3

*Means (and Standard Deviations) of the scoring on each DEX factor for the Participants with MS and ‘Others’ within each of the two Working Memory based Sub-Groups*

Factor	Working Memory Sub-Groups			
	Group A – Impaired		Group B – Unimpaired	
	MS	‘Others’	MS	‘Others’
1.Inhibition	1.1 (0.6)	1.4 (0.9)	1.1 (0.5)	1.0 (0.7)
2.Intentionality	1.1 (0.7)	1.4 (1.0)	1.2 (0.7)	1.1 (0.9)
3.Executive Memory	0.8 (0.7)	1.1 (1.0)	0.8 (0.5)	0.7 (0.8)
4.Positive Affect	0.7 (0.6)	1.1 (0.9)	1.1 (0.5)	1.1 (0.8)
5.Negative Affect	1.0 (0.8)	1.3 (1.0)	1.3 (0.7)	1.2 (1.0)

*Note.* Group A- Impaired = Working Memory Index scores < 85, Group B - Unimpaired = Working Memory Index scores => 85.

While Table 8.3 showed that the scoring levels on the questions within each factor was still low for each of these two groups, one notable difference was that for *Group A - Impaired*, the participant’s scores were lower than the ‘others’ scores for every factor. In contrast for *Group B - Unimpaired* the participant’s scores were all greater than (or equal to) the scores of the ‘others’. This suggested that for those

whose working memory was impaired their level of insight may be somewhat reduced.

One-way multivariate analysis of variance (MANOVAs) were again conducted within each of these two groups to determine whether there was any significant effect of MS (MS and 'Others') on the scoring for any of the five factors. Neither MANOVA was significant ( $F < .67$ ,  $p > .65$ ), which suggested that levels of insight were not significantly compromised within either of these two groups.

Therefore for this sample and within each of the sub groups that were examined the mean scoring levels for the questions that make up each factor were at the low end of the scoring scale (0 to 4) indicating that behavioural problems were not an issue for the participants in this sample. It was also evident from the analyses that the participants on average were well aware of their behaviour in relation to all the factors examined.

Finally, to examine on a more individual level whether any behavioural problems existed which had been masked by the group analyses, the percentage of participants and significant 'others' who scored 3 or 4 (scale 0 to 4) on any one question was examined, along with the difference in these percentages for each question. Scores of 3 or 4 were considered to represent the level at which there would be a problem with the behavioural issue that the question addresses (Burgess & Robertson, 2002).

As indicated by the previous analyses, the percentages of both the participants and 'others' who considered any of the behaviour assessed by the DEX questions to be at problem level was generally very low. Question 15, relating to not being able to sit still for any length of time, was the question most often scored highly by participants with 17% scoring this question at level 3 or 4. It was however, an issue

which was recognized almost equally often (16%) by the 'other'. Question 8, relating to the negative affect factor, was scored highly most often by 'others' overall, with 23% scoring this question at level 3 or 4, but was scored at these levels considerably less often by the participants (14%). The question which showed the greatest discrepancy between self perception and others ratings was Question 2 which related to impulsive behaviour, and was one of seven questions which made up the Inhibition factor. For this question only 4% of the participants scored themselves at level 3 or 4 compared to 21% of the 'others' who considered this issue to be somewhat of a problem for the participants.

Therefore, it seemed from these results that the behaviours addressed by this questionnaire did not characterize this sample of participants to any significant degree. As there was also little evidence of a lack of insight it would be expected that the impact of any executive dysfunction on the competence of daily functioning in this sample would be minimal.

## **Temporal Questions**

The five questions that were asked in this assessment were as follows:

1. How long do you think it would take to blow up a standard party balloon?
2. How long do you think it would take to boil a jug half full with cold water?
3. How many advertisement breaks do you think there are on television during the news hour – between 6.00pm and 7.00 pm?

4. How many times do you think the 13<sup>th</sup> fell on a Friday over the last 3 years – that is 1999 plus 2000 plus 2001?
5. How long do you think it would take a professional window cleaner to clean the windows of an average three bedroomed house on the outside only?

The accuracy of the responses to these five temporal questions was assessed by comparing the participant's estimations to those of the 'others' for the complete sample, within each 'impairment type' group and within each of the two subgroups formed on the basis of the working memory scores. As the analysis of the DEX questionnaire indicated that levels of 'executive' related behavioural problems were relatively low, it was not expected that a significant difference between participants and 'others' would be found on these temporal questions. Therefore, it was of interest to extend the analysis to determine the 'impairment group' distribution of those participants whose estimations were significantly higher or lower than the 'others' on one, two, or three or more questions.

### ***Results***

Because the responses to each of the questions (except Question 4) could only be estimates (not right or wrong) the means and standard deviations for the participants and 'others' on each question are presented in Table 8.4, along with the numbers of people who answered each question. This Table indicated that apart from a longer time estimation by the participants for question one and a smaller variance within the estimations of the 'others' for questions one, two and to a lesser extent question three, the mean estimates for the participants and 'others' were similar.

Table 8.4

*Means (and Standard Deviations) of the Estimates to each Temporal Question for the Participants with MS and 'Others'*

Question	MS			'Others'		
	N	M	SD	N	M	SD
1. – Time to blow up a Balloon (secs)	95	124.8	(248.3)	94	47.1	(99.5)
2. – Time to boil a jug (secs)	95	172.0	(141.7)	91	160.9	(86.1)
3. – Number of advert. breaks	94	5.5	(3.9)	92	5.2	(3.0)
4. – How many Friday 13 <sup>th</sup> in 3 years	95	4.7	(3.0)	91	5.1	(3.2)
5. – Time to clean Windows (mins)	95	75.2	(50.7)	92	77.7	(51.3)

*Note.* N = Number of Participants, M = Mean Estimate, SD = Standard Deviation, s = seconds, m = minutes

For the complete sample independent group t-tests for each question indicated a significantly different mean estimation only in relation to question one, which asked how long it would take to blow up a standard party balloon,  $t(185) = 2.82$ ,  $p < .01$ .

Within each impairment type group the only significantly different estimation was found in *Group 3 - Both*, again only for question one,  $t(132) = 2.95$ ,  $p < .01$ .

When any differences in temporal judgment between the two working memory based subgroups was examined, it was found that within *Group A - Impaired* the results mirrored those of the whole sample in that only question one was significantly different from the controls,  $t(113) = 2.75$ ,  $p < .05$ . For *Group B - Unimpaired* no significant difference between the participants and the 'others' was found for any question. From these results it would appear that compromised temporal estimation,

as far as it was measured by these questions was not an important factor for any participant group.

Participants' estimations were then assessed as being inaccurate if they were more than plus or minus one standard deviation from the mean of the 'others' estimation, or accurate if they fell within the range of plus or minus one standard deviation from the 'others' mean, and a further comparison between the four 'impairment type' groups was made. The numbers in each group, and the percentage of the group, that had one, two or three or more impaired estimations are shown in Table 8.5.

Table 8.5

*Accuracy of Temporal Estimation by 'Impairment Type' Group*

Number of Inaccurate Estimations	'Impairment Type' Groups			
	1. No	2. Memory	3. Both	4. Executive
None	9 (33.4%)	7 (41.2%)	11 (25.6%)	3 (37.5%)
One	12 (44.4%)	6 (35.3%)	13 (30.2%)	3 (37.5%)
Two	6 (22.2%)	3 (17.6%)	11 (25.6%)	0 (0%)
Three or more	0 (0%)	1 (5.9%)	8 (18.6%)	2 (25%)

*Note.* No = No Impairment, Memory = Memory Impairment Only, Both = Memory Impairment and Executive Dysfunction, Executive = Executive Dysfunction Only

The only notable differences between the groups that were evident in Table 8.5 was the lower percentage of participants in *Group 3 - Both* with no inaccurate estimations and a greater percentage of participants in both *Group 3 - Both* and

*Group 4 - Executive* which have three or more inaccurate estimations. Conversely there was shown to be a lower percentage of those with three or more impaired estimations in *Group 1 - No* and *Group 2 - Memory*.

As this distribution suggested that there could be some difference between the four groups regarding those participants whose inaccurate estimations were more general, the analysis was extended to examine this possibility. A Chi Squared analysis using the four 'impairment type' groups and the number of participants with three or more inaccurate estimates was not significant,  $\chi^2(3, N = 95) = 7.555, p = .056$ , however, the effect size was moderate. Therefore although there was not a significant difference in the distribution of those with three or more inaccurate temporal estimations, there was a tendency for those who were inaccurate on three or more of the five temporal estimates to belong to one of the two executive dysfunction groups

## **Summary and Discussion**

Overall the scoring on the questions within each of the five factors was similarly low throughout the sample and the subgroups. Executive Memory was consistently the lowest scoring of the five factors, indicating a lack of evidence of any of the dysexecutive behaviour that characterised that factor in particular. Although there was a tendency for those whose working memory was impaired to show a greater lack of insight than those whose working memory was unimpaired, lack of insight was not generally an issue for the participants in this sample. This was also reflected in the temporal estimations, which were shown to be reasonably accurate.

The measure of everyday behaviour that was used in this study was the Dysexecutive Questionnaire (DEX) in conjunction with five temporal judgment

questions. For this sample the results from the DEX questionnaire were found to lie somewhere between the results from the clinical population used in the validation of the test (Burgess et al., 1998), and those found in a study using the same assessment with a non-clinical sample (Chan, 2001). In the former, the behaviour ratings of the clinical population were significantly lower than those obtained from a population of significant others. In contrast to this, both the control group used in the Burgess study, and the non-clinical sample used in the latter study, saw non-significant 'difference' scores but a tendency for the participant to score more highly (perceiving a greater problem) in relation to themselves than the significant other did.

In keeping with the relatively mild to moderate executive dysfunction found in this MS sample, the difference in scores between the participants and the 'others', for this sample as a whole were not significant for any factor, and generally the 'others' scores tended to be similar to those of the participants. When the same analysis was conducted within each of the four 'impairment type' groups and the two working memory based subgroups, some difference between the groups was evident. Although there was no significant lack of insight for any group, it was notable that within the group with no impairment and the group whose working memory was not impaired, participants scores tended to be higher than those of the 'others'. In contrast for those in the group with both memory impairment and executive dysfunction and the group whose working memory was impaired the participant's scores were consistently lower than the 'others' scores. Therefore for those in this sample with no impairment their scoring patterns were similar to the non-clinical samples in both the Chan (2001) study and the Burgess et al. (1998) study, where as for those with both memory impairment and executive dysfunction and those whose working memory was impaired the pattern of scoring was more similar to the clinical sample used in

the study by Burgess et al. (1998), although the differences between the participants scoring and 'others' scoring in the current study were not significant.

It would seem then that the proposed 'insight' measure was not particularly revealing in this sample overall, in that there was generally no significant difference between the participant's ratings and the ratings of 'others'. Although some lack of awareness was indicated within some groups, it would seem that this measure would be more informative in those more severely impaired in their executive functioning. In this sample the scoring patterns in relation to the factors tended to be more informative.

Although the relative scoring on each of the factors was broadly similar within each of the groupings that were examined, there was one interesting difference. While the Executive Memory factor was most often the lowest scoring factor, for the group whose working memory was impaired it was the fourth lowest scoring of the five factors. Although this difference was not great it could indicate that this factor may bear some relationship to the working memory measures that were used in this research.

Another point of interest was that while the Chicago Multiscale Depression Inventory had indicated that depression was not an issue for those participants in this sample it seemed that for the DEX questionnaire the negative affect factor was scored most highly (greatest problem) in all but the group whose working memory was impaired. Although this possibly suggested some discrepancy between the two measures, the two questions that made up the Negative Affect factor related to being lethargic and being unable to show emotion. Therefore it was evident that for the first question at least a high score would have been more the result of MS symptoms than depression as such. Again this illustrated that in order to make an accurate assessment

of the levels of depression, its components do need to be examined separately, with disease symptoms in mind, for this and other clinical samples.

Of the three 'non-affect' factors that could have possibly been related to the D.KEFS analysis, the Executive Memory factor usually had the lowest score of the five factors, but the Intentionality factor most often scored at the second highest level after the negative affect factor. However most of the questions within this factor addressed issues relating to planning for the future and making decisions, thus again the scoring could well have been influenced by the many unknowns associated with Multiple Sclerosis rather than any behavioural issues.

The third of the three 'non-affect' factors was Inhibition, which included both the question that was most often scored at level 3 or 4 by the participants and the question with the greatest difference in these scoring percentages. For this factor, although the question most often scored highly by the participants related to being restless, again possibly a consequence of MS, the question with the greatest difference between the percentage of participants and 'others' scoring at levels 3 or 4 related to impulsivity. For this issue there was therefore little doubt that it did address an element of behaviour that was evident in this sample of participants with MS but was not well recognized by them.

It therefore seemed overall that many of the issues that made up the executive factors that the DEX addresses were not reflected in the results of the D.KEFS assessment. This may have been a testament to the gulf between test scores and real life problems, however, it could also be a consequence of lack of equivalence of the constructs.

Interestingly, although the behavioural issue addressed by one question in the 'executive memory' factor was regarded as a problem (scoring 3 or 4), by 10% of the

participants, rather short of the 17% of 'others' who considered the same behaviour a problem, in general, the behaviours characteristic of this factor were not rated at problem levels. As 25% of this sample was performing at impaired levels on the working memory measures of the Wechsler Memory Scales-III, this differential could again be due to the discrepancy between test scores and real world manifestations of a problem. However, the question that scored most highly in this factor related to getting events etc. muddled up – a phenomenon that should have had some impact on, and therefore shown some equivalence with, cognitive test results. In contrast, the other two questions that made up this factor related to confabulation and perseveration respectively, which in terms of the D.KEFS scoring would both have been categorized differently. This suggested that categorizing or labeling differences may have accounted for the seeming lack of relationship between the most commonly impaired D.KEFS categories and the relative scoring of the behavioural factors addressed by the DEX questionnaire.

However, in spite of the possible differences in the categorization of behaviour, overall it seemed that the level of scoring and the non-significant difference between the participants and the 'others' ratings on the DEX questionnaire would have reflected reasonably accurately the level of everyday problems associated with the level of executive dysfunction assessed in this study. Also it seemed that the 'insight' measure would only be 'insightful' when the severity of executive dysfunction was more considerable than that indicated in this sample. The potential utility of the 'insight' measure was indicated, however, in so far as working memory is an indicator of the degree of executive dysfunction, in that the group with lower working memory scores also produced a greater difference between the lower scoring

of the participants and the higher scoring of the 'others' than those whose working memory was not impaired.

Another aspect of executive functioning, which can affect efficient daily functioning, is temporal ordering and frequency judgments. These factors have in fact been shown to be impaired in some samples of those with MS (Fischer, 2001), but studies relating to this domain are limited. However, as they seem to be another characteristic of executive dysfunction, it was considered that these abilities should be examined within this sample of those with MS. These abilities were assessed in this study by way of a series of five questions, which required some temporal judgment of either frequency or duration. It was obvious from the comparisons between the 'others' and the participants that any temporal judgment impairment was certainly not global and the only trend evident was a disproportionate (but not significant) number of participants with unrealistic estimates for three or more questions, in the two groups with executive dysfunction. The one question that was judged most inaccurately by the participants related to the length of time it would take to blow up a standard party balloon. Although it was emphasized during the assessment that the question was general and did not relate to the participant specifically, it was the researcher's impression that the answer given did often relate to personal experience. As a number of those with MS were not as physically able as those in the control group, personalizing the estimate may have accounted for the discrepancies in estimated time seen in relation to this particular question.

Overall however, the trend evident in this sample suggested that any problems with temporal judgment were a failing in some 'executive' skill, and the results supported the view that impaired temporal judgment is related to that group of problems, rather than being a problem that may appear randomly in those with MS. It

was also evident however, that in this sample, compromised temporal judgment was not a significant issue.

Therefore, in spite of the seemingly limited value of the DEX questionnaire in relation to this sample, it has, in general terms, supported the test results. That is, in keeping with the relatively mild or moderate levels of executive dysfunction indicated by the D.KEFS assessments, the 'real consequences' of the assessed dysfunction has been shown to be minimal. Thus these results confirmed that the assessed level of executive dysfunction in this sample of participants with MS did not manifest in 'problem' behaviours or impact on daily functioning to any significant degree. Associated with this comparatively low level of scoring on the DEX questionnaire, evidence was also provided that where moderate behavioural problems did exist they were also reasonably well recognized by those affected. This was a very important conclusion for this community based sample as it suggested that it was probable that there were not numbers of those with MS in the community living with diminished awareness and therefore at a level of independence that is not appropriate. Additionally, as long as this is the case then measures to compensate for any difficulties that arise can be initiated and put in place.

## **Chapter 9**

### **GENERAL DISCUSSION**

First it must be said how much of a privilege it was to be conducting this research with such a willing group of participants. The collection of data for this research was a very time consuming (taking up to 6 hours), demanding and often tiring process for the participants, which could also have made the researcher's job somewhat uncomfortable. However, the process was more of a pleasure due to the friendly and welcoming nature of the participants who didn't ever need any encouragement to contribute maximum effort to each task.

The preceding chapters have indicated that levels of general ability in this sample of participants with MS were generally above average. While no impairment on memory measures was evident for the sample as a whole, a considerable number of individuals were subsequently shown to have difficulty with visual memory in particular. Fluency and reasoning were the executive categories most frequently impaired, and although there were a considerable number of different individual profiles, the degree of executive dysfunction was generally low in this sample.

Somewhat surprisingly processing speed was shown not to be compromised, but a simple test of attention was 'impaired' in some. When links to executive functioning were examined, it seemed that it was only working memory which indicated any relationship with other executive functioning. It was then demonstrated that lower working memory scores were associated with a greater degree of executive dysfunction, but there was no consistent or strong relationship between working memory and any other specific executive category. Finally, in accord with the low degree of executive dysfunction seen in this sample of participants with MS, the

measure of associated behaviours indicated that the participants in this sample did not exhibit any dysexecutive characteristics and their level of insight was not reduced.

It was evident to the researcher during the course of this study that this research included a good representation of the people affected by Multiple Sclerosis in New Zealand. This impression related to both the demographic characteristics of those that participated in this study, as well as to coverage of the many manifestations of the disease. The wide range of values that characterised the variables of interest in this study subsequently endorsed this impression. Thus, as the numbers in this study made up approximately 2.5% of the MS population in New Zealand, it was reasonable to assume that this sample was a good representation of those with MS in New Zealand. The one possible difference between those in this study and the broader MS population in New Zealand would be in relation to those who are more severely affected by MS, both physically and cognitively. Although this study included a small number in that category, for pragmatic reasons their numbers were limited. However, it is believed that this group constitutes only a minority of those with MS in New Zealand.

In presenting the characteristics of this sample of participants with MS, this study also demonstrated the advantages of using the special purpose Chicago Multiscale Depression Inventory. It was quite clear, when each scale was examined, that any indication of depression given by the aggregate score for this sample, was the result of an elevated Vegetative Scale score which included factors which were also symptomatic of MS. Therefore there has been shown to be an obvious advantage in using this specialized type of measure for MS, and similar clinical populations, as it makes clearer whether the obtained depression scores are indicative of a level of

depression per se or whether they are, as in this study, primarily the result of other disease symptoms.

In 1996 Rao suggested that some degree of cognitive dysfunction could be found in 43% to 65% of those with MS. For those with MS New Zealand, this study would suggest that 65% is somewhat of an overestimate even as an upper limit. However, when consideration is given to the probable under representation in this sample of those severely affected by MS, along with the numbers whose predicted levels of general ability suggested some cognitive decline which had not deteriorated to clinical levels, it could be that 65% is not too high a figure to put on an upper estimate of numbers of those with MS who may have some cognitive impairment.

Overall the general ability levels of the participants in this sample were above average, but within this group there were a number of participants whose performance had deteriorated significantly. Given the current levels of performance this would suggest that prior to MS the level of general ability for many in this sample would have been extremely high. Although in a minority of cases the deterioration may have been the result of compromised motor skills, the suggestion of a high level of premorbid performance is supported by the Australian study (Mathias et al., 2004), which found the scores predicted by the Wechsler Test of Adult Reading to be somewhat conservative. Thus for a number in this sample the recognition of declining cognitive skills would be a factor that must only add to the numerous personal frustrations that this disease brings.

Memory impairment was more evident in this sample than impairment on general ability measures, and although no difference was found between performance on long-term and short-term memory measures, there was a difference seen between visual memory and auditory memory. This difference between a higher auditory

memory performance and lower visual memory performance was not evident in those who had no impairment, therefore in so far as this group with no impairment could be regarded as a control group, it adds further support to the modality differences demonstrated in this study, compared to the results of the study by Fischer (Fischer, 1988). Based on a similarly lower visual memory performance compared to auditory memory performance of the control group used in the Fischer study, and the resulting non-significant group x modality interaction, the lower visual scores of that sample of participants with MS were not considered to represent a modality difference in memory performance. This current study has however demonstrated a modality difference in those with memory impairment, and as this difference remained constant over both short term and long term memory it suggested that for those with MS, memory impairment is either selectively related to the visual modality, or visual memory is more severely compromised than auditory memory. As the optic nerve is often a primary target of the degenerative processes of MS, the relationship between optic nerve damage and the level of visual memory impairment could be the focus of future research.

The level of executive dysfunction and the detailed profiles of executive dysfunction revealed in this sample of those with MS was a testament to the usefulness of the Delis-Kaplan Executive Function System. Whilst it is not always necessary to know the nature of executive dysfunction in the detail outlined in this study, if the assessment of executive dysfunction is limited, as discussed previously, there is always the danger of allowing some problems to remain undetected with the resulting possibility of undesirable consequences. This of course is a greater or lesser issue depending on the nature and the implications of the dysfunction.

If there are any limitations to the D.KEFS assessment it would be that there was no test that targeted working memory specifically. Rather, the battery included tests that required a varying degree of working memory involvement in order to successfully complete the task, but it was not possible to isolate the specific working memory contribution. Presumably in a clinical setting it would be sufficient to be able to gauge proficiency levels generally rather than know exactly the cause of the problem. However, in a research setting where it was desirable to be able to assess the different categories of executive functioning separately, this omission was regrettable.

The advantage of using the different levels of analysis for this heterogeneous clinical population was also evident in this study. Whilst levels of impairment on general ability measures remained low whether the analysis was based on the entire sample, 'impairment type' subgroups or was at an individual level, the same could not be said of the memory assessment. The method frequently used in previous research, where the means of the entire sample were used as an indication of impairment or otherwise, in this study suggested that this sample of participants with MS were not impaired on any memory measure. However when smaller subgroups were formed it became evident that there was at least one group of participants who were in fact impaired on all memory measures. When participant's scores were examined on an individual basis a further increase in the number impaired was revealed. Although it is not new to reveal that the individuals who make up a group can perform at levels that are at variance with the average of that group, the uniqueness of the MS population is, that unlike most human sub-populations, there is no 'typical' or average person with MS. This makes the use of the 'average' of a sample of participants with MS rather more meaningless than it would usually be.

One testament to the fact that it is difficult to generalize about those with MS, which was illustrated in this study, was the performance on the Attentional Capacity Test. Contrary to previous suggestions which had indicated that it was in the complex speeded attentional tasks where some limitations can be seen in those with MS, this simple test of attention revealed some level of impairment in this sample. It was even more surprising to find that the ability to pay attention seemed to have no selective part to play in executive functioning. Although not reported in this study subsequent analyses were conducted on this measure and contrary to the initial indications attention was shown to have a significant part to play in executive functioning. This relationship did however appear to become distorted when either memory alone or executive functioning alone were impaired, indicating an overriding influence of specific areas of impairment in the smaller groups, on the relationships involving this measure.

Likewise, it was surprising that no significant decrement in information processing speed was demonstrated. For this variable the mean processing speed (slope) did suggest a slightly slower speed for the two groups with executive dysfunction, but any difference between these two groups and the two groups with no executive dysfunction was not significant. Again further analysis was conducted but not reported, and it seems a link with executive functioning and working memory in particular did exist.

Although no clear link has previously been demonstrated between executive dysfunction and other cognitive impairment, the indications of this study were somewhat of a surprise, in that it was unexpected to see just how unrelated most of these cognitive processes were. The one exception was of course working memory which, being an executive function category itself, could have been expected to show

some link with other executive categories. However, the multiplicity of executive dysfunction profiles found in this study indicated that the integrity of executive functioning is not a product of working memory alone. The results instead lent support to those studies that concluded that working memory was a differentiable executive function. There is also no doubt however, that working memory does contribute, to a greater or lesser degree, to most other functions that have been considered 'executive'.

In terms of the various theories of executive functioning, this study suggested that it would be reasonable to assume, in so far as Spearman's 'g' represents those 'reasoning' skills that are part of ones executive behaviour, there will be a relationship between executive functioning and Spearman's 'g'. However the link between Spearman's 'g', which is regarded as the factor which underlies all other cognitive skills, and working memory, is probably closer than the relationship between 'g' and other categories of executive functioning. This is because working memory processes are also more generally implicated in other executive processes than are any other specific executive categories.

The element of control features in many theories of executive functioning, and if this equates to 'effortful' as opposed to 'automatic', again it obviously is an integral feature of executive functioning. However this is a very broad term and can be seen in the complete range of processes required to execute a task, from the (relatively) initial selective attention, through to shifting focus if necessary, maintaining attention, inhibiting irrelevant factors and all monitoring, updating, sequencing and manipulating processes required to facilitate task completion. Therefore if the failure of control as a process is behind the difficulties participants found with the D.KEFS tests, what is difficult to understand or explain is the wide variability in task

performance both within and between participants. Whilst control per se may be a major function of the frontal lobes, it is hard to imagine that 'control' as a process, has quite so many facets that it can provide the answers to the multiplicity of profiles of executive dysfunction seen in this study. Although the five 'control' processes outlined by Stuss et al. (1995), and evidenced in the many aspects of attention, go some way to differentiate the separate processes that may collectively constitute 'executive control' and thereby executive functioning, it still does not seem to provide the complete answer.

It could be that a multi process model such as that proposed by Fuster (2001) provides a more likely explanation of the multiple patterns of results. This theory proposes that the primary function of the frontal cortex is that of temporal organization. It is proposed that this primary function is subordinated by temporal integration processes, which in turn are facilitated by various contributing processes including attention, working memory, a prospective element (preparing for action) and control (monitoring), all of which are linked over time to achieve a goal. The multifaceted nature of this model seems to more readily provide multiple possible points of break down, in terms of both process or temporal ordering, thereby providing a seemingly more feasible explanation for the diverse set of results. In this model, focusing attention is the first stage in a chain of events that activates the neural networks necessary to access and bring on line relevant items from memory. At this stage the operational construct is working memory, which triggers anticipatory networks that prepare for the appropriate behaviour, which is then constantly monitored in relation to the achievement of a goal. Although this sequencing of events may appear somewhat different to, for example, an embedded process model of working memory, the primary difference, I would suggest, is the

focus of the model. The working memory model begins with a passive memory store an aspect of which then becomes the focus of attention and is utilized and controlled by a 'central executive' – all considered part of working memory. In contrast Fuster's model is an explanation of the function of the frontal lobes, which, in describing their influence, separates out the various processing stages, which in fact are very similar to those in the working memory model, but extend further to the monitoring of ongoing behaviour. Although, unlike other models, the primary emphasis in the Fuster model is the temporal integration of the various processes, other differences appear to be more those of definition or construct boundaries than major process differences.

Although most models of working memory show a strong relationship between memory and working memory, somewhat counter intuitively, working memory performances of those in this sample, seemed often to bear no relationship to performances on general memory measures. However the relationship between working memory and other executive functions meant that a poor general memory could be compensated for, in terms of the level of executive functioning, by a good working memory. Conversely a good general memory did not preclude executive dysfunction if working memory performance was comparatively lower. These relationships can best be illustrated by the following case studies:

**Case 1:** This participant in general terms was an example of someone with high memory scores in conjunction with high working memory scores. She was 56 years of age, lived alone, had completed 11 years of education and had a trade/professional (non-tertiary) qualification. She first noticed symptoms now recognizable as the beginnings of MS 29 years ago, the course of her MS was secondary progressive and her current Expanded Disability Status Scale (EDSS)

rating was 6.5 (Scale range = 0 – 10). Her Chicago Multiscale Depression Inventory (CMDI) scores (standardized mean = 50) were 64 (vegetative scale), 44 (evaluative scale), 56 (mood scale) and 55 (total CMDI), slightly on the high side, and she was not taking any medication. The memory scores for this participant ranged from 105 (Recognition), 116 (Immediate Memory), to 118 (General Memory) and 124 (Working Memory). Her Verbal IQ was 114, PIQ was 134 and FSIQ was 124, making all cognitive tests scores well above average. The processing speed slope was 0.02 (sample mean = 0.074) and her ACT score was 22 (sample mean = 18.68), also both better than the average. Needless to say this participant was a good example of someone with good overall cognitive ability including equally high working memory and general memory scores. In line with these other results she did not show any signs of being impaired in any category of executive functioning and had recently returned to University to study.

**Case 2:** In contrast this second participant, at 78 years 8 months was considerably older than case 1, though all tests were age adjusted, therefore comparisons should be possible. Similar to case 1, this participant was also female, lived alone, had 11 years education and had completed a non-tertiary qualification. She first experienced symptoms typical of MS 54 years ago, again a significant difference from case 1, however her current EDSS rating was the same as the previous participant at 6.5, and the course of her MS was also secondary progressive. This participant did however take medication (Rivotril). The CMDI scores for this participant were somewhat lower than those for case 1 at 45 (mood), 44 (evaluative), 36 (vegetative) and 41 (CMDI total), but her general memory scores were similar at 110 (Recognition), 120 (Immediate Memory), 118 (General Memory), but working

memory was considerably lower at 93. The VIQ score for this participant was similar to case 1 at 104, however PIQ was considerably lower (107) and FSIQ was somewhat lower (106). Processing speed was also slower, the slope gradient being 0.06, as was her ACT score of 16. Memory scanning rate did not differ significantly between the various age groups of the control group, so presumably age is not the underlying factor influencing the processing speed differential. However, there were found to be some disease variables that correlated with the age differential found in the sample of participants in relation to the ACT scores, so less can be made of that difference in the two cases. This participant, although not officially working, still led a very active life (especially mentally), participating to a very large degree in many community activities.

Although her primary memory scores were as high, or higher, than those of case 1, her Performance IQ and processing speed were somewhat lower. The Performance IQ score was largely influenced by the lower Perceptual Organization Index score, a pattern sometimes associated with MS, but not necessarily related to executive functioning. However the slower processing speed does possibly link with the assessed executive dysfunction which in this case related to the single category of 'planning'. Although the degree of executive dysfunction for this participant was limited, quite probably due to her above average results on most other measures, her lower working memory score would have correctly signaled some executive impairment. In this case the problem was also associated with a slowed memory scanning speed, a relationship which is also likely to be common. Therefore, although the general memory scores were high for this participant, the comparatively lower working memory score did correctly indicate some degree of executive dysfunction.

**Case 3:** The third example, at 17 years 2 months of age was the youngest participant in this study. She had completed 10 years of education, without achieving any qualifications. She had been diagnosed with relapsing/remitting MS and believed her initial symptoms began 10 years ago. Her CMDI scores were high at 76 (mood), 112 (evaluative) and 92 (vegetative), giving a CMDI total score of 103. She was taking medication (Ibuprofen, Paradex and Tegretol), was currently unemployed and had an EDSS rating of 6.0. Her WAIS-III indices showed the reverse trend to most other participants, with a PIQ score of 100 outperforming the VIQ score of 88. FSIQ was 93. The memory scores for this participant were lower than most at 59 (Immediate Memory), 66 (General Memory), 80 (Recognition) but a higher 91 for working memory. In spite of her low general memory scores, this participant was assessed as having only one category of executive dysfunction, and that was 'reasoning'. Her processing speed slope was 0.12, which was comparatively slow, and her ACT score, at 13, was well below average. This participant then was an example of someone whose general memory scores were very low, but, in spite of those scores, a considerably higher working memory score limited the assessed executive dysfunction to only one category.

**Case 4:** In contrast to case 3, the final example is a male of 64 years 10 months of age, and similar to the previous case had had 9 years of education but had no formal qualifications. He had primary progressive MS, and first noticed relevant symptoms 4 years ago. His EDSS score was lower than the previous example at only 3.5. He was taking medication for blood pressure but nothing for his MS, and he described his occupation as a retired farmer. His CMDI scores were in the average range, 42 (mood), 48 (evaluative), 47 (vegetative) and 48 (CMDI total), all

considerably lower than the previous participant. WAIS - III measures were also more closely allied to the expected performance pattern, with VIQ (92) being considerably higher than PIQ (76). FSIQ was 84. However, in common with the previous participant his memory scores were in the 'impaired' range and were as follows: 82 (Immediate Memory), 74 (General Memory), 80 (Recognition), but in contrast to the previous example his working memory score was only 76. Although the general memory scores of this case were slightly above those of the previous case, in contrast to the previous case, the equally low working memory score of this participant was associated with two other categories of assessed executive dysfunction (fluency and reasoning), which effectively meant this participant had three categories of executive dysfunction. This participant's processing speed slope was similar to that of the previous participant at 0.10, but his ACT score at 20 was considerably better. It would also appear that CMDI results did not influence the D.KEFS results. Therefore, for this participant, the working memory scores were in line with the low general memory scores, and these low scores, seen across all memory indices, were in turn associated with more extensive executive impairment.

These examples illustrate how those with similar memory performance levels can be differentiated in terms of executive impairment on the basis of their working memory abilities. The first two cases each had general memory performance levels well above average, and, for the participant whose working memory performance level was comparable to these other scores, no executive problems existed. However for the participant whose working memory performance level was comparatively lower (though still not impaired) this signified some, though slight, executive impairment.

Cases 3 and 4 are both examples of participants who had impaired general memory performances. In the case of the younger participant the levels of performance were very low, in contrast to her level of performance on the working memory measure, which was higher and in the average range. Once again this comparatively good working memory performance limited the assessed executive dysfunction to only one category. The other participant, however, whose level of general memory performance was slightly better than case 3, had a low level of working memory performance which was similar to his other memory ability and he was assessed with three categories of executive dysfunction. Again, these are two cases with similar levels of general memory ability, diverse working memory ability and therefore differing degrees of executive dysfunction.

Although the relationship between working memory and other executive functioning was evident in this sample, the influence of general memory on executive functioning was shown to be very limited. This was somewhat surprising although it does support to some extent the structural equation results obtained by Engle et al. (1999), which suggested very little relationship between the memory component common to both short term memory and working memory, and fluid intelligence. In the current study, there were, however, also some inconsistencies in the relationship between working memory and other executive functioning.

It can be seen from Figures 6.2 and 6.5 in Chapter 6, that for those with no impairment there was one cluster (cluster 3,  $n = 9$ ), and arguably both clusters ( $n = 8$ ) from the group with executive dysfunction only, that have similar profiles. Both groups were characterized by above average general memory scores and comparatively lower working memory scores, but for the one cluster in the group with no impairment there was no executive impairment. In an attempt to isolate what

may have been responsible for the difference in executive functioning between the two groups, all index scores from the WMS - III and the WAIS - III, plus the processing speed slope, were compared across the two groups. Only the Auditory Recognition Index score was significantly different, with the score from the group with executive dysfunction producing higher scores. An examination of the demographic variables indicated no significant differences between the groups in age, years since first symptoms, EDSS score or years of education. There was however a significant difference in the occupational make-up of the two groups. Of the eight members of the group with executive dysfunction 1 was a 'homemaker', 2 were sickness beneficiaries, 4 were retired and only 1 was in paid employment. For the 9 in the group with no impairment 1 was a student, 2 were retired and 6 were in paid employment. As this was the only discernable difference between the two groups, it appears to be a good argument for remaining mentally active. This assumes, of course, that a higher level of mental activity, either in terms of social interaction or job demands, is associated with the workplace.

Two other groups of participants with similar memory profiles but different 'executive' profiles were cluster 2 (n = 7) from the group with only memory impairment and cluster 2 (n = 14) from the group with both memory impairment and executive dysfunction (see Figures 6.3 and 6.4). These two groups both had average memory scores of around or below the 'impaired' cut off point, but working memory scores which were higher, and again only one of these two groups had executive dysfunction. The same comparisons as before were made between these two clusters and there were no significant differences on any of the WMS - III or WAIS - III measures. The Processing Speed Index mean for the cluster in the group with both memory impairment and executive dysfunction was, however, 17 points lower than

the mean Processing Speed Index score for the cluster with memory impairment only. This was an opposite result to that indicated by a non-significant difference found in the mean scanning speed slope obtained from the Sternberg assessment, which was greater, indicating a slower processing speed for the 'Memory Only' group. These different results illustrate the influence of physical ability on the Processing Speed Index score, and demonstrate how unreliable this can be as a measure of scanning speed in some clinical populations. Demographic data comparisons were also non – significant although those with only memory impairment were on average 6 years older and had had MS symptoms for an average of 8 years more than those with both memory impairment and executive dysfunction. Again, however, there was some difference in the occupational make up of the two groups. In the group with both memory impairment and executive dysfunction 1 (7%) was unemployed, and 1 was a homemaker, 4 (29%) were beneficiaries, 5 (36%) were retired and 3 (21%) were in employment. In contrast for the group with only memory impairment 1 (14%) were homemakers, none were beneficiaries, 4 (57%) were retired and 2 (29%) were in employment. Although these differences in employment were not quite as striking as for the two clusters examined previously the trend was still the same. The group with only memory impairment did have a greater percentage in the retired category but it also had a greater percentage in employment than the group with executive dysfunction. Thus, the group with no executive dysfunction was made up primarily of those either in employment or retired, with no unemployed or beneficiaries, suggestive, maybe, of a more active group of participants. Therefore, in spite of equivalent scores on cognitive measures, the group with a greater proportion of those who remain in employment tend to be less inclined to have executive dysfunction. However, remaining in employment is certainly not the simple answer to the problem

of executive dysfunction, as the argument unfortunately, is, amongst other things, somewhat circular in nature.

If working memory is seen as a good indicator of other executive functioning, but being in employment somehow either minimizes any detrimental effects of a limited working memory capacity on executive functioning, or maximizes its positive effects, then on the surface, it would appear that maintaining employment should be a priority. However, working memory integrity, as measured by a Speaking Span test, has been shown to relate significantly with a subjective difficulties questionnaire that addressed issues relating to concentration and memory (Matotek et al., 2001). Also an Elevator Counting with distraction, test of attention, was shown to be the highest correlate of the Environmental Status Scale, a scale which assesses difficulty in performing everyday tasks (Higginson, Arnett, & Voss, 2000). Although the latter study only related to those MS participants who had been assessed as having some cognitive impairment, attention as measured by the Elevator Counting test, is arguably, a measure of working memory. Therefore both sets of results indicate that deteriorating working memory functioning is closely related to perceived difficulties in everyday situations. It is very likely then, that working memory difficulties, and the related perceived deterioration in performance, contribute greatly to the decision to leave the work force.

That perceived and/or actual cognitive difficulties are a primary predictor of unemployment in those with MS has been shown in several studies, (Amato et al., 1995; Beatty, 1998; Rao, Leo, Ellington et al., 1991; Roessler, Fitzgerald, Rumrill, & Koch, 2001), and memory problems seem to be the most relevant factor. Therefore, if one of the main reasons for abandoning work is also, apparently, the same factor that benefits from remaining employed, the solution is a little difficult to see.

It should also be mentioned that a primary motivation for this study was the realization that levels of physical ability were the main benchmark for determining the level of care available for those with MS. Therefore, it seemed probable that equally important cognitive deterioration could have remained undetected thereby placing some in the community at risk. Fortunately, the assessment of dysexecutive behaviour, in support of the D.KEFS assessment, suggested that behavioural problems within this sample were not generally at a level to cause concern. However, in the course of this research it was evident that there were a very small number of participants with MS whose personal responsibilities exceeded a level that would have been optimal. What was reassuring however, was that in those instances it appeared that others in the community provided some level of support.

### *Limitations of the Study*

Finally it is necessary to discuss the limitations of this study. Potentially the most important limitation was the use of the standardized norms of the major test batteries as a benchmark instead of a demographically matched control group. The primary impact of this decision was to preclude any allowance for education effects in the test results. This decision was made, however, to maximize the number of clinical participants in this study. Given that those with MS present a very heterogeneous set of cognitive profiles, it was considered that to have any chance of isolating any common factors underlying whatever executive dysfunction was shown to exist, it was necessary to recruit a large sample. Maximizing the numbers in the clinical sample achieved two ends both of which were considered to outweigh any disadvantages that may have resulted from the lack of a control group. The first was that it was the patterns of cognitive impairment, rather than the extent of impairment

(numbers impaired) which was more important in this research, and it was predicted that patterns would only emerge if the numbers were sufficiently large. Secondly, by recruiting the maximum number possible for this study, the sample (pre MS), could have been expected to increasingly resemble the 'normal' population from which the standardized data were obtained, thereby giving greater validation to the comparisons made.

A related issue is that of the cut-off criteria used. Although to a certain extent the literature justified the one standard deviation level for the Wechsler Adult Intelligence Scales - III (WAIS-III) and the Wechsler Memory Scales-III (WMS-III), there was no equivalent justification in relation to the other measures. This decision was made originally so as to enable those borderline/mild cases to be included in the analysis. However, it was demonstrated, when using the one standard deviation benchmark, the actual numbers 'impaired' on the WAIS - III and WMS - III were less than would have been predicted. To support this it did transpire that the performance levels of this sample (based on WTAR predicted Full Scale IQ and actual Verbal IQ) were slightly biased toward the upper end of the normal distribution. For the WTAR predicted Full Scale IQ only 3% of the participants scored lower than one standard deviation below the mean, considerably less than the 16% that would be expected in a normally distributed population, especially if the Australian trend of under-estimation applies. The Verbal IQ scoring pattern (which unlike the Performance IQ would not have been confounded by physical limitations) was very similar, with only 6% of the participants scoring less than 85, and for this measure, all but two of these were identified by the WTAR as scoring significantly less than predicted, leaving only two participants falling naturally into this lower range, again well short of the 16% expected in a 'normal' distribution. Thus in so far as these results can be extrapolated

to the D.KEFS results it would appear that the chosen criteria was appropriate for this sample, however a supplementary analysis using 1.64 standard deviations from the mean as the cut-off criteria can be seen in Appendix F.

A third issue relates to medication. There was no attempt to exclude participants on the basis of any medication they were taking. The rationale behind this decision relates to one of the reasons for examining executive functioning in this sample of participants with MS. That is, to ascertain whether those participants with MS in the community had the ability to function appropriately and therefore be safely independent. Thus when gauging how appropriate the existing level of independence was, it was considered that any required medication was an integral part of this judgment.

Along similar lines, but with a rather more pragmatic rationale was the issue of visual acuity. There were no means at the researcher's disposal to accurately assess the participant's sight. If they wore glasses or indicated any visual problems they were asked, where relevant, if they could clearly see the stimuli. If there were any doubts, the pattern of results were carefully examined and although it would be fair to say there would have been some participants who did not see things as clearly as others, there was not in any of the results, a significant decrement that could be consistently related to impairments in sight. It would, however, be naïve to state categorically that no score was affected by visual weakness.

The final issue concerns the reliability of the categorization of executive dysfunction. There were difficulties in relation to the categorization of participants due to the lack of a direct relationship between specific D.KEFS scores and specific categories. This therefore necessitated some level of subjective judgment. If as was originally intended, the various executive profiles had formed the basis of the

analysis, the element of subjectivity may have been of greater concern. However, as the primary analysis was based on the more general executive impairment or otherwise, it would seem that any issues with the methods of categorization were limited.

In conclusion it seems that this study has reinforced previous indications that there are in fact a multiplicity of cognitive profiles evident amongst those with MS. What is reassuring, in so far as this sample is representative of those with MS in New Zealand, is that whilst some level of executive dysfunction was evident in the majority of those in this sample, the degree of dysfunction was not usually sufficiently severe to significantly impair the participants' ability to recognize their existing limitations. It seems likely, therefore, that where some deterioration is evident, the weakness would be recognized and steps taken to minimize its effects. The implications of this finding are especially reassuring as many with MS in New Zealand live with limited daily care.

It was also evident however, that executive dysfunction was present in a significant number of those with MS, but given the many manifestations of executive dysfunction that surfaced in this study, it was also obvious that in a clinical setting it would be impossible to examine all these possible areas of impairment. However in so far as the relationship between working memory and other executive functioning that was suggested in this research does apply, it could well be appropriate when cognitive assessments are first administered, to include a relatively demanding test of working memory. If there seems to be a disproportionate weakness in working memory then this could provide a reason to examine the integrity of other executive functions in more detail. This would be especially important if the person involved

was still in employment, particularly if their position was one of responsibility, or if the person was responsible for the care of other family members, or was living on their own.

Finally it needs to be said how much I admired the courage of all those who took part in this research, and I can only say that I whole heartedly look forward to the day that the many riddles of this disease are solved.

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## APPENDIX A

Covering Letter for MS Sample

15<sup>th</sup> July, 2002.

Dear MS Trust Member,

My name is Margaret Drew, I am a Doctoral Candidate at the University of Waikato and I am hoping you can help me with my Research.

The focus of my Research is people with Multiple Sclerosis and the purpose of my Research is to examine possible misconceptions about how, or if, MS affects cognitive processes. By cognitive processes I mean the way your brain deals with everyday activities and decisions. I am interested in the views of both the person with MS and someone who lives with them or is close to them.

I have enclosed an information sheet detailing what would be involved if you agree to take part in this project. If, however, you have any questions, please contact either myself (ph 853 5022), the MS Office (ph 8395506) or my Supervisor, Dr Robert Isler at the University of Waikato (ph 8562889 Extn 8401).

As a gesture of appreciation, those who participate in this study will go into a draw to win one of two vouchers for a massage in their own home, or if preferred, book or music vouchers to the same value. At the conclusion of my study I would also be happy to share the information I have gathered with those interested, either on an individual basis or collectively at a meeting.

I look forward to meeting you should you wish to become involved in this Research project.

Margaret Drew  
Psychology Dept.  
University of Waikato

**Please note:** This research has the support of the MS Waikato Trust and has been approved by the Ethics committee at Waikato University. Also to protect your privacy this letter has been sent out by the MS Office.

## **APPENDIX B**

### **Information Sheet for MS Sample**

## INFORMATION SHEET

**Title of project:** The cognitive effects of Multiple Sclerosis.

**Principal Investigator:** Margaret Drew  
Post-Graduate Student  
Department of Psychology  
University of Waikato.

**Telephone:** (07) 8535022. **E-Mail:** mdrew@wave.co.nz

**Supervisor:** Dr. Robert Isler (University of Waikato)

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This study is concerned with finding out about the types of cognitive difficulties (if any), faced by people with Multiple Sclerosis (MS). We are also interested in finding out how these difficulties affect the daily lives of people with MS.

The reason for this research is to gain a better understanding of the impact of the various types of cognitive problems on the lives of people with MS and their families. In this way it should be possible to provide more relevant assistance in the future to people with MS and their families.

If you agree to take part in this study the person who has MS will be seen on two occasions and another person who knows them well (and preferably lives with them) will be seen briefly on one occasion. You can be seen in your own home, at the home of the Researcher or at the University of Waikato depending on which is most convenient for you.

Each visit will last a maximum of 3 hours. During the visits the person who has MS will be asked to take part in a number of puzzle/game type assessments, which most people find enjoyable and stimulating. They will also be asked some questions about their daily lives. The person who does not have MS will be asked to complete a short questionnaire about how they see MS has changed the person with MS. The information that we receive during these visits will remain completely confidential, and you will not be identified in any future use of this information.

If you, or anyone you know with MS is interested in taking part in this research please contact my self – Margaret Drew on ph 8535022, or mobile 021 457 312, or via email at mdrew@wave.co.nz.

## APPENDIX C

### TEMPORAL JUDGEMENT QUESTIONS

**1:** How long do you think it would take to blow up a standard party balloon? \_\_\_\_\_

**2:** How long do you think it would take to boil a jug half full of cold water? \_\_\_\_\_

**3:** How many advertisement breaks do you think there are on television during the news hour – between 6.00pm and 7.00pm? \_\_\_\_\_

**4:** How many times do you think the 13<sup>th</sup> fell on a Friday over the last three (3) years – that is, in 1999 plus 2000 plus 2001? \_\_\_\_\_

**5:** How long do you think it would take a professional window Cleaner to clean the windows of an average three bedroomed house on the outside only? \_\_\_\_\_

## **APPENDIX D**

### **Consent Form**

University of Waikato  
Psychology Department  
**CONSENT FORM**

PARTICIPANT'S COPY

Research Project: \_\_\_\_\_

Name of Researcher: \_\_\_\_\_

Name of Supervisor (if applicable): \_\_\_\_\_

I have received an information sheet about this research project or the researcher has explained the study to me. I have had the chance to ask any questions and discuss my participation with other people. Any questions have been answered to my satisfaction.

I agree to participate in this research project and I understand that I may withdraw at any time. If I have any concerns about this project, I may contact the convenor of the Research and Ethics Committee.

Participant's Name: \_\_\_\_\_ Signature: \_\_\_\_\_ Date: \_\_\_\_\_



University of Waikato  
Psychology Department  
**CONSENT FORM**

RESEARCHER'S COPY

Research Project: \_\_\_\_\_

Name of Researcher: \_\_\_\_\_

Name of Supervisor (if applicable): \_\_\_\_\_

I have received an information sheet about this research project or the researcher has explained the study to me. I have had the chance to ask any questions and discuss my participation with other people. Any questions have been answered to my satisfaction.

I agree to participate in this research project and I understand that I may withdraw at any time. If I have any concerns about this project, I may contact the convenor of the Research and Ethics Committee.

Participant's Name: \_\_\_\_\_ Signature: \_\_\_\_\_ Date: \_\_\_\_\_

## APPENDIX E

### Demographic Questionnaire for Participants with MS



**Occupational Training Qualifications:** [ ]

- |                                 |                       |
|---------------------------------|-----------------------|
| 1. Nil                          | 2. School Certificate |
| 3.U.E./Sixth Form Certificate.  | 4. HSC/Bursary.       |
| 5. Trade – Specify. _____       |                       |
| 6. Professional –Specify. _____ |                       |
| 7. Tertiary. –Specify. _____    |                       |
| 8. Other – Specify. _____       |                       |

**Living Arrangements:** (Include number of people living with) [ ]

- |                           |              |
|---------------------------|--------------|
| 1. Alone                  | 2. Family    |
| 3. Relations.             | 4. Partner   |
| 5. Partner plus children. | 6. Flatmates |
| 7. Other – Specify: _____ |              |

**Number of Dependent Children:** [ ]

**Current Medication:** [ ]

- |        |                       |
|--------|-----------------------|
| 1. No. | 2. Yes: - Type. _____ |
| _____  |                       |

**Current Medical Conditions:** [ ]

(Do you currently have any condition other than Multiple Sclerosis which affects your eyesight, hearing, sense of smell or touch, or conditions of epilepsy, diabetes, etc?)

- |       |                      |
|-------|----------------------|
| 1. No | 2. Yes – Type: _____ |
| _____ |                      |

**Previous Medical Conditions:** [ ]

(Have you ever had any condition other than Multiple Sclerosis which affected your eyesight, hearing, sense of smell or touch, or conditions of epilepsy, diabetes, etc?)

- |       |                     |
|-------|---------------------|
| 1. No | 2. Yes. Type: _____ |
| _____ |                     |

**Previous Hospitalisations:** [ ]

- |        |                           |
|--------|---------------------------|
| 1. No. | 2. Yes – Diagnosis: _____ |
| _____  |                           |



**Suggested Control Subjects:**

Name: \_\_\_\_\_

Address: \_\_\_\_\_

Name: \_\_\_\_\_

Address: \_\_\_\_\_

## APPENDIX F

### Demographic Questionnaire for Control Group

**MULTIPLE SCLEROSIS NEUROPSYCHOLOGICAL STUDY.**

**Participant ID:** \_\_\_\_\_

**Name:** \_\_\_\_\_

**Address:** \_\_\_\_\_

**Date:** \_\_\_\_\_ **Time** \_\_\_\_\_

**Date of Birth:** \_\_\_\_\_ **Age:** \_\_\_\_\_

**Gender:** 1. Female 2. Male [ ]

**Dominant Hand:** 1. Right 2. Left [ ]

**Ethnicity:** [ ]

1. NZ European/Pakeha 2. NZ Maori  
3. Pacific Islander 4. Other – specify \_\_\_\_\_

**Marital Status:** [ ]

1. Never married 2. Married/De Facto  
3. Separated/ Divorced 4. Widowed  
5. Other – specify \_\_\_\_\_

**Relationship to Other Person Being Assessed:** [ ]

1. Spouse/partner 2. Parent  
3. Son/Daughter 4. Other relative  
5. Friend 6. Other – specify \_\_\_\_\_

**Education:** [ ]

Years of secondary Education: \_\_\_\_\_

Years of tertiary Education: \_\_\_\_\_

Age when left school: \_\_\_\_\_

Years of Education: \_\_\_\_\_

**Occupational Status:** [ ]

1. Student 2. Unemployed  
3. Homemaker 4. Sickness beneficiary  
5. Retired  
6. Paid Employment – Specify: \_\_\_\_\_ [ ]

**Occupational Training Qualifications:** [ ]

- |                                 |                       |
|---------------------------------|-----------------------|
| 1. Nil                          | 2. School Certificate |
| 3. U.E./Sixth Form Certificate. | 4. HSC/Bursary.       |
| 5. Trade – Specify. _____       |                       |
| 6. Professional –Specify. _____ |                       |
| 7. Tertiary. –Specify. _____    |                       |
| 8. Other – Specify. _____       |                       |

**Living Arrangements:** (Include number of people living with) [ ]

- |                           |              |
|---------------------------|--------------|
| 1. Alone                  | 2. Family    |
| 3. Relations.             | 4. Partner   |
| 5. Partner plus children. | 6. Flatmates |
| 7. Other – Specify: _____ |              |

**Number of Dependent Children:** [ ]

**Current Medication:** [ ]

- |        |                       |
|--------|-----------------------|
| 1. No. | 2. Yes: - Type. _____ |
| _____  |                       |

**Current Medical Conditions:** [ ]

(Do you currently have any condition which affects your eyesight, hearing, sense of smell or touch, or conditions of epilepsy, diabetes, etc?)

- |       |                      |
|-------|----------------------|
| 1. No | 2. Yes – Type: _____ |
| _____ |                      |

**Previous Medical Conditions:** [ ]

(Have you ever had any condition which affected your eyesight, hearing, sense of smell or touch, or conditions of epilepsy, diabetes, etc?)

- |       |                     |
|-------|---------------------|
| 1. No | 2. Yes. Type: _____ |
| _____ |                     |

**Previous Hospitalisations:** [ ]

- |        |                           |
|--------|---------------------------|
| 1. No. | 2. Yes – Diagnosis: _____ |
| _____  |                           |



## **APPENDIX G**

### **Executive Function Results using 1.64 Standard Deviations as the Impairment Criteria**

## **Results**

The following results are based on an impairment criteria of 1.64 standard deviations from the mean of the D.KEFS normative data.

Based on the same assessment methods as the original analysis 34% (n = 32) of the participants with MS remained impaired on at least one of the five categories of executive dysfunction. The most commonly occurring individual profiles of dysfunction were the combinations of fluency and reasoning (n = 4) and reasoning and planning (n = 4). The frequencies of these profiles were followed by the shifting and inhibition categories each in isolation, the combination of fluency and planning, along with more extensive profile of shifting, planning, reasoning and fluency, all with n = 3.

For this smaller sample of participants with executive dysfunction 10 (31% of those impaired) had only one category of impairment, 14 (44% of those impaired) had two categories of impairment and 8 remained with three or more categories of impairment but for this analysis that represented 25% of those with executive dysfunction.

The most frequently occurring categories were again fluency and reasoning, each occurring either in isolation or with other categories of dysfunction in 18 participants. The planning category was the next most frequent (n = 13), followed by shifting (n = 8) and inhibition (n = 7)

Therefore this more conservative criteria has reduced the numbers assessed with executive dysfunction, but this number remained greater than previous authors had indicated. The most notable difference between the two analyses was the reduced number of participants with only one category of executive dysfunction that were seen in this analysis.

## APENDIX H

*Means, Standard Deviations and Number Impaired on the WAIS - III Indices and IQ Measures*

WAIS-III	Number	Mean	Standard Deviation	Number Impaired
<b>Indices</b>				
VCI	95	101.9	12.5	7 (7%)
POI	94	100.7	16.1	15 (16%)
WMI	95	98.9	14.0	17 (18%)
PSI	86	92.3	15.6	32 (37%)
<b>IQ Measures</b>				
VIQ	95	101.7	11.6	6 (6%)
PIQ	94	97.8	15.2	19 (20%)
FSIQ	94	100.2	12.6	12 (13%)

*Note.* VCI = Verbal Comprehension Index, POI = Perceptual Organization Index, WMI = Working Memory Index, PSI = Processing Speed Index, VIQ = Verbal IQ, PIQ = Perceptual IQ, FSIQ = Full Scale IQ

## APPENDIX I

### *Means, Standard Deviations and Numbers Impaired on the WMS - III Indices*

Index	Mean	Standard Deviation	Number Impaired
Auditory Immediate	94.55	12.12	19 (20%)
Visual Immediate	89.03	16.89	49 (52%)
Immediate Memory	90.25	15.85	39 (41%)
Auditory Delayed	94.62	13.16	23 (24%)
Visual Delayed	88.68	15.72	43 (45%)
Auditory Recognition	96.11	14.73	19 (20%)
General Memory	91.20	15.26	38 (40%)
Working Memory	97.19	15.14	24 (25%)

## APPENDIX J

Table of the Range, Means and Standard Deviations of Twenty of the Primary D.KEFS scores, along with an indication of the executive category they each primarily contribute to

*Range, Means and Standard Deviations of Twenty Primary D.KEFS Scores and an Indication of the Category they each Contribute to*

D.KEFS Score	Range	Mean	SD	Executive Category
Trails Switching	13	8.54	3.90	Shifting
Letter Fluency	17	10.12	4.17	Fluency
Category Fluency	18	10.24	3.69	Fluency
Switching Fluency	18	8.85	3.79	Shifting
Design Fluency <sup>a</sup>	15	10.52	3.25	Fluency
Stroop Inhibition	14	8.77	3.57	Inhibition
Stroop Switching	14	8.82	3.79	Shifting/ Inhibition
CCST Correct Sorts	16	9.91	3.08	Reasoning
CCST Description	17	9.64	3.07	Reasoning
CCST Recognition	15	9.58	2.84	Reasoning
20 Questions Abstraction	14	10.39	2.91	Reasoning
20 Questions Total Asked	14	10.19	3.46	Reasoning/ Planning
20 Questions Achievement	14	9.74	3.50	Reasoning
Word Context <sup>b</sup>	14	9.66	2.69	Reasoning
Tower Total	16	10.01	3.12	Planning
Proverbs Total	11	10.44	2.46	General
Common Proverbs	12	10.35	2.67	General
Uncommon Proverbs	10	10.41	2.47	Reasoning
Proverbs Accuracy	11	10.36	2.33	General
Proverbs Abstraction	11	9.97	2.69	Reasoning

*Note.* <sup>a</sup> N = 93, <sup>b</sup> N = 94. CCST = California Card Sorting Test