Anomia in people with

Relapsing-Remitting Multiple Sclerosis

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List of Abbreviations

MS: Multiple Sclerosis

RRMS: Relapsing-Remitting Multiple Sclerosis

PPMS: Primary Progressive Multiple Sclerosis

SPMS: Secondary Progressive Multiple Sclerosis

PRMS: Progressive Relapsing Multiple Sclerosis

MRI: Magnetic Resonance Imaging

CIS: Clinical Isolated Syndrome

BNT: Boston Naming Test

PASAT: The Paced Auditory Serial Addition

JLO: The Judgment of Line Orientation test

SR: Selective Reminding test

SDMT: Symbol Digit Modalities Test

WAIS-R: Wechsler Adult Intelligence Scale-Revised

SRFT: Salford Royal NHS Foundation Trust

PIS: Participant Information Shee

IPNP: The International Picture Naming Project

ACE-R: Addenbrooke's Cognitive Examination–Revised

NART: National Adult Reading Test

SD: Standard Deviation

RT: Reaction Time

ms: Milliseconds

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Abstract

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Multiple Sclerosis (MS) is a neurodegenerative disease that produces plaques and inflammation throughout the central nervous system (CNS). MS can present in four different clinical courses, of which Relapsing-Remitting Multiple Sclerosis (RRMS) is the main clinical course, especially at early stages of the disease. The age of onset is typically between 20-40 years. MS can have a devastating impact in the personal, social and professional life of the sufferer. MS affects the grey and white matter and the subcortical pathways that connect these areas. This leads to impairment in both physical and cognitive skills. The majority of research about cognition in MS focuses on memory and processing speed deficits. Speech and communication deficits in MS have been relatively neglected in the current literature.

A systematic review of speech/language disorders in MS confirmed that there is a gap in the understanding of anomic deficits in people with MS. The research regarding speech and communication deficits in MS has been mainly focused on deficits such as verbal fluency. Anomic deficits have not been properly addressed in the MS literature, possibly reflecting difficulty in detecting milder presentations. Moreover, previous studies have failed to delineate the nature and extent of anomia. This study aimed to examine communication deficits in people with MS, with specific focus on anomic symptoms, as well as potential interaction with dysarthric symptoms. A communication screening assessment was conducted with participants (n=100) suffering from RRMS. The cognitive and linguistic skills of the participants were assessed with several behavioural assessments.

The mean participant performance was at the neuro-typical control cut-off in all tasks, although there was a wide range of performance across each test. There was a clinical performance across the cohort for 42% in picture naming, 43% in the ACE-R, 11% in the NART, and 32% in the Pyramids and Palm trees. The anomic symptoms presented as both difficulty in retrieving words and reduced speed of word retrieval. There was evidence of mild dysarthria for 33% of participants, although speed of word retrieval was still on average slower without these participants. The majority of participants presented with cognitive impairment in more than one domain. Statistical testing using correlation and regression analyses showed numerous correlations between test scores but not between test scores and years with MS. Within the regression model, semantic deficits were most strongly related to anomic symptoms.

Anomia in MS has been underestimated and requires further research across the MS range of presentations. Future research should aim to better understand the deficits that lead to anomic symptoms, develop sensitive and time-efficient assessments and evaluate treatment programmes through which people with MS can reduce the disabling consequences of anomia and related deficits.

Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Copyright Statement

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CHAPTER 1: Thesis Overview

Multiple Sclerosis (MS) is a neurodegenerative disease caused by neurological damage in both white and grey matter of the brain (Chiaravalloti & DeLuca, 2008). Patients suffering from MS develop motor and cognitive deficits that can be highly disabling. Whether deficits in language processing are a typical feature of MS has been a controversial clinical and research topic. However, the findings of some previous research studies have supported the suggestion that language impairment is among the cognitive deficits typically produced by MS (Lethlean & Murdoch, 1997).

Language is one of the most complex cognitive domains. Nonetheless, it is a basic skill required to conduct all our daily tasks. Without it, we cannot satisfy the demands of our personal and professional life. Language entails several different aspects from complex understanding of metaphors, to more simple activities such as naming an object, reading and spelling.

Everyday interaction requires rapid and fluent access to a substantial vocabulary. Yet, this ease of access can be subtly limited by the gradual onset of neurological diseases such as Parkinson's, Dementia and Multiple Sclerosis. MS is a disease that can produce severe cognitive deficits because of disruption between subcortical and cortical pathways (Drake, Allegri, & Carra, 2002). Moreover, this disease can also interfere with different aspects of language processing, including word retrieval, spelling and higher level comprehension.

Anomia is the formal term to describe inaccurate or delayed word retrieval caused by brain damage (Laine, 2013). The difficulty of diagnosing this problem lies in the wide spectrum of impairment that a person can present. Anomia can be present from a mild level such as "tip-of-the-tongue" problems, to severe anomia such as aphasia (Laine, 2013). Due to the progressive changes in brain structure and function associated with MS, it is possible that people with MS may suffer from anomia, and likely that the severity of this may alter with progression of the disease. When an individual with MS suffers from mild anomia, it may be relatively easy to compensate or cover up this problem, although even mild symptoms can be very frustrating. However, with time anomia may become more severe as brain damage increases. After a certain point, anomic symptoms may become more severe and directly impact on everyday conversation functioning as well as vocational needs and quality of life.

This research study aimed to assess naming skills in patients with MS in the context of wider cognitive and communication assessment. As a starting point, a systematic literature review on the topic of speech and language disorders associated with MS was conducted. Then, the empirical study which is the core of this thesis was implemented. This empirical study aimed to conduct a cognitive-communication screen with a large number of people with RRMS (target n=100) at the Neurology Department in Salford Royal NHS Foundation Trust (SRFT). The behavioural assessments selected as part of this screen were focused on assessing individually the main cognitive domains that can be impaired in people with MS (memory, attention, language). Moreover, this assessment included a task to assess motor speech problems (dysarthria) given the extent of physical disability in MS. Finally, in order to assess naming skills in people with MS (anomia), a bespoke Picture Naming Task was developed and included in the assessment. This task aimed to provide a sensitive measure of word retrieval skills by measuring both the accuracy and reaction time of the participants. Speed of word retrieval is an important index of milder anomic symptoms and particularly important as a measure in gradually progressive neurological disease. Reliable and sensitive diagnosis of anomia is a prerequisite to understanding the extent and nature of language deficits in MS and to development of disease-specific clinical management and treatment approaches.

CHAPTER 2: Introduction

Research motivation

Maximising physical and cognitive functioning in the face of neuro-degenerative disease is becoming increasingly important given the rapidly increasing prevalence of these conditions. Multiple Sclerosis (MS) is a degenerative disease that leads to a range of disabilities which affect vocational opportunities, social participation and quality of life. Most people diagnosed with MS report restrictions in social activities because of the physical and cognitive symptoms of the disease (Chiaravalloti & DeLuca, 2008).

The average age of onset of MS is around 30 years old (Moreno, García, Marasescu, González, & Benito, 2013). Therefore, there is a marked clinical need for active rehabilitation which can support people with MS to maintain life roles such as employment and family responsibilities, which could alleviate the costs health and social care budgets (Amato et al., 2013).

Language impairment is a symptom that is potentially highly disabling to people with MS. Moreover, it is a topic that has been barely studied in MS. Among language impairment, the nature and extent of anomia is unclear and warrants research.

Multiple sclerosis

MS is a disease that attacks the central nervous system (CNS) by damaging the myelin sheaths of the nerves (Lethlean & Murdoch, 1997). It is a progressive disease that produces inflammatory lesions and plaques throughout the CNS, specially next to periventricular regions (Bagert, Camplair, & Bourdette, 2002). New findings have detected damage not only in the white matter but also in the grey matter (Chiaravalloti & DeLuca, 2008; Lethlean & Murdoch, 1997; Rosti-Otajärvi & Hämäläinen, 2011). Conventionally, axonal loss was not regarded as a consequence of the disease. Nevertheless, with the development of new techniques, these lesions have been found in numerous situations, even at the beginning of the disease (Chiaravalloti & DeLuca, 2008).

The enormous diversity of locations of the plaques that MS provokes, results in a wide diversity of symptoms. These symptoms impede the neurons which make synapses to transfer information (Chiaravalloti & DeLuca, 2008). At early stages in the disease, the most common symptoms associated with MS are motor (physical disability) and sensory deficits. Nowadays, the implications of the disease for cognitive impairment are more widely recognised. This is especially in areas such as memory, attention or language. The possible presence of neuropsychiatric deficits has also been studied (Rosti-Otajärvi & Hämäläinen, 2011). These deficits are difficult to detect because of the lack of sensitive standardised assessments, and given that they can be subtle in terms of degree of symptom presentation. Furthermore, cognitive symptoms can often be overshadowed by physical disability, although they can in some cases appear at the beginning of the disease and when there is no physical disability.

MS is the most frequent degenerative disease that affects the CNS in northern Europe and northern United States (Baylor, Yorkston, Bamer, Britton, & Amtmann, 2010). The typical age of onset of the disease is between 20-40 years of age; however, there have been cases of patients with an earlier or later onset. It is also known that MS affects more females than males, it being three times more frequent in women (Baylor et al., 2010).

The presence of cognitive dysfunction is estimated to occur in 40-60% of cases of MS. These figures vary according to the sample of patients examined, since it varies according to clinical course, type of evaluation, years with the disease etc. The symptoms and cognitive impairment that MS produces are disabling and can be even present as frank dementia in certain types of plaque changes (Rogers & Panegyres, 2007).

Currently, there is no definitive information as to the aetiology of MS. There are a few factors that have been detected as precursor to MS such as some viruses and environment factors (Lin, Charlesworth, Van Der Mei, & Taylor, 2012). Apart from these, there are two main variables which seem to be significant in the development of MS. The first one is related to differences between individuals. In this category, there are several different variables such as age (linked to cognitive status), gender and lifestyle habits such as smoking and diet.

Genetic factors are also involved in the development of MS. There have been studies focused on the impact of the genes such as “HLA-DRB1” (human leucocyte antigen) and “IL7R” (interleukin 7) receptor alpha chain in MS (Gregory et al., 2007; Lin et al., 2012). The first gene leads to a three-fold increase in risk of MS and it has been found in 70% of MS patients (Lin et al., 2012). Regarding IL7R, its involvement in inflammatory responses and the immune system plays an important role in the development of MS (Gregory et al., 2007). A modification in this gene can produce damage in the myelin sheaths that increases the damage of the disease (Gregory et al., 2007). “APOE” (apolipoprotein E) is another gene that has been studied as a cause of cognitive impairment not only in MS, but also in Alzheimer´s disease (Benedict & Zivadinov, 2011). The interaction of these variables is complicated and poorly understood, making it harder to predict the course of the disease and manage its symptoms (Amato et al., 2013; Chiaravalloti & DeLuca, 2008).

Clinical course

The clinical course of a disease refers to its progression. In MS there are four general clinical courses that differ in the time between outbreaks and the recovery between them (Chiaravalloti & DeLuca, 2008). These courses are:

- **Relapsing-Remitting MS (RRMS):** This is the main clinical course of the disease, especially at the beginning. What is distinctive about this course is the complete recovery from symptoms after the initial outbreak (Chiaravalloti & DeLuca, 2008).

- **Primary Progressive MS (PPMS):** The main characteristic of this clinical course is that the effects of the disease keep increasing with time and without recovery (Lublin et al., 2014).

- **Secondary Progressive MS (SPMS):** This clinical course is composed by two stages. The first stage starts with exacerbations and then recovery after them, although there is no full recovery. In the second stage, the disease progresses gradually with time like in PPMS (Lublin et al., 2014).

- **Progressive Relapsing MS (PRMS):** This is a rare clinical course at the beginning of the disease. It is characterised by the lack of improvement after the first outbreak. The negative effects of the disease keep increasing with time. Occasionally, there is a small recovery (Chiaravalloti & DeLuca, 2008).

RRMS, PPMS, SPMS and PRMS have been traditionally used to classify MS patients. However, there are two new categories that have been created as these terms were not appropriate for some patients. These two new classifications are:

- **Clinically Isolated Syndrome (CIS):** This term was required to be included as a clinical course because it is known as the onset of the disease. At this point, the patient does not have all the characteristics of MS. However, is the first sign of the disease (Lublin et al., 2014).

- **Radiologically isolated syndrome:** This syndrome created some problems regarding the possible diagnosis of MS when it was discovered. Radiologically isolated syndrome refers to when there are findings of loss of myelin sheaths but there are no other symptoms. These findings cannot guarantee the presence of MS. Close monitoring of the patient is required to detect changes that can suggest that the person actually has MS (Lublin et al., 2014).

Treatment

There are three main approaches to treatment of symptoms associated with MS. They vary according to the main objective of the treatment, although they all focus on minimising the progression of the disease. Nonetheless, bearing in mind that MS is a progressive disease, this is a difficult task (Wang, 2005):

- Disease-modifying treatments aim to alter the clinical course of MS for patients. However, not all clinical courses respond to this kind of treatment. This treatment has been useful only for RRMS and SPMS. For example, drug treatment may serve to delay the progression of cognitive symptoms (Baylor et al., 2010; Feinstein, Freeman, & Lo, 2015).

- Symptomatic treatments can be described as secondary treatment, in that the focus is on the various symptoms (e.g., fatigue, dysphagia, spasticity etc.) rather than the disease itself. Here the aim is to reduce the overall effects of the disease by managing different symptoms separately (Merino & Quílez, 2007).

- Treatment of the outbreak is a technique that aims to relieve the negative effects of the outbreak. An outbreak is when the disease progresses producing adverse symptoms in the patient (Merino & Quílez, 2007).

Range of symptom presentation in multiple sclerosis

MS is a disease characterised by the wide variety of impairments according to the extent of the parenchyma affected by plaques. Typically, there are time points in the clinical course when symptoms are very marked, followed by some period of remission, during which symptoms lessen in severity although they tend not to disappear (Bagert et al., 2002; Finkelsztejn, 2014). When cognitive dysfunction was first noted, there was little research interest because of the perception that such involvement was atypical. Moreover, distinguishing cognitive impairment and depression can be challenging (Benedict & Zivadinov, 2011). However, with the development of better clinical assessment, cognitive impairment has been found to be commonplace in MS.

Bearing in mind that MS is a subcortical dementia, most of the symptoms related to the disease are physical and motor problems. The most common physical deficits presented in people with MS are visual problems, lack of coordination or fatigue

(Finkelsztejn, 2014). However, the majority of these deficits appear after an outbreak of the disease and are only temporarily present in its maximum intensity (Finkelsztejn, 2014).

These patients also suffer from memory problems, problems making decisions, distractibility, verbal impairment, visuospatial deterioration and slower speed when handling different information (Achiron et al., 2013; Amato et al., 2007; Moreno et al., 2013). Though these are the most common deficits of the disease, MS can cause other types of neuropsychological impairments to varying degrees (Jønsson, Korfitzen, Heltberg, Ravnborg, & Byskov-Ottosen, 1993). The most common problems are difficulties with memory, processing speed and language (Achiron et al., 2005).

These kinds of problems occur when there are demyelinating changes in the grey matter. However, changes in white matter have been recently associated with cognitive deficits. This has led to a different approach to diagnosis and clinical assessment in MS and has led to new findings about how MS progresses (DeLuca, C, Yates, Beale, & Morrow, 2015). These have been possible due to the use of new techniques such as Magnetic Resonance Imaging (MRI) which have helped to detect lesions that were not possible to observe previously (DeLuca et al., 2015).

The prevalence of cognitive deficits in MS varies across the different researchers that have investigated this aspect. Nevertheless, approximately 40-60% of patients with MS present cognitive dysfunction (Denney, Sworowski, & Lynch, 2005). Contrary to what was initially believed, cognitive dysfunction can appear at any phase of the disease, not only when the disease has been present for several years. The dysfunctions are caused because of the brain atrophy produced by demyelination (Achiron & Barak, 2006; Amato et al., 2007). The magnitude of the deficits is frequently connected to the development of the disease and the intensity of the lesions. This is typically more noticeable in the progressive courses (Ferreira, 2010; Filippi & Rocca, 2010). However, this correlation is not fully consistent. There are multiple factors involved in cognitive dysfunction. For example, the location of the damage and characteristics of every person can help or hinder the progression of the symptoms. Moreover, there is no proof of the relationship between years with MS and physical deterioration, and cognitive deficits (Rogers & Panegyres, 2007). There is a clearer link between brain atrophy and cognitive impairment that has been found using MRI.

This relationship is especially noticeable when the damaged area is the frontal lobe because of the key role this brain region has in executive control and planning (Calabrese et al., 2007; Cox & Julian, 2005; Lethlean & Murdoch, 1997; Rossi et al., 2012).

Overall, patients with MS suffer from a marked decline in their cognitive skills as time living with the condition increases. This happens even if they are being treated with drugs (Achiron et al., 2005).

Cognitive impairment in people with MS can be seen in areas of cognition such as:

- **Memory:** Memory impairment is the most frequent symptom in people with MS (40-65%) and is frequently reported by patients and their families (Chiaravalloti & DeLuca, 2008). Problems retrieving and encoding information can be disabling for the patient because they forget appointments with their doctor or friends (Brissart, Morele, Baumann, & Debouverie, 2012; Chiaravalloti & DeLuca, 2008). The biggest problem that MS patients suffer with memory is when trying to retrieve information from long-term memory. Also, verbal memory deficits restrict learning of new information, where MS patients have problems storing and accessing the information (Langdon, 2011). There is also evidence of impairments in episodic memory. This is the memory for events, although the prevalence of this problem differs across studies (Brissart et al., 2012). Nonetheless, not all types of memory are impaired by MS; for some patients, immediate memory is preserved (Rogers & Panegyres, 2007).

- **Learning skills:** Closely related to memory problems, patients with MS also suffer from difficulties in trying to acquire information. These individuals need more time to learn and the process to acquire the information needs to involve several repetitions of the information in order to learn the information successfully (Ferreira, 2010).

- **Attention:** Another of the most common areas of cognition that is damaged because of MS is attention. Symptoms included difficulty dealing with different types of information simultaneously and while performing tasks that require a heavy attentional load. The greater the attentional loads of the task, the poorer the performance. Deficits in attention have been found at all stages of the disease, even early stage (Rogers & Panegyres, 2007).

- **Language:** Language is a topic that has been relatively neglected by researchers, possibly because impairments have been too difficult to detect. However, recent investigations have detected deficits in multiple aspects of language. This function can be altered at an early stage of the disease although it is usually a subtle change. The symptoms reported are usually in verbal fluency, comprehension deficits or semantic memory (Langdon, 2011) which reflect atrophy of subcortical pathways that connect the relevant brain regions (Lethlean & Murdoch, 1997). There have also been reported findings of people with MS and aphasia, as well as patients with deficits understanding metaphors and information with dual meanings (Laakso, Brunnegård, Hartelius, & Ahlsén, 2000).

- **Ability to process information:** This aspect of cognition refers to whether the individuals with MS have the ability to process and operate information for a short period of time. This ability is part of short term memory and has been largely known as "working memory", which is closely linked to speed while processing information (Chiaravalloti & DeLuca, 2008). Sometimes, this deficit is difficult to detect because it can be identified as a deficit in another area of the cognition such as attention. Because of the latter, special attention must be taken when assessing this aspect of cognition (Ferreira, 2010).

- **Processing speed:** This ability has been found to be damaged in most of the individuals with MS because of the axonal loss that produces difficulties with the transfer of information. MS causes problems when processing information, making it necessary for these patients more time to fulfil an exercise (Rogers & Panegyres, 2007). This process involves information processing, an ability which is also affected by the disease (Langdon, 2011). This dysfunction is certainly important because it means decision-making becomes slower which can have substantial effects on daily functioning and engagement in work (Bagert et al., 2002).

- **Executive functions:** Executive function is a term that denotes the skills required to carry out a complex sequence of behaviours requiring planning, ordering of tasks and monitoring of progress. Executive functions are cognitive processes that can readily be damaged in MS (Chiaravalloti & DeLuca, 2008). People with MS have considerable difficulties in this domain. For example, when they make a mistake and subsequently try to correct it, they may make perseverative errors because of their inability to modify the original error (Rogers & Panegyres, 2007).

- **Vision:** Although deficits in vision are not frequent, approximately 15 % of sufferers of MS present this deficit. This function can be damaged in different aspects such as recognising or perceiving objects/stimulus **(**Chiaravalloti & DeLuca, 2008**).**

All these cognitive dysfunctions can be present in sufferers of MS and can interact with each other detracting from the patient's cognitive status. It is also essential to point out that there are other important variables that interact with the damage produced in the brain. Some of these variables are age and the role of neuroplasticity, gender and years of education (Ferreira, 2010; Potagas et al., 2008). In Table 1, a summary of the main cognitive deficits found in MS is shown.

Table 1- Frequency of cognitive deficits in MS (Bagert et al., 2002)

Cognitive Deficits	**Frequency in MS**
Attention	+++
Information processing	+++
Encoding memory	+++
Free recall memory	+++
Verbal fluency	+++

Auditory/visual span	++
Recognition memory	++
Executive function	++
Conceptional reasoning	++
Visuoperceptual function	++
Loss of stored factual knowledge	+
Motor learning	+
Apraxia	+
Agnosia	+
Aphasia	+

+Indicates frequency from rare (+) to common (+++)

Other frequent symptoms which can affect cognition include:

- **Fatigue:** This is the symptom that most of the people with MS experience throughout the disease. Fatigue not only occurs physically because of motor problems that the disease causes, but also cognitively because of the higher cognitive demand required to accomplish a task due to the cognitive deficits. Because of the feelings that it provokes, this is a symptom that produces a huge impact in the lifestyle of the individuals (Ferreira, 2010; Hartelius et al., 2004).

- **Depression:** This symptom is usually present in half of the patients with MS and it can appear at any stage of the disease. It is not yet known why patients may present with depressive symptoms during the clinical course of the disease. Notwithstanding, it can appear because of the presence of cognitive deficits or some medical treatments (Ferreira, 2010).

- **Motor impairments:** Physical restrictions are the most recognised symptoms of MS and can restrict engagement in everyday activities requiring cognitive skills (Ferreira, 2010).

- **Verbal expression:** The presence of dysarthria is very common in MS patients and restricts speech intelligibility and speed and ease of word production and general communication (Bringfelt, Hartelius, & Runmarker, 2006; Ferreira, 2010).

The aforementioned deficits occur because of the damage to pathways and structures that are involved in cognitive functions. When these pathways are impaired, there is a disconnection between cortical and subcortical regions that contributes to cognitive dysfunction (Filippi & Rocca, 2010). Some studies have related the disruption in the connections between the cortex and subcortical areas to deficits in linguistic aspects (Lethlean & Murdoch, 1997).

Specific brain regions and cognition in multiple sclerosis

Researchers have reported that patients with MS have a lower hippocampal volume than people without the disease. There is a strong link between intact cognitive functioning and the functionality of this area (DeLuca et al., 2015). The third ventricle has also been measured in these patients, to relate its width with brain atrophy. When this ventricle becomes bigger, there is an increase of cerebrospinal fluid in the brain, which means that this fluid is taking over areas where there was parenchyma. This area is highly related to cognitive dysfunction because of its contiguity to the thalamus (DeLuca et al., 2015; Houtchens et al., 2007). The thalamus, which is implicated in MS, is involved in processing speed and planning among other cognitive functions. Some patients with cognitive impairment in many different tasks also have a reduced thalamus. This area is linked to cortical areas. It works by exchanging information from different areas of the brain and is one of the main components of the limbic system (Batista et al., 2012; DeLuca et al., 2015; Houtchens et al., 2007).

The caudate nuclei are another area frequently affected by MS. It has been linked to some tasks such as verbal fluency and the ability to recall information after repeated exposure. MRI techniques have shown that the caudate nuclei in people with MS are smaller than individuals without the disease (DeLuca et al., 2015). Finally, the corpus callosum, which is also damaged by MS, has been associated with cognitive functions. The ability to solve a problem or the time required to process information are skills closely linked to this major white matter pathway (Filippi & Rocca, 2010).

Consequently, cognitive dysfunction affects people with MS in many different ways. The atrophy of the central areas of the brain is the one that is most related to cognitive deficiency (Filippi & Rocca, 2010). This impairment appears in all the clinical courses of the disease. With time, cognitive impairment can reach a level where the problem is more severe and the patient finally suffers from dementia (Amato et al., 2013). Dementia is characterised by the presence of cognitive impairment in at least two cognitive domains. In MS patients it is usually found by the dysfunction in memory and another domain like executive functions (Cox & Julian, 2005).

Relationship between time and cognitive impairment

Multiple studies have tried to find a relationship between the time with the disease/duration of living with MS and level of cognitive impairment. As stated previously, when understanding MS it is necessary to pay attention to the relationship between variables instead of studying one variable at a time. Severe cognitive impairment is usually present later in the disease. However, depending on the damage that MS causes in the brain, it can be also found early in the disease. It happens even when there has been only one outbreak. Along with the latter, the clinical course, T2 load lesion and procedures to assess cognitive impairment play an important role in estimating the intensity of cognitive impairment. Regarding the clinical course, progressive clinical courses are known to be the ones that produce the most severe impairment compared to relapsing courses (Amato et al., 2006; Ferreira, 2010). The typical impairment produced in each course is also different. While progressive courses create greater problems in the frontal lobe; relapsing courses produce more problems recalling information (Zakzanis, 2000). With respect to T2 lesions, it seems clear that the greater the extent of T2 lesions, the worse the cognitive status. This has been seen using MRI that allowed researchers to examine directly the effects of MS in the brain (DeLuca et al., 2015). Finally, the patients included in each study can modify the results regarding cognitive impairment and time with MS. In this disease, each patient’s clinical presentation is unique. Hence, the possible association between variables is difficult to assess because of the heterogeneous sample of participants (Achiron et al., 2013).

Regarding the association between time with MS and cognitive impairment, the results have been mixed. Some studies state that there is no relationship between number of years with the disease and intensity of the cognitive dysfunction (Denney et al., 2005). The reason why they support the lack of connection between these two aspects is because of their perspective that the number of plaques in the brain or the brain atrophy is more important than years with MS. For example, sometimes the disease process has been present for several years but the damage that it produces is mild. On the other hand, the disease can produce severe damages in the brain only in a few years (Denney et al., 2005). Certain studies, however, have found an association between impairment and years with MS (Achiron et al., 2013). The findings provide a lower score in different cognitive domains for people with more years with MS. However, there were methodological problems with some previous studies. For example, in some of them, the number of participants was small and there were problems with the control of variables (Achiron et al., 2013).

There has been one attempt at a definitive study with a relatively large sample of people with MS (Achiron et al., 2013). Here, participants were divided into groups according to the number of years with the disease. After assessing several cognitive domains, the results showed that the longer the time with MS, the worst the performance in the assessment. This decrease in the performance only happened with individuals that had been diagnosed for more than five years. This fact may have reflected the effects of the treatment that patients receive when MS was originally diagnosed. Overall, time influences the development of cognitive dysfunction in MS, although it can appear at an early stage of the disease (Achiron et al., 2013). Other studies supporting this relationship have found a worse performance in patients who have had MS for several years, and these findings were especially significant in language dysfunction (Velázquez-Cardoso, Marosi-Holczberger, Rodríguez-Agudelo, Yañez-Tellez, & Chávez-Oliveros, 2014).

A variable that does not appear to affect cognitive impairment is the degree of physical disability. Although it has sometimes been believed that these two variables where closely related, it has been recently suggested that they are independent (DeLuca et al., 2015).

A relationship that is more consistent is between cognitive dysfunction and social relations. Individuals with high levels of impairment opt for less social activities and this can lead to a higher level of cognitive impairment with less interaction with other people (Bagert et al., 2002).

Language disorders in multiple sclerosis

When considering the cognitive disabilities caused by MS, it is clear that MS can been seen as a form of subcortical dementia, and as such it shares certain characteristics regarding the presence of language deficits with other subcortical dementias. Subcortical dementias are characterised by the degeneration of the basal ganglia and white-matter tracts of the brain (Cummings & Benson, 1988; Savage, 1997). Other neurological diseases which are also marked by subcortical dementias apart from MS are Parkinson’s disease and Huntington’s disease. The damage produced in the subcortical areas of the brain produces deficits in cognitive processing, memory, executive functions, physical deficits or visuospatial alterations (Savage, 1997).

Language deficits are usually relatively preserved in people with subcortical dementias. This type of deficit is more common in cortical dementias where cortical regions of the brain have also been damaged (Cummings & Benson, 1988). When language deficits have been found in people with subcortical dementias this has been associated with generalised cognitive impairment, more than specifically language deficits as a characteristic of the disease (Beatty & Monson, 1989). However, further research with people with Parkinson’s disease, Huntington’s disease and MS has shown that deficits such as anomia (difficulty retrieving words) in confrontation naming tasks (Bayles & Tomoeda, 1983; Beatty & Monson, 1989). Moreover, both people with MS and Parkinson’s disease are usually slower than neurotypical participants when retrieving words in confrontation naming tasks (Beatty & Monson, 1989). Problems with lexical processing have also been found in people with Parkinson’s disease, regardless of their performance on confrontation naming tasks (Beatty & Monson, 1989). Deficits with verbal fluency have also been found in people with Parkinson’s disease, and this is the most common language impairment present in people with MS (Cummings, 1986; Henry & Beatty, 2006). Apart from these language deficits, subcortical dementias are also known for presenting speech deficits. One of the most common speech deficits that can be found in different subcortical dementias is dysarthria (Cummings, 1986). This deficit is produced because of the damage in the motor system involved in speech production.

Overall, MS shares certain language deficits with other subcortical dementias such as Parkinson's or Huntington's disease because of the initial location of the damage in the brain. However, as the damage produced by MS progresses, cortical areas of the brain are also affected, increasing the severity of cognitive dysfunction (Chiaravalloti & DeLuca, 2008). The impact the damage in both cortical and subcortical areas of the brain has increases the degree and nature of the language deficits that can be found in people with MS (Chiaravalloti & DeLuca, 2008). Therefore, the neuropsychological profile of people with MS shares characteristics with both cortical and subcortical dementias. In fact, these deficits can even be present as frank dementia when the damage is severe (Rogers & Panegyres, 2007).

One of the reasons why it is challenging to compare language deficits in people with MS and other subcortical dementias is because subcortical dementias do not form a homogeneous clinical condition (Cummings, 1986). On the contrary, dementias tend to be of variable character. Moreover, the presence of language deficits has always been characteristic of cortical dementias, in fact, the language deficits found in subcortical dementias have usually been mild deficits (Cummings, 1986).

Whether there are language disorders in people with MS or not has been a source of controversy because of the conflicting results that have been found in different research studies. There are multiple reasons for this. For instance, one of them is the subcortical nature of the disease. As has been mentioned, at the early stages of the disease, language deficits were not expected in people with MS because of the location of the damages (subcortical lesions). These types of deficits were linked to cortical dementias such as Alzheimer's disease (Lethlean & Murdoch, 1997; Mackenzie & Green, 2009). Another reason can be the lack of widely used reliable assessments for sensitive measures of language. Finally, it can be also included some methodological reasons such as the diversity of participants selected in the studies (Laakso et al., 2000; Lethlean & Murdoch, 1997). MS is a disease in which symptoms vary according to several variables such as clinical course or physical deficits (Friend et al., 1999; Mackenzie & Green, 2009). As a consequence, not all MS sufferers have the same cognitive impairment, with the types of deficit observed depending on the impaired area, acuteness of the damage and clinical course of the disease (Friend et al., 1999). This final point makes it more difficult to find a precise association between the disease and the impairment that it can produce in language.

Language is a complex cognitive function that operates from an interrelationship of brain structures, which are usually located in the left hemisphere. Nowadays, there is a greater interest in the involvement of cortical and subcortical pathways in language. This is because researchers have more recently reported patients with brain atrophy in subcortical structures and white matter pathways and impaired language skills (Friend et al., 1999; Laakso et al., 2000). MS damages large areas of the brain including the arcuate fasciculus. Impairment in this area has a major impact on language processing, leading to severe problems repeating words (Fridriksson et al., 2010). The thalamus and basal ganglia are also affected by the disease and they are highly involved in language (Laakso et al., 2000; Mesulam, 2003), specifically in verbal learning and verbal fluency (DeLuca et al., 2015).

Apart from brain atrophy, other variables have been studied in relationship with language dysfunction. Some authors have tried to find a relationship between years with MS and language impairment. However, consistent with other cognitive impairments, the results that have been found are not conclusive, and they vary according to the study (Mackenzie & Green, 2009).

Recent investigations assessing language in MS patients have found that these patients usually perform below the control group (Lethlean & Murdoch, 1997). Deficits in tasks that involve high-level language are commonly present in these individuals. Furthermore, they complain about some speech problems (Sepulcre et al., 2011). Many individuals with MS report information using less accurate vocabulary and less informative expressive language (Mackenzie & Green, 2009). The areas of language that are usually impaired because of MS are word retrieval, comprehension and fluency. Despite the fact that sometimes these deficits are difficult to detect, they are frequently found in these individuals. However, problems with the type of assessment, reduces the figures of people with language impairment. This is because the tests used to assess changes in language skills in MS patients may not be specific or sensitive enough (Tallberg & Bergendal, 2009). For example, some studies only consider the accuracy scores in a naming test. By doing so, they exclude the possibility of a fuller examination about the performance of the participants. In verbal fluency tasks, patients with MS perform less well than control groups. Nonetheless, depending on the category (semantic, phonologic, etc.), these individuals can reach the same level of performance as individuals without impairment (Sepulcre et al., 2011). Several research studies have found that the general population uses two techniques in verbal fluency tasks in which participants are asked to generate a list of items in a category (e.g. animals) within a minute; these tactics are “clustering” and “switching”. Clustering refers to the use of words that belong to the same category. This has been linked with temporal areas of the brain because of the importance of lexical information in that area. Switching refers to the change of cluster when they do not know more words from that category. Frontal areas are required to be able to switch properly between categories because the executive functions are controlling the task. These two tactics can help participants to improve their scores in the task despite the presence of language deficits (Sepulcre et al., 2011; Tallberg & Bergendal, 2009).

In most of the studies assessing language, women exceed the level of males (Friend et al., 1999). Naming problems have been reported in patients with MS. This difficulty varies according to different variables such as clinical course of the disease. This relationship between naming and clinical course is still unclear. However, some findings may indicate that this deficits appears early in the illness (Friend et al., 1999).

It is also common for people with naming problems to produce words that do not exist or irrelevant answers in naming tasks. This happens because of their inability to access the correct word (Kujala, Portin, & Ruutiainen, 1996). Problems retrieving words have been found in several studies although sometimes they have been related to a memory inadequacy (Friend et al., 1999). One of the main problems here is that this deficit prevents these individuals from communicating effectively (Laakso et al., 2000). As well as expressive problems, some people with MS have been noted to have difficulty with understanding metaphors, drawing inferences or understanding sentences with dual meanings.

It is not yet clear why people with MS have problems recalling words. These language problems are usually linked to brain dysfunction and the damage of pathways that are involved in language. They can also happen because of the effects of some medicines. The problem is that this relationship is not clear yet, because depending on the dose and the drug, the effects vary considerably (Hodgson, 1993). Additionally, there are other factors which may influence language performance in MS. Depression can be one factor that affects retrieval tasks because it produces an adverse influence on memory skills. Finally, another factor that is also involved in the language skills of people with MS is the presence of memory impairment. Sometimes these patients present problems understanding language because they cannot access the meaning of the word as a result of memory impairment (Klugman & Ross, 2002). Difficulty in retrieving a word that is already known has usually been referred to as: "on the tip of the tongue". The term alludes to when the person has a sense of familiarity with the object but access to the exact term is not possible (Burke, MacKay, Worthley, & Wade, 1991).

As well as cognitive impairment affecting language processing, dysarthria is a common symptom in MS patients which has been noted in 40% of individuals. However, dysarthria is caused by the motor symptoms of the condition leading to muscle weakness in the voice and articulation tract. Dysarthria can also restrict social interaction in people with MS (Bringfelt et al., 2006). The characteristics of this deficit are varied, but it is usually marked by poor articulation, pauses between words, poor breath support for speech and compromised speech intelligibility. Dysarthric symptoms can occur separately from or in combination with language disorders (Baylor et al., 2010; Bringfelt et al., 2006; Klugman & Ross, 2002). Wider factors related to MS can also interact with dysarthria and/or language disorders in affecting communication, such as fatigue.

In MS it is extremely difficult to categorise individuals by their performance in different tasks because of the variety of brain damage that they present with. However, the location of the damage may be a good indicator of the type of deficits that can occur. Specifically, it is usually more frequent to find language difficulties in patients with brain atrophy in subcortical structures and/or their connections with cortical areas of the brain. This is especially the case when the damage is in the left hemisphere of the brain because it is usually more related to language.

When trying to categorise individuals by their language skills, there are a wide range of groups according to the language disorders that are present. It has been suggested that there are three main types of language presentation in MS: substantive language impairment; selective high-level language impairment; and, normal language skills (Murdoch & Theodoros, 2000).

People with substantive language impairment present with generalised deficits across all areas of language processing. Word retrieval problems can be particularly prevalent in this group. Other symptoms can include difficulty producing synonyms and antonyms and problems generating sentences. Sentence production can be marked by grammatical errors and some sentences may lack meaning. Another common problem is related to the inability to understand metaphors. This problem is present in the majority of patients with severe language impairment. Other difficulties typically include dysarthria and problems understanding verbal information (Murdoch & Theodoros, 2000).

Regarding selective high-level language impairment, the main symptoms found are in expression, reception and comprehension of language. These are usually accompanied by other deficits such as word-finding difficulties, problems defining words or finding synonyms/antonyms for a given word (Murdoch & Theodoros, 2000).

Finally, there is a group of MS patients whose level of language skill is close to neuro-typical performance. In this category, patients usually have only a mild deterioration of high level language in expressive and receptive skills. These individuals are able to understand metaphors and make inferences, as well as the preserved ability to define words. Nonetheless, sometimes they can have problems finding words when talking, although this capacity is usually preserved (Murdoch & Theodoros, 2000).

Verbal fluency in multiple sclerosis

Verbal fluency tasks have been widely used in patients with MS to assess language skills and other cognitive areas. These types of test are straightforward to use and they are sensitive to subtle cognitive deficits. When assessing a patient with MS with this kind of test, there are several variables that may affect the results obtained. For instance, the reduction of processing speed may affect the level of performance. This leads to a lower score although arguably the main function that is being assessed remains unaffected (Henry & Beatty, 2006). Although these tests have been useful when assessing language skills, they have some drawbacks. The main one is related to the brain areas required to perform properly in the task. These tests involve large areas of the frontal lobe of the brain which means that executive functions are especially present while performing (Tallberg & Bergendal, 2009).

Problems in verbal fluency test are often more noticeable in the clinical subtypes of MS characterised by a progressive course. They are frequently connected to factors such as gender, age of the patient or duration of the disease. There are two types of possible deficits when talking about verbal fluency. The first deficit refers to the ability of the person to name words with a specific first letter (phonemic fluency). The second deficit involves the capacity of the patient to retrieve words from a specific semantic category (semantic fluency). For those people with MS who have problems with attention and other aspects such as processing speed, these people generally perform poorly in these tasks. Although the task seems simple, it involves a lot of different cognitive procedures from retrieving a specific word, to inhibit competing lexical options (Connick, Kolappan, Bak, & Chandran, 2012; Viterbo, Iaffaldano, & Trojano, 2013).

Anomia

Anomia is a term used to describe specific problems in retrieving words, one of the most fundamental aspects of language. The presence of word-retrieval deficits are the main characteristic of aphasic disorders. This deficit substantially impacts on the ability to take part in a well-organized and meaningful conversation. There are multiple simple tasks that can be used to identify this symptom. Most commonly, testing takes the form of confrontation naming of pictures, for example, different common objects, to see if the person can access and produce the name of the item accurately and quickly (Mesulam, 2003). This type of task helps to detect whether or not a person has a deficit retrieving words, the severity of the deficit and the type of errors made by the participant (Hillis, 2015).

The cognitive steps in naming an object follow a series of complex processes. This firstly involves the visual recognition of the object, access to the semantic knowledge of the word and production of the lexical phonological output of the target word (Hillis, 2015). Impairment in the semantic or phonological stages of the lexical processing will be associated with the presence of aphasia (Hillis, 2015). On the contrary, deficits in the visual recognition of the object would be associated to agnosia (visual recognition of objects impaired) (Hillis, 2015).

Anomia has been studied extensively in order to inform cognitive models of core language functions, such as comprehension and expression of single words. The original models were proposed to account for symptoms of stroke aphasia and explain different types of word retrieval breakdown (Laine, 2013). One of the most important models was created by Wernicke and Lichtheim (Laine, 2013). They identified different phases required to produce a word. The process goes from recognising the sound of the word, to producing the motor order to articulate the word (Laine, 2013). Subsequent models have focused on brain areas and the implication of each area on language. These models have focused on where language was located in the brain, placing every function of the language in a different area and processing level (Laine, 2013). They have identified a number of brain regions (and their connections) important for the processes involved in word retrieval, especially those in posterior temporal and inferior frontal regions. Such regions, and the white matter connections between them, may become damaged in MS, and consequently may produce underlying processing deficits resulting in anomia.

One aspect that may affect the success or failure of word retrieval is the type of word. Important psycholinguistic variables, and the areas of the brain involved in retrieving words are different depending on whether the word to be retrieved is a verb or a noun (Damasio & Tranel, 1993). This can result in differential abilities in retrieving the different types of words. It has been suggested that the organisation of concrete nouns in the brain is more complex than the organisation of verbs, as nouns are usually more hierarchically structured than verbs (Damasio & Tranel, 1993). Therefore, someone can have problems, for example, retrieving names of animals although the retrieval of words that express actions may be intact. Moreover, these problems retrieving words also vary according to the condition under which a word needs to be retrieved, with performance differences found between (single word) confrontation naming and connected speech (Damasio & Tranel, 1993). The different stages of word production may be differentially affected by these variables, and all this considered together may suggest that the problem retrieving words vary according to the stage of word production impaired (Damasio & Tranel, 1993).

In order to understand word-retrieval deficits, it is informative to review the different types of cognitive models of lexical retrieval. These models illustrate the process in which language is produced and how language is understood (Laine, 2013). Moreover, they provide information through which to understand why word-retrieval deficits happen and which aspects of language processing are impaired, hampering word-retrieval processes.

These cognitive lexical models can be divided into three main categories according to the different types of connections between levels of language processing. These models are:

- Functional Models: This type of model is characterised by understanding the relationship between language and the neuroanatomical processes of different aspects of language. In this type of model, a language disorder would be caused by damage in a specific area of the brain or cognitive process. Functional models can be of significant relevance when diagnosing and treating language deficits (Laine, 2013).

- Local Connectionist Models: This type of model is considerably more complex than the functional models. In local connectionist models the different stages required to retrieve a word interact with each other as the speech or language is produced. For this reason, when producing speech or retrieving a word, different stages of word retrieval such as identification of semantic features or access to lexical network interact with each other with bi-directional activation (Hillis, 2015).

- Distributed Connectionist Models: Contrary to the local connectionist models where there is a relationship among “single units” (i.e.: grapheme, phoneme), in distributed connectionist models there is a relationship among patterns of activation. The strength of the activation of each pattern will determine which concept is activated (Dell, Schwartz, Martin, Saffran, & Gagnon, 1997; Hillis, 2015).

The type of anomic deficits present in people with MS can be understood with reference to Dell’s model of lexical production. Dell’s model is a distributed connectionist model of speech production (Dell et al., 1997). This model is characterised by word retrieval processes occurring in two stages. These stages were highly connected and all levels of representation of the model can interact with each other in any direction (Laine, 2013).

Dell's model has been used to understand word retrieval deficits with both clinical participants (aphasic participants) (Dell et al., 1997) and neurotypical participants (Laine, 2013; Stemberger, 2004). This model explains the type of errors that can occur during a picture naming task (Dell, Chang, & Griffin, 1999). These errors can be categorised in:

- Semantic errors: Retrieve a word semantically related.
- Formal errors: Retrieve a word with similar phonological characteristics.
- Mixed errors: Retrieve a word semantically related to the target and also with a similar phonological structure.
- Unrelated: Retrieve a word without any type of semantic or phonological relationship with the target word.
- Non-words: Retrieve a word that does not exist.

This model consists of three levels of representation or nodes (semantic features, lexical and phonological) (Laine, 2013). Every node represents a single unit (Dell et al., 1999).When trying to name an object, the activation starts in the semantic features of the word, then the next stage includes the access to lexical knowledge and concludes when the phonological output of the word has been activated and the person produces the word (Laine, 2013). Moreover, since there is a bi-directional relationship between these nodes, there is also "feedback" activation in this process. This means that when the node of lexical knowledge is activated, it send information back to the semantic node activating nodes with similar semantic characteristics, as well as the phonological node will activate lexical nodes that share similar phonological characteristics (Laine, 2013). The word with the highest level of activation of the correct semantic and phonological category is the word that is retrieved; however, if there is activation noise in any of the stages, sometimes an unrelated word can be selected producing the errors mentioned above (Dell et al., 1999). For this reason, Dell's model can explain mixed errors without including an extra stage in the lexical processing (Laine, 2013).

As previously mentioned, these three nodes are connected to each other bidirectionally. Hence, the semantic features can be connected to the phonological level and vice versa. This interaction between the semantic and phonological levels has an impact on word retrieval mechanisms. Therefore, when a person is trying to retrieve a word, this process will depend on the intensity of the activation between semantic and phonological representations (Laine, 2013).

Regarding the type of errors that a person with word retrieval deficits can make, this can be distributed from normal pattern errors (produced by neurotypical population) to random pattern errors (error produced when there is no information about the word) (Dell et al., 1999). The type of errors made by neurotypical population would be closer to semantic and mixed errors without producing non-words or unrelated words (Dell et al., 1999). However, the random pattern errors would be typically characterised by the production of non-words and the rest of errors would be present to a lesser degree (Dell et al., 1999). Considering this, a person with a greater difficulty retrieving words will produce more non-words than other type of responses, and a person with a milder deficit will produce less non-word errors.

The type of anomic deficits a person presents depends on which stage of the lexical production presents deficits. To classify these deficits three categories can be defined:

- **Semantic anomia:** This type of anomia appears when a person has a deficit in the first level (semantic features) of the Dell's model of lexical processing. An individual presenting with semantic anomia presents with difficulties when trying to access the meaning of the target word. Symptoms include difficulties understanding and producing words across modalities as it involves a general impairment of semantic knowledge. The problems in this type of anomia would appear only if the process required to name an object entails the use of semantic information. The intensity of the impairment may differ according to the modality and familiarity with the word (Laine, 2013).

- **Word form anomia:** This type of anomia corresponds to problems in the second level (lexical level) of the Dell's model of lexical processing. An individual with this type of anomia will not present with difficulties understanding the meaning of the picture but, they will not be able to access the target word. In this type of anomia there is sufficient semantic activation to ensure comprehension; however, this activation is not sufficient for generating or selecting the required lexical node from the semantic lexicon. This symptom varies according to the category of word. Nouns and verbs are processed in different ways in the brain; hence, the impairment in these categories is not always the same. Verbs entail a higher processing level than nouns. Another dissociation that can be found in this type of anomia is between concrete and abstract (Laine, 2013).

- **Disordered phoneme assembly:** This type of anomia corresponds to problems in the third level (phonological output) of the Dell's model of lexical processing. The problem in this category occurs after the meaning and the target word, but before production of the sequence of sounds/phonemes that make up the word. It is not possible for the individual to access the phonemes that needs to be articulated. This type of anomia involves a disconnection between the semantic information and the production of the word (Laine, 2013).

Apart from these types of anomia, pure anomia (complete inability to retrieve words) can be also found in individuals although it is relatively rare. The majority of errors made by a person with this type of anomia would be classified as non-words or unrelated words from the classification of errors from Dell's model (Dell et al., 1999). Anomic problems can also appear as a result of other deficits before or after the "retrieving words process" (Laine, 2013). Agnosic deficits that impede the proper visualization of an object in a confrontation naming task would hamper the retrieval process (Laine, 2013). This type of deficit acts before the processes required to retrieve the word. On the contrary, deficits such as dysarthria can hamper the production of the phonological output regardless of the processes involved in retrieving the word (Laine, 2013). This type of deficit acts after the word has been retrieved.

Nature and prevalence of anomia in people with multiple sclerosis

Anomia in people with MS has been found in several investigations. However, there has not been a precise percentage of patients that present with this symptom. Studies have found evidence for the presence of deficits in picture naming. These deficits have been related to a failure in different stages of naming such as perception, semantic information and access to lexical modules. This is because to name a picture entails several different processes. They go from perceiving the characteristics of the picture, to linking the image with the idea that it represents, to the pronunciation of the correct name (Snodgrass, 1984). However, in addition to the involvement of multiple stages of word retrieval, other cognitive processes are also required. This makes it difficult to identify differences between perceptual problems, memory problems or true anomic problems (Lethlean & Murdoch, 1994).

The nature of anomic problems in MS patients is usually linked to semantic impairment. This is because these individuals are thought to have some type of semantic knowledge impairment that disturbs the connection between the process required to access the semantic information (Lethlean & Murdoch, 1994). In support of this idea, an investigation carried out by Lethlean and Murdoch (1994) found that people with MS usually make more semantic than other type of errors. This suggested that these patients had difficulties recovering the correct term from all the possible words that they can use.

Such problems with accessing semantic information or retrieving the correct term from amongst related items is similar to deficits associated with aphasia, and would be suggested to reflect deficits with the retrieval system itself. However, others have proposed that such retrieval deficits may not be due to impairments within the language system itself, but related cognitive functions important for language and other skills. Some studies have tried to determine the relationship between anomic problems and cognitive impairment. To do so, researchers have studied the differences in the time required to respond to different items. The results have indicated that people with MS have numerous errors when trying to retrieve a word and they need more time to respond (Tallberg & Bergendal, 2009). This problem retrieving semantic information can be linked to other cognitive skills like attention and memory. These together may interact and lead to patients having a poor performance in tasks that require word-retrieving (Le Dorze & Nespoulous, 1989).

For example, anomic problems on people with MS have on some occasions been linked to attention problems due to the subcortical nature of MS. As a result, when a person with MS presents with this type of disorder, it may be associated with deficits in attentional skills. However, not all researchers agree with this association. MS is a disease that affects the white matter of the brain, and eventually ends up affecting also the grey matter. Therefore, when trying to understand anomic problems presented in people with MS, it is necessary to know if there are deficits in both white and grey matter of the brain. If a person with MS presents with naming deficits and disruption of cortical areas, the anomic deficits this person makes may be the same as those patients with cortical dementias, problems not associated with attentional deficits (Lethlean & Murdoch, 1994).

Other studies have linked anomic problems with memory. The argument is that individuals with MS have severe problems recalling information from long-term memory, which leads to problems retrieving words. These patients do not have problems learning the word or keeping the information in memory. What happens is that when trying to retrieve a word, although it is present in their lexicon, the process to access the information is damaged (Zakzanis, 2000).

The relationship between cognitive impairment and anomic problems is challenging to delineate. When there is widespread cognitive degeneration, anomic problems are more likely to occur. Problems naming can occur because of the disconnection in pathways that connect the thalamus with other areas of the brain. This type of problem appears at any moment of the disease. According to age, level of education and other variables present in the disease, the intensity and presence of anomia varies. However, there is no relationship between variables such as clinical course and naming problems (Rao, Leo, Bernardin, & Unverzagt, 1991).

During the clinical course of MS, the patterns of demyelination produced in the brain affect many different areas of cognition. Depending on the type of MS, and both the intensity and duration of the exacerbations, patients will present different dysfunctions. SPMS is usually the MS subtype that provokes the most severe impairment compared to other courses. This may be because the above subtype of MS is typically characterised by lesions in the frontal regions of the brain. Moreover, there are indications that the more years with the disease, the greater the impairments in tasks such as verbal fluency (Denney et al., 2005; Velázquez-Cardoso et al., 2014). It is also noteworthy that there is no direct connection between physical disability and the cognitive state of the patients. In this association the influence of the clinical course is not considered (Denney et al., 2005).

Relationship between underlying linguistic skills and degree of cognitive disability

The degree of disability present in each person with MS depends on some factors that help to preserve the proper cognitive functioning. One of these factors is the “cognitive reserve”. Cognitive reserve is acquired throughout the lifetime and is different in every person according to job, level of education and daily tasks. Furthermore, it is also affected by genetic and environmental factors, as well as characteristics of the disease. The different variables involved in the cognitive reserve are thought to be able to protect individuals against harmful factors. This means that it helps to diminish the effects of brain damage. Cognitive reserve works by increasing the number of connections between neurons so it compensates for the damage caused by the disease (Da Silva et al., 2015; Pinter et al., 2014).

Among all the different variables that have been studied within this topic, the level of academic attainment and intelligence are the ones that have captured most attention. People that have studied for longer preserve their cognitive skills to a greater extent. Nonetheless, the level of academic attainment depends on the age of the individual, and this has been barely verified for all ages. Regarding the level of intelligence, there are studies that suggest its impact in the preservation of cognitive skills (Da Silva et al., 2015).

There is little known about how cognitive reserve works. This reserve is also present in people without any neurological disease. The only means by which cognitive reserve is detectable in people without cognitive impairment is when their cognitive skills are measured by neuropsychological assessment. Among people with MS, there is evidence of the effects of this factor in their performance in different tasks. Patients with a higher level of education preserve their cognitive skills for longer. They perform better when their attention, memory or language skills are evaluated (Sumowski, Chiaravalloti, & DeLuca, 2009). This effect has not only been observed in MS patients but also in several different diseases such as degenerative diseases or traumatic brain injury (Sumowski et al., 2009).

Treatment of anomia

The disabling consequences for communication caused by anomia have led to some research focus on the treatment of anomic symptoms. In order to treat anomia, it is necessary to determine which stage of the retrieval process is impaired. This information will give a valuable indication as to the most useful treatment techniques that can be used. Once this is defined, different treatment options can be utilised (Laine, 2013). Given the continual atrophy of parenchyma in MS patients, methods based on compensatory strategies may enhance language skills more effectively than restorative techniques (repetition) (Hartley, 1995).

Regarding possible treatments for anomia, psycholinguistic functional models of naming have been utilised to develop naming treatments. The process of articulating a word can be divided into two phases. First the meaning is retrieved and then the phonological structure of the word. The impairment can be in one of these stages or in both of them. The treatment most of the time matches the impairment of the sufferer although it does not always need to be this way (Laine, 2013).

The anomic problems that MS produces are different to the ones produced by other aetiologies. Because of the neurodegenerative nature of MS, its effects cannot be compared with the anomic problems created by other diseases. Subtle deficits in language are common in degenerative diseases although at the beginning they are difficult to spot. Anomia is among the first deficits that usually occur. Through the course of MS, there may be a continuous loss of cognitive abilities (memory, attention, processing speed, etc.). The treatment needs to aim to keep accessible as many words as possible and for the longest period of time (Laine, 2013).

The techniques that are used to treat anomia need to change with time as the disease progresses. Moreover, every person needs to be treated with specific methods according to their necessities. Another requirement for the treatment is its adequacy to the social life of the sufferer. It should provide useful information about how to solve problems during their routine (Murdoch & Theodoros, 2000).

The latter techniques that have been explained are part of treatments that have proven to be effective to treat anomia. In addition to those techniques, there are specific treatments for anomia that vary according to what are they focused on (Bruce & Gatehouse, 1997). The main treatments are:

- **Semantic treatment:** This treatment consists on performing tasks where the visual form of a word needs to be associated to its photograph. The meaning of the word helps in this task to link different words (Bruce & Gatehouse, 1997).

- **Lexical treatment:** In this case, knowing the structure of the word is the main target. To do so, there are multiple tasks that involve reading incomplete words. In this tasks new clues are given while the task advances or reading words followed or not by its image (Bruce & Gatehouse, 1997).

- **Orthographic treatments:** The main objective of this treatment is to relate the graphical structure of a word with its sound. This works as an assistance to understand and recognise better the word (Bruce & Gatehouse, 1997).

Conclusion

This Introduction has focused on the cognitive symptoms that people with MS typically present, with a particular focus on language disorders. Relatively few studies have investigated symptoms of language disorders in people with MS. Moreover, the information about language skills in people with MS varies between different research studies. Among these research studies, some of them have found symptoms of language disorder (Friend et al., 1999; Kujala et al., 1996), while others have not (Langdon, 2011). Anomia has been implicated as one of the most common cognitive symptoms of language disorder in MS (Nicholas, Brookshire, Maclennan, Schumacher, & Porrazzo, 1989).

Further experimental and theoretical investigations are needed in this area to estimate the extent and nature these clinical symptoms. This will be of substantial importance for the field as it will help to fully understand how MS works and hopefully inform more effective rehabilitative methods.

CHAPTER 3: Speech and Language Disorders in People with Multiple Sclerosis: A Systematic Review

Abstract

***Background*:** Multiple Sclerosis (MS) is a neurodegenerative disease that produces impairment in both cortical and subcortical areas of the brain. People diagnosed with this disease often present with speech and language disorders. The main communication deficits studied in MS have been verbal fluency deficits and dysarthria. Verbal fluency deficits may reflect deficits in cognitive skills, including problems with memory, processing speed and language amongst others. The presence of anomia in people with MS, which refers to word retrieval problems, has not been extensively researched to date.

Aim: To understand the extent and nature of speech and language disorders in adults with MS according to the current literature.

Methods & Procedures: A systematic review of speech and language disorders in people with MS was conducted across four electronic databases. The search was conducted in PubMed, Medline, Web of Science and PsycINFO. The aim was to synthesise findings from the current literature with regard to the range of speech and language disorders observed, and interaction and overlap of underlying symptoms of cognitive and communication disorder in the context of physical disability and MS as a whole.

Main Contribution: Twenty-eight articles related to speech and language disorders in people with MS were included in this review. A synthesis of the reported deficits found across the studies selected highlights the diversity of speech and language disorders present in people with MS. Dysarthria, limited verbal fluency and anomia are the main speech and language disorders found. The interaction between physical and cognitive deficits is an aspect of increasing relevance to understanding these disorders.

Conclusions & Implications: People living with MS frequently suffer from speech and language disorders. The intensity or type of deficit varies according to variables such as clinical course or years with the disease. Evidence suggests that these deficits appear even during the first stages of the disease. Further research needs to be conducted to understand anomia/naming deficits, since the majority of the existing research on this topic has been limited to problems retrieving information from memory.

Keywords: MS; word retrieval problems; nature; language; memory.

Introduction

The main reason for conducting a systematic review of literature on the topic of speech and language disorders in people with MS is to attempt to understand the nature and prevalence of the various forms of communication disorder which can affect people living with this condition. Communication disorders in MS include impairments in speech production, with symptoms of dysarthria or apraxia of speech reported. However, impairments in cognitive skills may overlap and interact with motor impairments such as dysarthria. To date, there has been a lack of clarity as to whether communication impairments in MS should be considered as aphasic symptoms, stem from broader information processing deficits, or a combination of both.

This systematic review will investigate whether the current literature can clarify some of these complex issues. Better understanding of the nature and prevalence of speech and language disorders in MS is a prerequisite to the development of effective rehabilitative treatments to minimise communication disability and enhance quality of life of MS sufferers.

Methods

Literature search: The following literature databases were accessed in order to systematically review the topic of speech and language disorders in people with MS: PubMed, Web of Science, Medline and PsycINFO. The search was conducted in four different databases to ensure the findings were comprehensive and representative of the literature as a whole. Studies in all languages were included to reduce the risk of bias. The filters of "human" and "adults" were used to constrain the search. No restrictions in year of publication were set. The keywords inputted into the databases were: multiple sclerosis, word retrieval, language disorders, speech disorders, speech problems, anomia, word finding problems and language dysfunction. These keywords were searched in different combinations.

After conducting each search, the title and abstract of each article found during the search was analysed to determine their relevance to the topic under review. All articles selected included information about information/word retrieval skills or speech disorders such as dysarthria in patients with MS.

Data collection: After selecting all relevant studies for the systematic review, the manuscripts were obtained and analysed more fully. All studies were read in full, and further classified as relevant or not relevant to the systematic review. The included studies have been summarised in this review as follows: name of the authors and year of publication; number of participants with MS included in the study; speech/language disorders reported; specific description about deficits; assessments used to measure deficits and results obtained by participants. In addition, where available within each study, the mean and standard deviation (SD) of the assessment data were extracted.

For those studies which provided assessment data divided by gender or clinical course of the disease, this information was converted into one measure (mean of provided values), as the majority of the studies included information across both gender and/or clinical course combined.

Search methods

The first search conducted was "multiple sclerosis" and "language" or "speech". Figure 1 shows a summary of the number of results found in this first search across all the electronical databases selected for this review. Due to the large number of articles initially identified, additional searches were conducted in each database including more specific terms.

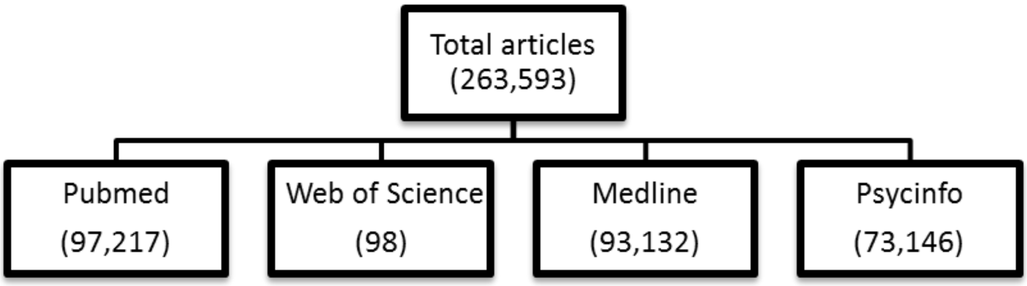


Figure 1- Summary of the number of results found in the first search across all databases

In order to help constrain the search and obtain articles restricted to a specific type of participant, the following searches conducted using more specific terms also included the filters "humans" and "adults (19+years)". The terms used in these more refined searches were structured in such a way that all articles related to the topic of the review could be found. Some of the searches conducted were: "multiple sclerosis" and "word retrieval"; "multiple sclerosis" and "language disorders" or "speech disorders" and "word retrieval problems"; "multiple sclerosis" and "language disorders" and "speech disorders" and "anomia"; "multiple sclerosis" and "word finding problems"; "multiple sclerosis" and "anomia"; the last search was "multiple sclerosis" and "speech problems". These searches helped to greatly reduce the number of relevant articles for the systematic review in all databases except for Web of Science. In this electronic database, the number of relevant articles increased from 98 in the first search to 129 in the following searches. Figure 2 shows the reduction in the number of articles found in the databases using the terms mentioned above.

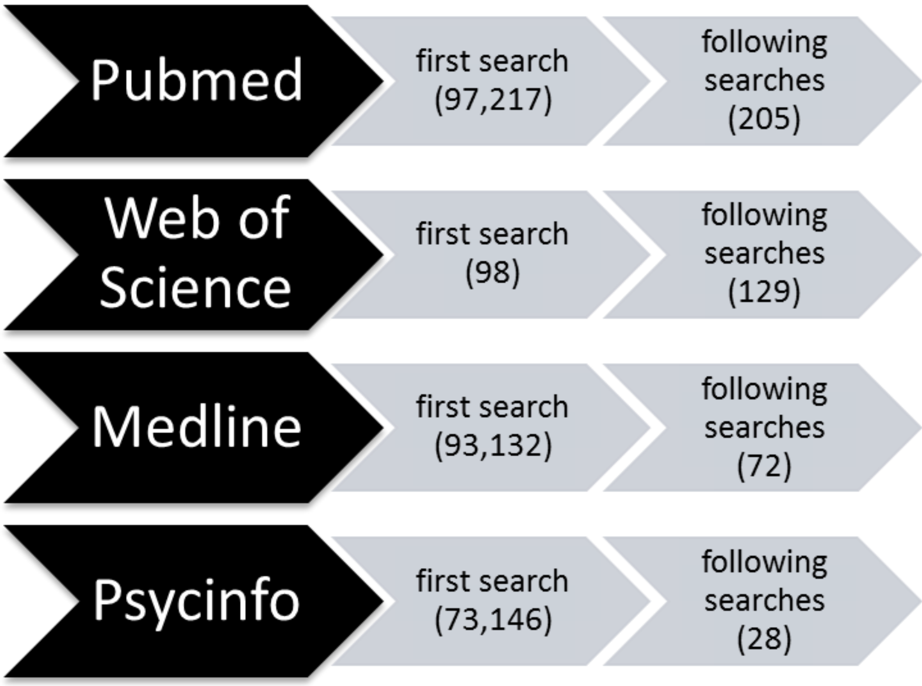


Figure 2- Reduction of article numbers after searching using more specific terms

Regarding the studies found in each individual database, the articles retrieved in each search were excluded or included in the review according to their relevance to the topic. Figure 3 shows a summary of the steps in which relevant studies were collated across the four databases for this review.

As previously stated, the keywords inputted into the databases were multiple sclerosis, word retrieval, language disorders, speech disorders, speech problems, anomia, word finding problems and language dysfunction. During the search, only one modification of the terms mentioned above was required. Anomia was searched as a key word (anomia.mp) in PsycINFO because this database does not recognise anomia as a Medical Subject Heading term (Mesh term). Several searches were conducted in each database to ensure finding all articles related to the topic.

There was redundancy in the articles identified across databases, with the majority of the articles found in more than one database and in more than one search. This lends support to the presumption that all studies related to the topic were identified. Thirty-nine studies provided relevant data regarding speech and language disorders in MS.

These were carefully reviewed and a further eleven were excluded. Four studies were excluded because they focused only on treatment of dysarthria and did not describe or characterise patients or provide assessment data. Five studies were excluded because they only offered general information about impairments in MS and there was no specific information regarding communication skills. One study was excluded as it described how to diagnose MS, rather than specific communication symptoms. Finally, one other study was excluded as it had not been peer reviewed.

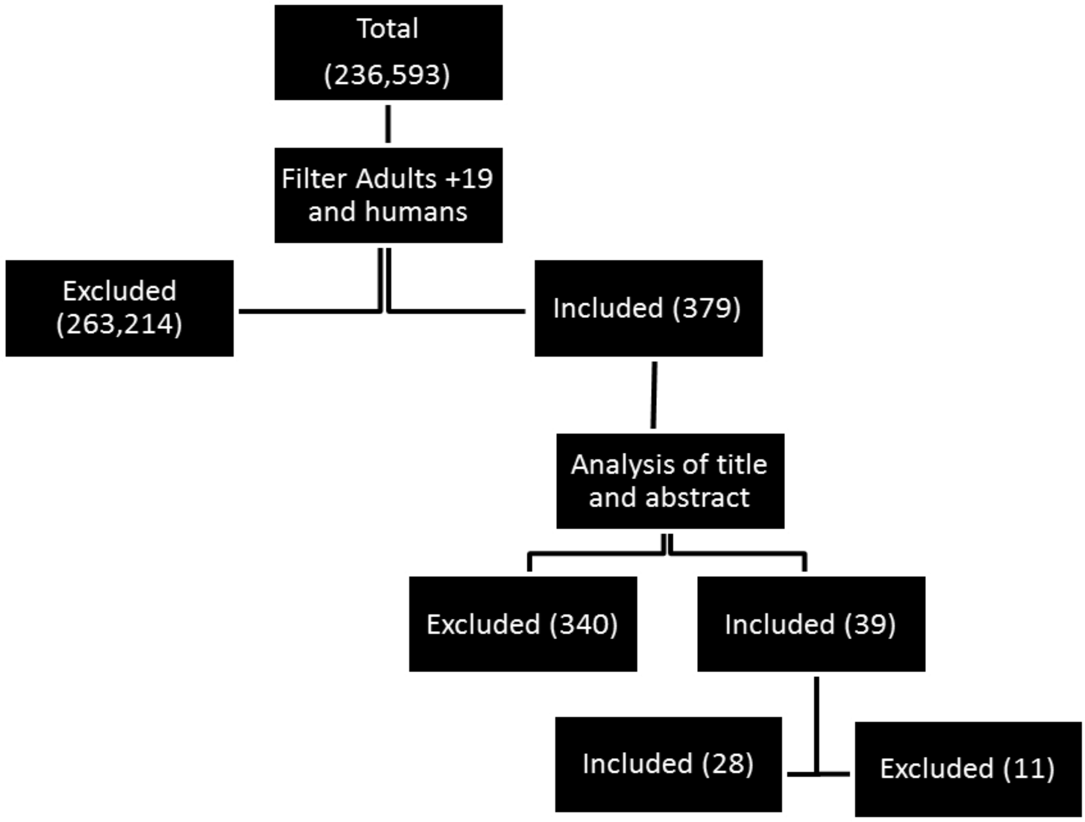


Figure 3- Collation of relevant studies

Results

Twenty-eight studies were selected for inclusion in the systematic review**.** The most striking feature of the existing literature is the apparently wide variety of findings reported. In terms of core deficits, several studies described cognitive-linguistic deficits relating to memory and information processing (n=8 studies). The next largest group of studies identified language deficits (i.e., of naming and/or verbal fluency) (n=6 studies) as being common MS characteristics. Other relevant findings were the presence of dysarthria (n=4 studies), and impairment of multiple cognitive domains that hinder the performance on speech/language tasks (n=10). Figure 4 summarises this findings. It should be noted that these descriptors are not mutually exclusive, with some studies fitting into more than one category. However, within the current review the studies have been classified in only one group according to their main finding. Although the description of 'impairment of multiple cognitive domains" was the largest with ten studies, this represents a heterogeneous set of findings which described the interaction between memory, language and speech problems overall.

Cognitive-linguistic symptoms related to memory and information procesing deficits

- Andrade et al. 2003; Armstrong et al. 1996; Brissart et al. 2012; Coolidge et al. 1996; DeLuca et al. 2013; Gaudino et al. 2001; Godoy et al. 1996 and Sicotte et al. 2008.

Language deficits

- Beatty et al. 1989; Drake et al. 2002; Lethlean et al. 1997; Pijpers-Kooiman et al. 1995; Tallberg et al. 2009 and Vlaar et al. 2003.

Dysarthria

- Feenaughty et al. 2013; Mackenzie et al. 2009; Smith et al. 2007; Yorkston et al. 2003.

Impairment of multiple cognitive-linguistic domains

- Beatty, 2004; Bodling et al. 2008; Connick et al. 2013; DeLuca et al. 1998; Friend et al. 1999; Hamilton et al. 2009; Henry et al. 2006; Huijbregts et al. 2004; Jennekens-Schinkel et al. 1990; Kujala et al. 1996.

Figure 4- Patterns of cognitive-linguistic deficits found across studies

A summary of the studies describing speech and language disorders in people with MS is presented in Appendix A.

Participants per study

Regarding participant numbers, the total number of participants across the studies was n=4628, with a mean and standard deviation of 170.6 (451.1). The standard deviation was larger than the mean itself due to the considerable variation in participant numbers across studies. For this reason, the studies included in this review are best compared in two different groups according to whether the number of participants was more or less than 100. Figures 5 and 6 show the studies containing less than 100 or more than 100 participants, respectively.

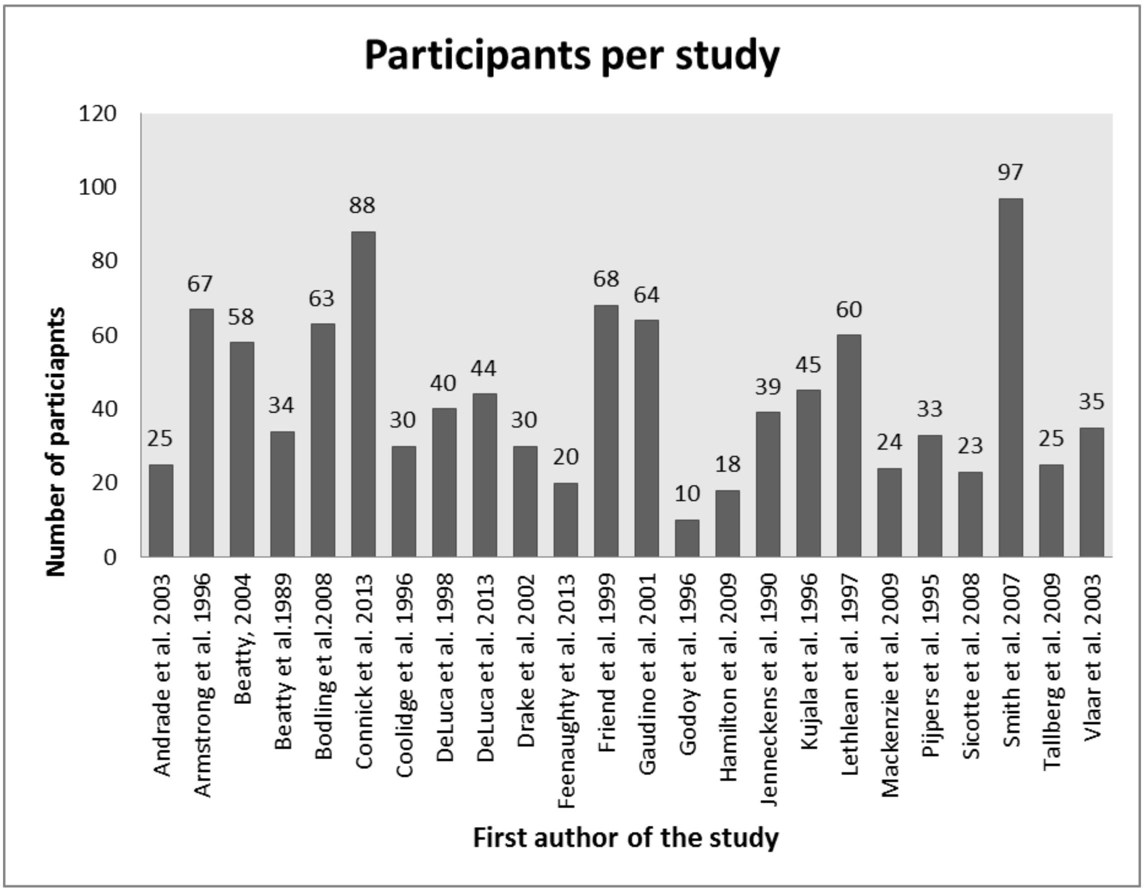


Figure 5- Studies with less than 100 participants

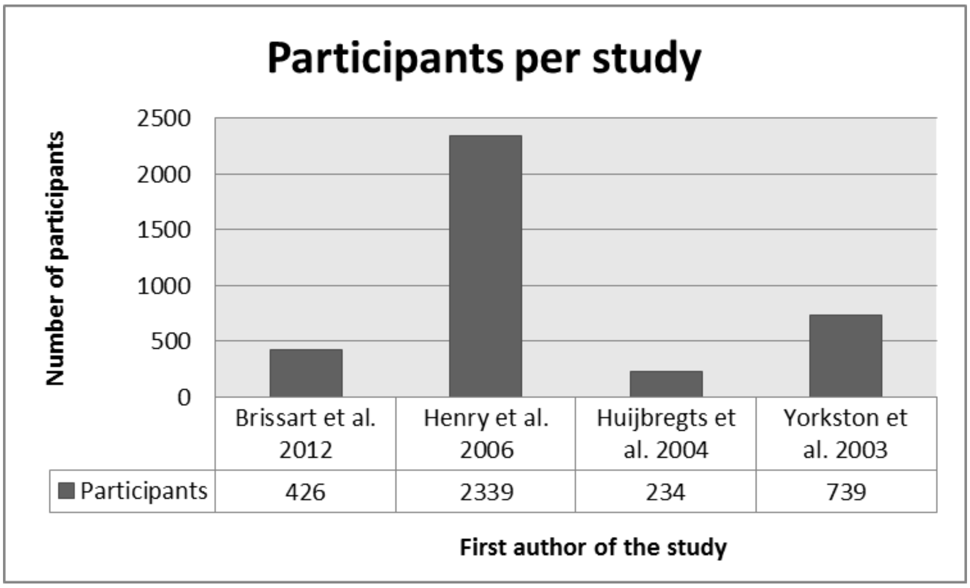


Figure 6- Studies with more than 100 participants

As can be seen from a comparison of the number of studies included in the two groups, the vast majority of studies included in the current review involved fewer than 100 participants (24/28 studies). The studies that included less than 100 participants (Figure 5) included between 10 and 97 participants, with a mean and standard deviation of 43.33 (22.61). In contrast, the studies included with more than 100 participants (Figure 6) included 234 participants as minimum, with the study of Henry and Beatty (2006) containing the largest sample, with 2339 participants. The large sample size included in the Henry and Beatty (2006) study resulted from the fact that this was a review of multiple studies about verbal fluency. The vast difference in the number of participants between studies with more than 100 participants made the standard deviation increase substantially to 170.64 (451.12).

Domains tested across studies

There was a wide variety of domains assessed across the studies included in this review. The main domains assessed in these studies were memory, language, information processing and dysarthria. When assessing these domains, all studies found that people with MS performed less well than healthy control participants.

Regarding the range of domains assessed within studies, a number of the studies included in this review conducted a relatively narrow evaluation focussing only on one aspect of cognitive-linguistic functioning. For instance, Armstrong et al. (1996) conducted a narrow assessment focused only on long-term memory deficits. The drawback of these types of studies is that the information obtained in the assessment is highly specific and does not provide information about the reported deficit in the context of other cognitive-linguistic domains. However, there were several studies which did conduct an in-depth assessment of several cognitive-linguistic domains (e.g., Friend et al., 1999). These types of studies can be more informative as the results obtained provide broader and more comprehensive data. These results provide both an overview of how some cognitive-linguistic domains work individually in MS, as well as information about how they interact, which is of major importance in a disease like MS.

Regarding the materials used to assess the participants with MS in each study, there was a wide variety of tests used. Tests used across more than one study included The Boston Naming Test (BNT), The Paced Auditory Serial Addition Test (PASAT), The Judgment of Line Orientation test (JLO), Addenbrooke's Cognitive Examination Revised (ACE-R), 7/24 Spatial Recall Test, Selective Reminding test **(**SR), Picture Naming Test, Symbol Digit Modalities Test (SDMT), Stroop test, and the subtests of vocabulary and information of the Wechsler Adult Intelligence Scale-Revised (WAIS-R). Table 2 shows the mean and standard deviation of the results for these tests found combined across the studies in the review.

Table 2- Summary of results (mean and SD) for test used across multiple studies

	Mean (SD) MS Group	Mean (SD) Control Group
BNT	**49.98(5.64)**	**54.42 (3.12)**
ACE-R	**91.03(7.39)**	**-**
7/24	**6.66(4.06)**	**3.45(-)**
WAIS-R (Vocabulary)	**49.75(10.9)**	**-**
JLO	**24.48(4.99)**	**-**

The BNT was the most commonly used test used across the studies included in this review, having been used in five of the studies. However, it should be noted that the mean and standard deviation of the BNT shown in Table 2 was calculated using data from only four studies (Beatty & Monson, 1989; Drake et al., 2002; Kujala et al., 1996; Tallberg & Bergendal, 2009). Data from the fifth study (Henry & Beatty, 2006), was excluded in the analysis due to the fact that as a review, the results provided related to effect size only and did not include raw data with mean and standard deviation. The average score of the BNT for the MS group suggests a relatively intact level of word retrieval skills (compared to conditions associated with prominent language deficits, such as post-stroke aphasia). However, it is important to note that the control groups in these studies still outperformed the MS group. In addition, when compared to the age-based normative data provided with the BNT, a deficit in word retrieval was also indicated. The participants with MS included in the four studies that used the BNT can be divided into two age groups. For the first group involving participants aged 40-49 years (Drake et al., 2002; Kujala et al., 1996; Tallberg & Bergendal, 2009), the performance mean and standard deviation was 49.55 (6.15), which is lower than the respective BNT normative data of 56.8 (3.0) (Kaplan, Goodglass, Weintraub, Segal, & van Loon-Vervoorn, 2001). For the second age group involving participants aged 60-69 years (Beatty & Monson, 1989), the mean and standard deviation was 51.3 (4.13), which again is lower than the 53.3 (4.6) BNT norms (Kaplan et al., 2001). Therefore, results of these studies indicate that participants with MS may have difficulties retrieving words, although, speed rather than simply accuracy of retrieval could potentially be a more sensitive index of this function.

Aside from the BNT, the remaining assessments shown in Table 2 were each used in two different studies. Performance on the WAIS-R, JLO and 7/24 Spatial Recall Test was compared between participants with MS and healthy controls in the studies of DeLuca et al. (1998) and Gaudino et al. (2001). Both studies failed to find statistically significant differences between participants with MS and the control group for the WAIS-R (subtest of vocabulary) and JLO. However, for the 7/24 Spatial Recall Test, the MS group needed more trials than the control group to achieve the criterion in both studies, with an average number of trials of 6.66 for the MS group compared with 3.45 for the control group. Performance on the ACE-R for participants with MS and healthy controls was examined in the studies of Connick et al. (2013) and Hamilton et al. (2009). Connick et al. (2013) did not provide any information about the differences between MS participants and control group for the task. However, Hamilton et al. (2009) found statistically significant differences between the scores for the MS group (mean = 91.17, SD = 6.49), and the control group (mean = 96.70, SD = 2.64).

In addition to the quantitative measures provided in Table 2, it is important to also mention some of the qualitative information provided in these studies about the performance of the participants with MS compared to those in control groups. DeLuca et al. (1998) and Gaudino et al. (2001) conducted studies to understand memory deficits in MS, with both using common assessment tasks including the JLO, WAIS-R subtest of vocabulary and 7/24 Spatial Recall Test**.** The results showed that for learning tasks, again, participants with MS usually need more trials than their matched control group to equal the level of learning of the control group (DeLuca, Gaudino, Diamond, Christodoulou, & Engel, 1998). Nonetheless, once the information had been learnt, both healthy control and MS groups performed at the same level (DeLuca et al., 1998). While consistent patterns of performance were generally observed across the two studies, they did differ in one aspect of memory performance. DeLuca et al. (1998) found that participants with MS performed worse than the control group for visual recall and recognition, while Gaudino et al., (2001) did not find any such difference between the control and MS groups.

Overview of clinical symptoms

The variable and heterogeneous, neurodegenerative character of MS is reflected in the wide diversity of speech and language disorders described in the studies examined in the current review. Four studies reported symptoms of dysarthria (Feenaughty, Tjaden, Benedict, & Weinstock-Guttman, 2013; Mackenzie & Green, 2009; Smith & Arnett, 2007; Yorkston et al., 2003). This deficit interacts with other cognitive impairments such as deficits in working memory leading to greater difficulty in carrying out assessment tasks (Hamilton et al., 2009; Mackenzie & Green, 2009). Dysarthria is caused by impairments to the motor and sensory systems for speech production which can be distinct from cognitive-linguistic deficits causing communication disorders but may often overlap with these also (Duffy, 2013). Seven studies found word retrieval deficits due to impairments in memory skills (Andrade et al., 2003; Brissart et al., 2012; Coolidge et al., 1995; DeLuca et al., 2013; Gaudino et al., 2001; Godoy et al., 1996; Sicotte et al., 2008). The possible underlying deficits causing memory impairments were found to include problems acquiring new information or in retrieving already encoded information. Finally, there were also four studies which reported anomic symptoms (impaired word retrieval) in people with MS against the background of different levels of cognitive-linguistic impairment (Beatty & Monson 1989; Drake et al., 2002; Friend et al., 1999; Tallberg & Bergendal 2009). Table 3 shows an overview of the types of symptoms noted in the results of the systematic review.

Table 3- Summary of symptoms found in the review per article

Study	Presence of dysarthria	Memory deficits	Anomia	Deficits processing information	Language and semantic impairments	Mixed
(Andrade et al., 2003)		✓				
(Armstrong et al., 1996)		✓				
(Beatty, 2004)		✓				✓
(Beatty & Monson, 1989)			✓			

(Bodling, Denney, & Lynch, 2008)	✓			✓		✓
(Brissart et al., 2012)		✓			✓	
(Connick, Chandran, & Bak, 2013)	✓			✓	✓	✓
(Coolidge, Middleton, Griego, & Schmidt, 1996)		✓				
(DeLuca et al., 1998)		✓			✓	
(DeLuca, Leavitt, Chiaravalloti, & Wylie, 2013)		✓		✓		
(Drake et al., 2002)			✓			
(Feenaughty et al., 2013)	✓					✓
(Friend et al., 1999)			✓	✓	✓	✓
(Gaudino, Chiaravalloti, DeLuca, & Diamond, 2001)		✓				
(Godoy et al., 1996)		✓				
(Hamilton et al., 2009)						✓
(Henry & Beatty, 2006)					✓	
(Huijbregts et al., 2004)						✓
(Jennekens-Schinkel, Lanser, Van der						✓

Velde, & Sanders, 1990; Kujala et al., 1996)						
(Kujala et al., 1996)					✓	✓
(Lethlean & Murdoch, 1997)					✓	
(Mackenzie & Green, 2009)	✓			✓	✓	
(Pijpers-Kooiman, van der Velde, & Jennekens-Schinkel, 1995)		**NO**				
(Sicotte et al., 2008)		✓			✓	
(Smith & Arnett, 2007)					✓	
(Tallberg & Bergendal, 2009)			✓		✓	
(Vlaar & Wade, 2003)					✓	
(Yorkston et al., 2003)	✓					

Description of specific clinical symptoms

Word and information retrieval problems

Before analysing the information found in the studies, it is important to clarify the differences between word retrieval problems and information retrieval problems. Although both tasks measure the number of words retrieved by a participant, they differ on the procedure and brain mechanisms involved in the task. The tasks used to measure word retrieval problems typically require a participant to name an object that is being presented to them. When measuring information retrieval problems, participants need to retrieve the name of objects previously presented to them after a delay period, for instance, 30 minutes after the presentation of the objects. The first naming task measures the skills a participant has retrieving verbal labels, while the second retrieval task is more focused on memory skills and the ability of acquiring and retrieve information previously presented.

Regarding the presence of word retrieval problems in MS, those studies which identified or discussed this symptom have been equivocal in delineating its nature and underlying cause. It is also important to note at this point that in reference to the distinction mentioned above, when studying retrieval problems in MS, most of the studies conducted to date in this area have studied information retrieval problems. For instance, authors such as DeLuca et al. (1998), Andrade et al. (2003), and Coolidge et al. (1996) conducted studies examining information retrieval deficits in MS, using lists of words as stimuli for studying possible deficits. In these studies, the number of words retrieved for a participant after a certain time was used to measure the skills a participant had retrieving words. Only a few studies have focused on word retrieval problems caused due to language impairment. An example of these types of studies is Drake et al. (2002), who conducted a study using word retrieval performance measures such as the BNT and verbal fluency tasks.

The lack of research studies on the topic of word retrieval specifically makes it difficult to understand the nature of any observed word retrieval deficits, or indeed, even how prevalent such deficits are. The variability of results found by different research studies also makes the task of arriving at a clear conclusion more challenging. In order to fully resolve the various accounts of word retrieval problems in MS, analysis of all research studies that have investigated word retrieval problems in MS is required.

Information retrieval problems

In order to process and use information, our brains need to be able to encode, store and retrieve this information (Brissart et al., 2012). A problem in any of these stages, such as those found in memory deficits, can produce impairments when trying to use information already known. Indeed, among the cognitive deficits produced by MS, memory deficits have been one of the most commonly observed impairments in MS sufferers (Andrade et al., 2003). Consequently, memory deficits have been studied as the main cause of information retrieval problems in MS. In fact, this review found eight research studies specifically focused on this.

While information retrieval deficits have been commonly observed in people with MS suffering from memory impairments, not all types of memory are impaired at the same time or impaired to the same degree (Andrade et al., 2003). There is increasing evidence of long-term memory problems in people with MS; however, the causes of this problem are not yet clear (Armstrong et al., 1996). The most plausible causes of long-term memory problems in people with MS are either deficits retrieving information or deficits acquiring information. With respect to other types of memory, for episodic memory, which refers to memory about autobiographical events, both acquisition and retrieval processes may be impaired. Moreover, both are considered to have an equal impact in the development of the information retrieval deficit (Brissart et al., 2012). As such, an information retrieval problem may result from a difficulty in retrieving stored information (Coolidge et al., 1996), or in the initial acquisition of that information which hinders the processes of information retrieval (Brissart et al., 2012).

Studies have found information retrieval problems in MS when trying to determine whether memory problems are caused by a deficit acquiring information or retrieving information (e.g., Godoy et al., 1996). One of the most widely considered possible causes for information retrieval problems related to memory impairment is the presence of deficits with the retrieval process specifically, with proper functioning regarding the acquisition of information (Armstrong et al., 1996; Coolidge et al., 1996). This type of underlying deficit has been supported by studies such as Armstrong et al. (1996), who found participants with MS had problems retrieving information from long-term memory. However, while such long-term memory deficits have been examined with reference to with problems retrieving information, the mechanisms used by MS patients to acquire information are often not explored or specified (DeLuca et al., 1998). The relevance of understanding the mechanisms to acquire information has arisen from the fact that people with MS have problems both recalling and recognising information; hence, the problem when retrieving information is caused by impairment in one of the initial stages of learning (encoding or storing) (DeLuca et al., 1998).

Information retrieval problems have been linked to deficits acquiring information that impede proper retrieval and recall of that information (Brissart et al., 2012). For example, in a study examining verbal memory impairments in people with MS, DeLuca et al. (1998) required participants to learn a list of words and then recall the list after 30 minutes, 90 minutes and 1 week. It was found that for this task, participants with MS needed more trials to learn the list; however, once the list was known, there were no differences between participants with MS and the control group. DeLuca et al. (1998) concluded that deficits in acquiring information accounted for the poor retrieval skills observed in people with MS. In this case, patients with MS cannot retrieve words from a previously studied list not because they cannot access the information, but because when learning the list there is a failure codifying information. This new point of view is of major importance to consider when studying retrieval problems from memory in MS. There are several modalities of acquisition of information involved in the first stages of learning. Visual and verbal learning are the modalities that are usually impaired in MS patients.

Whether the observed information processing deficits in MS are attributable to an acquisition or retrieval problem can be largely attributable to differences in participants, assessment and characteristics of the brain damage in each participant. For instance, the hippocampus is well known for its major importance retrieving information and working with episodic memory (Sicotte et al., 2008). Sometimes, MS produces brain damage in the hippocampus, and a lesion in the hippocampal sub-region CA1 can produce problems retrieving and encoding information in people with MS (Sicotte et al., 2008). The intensity or type of problem varies according to clinical course or stage of the disease (Gaudino et al., 2001). Given that MS is a degenerative disease, the brain damage that it produces degrades the white and grey matter tracts leading to a degree of difficulty storing information (DeLuca et al., 2013). As previously stated, the clinical course of the disease also plays an important role when studying the extent of this problem. This is because the progressive courses of the disease cause more severe cognitive impairment (Gaudino et al., 2001). Some variables that can be considered as relevant in word retrieval deficits and by extension to cognitive deficits caused by MS are the effect of physical disability, years with the disease and clinical course. While, there is evidence of the lack of relationship between these variables and their influence in retrieval deficits (Gaudino et al., 2001), the clinical course of the disease has an impact in language impairment (Friend et al., 1999). Consequently, the interaction between deficits plays an important role in the development of cognitive deficits. Overall, it can be said that problems acquiring information are involved in the development of retrieval problems, although, they are not the only cause.

Word retrieval problems

The next stage in understanding retrieval deficits in MS is to analyse studies which consider word retrieval deficits caused by impairments in language processing. Anomia is the term used to refer to problems retrieving words including both accuracy and speed of retrieval. Difficulties in word retrieval skills have been found among the studies of this review (Beatty & Monson, 1989; Drake et al., 2002; Mackenzie & Green, 2009). Nonetheless, there are also research studies denying the presence of this type of symptom in MS (Pijpers-Kooiman et al., 1995). The nature of the problem seems to be as yet unclear.

The first research studies that investigated cognitive-linguistic functioning in MS stated that MS sufferers did not usually present with language deficits (Rao, 1986). However, it is now clear that contrary to this assertion, some people with MS do indeed seem to present with language deficits (Friend et al., 1999). Furthermore, when word retrieval problems were identified in the cognitive sequelae associated with MS, they were considered to appear only in the last stages of the disease when there is a marked generalised cognitive impairment (Beatty & Monson, 1989). However, there is now evidence that this is not the case. For example, one research study found evidence of word retrieval deficits in almost 40% of participants with MS, despite the lack of a severe cognitive impairment in these participants (Beatty & Monson, 1989).

The principal reason why word retrieval deficits were thought to occur only in the last stages of the disease was due to the large number of investigations which did not find language impairments in MS (Friend et al., 1999). For example, a study about cognitive dysfunction in MS did not find language impairment in people with MS (Rao, 1986). Nonetheless, word retrieval deficits have been found in the first stages of the disease, and in both chronic progressive and relapsing remitting forms of the disease (Friend et al., 1999). These findings suggest that MS may indeed produce language impairments, despite the early views to the contrary (Friend et al., 1999).

Evidence for word retrieval deficits in MS have come from studies which have administered naming tasks. Picture naming tasks have frequently been used in patients with cortical dementia to evaluate anomia. However, as noted above, subcortical dementias such as MS have generally been believed not to produce word retrieval deficits, and as such, naming tasks have not always been implemented (Beatty & Monson, 1989). For those studies which have assessed naming in people with MS, the assessment most commonly used has been the BNT (Drake et al., 2002; Beatty & Monson, 1989; Tallberg & Bergendal 2009). In these naming tasks, participants with MS have been found to present with a higher number of errors compared to control group; moreover, these errors are more severe than the ones made by neuro-typical participants (Tallberg & Bergendal, 2009). As such, word retrieval impairments do indeed appear to be present in at least some people with MS.

With regard to word retrieval deficits evident in object naming tasks, there is a large set of skills involved in the task, and in order to understand the deficits observed, it is necessary to properly understand how this task works. Object naming or picture naming tasks refer to tasks where participants are presented with a picture of an object and then asked to name the object. This requires retrieving the correct word of the object. Although picture naming tasks may seem simple, there are four stages of cognitive processing that need to work sequentially to produce the correct output. The first stage involves the perception of the object and differentiation of physical characteristics of the object (Drake et al., 2002). Next, participants need access to semantic knowledge that will help to classify the object into a specific category and identify the concept presented in the picture (Drake et al., 2002). At this point the correct word is retrieved following which the participant needs to produce the correct phonological output (Drake et al., 2002). Problems may occur at one or several of these processing stages.

As noted above, research has found evidence that people with MS may indeed show naming deficits, producing more errors than healthy participants in picture naming tasks. When looking at naming errors in MS, it is important to analyse not only the rate of errors but also the type of error produced (Drake et al., 2002; Tallberg & Bergendal, 2009). The main errors are caused by perceptual problems and problems accessing to the lexicon (Drake et al., 2002). Another measure of relevance in the naming task is reaction time, which refers to the time required to name the picture since it was presented. Participants with MS have generally been observed to need more time to retrieve the word that corresponds with the picture than healthy participants (Beatty & Monson, 1989). A longer reaction time can be interpreted as a processing speed problem or deterioration of language skills (Beatty & Monson, 1989). Sometimes, the observed naming deficits can be improved if semantic or phonological cues to the word are presented to participants, resulting from the fact that these cues reduce the effort required to access to the mental lexicon (Beatty & Monson, 1989). The causes of the word retrieval problems observed in people with MS may be complex and varied. Since MS is a subcortical disease that produces deterioration of the grey and white matter, the deterioration of subcortical structures and different white matter language pathways may be an important contributing factor to the development of the deficit in retrieving words (Drake et al., 2002). Such neuroanatomical deficits have been found to produce language problems in individuals post-stroke (Kuljic-Obradovic, 2003).

Word retrieval problems caused by interaction of variables

The last point of view to consider in trying to understand word retrieval deficits in MS is the interaction of variables in the disease. This refers to the interaction between different impaired cognitive-linguistic domains, perceptual and motor systems. Indeed, it has been argued that the conflicting results that have been found in different research studies are not truly representative of the deficits presented by MS patients (Beatty, 2004). A range of variables can interact to cause a heterogeneous presentation of anomia: MS lesion site, presence or not of depression, extent of physical disability or years with the disease may interact with each other and the cognitive functioning of patients varies according to this interaction. Therefore, although MS can produce word retrieval problems, the cause and extent of the problem can be different in each person affected (Beatty, 2004).

As discussed above, there have been studies which have concluded that word retrieval problems do not typically occur in MS. One key reason why some authors have made this assertion is due to the fact that during assessment, when a task has been modified to make it easier, participants with MS have performed at a level close to that of the control group (Andrade et al., 2003). The next main reason to refute the presence of word retrieval problems in MS is because of its subcortical nature. Traditionally, subcortical diseases did not imply language processing deficits (Pijpers-Kooiman et al., 1995). Furthermore, a study using free word association tasks found that both healthy participants and those with MS produced the same type of responses, suggesting the core retrieval skills were intact (Pijpers-Kooiman et al., 1995). However, there is an important limitation with the study of Pijpers-Kooiman et al. (1995) in that there was no focus on the time required to name (latency), only on response accuracy. Word retrieval deficits, if present, are difficult to detect because they might be subtle and vary according to the cognitive characteristics of each individual. For this reason, the measurement of reaction time is of great value in these types of tasks, since a longer reaction time might be evidence of a greater difficulty retrieving words.

Having reviewed the evidence regarding whether people with MS typically present with word retrieval deficits or not, a final conclusion cannot as yet be arrived at. First of all, in the existing research studies there have been problems with the variables measured, since some studies failed to evaluate reaction time when retrieving words (Pijpers-Kooiman et al., 1995). Another possible problem could be the variability of cognitive deficits that MS produces. Additionally, differences between variables such as clinical course, years with the disease, degree of physical disability, presence of dysarthria etc., may vary across people with MS and impact on the deficits observed. Given this complexity, it is important that results regarding the presence or absence of word retrieval problems in MS should be analysed for each individual and not only at the group level. Finally, it is important to note that there have not been many research studies focused on the presence of word retrieval problems in MS caused by language disorders. Most research studies to date have focused on studying problems retrieving words from memory rather than examining the deficit as impairment to the language system. As such, further investigation into word retrieval problems caused by language impairment in MS, utilising tasks such as picture naming rather than memory and learning, is warranted. Furthermore, the topic would benefit from more systematic approaches to the sampling of patients as well as the techniques used to assess (Friend et al., 1999).

Language processing deficits

Apart from word retrieval problems in MS, there has also been research in other language deficits which may be produced by the disease. Processing deficits in MS can be found in multiple aspects of language. For instance, Friend et al. (1999) found patients with MS performing under the level of healthy participants in naming, verbal fluency, verbal memory and language comprehension. The most commonly reported deficits have been naming problems, verbal fluency deficits and deficits understanding complex language. Among the language deficits that have been found in patients with MS, verbal fluency deficits have been the most widely reported. The majority of these deficits are caused due to cognitive impairment; however, some symptoms may also be related to physical impairment (i.e., dysarthria). This results from the fact that while MS is a subcortical dementia, it may also affect cortical areas, such as those associated with motor planning and execution (Drake et al., 2002). Despite the fact both cognitive and motor linguistic deficits may interact with each other in MS, the majority of studies have analysed the two impairments independently (Feenaughty et al., 2013).

Impairments in verbal fluency have been commonly reported in people with MS when compared to healthy participants, and as such have been relatively extensively studied (Tallberg & Bergendal, 2009). This deficit is thought to be present in 25% of people with MS (Vlaar & Wade, 2003). However, this prevalence finding may be an under-estimate. The problem with such findings is that the nature of the language deficits can sometimes be subtle and the techniques used to measure the disability have not been sufficiently sensitive (Tallberg & Bergendal, 2009).

Deficits in verbal fluency have been linked to cognitive deterioration, but specifically to the deterioration of both memory and language impairment. When it has been related to memory impairments, the nature of the problem has been related to difficulty in accessing semantic memory (Andrade et al., 2003), or deficits in working memory (Friend et al., 1999; Henry & Beatty, 2006; Vlaar & Wade, 2003). When it has been related to language, the nature of the impairment has been related to problems in any level of linguistic processing as it is not clear at which level there is a disruption (Friend et al., 1999). Problems in executive functions have also been thought to be the cause of verbal fluency deficits (Henry & Beatty, 2006). In this case, participants may perform below the neuro-typical level because they do not employ the range of cognitive strategies to conduct the task effectively.

Regarding types of verbal fluency tasks, it is not clear whether semantic tasks (e.g., list of animals in one minute) or phonological tasks (e.g., list of words starting with 'f-' in one minute) are most affected by MS, since the results of different studies assessing verbal fluency have not been conclusive (Henry & Beatty, 2006). However, some research studies have related a poorer performance in the category of letter fluency to impairment in the prefrontal lobe and executive functions (Tallberg & Bergendal, 2009). Examples of MS and verbal memory impairment have also been found, but to a lesser degree (DeLuca et al., 1998; Friend et al., 1999).

The most common language deficits that occur in MS have been described so far. As stated previously, one characteristic people with MS have in common is that many suffer from remarkably varied changes in cognitive-linguistic functioning. This fact hampers investigations that try to establish the extent of different language deficits in MS. However, verbal fluency deficits, naming deficits and dysarthria have been found in several research studies, and could be considered as distinctive speech/language disorders in MS (Beatty & Monson, 1989; Bodling et al., 2008; Friend et al., 1999).

Apart from these language deficits, MS can also produce impairment in other aspects of language processing that have not yet been mentioned in this review. These symptoms have been noted in higher level language processing tasks. Typical symptoms include problems understanding metaphors, difficulties drawing inferences or understanding double meaning sentences (Lethlean & Murdoch, 1997). In order to be able to understand metaphors or draw inferences, a person needs to be able to process linguistic information at multiple levels and incorporate semantic and pragmatic understanding of real world contexts and/or the intention of the speaker. These processes are multi-faceted and the lower performance of people with MS could be attributable to a range of cognitive-linguistic deficits (Lethlean & Murdoch, 1997). Regarding the underlying neuroanatomical cause of such high level language deficits, these impairments have been related to the loss of myelin sheaths and damage of subcortical pathways (Lethlean & Murdoch, 1997). Furthermore, the disconnection between cortical and subcortical structures has also been implicated as a possible cause of higher level language deficits in MS (Lethlean & Murdoch, 1997).

Dysarthria

Dysarthria is one of the most common motor speech disorders that can be present in patients with MS. It refers to an oral-motor dysfunction present in between 40% to 50% of people with MS (Bodling et al., 2008; Mackenzie & Green, 2009). Dysarthria in MS derives from the motor and sensory symptoms arising from lesions in the CNS caused by demyelination which restricts speech production and detract from speech intelligibility (Smith & Arnett, 2007). This disorder presents different characteristics according to which areas of the brain have been damaged. The main types of dysarthria that can be found in MS patients are ataxic, when the damaged has occurred specifically in the cerebellum, and spastic, when the damage has occur in the upper motor neurone which carries motor information (Mackenzie & Green, 2009). The intensity of this disorder is measured by techniques that measure speech intelligibility (Feenaughty et al., 2013). This dysfunction is usually accompanied by body tremors and nystagmus, and it is not linked to years with the disease (Smith & Arnett, 2007; Yorkston et al., 2003).

Dysarthric symptoms have been widely reported in MS sufferers, and have a considerable impact on the performance in tasks assessing language processing (Bodling et al., 2008; Connick et al., 2013; Feenaughty et al., 2013). Deficits in comprehension and expression usually appear in people suffering from moderate dysarthria because of the interdependence between language and other cognitive domains (Mackenzie & Green, 2009). One of the principal causes of language deficits resulting from dysarthria is the fact that patients suffering from the deficit present with slower and slurred speech, and impaired articulation (Smith & Arnett, 2007). In fact, studies have found that this deficit hampers the performance of participant leading to worse results, not because of cognitive deterioration but because of difficulties articulating language (Bodling et al., 2008).

Although there is evidence of the difficulties dysarthria causes when performing a language test, to date there is no research study that has explicitly examined whether there is a relationship between anomia and dysarthria. Moreover, although it is known that dysarthria has a negative impact on performance in language tasks, there is no information about the degree of that impact.

Mixed presentations

This literature review has established that MS produces deficits in several cognitive-linguistic domains. As has been previously stated, people with MS can suffer from language deficits at different levels of processing to different degrees. To these it must be added cognitive-linguistic impairment stemming from other cognitive domains. The deficits MS produces interact with each other while conducting a task. This interaction is not yet clear; however, there is evidence of the negative impact that it produces in the results obtained in different assessments (Beatty, 2004; Feenaughty et al., 2013; Hamilton et al., 2009). For example, a patient can perform poorly in a language task because of problems with, for instance, working memory (Hamilton et al., 2009). In this situation, the result obtained in the task is not reflecting the real level of knowledge/ability of the participant, but the result of an interaction between deficits. In fact, there is evidence suggesting that speech problems such as dysarthria and performance in cognitive-linguistic tasks might be associated in people with MS (Feenaughty et al., 2013). Although further research is required to understand this association, a poor performance in motor speech tasks can worsen the performance in cognitive-linguistic tasks (Feenaughty et al., 2013). Another example could be problems with processing speed, which along with dysarthria or oculomotor problems can make participants obtain lower scores in picture naming tasks. Such a result is not due to language impairment per se but to the interaction between deficits (Bodling et al., 2008). In fact, when stimuli in a picture naming task are presented in different regions of the screen, instead of always in the centre, participants with MS perform worse than when all pictures are presented in the same region, indicative of factors affecting performance outside of the language system (Bodling et al., 2008).

The interaction between variables is important in understanding the nature of deficits such as naming problems, although this has sometimes been related to physical problems (such as visual or motor deficits) instead of cognitive-linguistic problems (Beatty, 2004; Kujala et al., 1996). This happens because language is a cognitive domain that can be easily affected by problems in other domains, since it is a complex domain that involves processing across multiple levels (Beatty, 2004). As can be seen, the interactions between variables make MS participants perform under the level of the control group. For these reasons, the relevance of the interaction between different cognitive deficits is becoming increasingly important.

The interaction between factors needs to be considered when assessing patients with MS because the results may not show their real level of cognitive impairment, but lower performance caused by other deficits that are also contributing to the result (Connick et al., 2013). This is an especially important consideration in two situations. Firstly, when assessing a group of participants which present both progressive and relapsing clinical courses. Patients with progressive clinical courses usually have more severe cognitive deficits; however, the data of both clinical courses is commonly analysed at the same time, although they do not always present with the same deficits (Connick et al., 2013). Secondly, when providing therapy to patients with cognitive dysfunction in several cognitive domains, since the interaction between deficits can reduce the effect of the therapy (Feenaughty et al., 2013). Nonetheless, there is currently no information about the intensity of the interaction between different cognitive deficits and variables of the disease (Feenaughty et al., 2013).

The interaction between variables, both cognitive and disease-related, is complex and is currently poorly understood. There are a number of factors which may interact in unknown ways to affect performance on a given assessment. For example, there is evidence that the nature of the assessment task can influence cognitive-linguistic performance. For example, studies have found that people with MS perform better in a cognitive-linguistic domain when this is assessed with a general battery of cognition, than when assessed with a specific test for the aforesaid domain (Jennekens-Schinkel et al., 1990). A small number of participants and selection of assessments with doubtful validity can be also added as problems when assessing and comparing the cognitive status of a participant with MS within these studies (Beatty, 2004; Jennekens-Schinkel et al., 1990). In addition, the variety of participants within the sampled groups also leads to challenges in drawing lessons from the literature. Every clinical course produces different profiles of deficits, and impairments that are observed do not have the same level of intensity (Huijbregts et al., 2004). Continued research is required to unravel the impact of these issues on the findings and interpretations across studies regarding the prevalence and nature of cognitive-linguistic deficits in MS.

Discussion

Multiple sclerosis is a neurodegenerative disease that produces several speech and language disorders caused by motor-sensory and cognitive-linguistic deficits stemming from damage to subcortical and cortical pathways in the brain (Lethlean & Murdoch, 1997). Due to its neurodegenerative nature and the accumulation of an array of disabilities across the lifespan, it has always been difficult to identify the main characteristics of the deficits produced by MS. This is exacerbated by the fact that the location of lesions in the brain varies across patients, leading to different patterns of symptom presentation. The current systematic review aimed to identify the degree and nature of speech and language disorders found in MS. The deficits reported in studies included in this review are depicted in Figure 7.

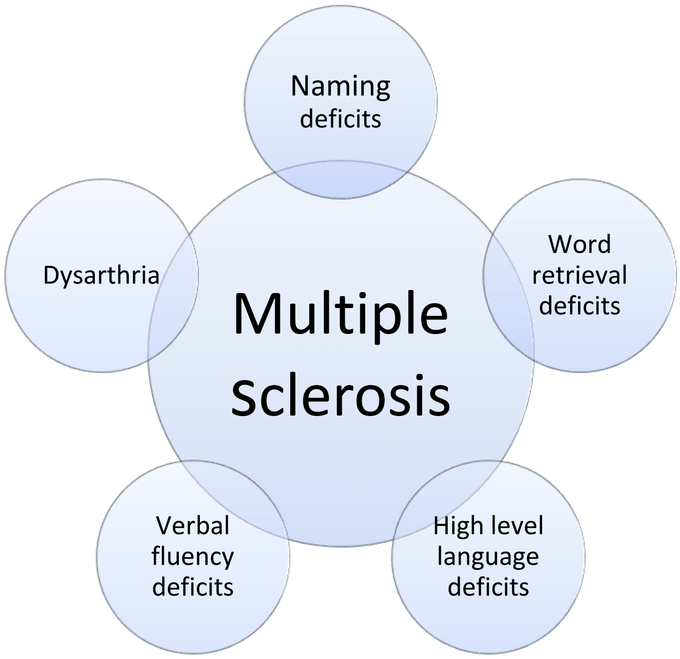


Figure 7- Speech and language disorders found in the review

Overall, and despite the growing literature, the nature of word retrieval problems in MS remains challenging to define because of the large number of variables interacting in MS. Some of the main variables involved in the development of word retrieval problems include working memory deficits, problems accessing the mental lexicon or problems recognising objects. To this, the complexity of language processes must be added. Most of the results found in different research studies show conflicting findings, with a failure to find the same deficits or similar degrees of impairment across studies. For example, while some studies (e.g., Drake et al., 2002) have found language deficits such as anomia, others (e.g., Rao, 1986) , have not found this deficit. The variability in the nature of MS has helped to contribute to the discrepancy in findings between studies and the resulting controversy, with wide variability between lesion site, extent of the lesion in the brain and clinical course across people suffering from the disease.

While it was initially postulated that MS was not commonly associated with language deficits, studies have revealed problems in a number of linguistic domains, most notably word retrieval (Drake et al., 2002; Beatty & Monson, 1989; Tallberg & Bergendal 2009). Regarding the information found about word retrieval problems in MS, the majority of research studies have focused on retrieval problems due to memory failure (Andrade et al., 2003; Armstrong et al., 1996). In contrast, there has been little research into word retrieval problems due to language impairment specifically. This may be because this deficit is difficult to detect. However, although the consequences may go unnoticed in early stages of the disease, studies have suggested that with disease progression the impairment may have a major impact. In addition to word retrieval problems, other prominent speech/language symptoms reported in this review included the presence of verbal fluency deficits and dysarthria.

With regards to verbal fluency deficits, it seems clear that people with MS typically have problems with this type of task. Several studies, such as Friend et al**.** (1999) and Vlaar and Wade (2003), have found impaired performance across both phonological and semantic fluency. The nature of this deficit has been associated to language disorders that reduce the skills of MS participants to find words. Problems with executive function or working memory have also been studied as causes of a reduced verbal fluency (Henry & Beatty, 2006). This situation is a perfect example of the impact that the interaction between variables has. For this reason, in order to understand and provide a proper diagnosis, it would be necessary to conduct more comprehensive assessments to differentiate the precise nature of the impairment producing the observed verbal fluency deficit. This will lead to a better understanding of the cognitive profile of participants with a poor performance in verbal fluency tasks.

With regards to dysarthria, there have been multiple research studies focused on the presence of dysarthria in people with MS. Several studies, such as Mackenzie and Green (2009), Smith and Arnett (2007), and Yorkston et al. (2003), have investigated the interaction of dysarthric symptoms with cognitive or physical tasks. However, although they emphasize the likelihood of dysarthria having a negative impact on the performance in some tasks, they failed to specifically investigate its impact. The result of this is that, although it is known that dysarthria hinders performance in some tasks, there is no information about which aspects of task execution are most affected, or what is caused by dysarthria and not by other deficits.

Apart from the range of speech and language disorders that can be found in many people with MS, understanding the interaction between them is of critical importance. Sometimes when assessing one cognitive-linguistic domain, it is practically impossible to eliminate the influence of other cognitive-linguistic domains and physical disability. For this reason, the level a participant can attain in a task depends on all the variables involved in the task. This should be controlled in order to obtain an exact measure of the impairment a person has in a specific domain. However, no matter how specific tasks are for a given cognitive-linguistic domain, they always involve more than one cognitive process and by extension cognitive domain.

What is clear, and has been found across all studies, is that people with MS invariably tend to perform less well than healthy participants in linguistic tasks, showing reductions in accuracy or increased latencies. However, there is currently not enough evidence to confirm or refute whether patients with MS typically suffer from anomia. Furthermore, when anomia has been found in people with MS, the information thus far available has been insufficient to allow understanding of what is causing this problem. For example, Beatty and Monson (1989) found that participants with MS present this type of deficit even when the level of cognitive impairment has not reached a severe level (Beatty & Monson, 1989). Problems with processing speed or accessing lexical knowledge can be causing this deficit; however, the relative contribution of each factor is unknown (Beatty & Monson, 1989). An approach that could be taken to solve these problems could be introducing regular cognitive evaluations to people with MS. There should be regular evaluation on how cognitive-linguistic skills vary throughout time to have a better understanding of the interaction between variables. This might help to clarify some of the current questions regarding the relationship between variables such as motor speech problems and cognition or the nature of anomic problems in MS. However, despite the relevance of assessing cognitive-linguistic skills in people with MS, this is not common nowadays (Hutchinson, 2016). The lack of funding, people with enough qualifications to conduct the evaluation and time hamper the introduction of this routine (Hutchinson, 2016).

For this reason, further research should be conducted to fully understand the nature and extent of word retrieval problems in MS and if there is an interaction between deficits (i.e., dysarthria and anomia). With a better understanding of the presence of these deficits in MS, the development of new therapies that will be better matched to the needs of each individual will be possible. This is of major importance since communicative problems have a negative impact in the personal, social and professional functioning of people with MS.

CHAPTER 4: Investigating Anomia in People with Relapsing-Remitting Multiple Sclerosis

Given the lack of clarity provided in the existing literature on the nature and extent of MS, as reflected in both the Introduction and Systematic Review above, an empirical study to investigate anomia in people with MS was conducted. After liaison with regional Neurology services, the TYSABRI clinic at one Regional hospital was identified as offering the most reliable access to people with MS. This, however, restricted the study to people with Relapsing-Remitting Multiple Sclerosis (RRMS) given that this is the population that TYSABRI targets. Although this has some disadvantages in that it would not throw light on the topic of anomia in people with MS more broadly (including those with primary and secondary progressive sub-types for example), it had the advantage of focusing on RRMS which includes people with a wide spectrum of physical and cognitive disability, many of whom were likely to be engaged in employment where language deficits may place some restrictions on their everyday functioning. A copy of the testing protocol submitted to the National Health Service Research Ethics Committee (REC) is attached in Appendix B.

This section provides information about the characteristics of the participants and the assessments included in this research study into anomia in people with RRMS. A rationale for the selection of the tasks and information about items included in each assessment is also provided.

Setting

To investigate the nature and frequency of anomia in people with MS, we liaised with the Neurology clinic at Salford Royal NHS Foundation Trust (SRFT). SRFT is a foundation teaching hospital which serves patients from Salford and Greater Manchester. Given the dearth of existing knowledge as to speech and language skills in people with MS, we aimed to conduct a broad, time-efficient screening assessment which would allow us to capture a general profile of the speech and language skills of a relatively large database of people with RRMS. We therefore aimed to obtain screening assessment data for 100 people with MS.

Methods

The tasks selected for the screening assessment in this research project were a brief interview and four distinct behavioural assessments.

Interview

The interview consisted of questions that aimed to obtain information about number of years with the disease, years of education or working status. Moreover, it aimed to help participants to feel comfortable with the researcher and the environment in which the assessment was going to be conducted. Some examples of questions included in the interview are:

1) Approximate number of years diagnosed with MS
2) Years of education
3) Handedness

Addenbrooke's Cognitive Examination –Revised

The first behavioural assessment was the Addenbrooke's Cognitive Examination – Revised (ACE-R) (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006). This test battery is used to assess severity and progression of symptoms of dementia. It encompasses tasks to assess orientation, registration, attention and concentration, memory, language and perceptual abilities. These cognitive domains are assessed in different subtests; each of them has a specific score. The scoring of the test consists of counting the number of correct answers in each subtest and adding up the scores of every task according to their value. Information about how to score the ACE-R is provided within the questionnaire of the ACE-R. The highest score is 100 points with a cut-off at 88 points that gives 94% sensitivity and 89% specificity for dementia (Mioshi et al., 2006). This task is usually administered in approximately fifteen minutes.

The subtests included in the ACE-R (Mioshi et al., 2006) are divided according to the cognitive domain that is being assessed. The first subtest starts with an orientation task with questions about the date and place where the assessment is being conducted.

Once this part is concluded, attention is assessed with tasks such as counting backwards and a spelling task. For memory, which is the next cognitive domain to be assessed in this test, there are different tasks according to the type of memory that is to be assessed. The types of memory included are recall, anterograde memory and retrograde memory. The tasks included to measure participant's language skills are verbal fluency, comprehension, writing, repetition, naming, and reading. An example of the questions participants are asked to answer in this test is the verbal fluency task which is divided in phonological and semantic fluency. In this task, participants are required to name words that start with either a letter (e.g., the letter "P") or from a particular category (e.g., animals) respectively in each condition. The last tasks of the ACE-R (Mioshi et al., 2006) aim to measure visuospatial and perceptual abilities.

The importance of this test battery lies in the wide range of cognitive domains that are addressed, as it helps to obtain a general measure of the cognitive status of the participants. Given that MS produces cognitive deterioration in multiple cognitive domains, by using this test, a comparison between different cognitive domains is provided when analysing the results of each subtest (Achiron et al., 2013; Amato et al., 2007). This is practical because instead of using different behavioural assessments that are specifically focused on one aspect of cognition, this test measures all relevant cognitive domains. Moreover, it reduces the time required to conduct the assessment and therefore, it reduces cognitive fatigue.

The ACE-R (Mioshi et al., 2006) has been used in previous studies with people with MS, proving to be sensitive to detect cognitive impairment in people with MS (Connick et al., 2013; Hamilton et al., 2009). In both studies, participants performed slightly above the cut-off (score 88) with a mean and standard deviation of 90.9(8.3) and 91.17(6.49) for the studies of Connick et al. (2013) and Hamilton et al. (2009), respectively. The average score of the participants with MS was particularly close to the cut-off.

Picture Naming Task

The next assessment was a Picture Naming Task. As previously mentioned, this type of task has been widely used to assess naming/retrieving skills in people with MS (Bodling et al., 2008; Jennekens-Schinkel et al., 1990). For example, the Boston Naming Test (BNT) has been widely used when studying naming skills in people with

MS (Beatty & Monson, 1989; Drake et al., 2002; Henry & Beatty, 2006; Kujala et al., 1996; Tallberg & Bergendal, 2009). This research project aimed to further the knowledge in the differences between the MS and control group in naming skills by analysing both accuracy and reaction time using a bespoke naming assessment.

The Picture Naming Task included in this assessment was displayed on a computer screen and took approximately eight minutes to complete. The computer was located on top of a table and approximately 20-30 centimetres away from the participant. The task consisted of sixty pictures selected from The International Picture Naming Project (IPNP) (Bates et al., 2000). The sixty pictures selected depicted objects (i.e., were nouns with no verbs) since there is a different response in the brain to nouns and verbs (Damasio & Tranel, 1993). Three other pictures were displayed at the beginning of the task as examples to familiarise participants with the procedure, with the sixty pictures selected then presented after the initial examples.

The sixty pictures of the task were selected and divided into four homogenous groups of 15 pictures based on the reaction time (RT) in milliseconds (ms) required to name the picture, obtained from the normative data provided by the IPNP (Bates et al., 2000). Reaction time was chosen to divide the groups so that deficits in processing speed and naming latency could be assessed as well as accuracy. The four different reaction time groups were:

Group A: 15 pictures with a reaction time <800 ms;

Group B: 15 pictures with a reaction time between 801-1000 ms;

Group C: 15 pictures with a reaction time between 1001-1220 ms;

Group D: 15 words with a reaction time between 1220-1500 ms.

Psycholinguistic variables associated with language performance were also obtained, specifically frequency, age of acquisition and length of phonological syllables. The information regarding the psycholinguistic variables (frequency, age of acquisition and length of phonological syllables) was also obtained from the normative data from the IPNP (Bates et al., 2000). Appendix C shows the words included in each subgroup of words and information about psycholinguistic variables of each subgroup.

Regarding the differences between the words of each group in frequency (the number of times a word is used in oral language, measured in occurrences per million), group mean frequency decreased as the group mean reaction time increased. Therefore, words in the group with the longer average reaction time (Group D) had a lower frequency while words in the group with a faster reaction time (Group A) had a higher frequency. In Figure 8, a summary of the comparison of the frequency between groups is shown. A higher value in frequency means that the word is commonly used in oral language. The information regarding the frequency of each word was obtained from the IPNP (Bates et al., 2000).

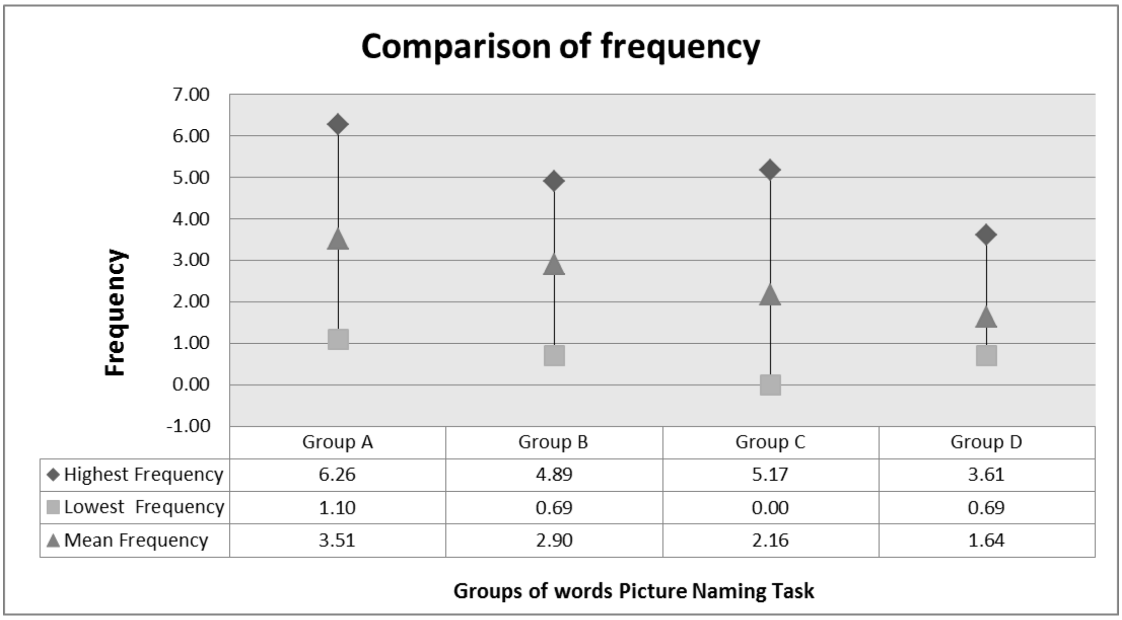


Figure 8- Comparison of frequency between subgroups of words included in Picture Naming Task

Another variable of interest considered in the selection of words in each group was age of acquisition, the average age at which people usually learn a word. This value was obtained from the IPNP (Bates et al., 2000). Age of acquisition values are divided into three groups: Group 1, with value equal to 1, is for words learned between 8 and 16 months; Group 2, with a value equal to 2, is for words learned between 17 and 30 months; Group 3, with a value of 3, is for words learned with more than 30 months (Bates et al., 2000). As can be seen in Figure 9, the average age of acquisition of each group increases as the reaction time of the group increases.

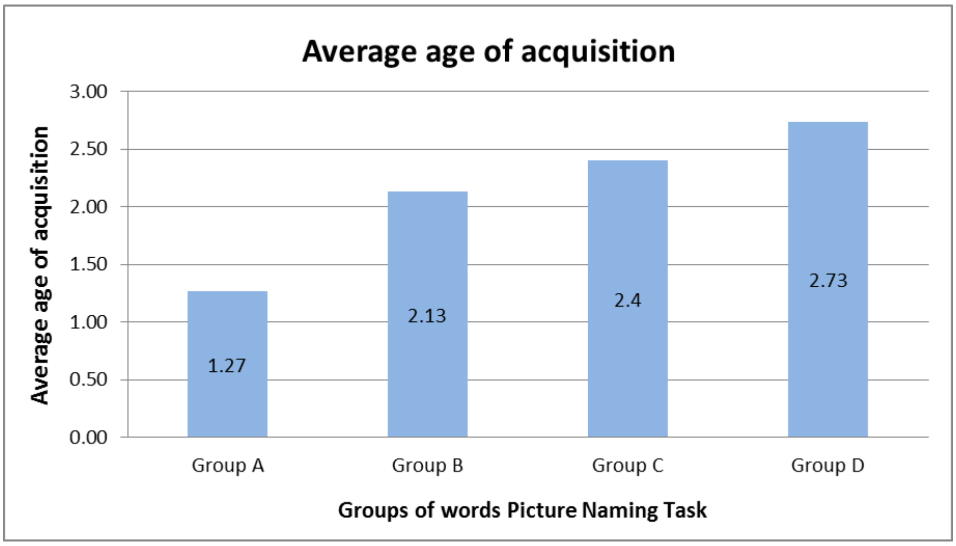


Figure 9- Comparison of age of acquisition between subgroups of words included in Picture Naming Task

Finally, the last variable considered to create the groups of words was word length as measured by number of phonological syllables. This value was obtained from the IPNP (Bates et al., 2000). In this case, three out of four groups share the same average length of phonological syllables (1.73). The remaining group (Group D) has a higher average in this variable (2.0). In Figure 10, a comparison between groups in length of words in phonological syllables is shown.

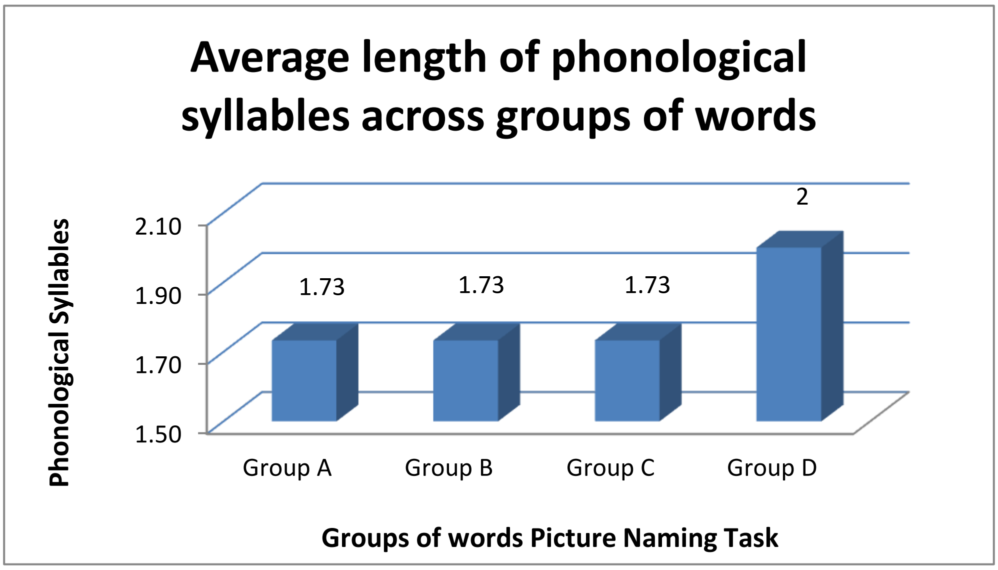


Figure 10- Comparison of length of phonological syllables per word in each subgroups of words included in Picture Naming Task

Overall, Group A (<800 ms) which consists of words with a faster average reaction time, also consists of words commonly used in oral language, which are learned at an earlier stage in life. Regarding the length of acquisition of this group (1.73), it is the same as Groups B and C. On the other hand, Group D (1221-1500 ms) with the slowest average reaction time consists of words less common used in oral language, are learned at a later stage in life and are slightly longer to name. The interaction between these variables means that it would be harder for participants to name these words in comparison with the words from the rest of the groups. Group B (801-1000 ms) and Group C (1001-1220 ms) have the same average length of phonological syllables; however, the words included in Group B are learned somewhat earlier than the words included in Group C. Finally, Group B consists of more commonly used words than Group C with an average frequency of 2.9 and 2.16 respectively.

Regarding the development of the task, this was carried out using Open Sesame software which is used to devise psychological experiments. The task consisted of the presentation of the pictures selected from the IPNP (Bates et al., 2000), along with the simultaneous presentation of a sound (for reaction time analyses), with the participant instructed to name the picture aloud. Before the picture appeared, a fixation dot was presented in the centre of the screen for one second where the picture was to appear to ensure the participant was looking at the correct location. There was a six seconds interval between the presentations of pictures for the participant to name the picture that appeared on the screen. The picture stayed on the screen for six seconds and then moved on to the next picture automatically. The fixation dot was presented for one second. The stimuli from the four groups of pictures were distributed randomly, but presented in the same order to all the participants. Figure 11 shows an example of the presentation of the stimuli for this test.

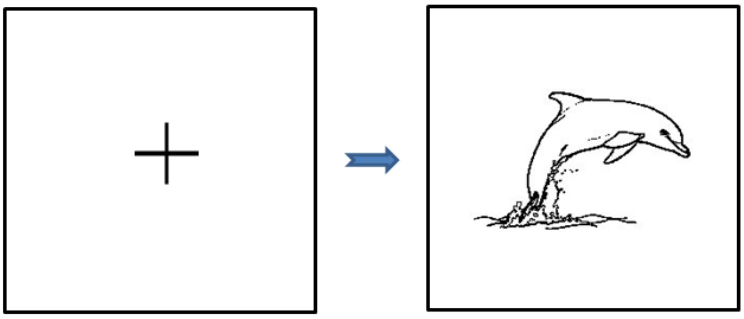


Figure 11- Example Picture Naming Task ***(Fixation dot displayed for 1 second/ Picture displayed for 6 seconds)***

During this task, participants were audio-recorded with a sound recorder, which allowed measurement of the reaction time required for each participant to name the picture.

The time required for participants to name the pictures was compared to the normative data of the reaction time obtained from the IPNP (Bates et al., 2000) to detect any deficits in naming latency. The maximum accuracy score for the task was 60 points. Each correct answer was considered as 1 point, on the contrary an incorrect answer or omission was considered as 0 points. A list including the words accepted as correct answers in the Picture Naming Task is included in Appendix D.

National Adult Reading Test

The National Adult Reading Test (NART) (Nelson & Willison, 1991) was the next behavioural assessment. This task was included for two reasons. Firstly, it can be used to derive an estimate of pre-morbid IQ. Secondly, as it requires participants to read words aloud, it allowed us to screen for the presence of dysarthria through recording single word reading production.

This assessment consists of 50 irregular words displayed on a screen of a computer which participants are asked to read aloud. The computer was on top of a table approximately 20-30 centimetres away from the participant. Examples of the words included in this behavioural assessment are the words ‘chord’, ‘ache’, ‘depot’ and ‘aisle’. According to how a participant pronounces the words, they would be classified as correct or incorrect. The maximum score for this task is 50 points, as the task consists of 50 items. The time required for this task is approximately five minutes.

As well as the Picture Naming Test, this task was audio-recorded to further analyse the responses of participants. By recording the answers, the presence or not of dysarthria reading isolated words could be detected. To assess the level of dysarthria of each participant, the Therapy Outcome Measure for Dysarthria was used (Enderby, John, & Petheram, 1997). This allowed scoring of the severity of the problem across a five point scale. The descriptors of this five point scale are: "0" profound dysarthria, "1" severe/ moderate dysarthria, "2" moderate dysarthria, "3" moderate/mild dysarthria, "4" mild dysarthria, and "5" no dysarthria (Enderby et al., 1997).

The NART (Nelson & Willison, 1991) has been widely used to assess premorbid intelligence in people with different types of neurological diseases, including a research study that used it with people with MS (Friend & Grattan, 1998; Friend et al., 1999). The efficacy of this test relies on the assumption that the skills someone has reading words that are not regular (i.e., violate spelling-sound correspondences), are not related to brain damage, and can help to predict the premorbid level of intelligence of a person (Bringfelt et al., 2006). However, there is evidence with the American version of this test (NART-R) that suggests that this task cannot be used to estimate premorbid intelligence in people with MS because of the language deficits caused by the disease (Friend & Grattan, 1998). For this reason, in the present research study this test has been used to detect the presence of dysarthria reading isolated words (as it involves reading aloud) and as a measure of reading skills, and has not been utilised as an estimate of general intellectual functioning. Regarding the differences between the MS and normative data for this task, the study of Friend et al. (1999) found that people with MS had a mean error rate and standard deviation of 24.6 (11.4), which is considerably close to the cut-off for the task which is 24 errors. As such, it seems that there is only a narrow difference between both MS and normative data in this task. However, as mentioned above, the score obtained by the MS group does not represent the level of premorbid intelligence of the group.

Pyramids and Palm Trees

The last behavioural assessment utilised in the screening assessment was the Pyramids and Palm Trees (Howard & Patterson, 1992). This task is used to assess semantic processing of concepts. Although there is no evidence of the use of this technique in people with MS in the literature reviewed so far, this is a task designed to assess semantic knowledge, which may contribute to language deficits such as anomia. Since this research project aimed to further the knowledge of language skills in people with MS, this task was included to provide information to complement the findings from the rest of the tasks.

The Pyramids and Palm Trees (Howard & Patterson, 1992) consists of 52 items, each one of which includes three pictures. The three pictures are presented to the participants in a paper format at the same time, with participants required to select which of the two alternatives presented on the bottom is more related to the target picture located above them. Participants need to access the meaning of the pictures that are presented to them, and to establish a semantic relationship between two of the pictures. Figure 12 shows an example of this test.

Figure 12- Example Pyramids and Palm Trees Test (Howard & Patterson, 1992)

In this task, oral language is not required, as participants are not asked to name the pictures, only to point to their answer. The time required for this task is approximately five minutes. The maximum score for the task is 52 points, as the test consists of 52 items. Every correct answer counts as one point, omissions are considered as errors. The cut-off for the normative data is 49.

This task is relevant for the assessment because in order to conduct the task, participants need to be able to activate the concept or meaning of the pictures and the relationship between them. When the correct meaning of the target picture is activated, the person would be able to link two of the pictures because of their semantic relation. However, if there is a problem in this stage, the participant would have problems establishing semantic relations between the three pictures. This type of difficulty accessing semantic knowledge is very common in anomia, and is in fact, the main characteristic of semantic anomia (Laine, 2013).

Implementation

The aim of the assessment battery designed for the current project was to screen the communication skills of a large dataset of participants with MS. Before the recruitment of participants, the researcher obtained a Research Passport to be able to access to an NHS hospital.

Once the Research Passport was obtained, the first step consisted of recruiting participants at the Neurology clinic at SRFT. The researcher attended the Neurology clinic three times per week over two months to recruit participants. Before the assessment, all possible participants were informed about the study by the investigator. Once the participants showed interest for the study, they were given a Participant Information Sheet (PIS). This document provides further information regarding the experiment and a contact number and email for any queries about the study. A copy of the PIS can be seen in the Appendix E and a copy of the Consent Form can be seen in the Appendix F. Once the participants had had the opportunity to ask questions about the research project, they signed the consent form if they were happy to proceed with the assessment.

All participants were assessed at the hospital, during their infusion (TYSABRI) time. This medication is prescribed as treatment for people with RRMM. The infusion does not produce any type of cognitive side effects that can have a negative influence in the performance of the participants. In fact, this medicine helps to reduce the number of outbreaks of the disease and thereby decrease the negative impact MS has in cognition. However, since these participants were assessed during their infusion time, this atypical testing condition (i.e., a needle...) may have hampered their performance in different tasks.

Because participants were assessed during their infusion time, they only had approximately one hour to participate in the research. The time required to complete the interview and the four behavioural assessments was approximately 45 minutes. However, this time varied between 35 to 60 minutes according to the participant.

During the assessment, participants were audio-recorded to help detecting dysarthria and evaluate their naming skills and reaction time. The participants were assessed in either the room in which they received their TYSABRI infusions or in a different room in the same ward to help them focus on the tasks. The order of the tasks of the assessment was as follows: interview, ACE-R (Mioshi et al., 2006), Picture Naming Task, NART (Nelson & Willison, 1991), and Pyramids and Palm Trees (Howard & Patterson, 1992).

Participants

Screening assessments were carried out between March and April in Salford Royal NHS Foundation Trust. By the end of this time frame, 105 participants with RRMS had consented and taken part in the screening assessment. All participants were assessed while they were getting their monthly infusion of TYSABRI.

Inclusion criteria were: (1) presence of MS, (2) participants over the age of 18, (3) native English speakers, and (4) enough physical ability in the upper limbs to allow participants to fill in the questionnaires. The reasons for conditions 3 and 4 were primarily because language is the main cognitive domain to be assessed. Hence, participants needed to be able to fully understand the instructions in English. If a participant did not have English as native language, the results in some tasks would have little value, since the result does not show the real level of cognition in that domain particularly in relation to the Picture Naming Task and NART (Nelson & Willison, 1991). Regarding the ability to complete questionnaires on their own, participants needed to be able to read and answer the questions alone to ensure the quality of the results obtained.

Within the 105 participants recruited, only one presented with visual problems that affected the results in the Picture Naming Task because of difficulty in identifying five out of sixty objects. For this reason, this participant was excluded. Three other participants were also excluded because they could not complete some of the visuospatial tasks of the ACE-R (Mioshi et al., 2006) because of the presence of tremors and/or difficulty in holding a pen. Finally, another participant was excluded because he was a habitual consumer of illicit drugs which was deemed likely to have a marked effect on cognitive functioning not related to MS. Data for the remaining participants (n=100) is presented in the Results section.

CHAPTER 5: Results

The first section of the results provides an overview of the demographic characteristics of the 100 participants included in the study. The second section of the results is focused on the data collected from the interview and the behavioural tests: ACE-R (Mioshi et al., 2006), NART (Nelson & Willison, 1991), Picture Naming Task and Pyramids and Palm Trees (Howard & Patterson, 1992). These data are presented in the following order: firstly, mean scores across MS participants compared to control scores; then, showing individual results for each participant in each task; and, lastly, showing the scores from the participants with MS in rank order (from strongest to weakest) against the control cut-off. Finally, the last section includes statistical analyses of the data.

Demographic data

All 100 participants presented with Relapsing-Remitting Multiple Sclerosis (RRMS) and were being treated with TYSABRI. Table 4 provides a summary of the demographic information of participants included in the present study.

Table 4- Average information of demographic data

Gender	Number	Average age	Average years with MS	Average years education
Male	32	41.41	8.11	14.81
Female	68	40.60	7.62	14.68

There were only two missing data points in the demographic data reported. The first missing value was the years with MS for one participant (no.56). The second missing value was the number of years of education for another participant (no.14). The demographic data is consistent with previous studies regarding these variables, and appears a good representation of the population of individuals with MS.

Global data

Demographic information

Table 5 shows demographic data for each participant.

Table 5- Demographic data

Participant	Gender	Handedness	Age	Years MS	Years Education	Work	Type of work
1	Female	Right	38	1.5	16	Yes	Radiographer
2	Female	Right	38	12	17	No	
3	Male	Left	30	8	14	Yes	Account manager
4	Female	Right	45	8	16	No	
5	Female	Right	66	4	18	No	
6	Female	Right	36	9	17	Yes	Retail manager
7	Female	Left	26	3.5	12	Yes	Director
8	Male	Right	51	4	17	Yes	IT services
9	Male	Left	25	6	17	Yes	Student
10	Female	Right	38	11	12	Yes	Clinical data manager
11	Female	Right	30	2.5	17	Yes	Business manager
12	Female	Right	37	2	18	Yes	Spiritual companion
13	Female	Right	32	8	18	No	
14	Female	Right	55	17	/	No	
15	Male	Right	49	2	12	Yes	Plumber
16	Female	Left	52	11	16	No	
17	Female	Right	48	24	15	Yes	Full time worker
18	Female	Right	41	11	17	Yes	Civil servant
19	Female	Both	29	13	12	No	
20	Male	Left	30	4	15	Yes	Driver
21	Female	Right	48	21	14	No	
22	Male	Right	45	8	14	No	
23	Female	Right	45	9	12	Yes	Sales (part-time)
24	Female	Right	49	15	16	No	
25	Female	Right	49	5	14	No	
26	Male	Right	47	12	12	Yes	General manager

27	Female	Right	56	9	14	No	
28	Female	Right	42	7	14	Yes	Teacher assistant
29	Female	Right	41	11	14	Yes	Dietician
30	Male	Right	27	3	17	No	
31	Male	Right	46	4	15	No	
32	Male	Right	57	34	13	No	
33	Female	Right	48	5	14	No	
34	Female	Right	56	6.5	14	No	
35	Male	Right	43	12	14	Yes	Fire service
36	Male	Right	31	1	17	No	
37	Male	Right	47	8	17	No	
38	Female	Right	52	22	12	No	
39	Male	Left	32	5	14	No	
40	Female	Right	30	8	17	No	
41	Male	Right	49	28	12	Yes	Worker in a shop
42	Male	Right	35	1	17	Yes	Office work
43	Male	Right	51	14	12	No	
44	Male	Right	47	1	17	Yes	Architecture
45	Female	Right	38	8	12	No	
46	Male	Right	30	1	12	No	
47	Female	Right	56	12	20	No	
48	Male	Right	45	15	17	No	
49	Female	Right	42	1	14	No	
50	Female	Left	27	7	14	No	
51	Female	Right	49	7	14	Yes	Interior designer
52	Female	Right	32	2	12	Yes	Hairdresser
53	Female	Right	33	3	14	Yes	Night club
54	Female	Left	43	14	17	Yes	Sales
55	Female	Right	44	5	12	Yes	Selling cosmetics
56	Male	Right	52	/	12	No	
57	Female	Right	34	2	17	No	
58	Male	Right	52	16	22	No	
59	Female	Right	38	8	22	Yes	Bioinformatics analyst
60	Female	Right	29	5	14	No	
61	Female	Left	41	8	14	Yes	Teacher assistant
62	Female	Right	36	5	17	Yes	Medical counsel
63	Female	Left	42	12	17	No	
64	Female	Right	49	1	17	No	

65	Female	Right	31	6	16	No	
66	Female	Right	31	15	14	No	
67	Male	Right	30	6	17	Yes	Research
68	Female	Right	28	3	16	Yes	Hairdresser
69	Female	Right	35	6	14	Yes	Help MS
70	Female	Right	48	10	12	No	
71	Female	Right	23	5	17	Yes	Teacher assistant
72	Female	Right	38	6	10	No	
73	Female	Right	45	4	10	No	
74	Female	Right	43	4,5	16	Yes	Sales
75	Female	Right	30	5	17	Yes	Office
76	Female	Right	44	3	17	Yes	Teacher
77	Male	Right	35	6	12	No	
78	Male	Right	38	14	17	No	
79	Female	Left	49	8	12	No	
80	Male	Left	40	5	12	Yes	Cleaner
81	Male	Right	37	10	12	No	
82	Female	Right	32	6	14	Yes	Personal assistant
83	Male	Right	29	3	14	No	
84	Female	Right	37	3	12	No	
85	Female	Right	43	15	17	Yes	Teacher
86	Male	Right	61	8	12	No	
87	Female	Left	46	13	17	Yes	Speech therapist
88	Male	Right	47	15	17	Yes	Office
89	Female	Right	45	4	17	Yes	Teacher
90	Male	Right	38	2.5	16	No	
91	Female	Right	44	7	12	No	
92	Female	Right	31	2	17	Yes	
93	Female	Right	33	5	14	Yes	Police
94	Female	Right	40	7	16	No	
95	Female	Right	27	2	14	Yes	Social services
96	Female	Right	45	4	12	Yes	Civil servant
97	Female	Right	41	6	14	Yes	Corporative banking
98	Female	Left	44	11	16	No	
99	Female	Right	48	2	12	No	
100	Male	Right	49	3	16	No	
MEAN			**40.86**	**7.85**	**14.72**		
SD			**8.97**	**5.95**	**2.4**		

As can be seen, the average age of the group (40.86) is consistent with the average age of onset of MS (20-40 years). Moreover, the group consists of participants from a wide range of ages. The age of the group varies from 23 years old the youngest participant to 66 years old the oldest participant. The range of years living with MS is also very wide; this varies from 1 year to 34 years with MS. This is relevant to observe whether or not years with MS has an effect on the performance of a participant in a task. Finally, it is noteworthy that many of the participants were unemployed, despite being of working age. This reflects the challenges the MS has meant for them in keeping employment in the context of physical and cognitive disability.

Results from main tasks

Table 6 provides an overview of the mean scores and standard deviation (SD) obtained by the participants in each task. As can be seen, the mean score of the participants with MS was close to the cut-off score for all tasks except for the NART (Nelson & Willison, 1991) on which they performed well above the cut-off score. While close to the cut-off values, there were two tasks in which the group scores were below, namely the ACE-R (Mioshi et al., 2006) and the Pyramids and Palm Trees (Howard & Patterson, 1992), indicating a level of mild impairment as a group in these tasks.

Table 6- Overview of the mean scores for participants with MS across the different tasks

	ACE-R (0-100) Cut-off 88	NART (0-50) Cut-off 26 (24 errors)	Picture Naming Task (0-60) Cut-off 52	Pyramids and Palm Tree (0-52) Cut-off 49
Mean	**87.37**	**34.41**	**52.02**	**48.91**
SD	**7.17**	**8.36**	**5.21**	**2.52**

The results obtained by each participant with MS in the four behavioural assessments included are presented in a summary table in Appendix G. This appendix also provides an individual table of each behavioural assessment with the scores obtained by each participant.

ACE-R

The ACE-R (Mioshi et al., 2006) consists of five subtests. The maximum overall score is 100 points and it is obtained from the score of the five subtests that form part of this task.

Table 7 shows the average score and SD in the global task and in the five separate subtests for the participants with MS in the ACE-R. Next to the name of each subtest appears the maximum possible score for each subtest, as well as the cut-off representing impaired performance.

Table 7- Mean performance across 100 participants with MS in the ACE-R

	ACE-R (0-100) Cut-off 88	Attention Orientation (0-18) Cut-off 17	Memory (0-26) Cut-off 18	Verbal Fluency (0-14) Cut-off 9	Language (0-26) Cut-off 24	Visuospatial Skills (0-16) Cut-off 15
Average	87.37	16.25	21.85	10.72	23.79	14.77
SD	7.17	1.45	3.61	2.34	2.01	1.54

The average score and SD of the MS group for this task is 87.37 (7.17) points, which is very close score to the cut-off score of the task (88 points), but is below it indicating impairment. Looking at individual performances across the group, there were 43 participants with MS under the cut-off score of the task. This means that 43% of participants with MS assessed performed under the lowest possible level within the neuro-typical limits for the task. A performance of 88 points (cut-off) or lower can be a signal of presence of some degree of dementia.

Regarding the performance of the MS group in the five subtests, there are no cut-off scores for a group with an average age of 41 years old (the MS group). However, there are data as to the cut-off score for the group age between 50-59 years of age. For this reason, the comparison has been made between these two different age groups. Performance of the older age group would be expected to be less than that of a younger age group (meaning cut-off scores indicative of impairment would be higher), and as such this comparison provides a conservative assessment of impairment.

In this comparison, the MS group performed at a mean level, which was lower than the cut-off score for the task. However as can be seen in Table 8, when compared to the group aged between 50-59 years old, the MS group had a better mean performance in the global score and in the subtests of memory and fluency. Conversely, the MS group performed less well than the group aged between 50-59 years of age in tasks such as attention and orientation, language and visuospatial skills.

Table 8- Cut-off for ACE-R

Age range	Education	Total ACE-R	Attention/ Orientation	Memory	Fluency	Language	Visuospatial
50-59	12.7	86	17	18	9	24	15
41	14	87.37	16.25	21.85	10.72	23.79	14.77

Picture Naming Task

The performance of the MS group compared to the normative data for the Picture Naming Task can be reported as both measures of accuracy and reaction times. Also, these data can be analysed for the naming of the full 60 items as a whole or according to performance on the four reaction time subgroups of words.

The Picture Naming Task consisted of 60 items. The mean of the MS group for this task was 52.02 correct answers, which was the same value as the cut-off score (52 correct answers). Z-scores were computed for raw scores in the accuracy of the Picture Naming Task. Participants who scored below a z-score of -1.96 were considered as participants with a significantly lower accuracy than the accuracy of the normative data. On the contrary, a participant with a positive z-score above 1.96 would be more accurate than the normative group. The value of the z-score was selected because in a standard normal distribution, the probability of obtaining a score between z= -1.96 and z=1.96 is 95%. In this case, there were 42 participants with a significantly lower accuracy than the accuracy of the normative data.

In order to understand whether or not there is a statistically significant difference in the performance of the participants with MS compared to the normative data in the condition of accuracy of the Picture Naming Task, the Mann-Whitney test was conducted. This non-parametric method was selected instead of T-Test because the normality of the distribution of the data collected cannot be assumed. Descriptive statistics showed that for the Picture Naming Task participants with MS were less accurate retrieving words than the normative group.

The Mann-Whitney test was conducted to analyse whether or not there is a statistically significant difference between the accuracy of both the participants with MS and the normative data for the Picture Naming Task. The Mann-Whitney Descriptive statistics showed that the accuracy of participants with MS was lower (median=90.5) than the accuracy of the normative data (median=98). The Mann-Whitney U was found to be U= 1110.00, p=.000, r=.34. This shows that the MS group was significantly less accurate than the normative data in the Picture Naming Task.

Amongst the group of MS participants, there was substantial variability in performance. This difference can be seen in the highest and lowest scores obtained by the participants in the task. The highest score obtained by a participant with MS was 60 correct answers (100% accuracy), which is the maximum possible score; however, the lowest score obtained by a participant was 35 correct answers (58.3%, a 25 point difference). While the first participant showed intact naming skills in the task, the other participant presented with a marked difficulty naming pictured items.

After understanding the performance of the MS group in the Picture Naming Task according to accuracy, it is necessary to analyse their reaction time. The time required to retrieve a word can be a sign of an increased processing difficulty retrieving words. A participant can be accurate retrieving the names of the pictures; however, they might also need more time to retrieve a word because their naming skills are impaired. For this reason, the next section of the results of the Picture Naming Task is focused on the study of the reaction time of the MS group.

The average processing speed of the MS group was slower than the average reaction time of the normative data. On average across all 60 items, participants with MS needed more time to name a word compared to the normative data. The MS group was, overall, 27.94% slower than the normative data of the IPNP for the pictures selected in the Picture Naming Task.

As well as noting the difference in reaction time for the global task, it may be more informative to analyse the difference in the reaction times between subgroups of words. As previously mentioned the words included in this task were selected according to their neuro-typical reaction time (among other variables) and divided into four groups accordingly. This division helps to see the group of words that are a major challenge.

The first group (Group A) encompasses fifteen words with a reaction time faster than 800 ms. Table 9 shows the words included in this group and the comparison of the reaction time between both the MS group and the normative data for the words included in Group A. Figure 13 shows the differences in reaction time between both the MS group and the normative data for all the words included in Group A.

Table 9- Reaction time of words included in Group A for the MS group and normative data

Group A (<800 ms)	RT Normative Data (ms)	RT MS group (ms)
BABY	729	770.89
AIRPLANE	778	807.96
CLOCK	772	865
MUSHROOM	746	941.85
ARROW	758	917.33
SCISSORS	741	863.25
EYE	700	909.39
FISH	777	883.68
BALLON	702	862.97
FOOT	758	952.23
GIRAFFE	783	1061.99
CAR	751	853.18
BICYCLE	731	901.43
HAT	684	839.08
BUTTERFLY	720	975.72
AVERAGE RT	**742**	**893.73**
SD	**30.72**	**71.47**

The average reaction time for both the normative data and the MS group was 742 ms (30.72) and 893.73 ms (71.47) respectively. The reaction time of the MS group was 20.44% slower than the reaction time of the normative data for the words included in Group A (RT <800 ms). Moreover, 68% of participants scored lower than the cut-off (803.44 ms) of the normative data for this group of words.

This result showed that the MS group needed more time to name the pictures. Moreover, the difference in the reaction time between the participants with MS as a group and the members of the group as individuals shows again substantial variation across participants.

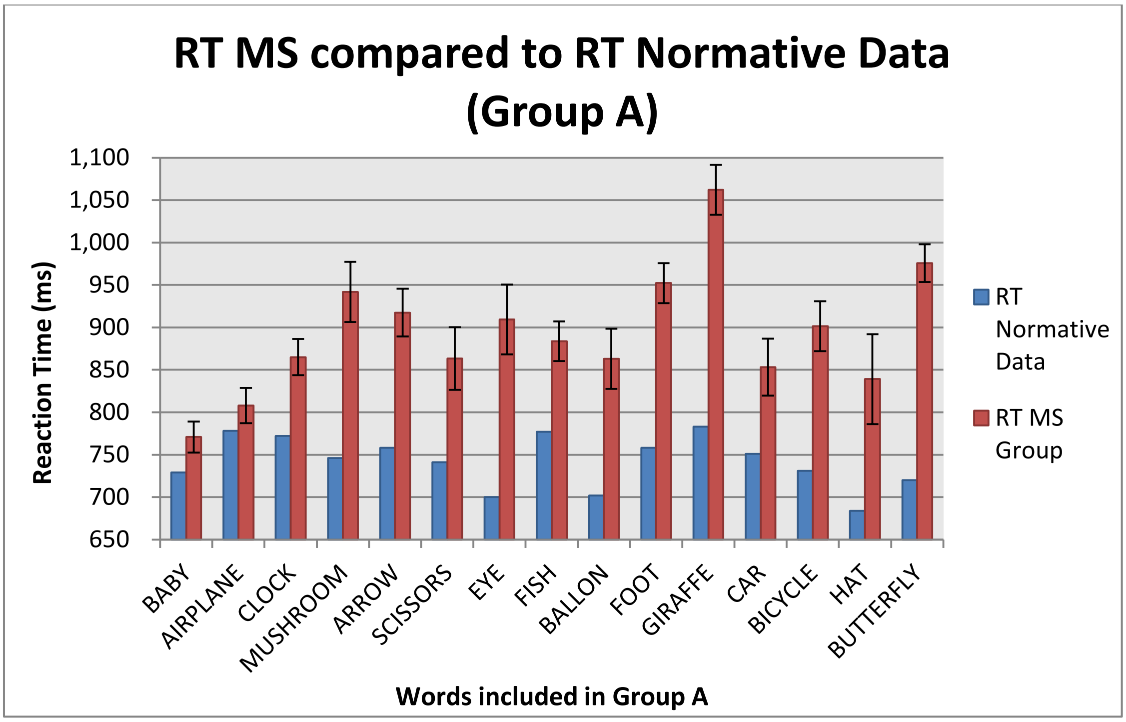


Figure 13- Comparison of reaction time between MS and normative data (Group A)

The second group (Group B) included fifteen words with a reaction time between 801 and 1000 ms. Table 10 shows the words included in this group along with the average reaction time of both the MS group and the normative data for each word included in this group. Figure 14 shows the differences in reaction time between both the MS group and the normative data for the words included in Group B.

Table 10- Reaction time of words included in Group B for the MS and normative data

Group B (801-1000 ms)	RT Normative Data (ms)	RT MS group (ms)
FAN	865	960.4
CAN	940	1281.02
HORSE	809	881.89
IGLOO	963	1091.67
BANANA	808	859.66
CACTUS	933	1289.13
APPLE	810	916.09
KING	898	1236.9
HELMET	921	1204.16
BALL	886	1076.01
FEATHER	977	1059.22
DOLPHIN	894	1242.57
FOUNTAIN	966	1350.62
ELEPHANT	837	904.72
CHEESE	843	1266.25
AVERAGE RT	**890**	**1108.02**
SD	**59.41**	**170.50**

The average reaction time for both the normative data and the MS group was 890 ms (59.41) and 1108.02 ms (170.50), respectively. For this group of words, there were 55 participants who scored lower than the cut-off score (1008.81 ms). The difference in the reaction time of the MS group compared to the normative data means that the MS group was 24.49% slower than the normative data for the words in Group B (RT 801-1000 ms).

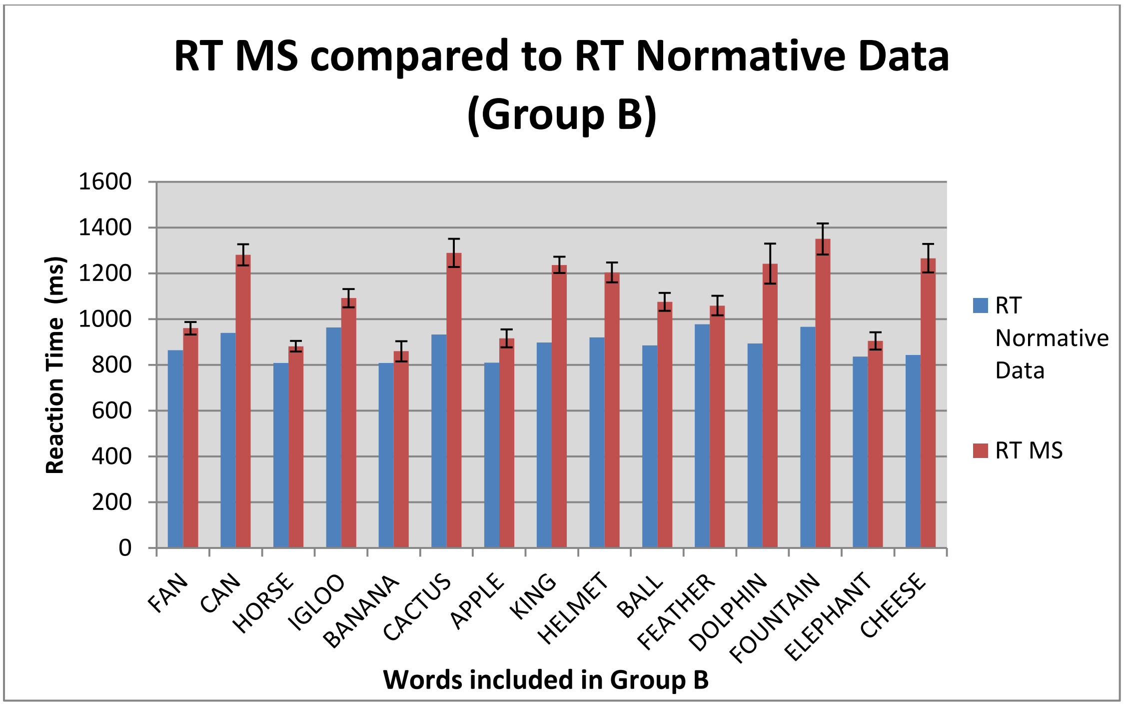


Figure 14- Comparison of reaction time between MS and Normative Data (Group B)

The third group (Group C) included words with a reaction time between 1001 and 1220 ms. Table 11 shows the words included in this group and the comparison of the reaction time between both the MS group and the normative data for the words included in this group. Figure 15 shows the differences in reaction time between the MS group and the normative data for the words included in Group C.

Table 11- Reaction time of words included in Group C for the MS and Normative Data

Group C (1001-1220 ms)	RT Normative Data (ms)	RT MS group (ms)
BARBECUE	1012	1413.58
DEER	1180	1461.3
LEG	1019	1065.61
CAROUSEL	1121	1667.06
PANDA	1071	1226.44
PEAS	1201	1881.45
KNOT	1122	1363.3
PIRATE	1118	1804.01
DENTIST	1075	1659.02
COW	1079	1426.76
CANOE	1164	1697.73
LETTUCE	1037	1541.51
PRIEST	1077	2224.71
HANDCUFFS	1113	1311.18
ANT	1171	1613.82
AVERAGE RT	**1104**	**1557.17**
SD	**58.33**	**287.02**

The average reaction time for both the normative data and the MS group for the words in this group of words were 1104 ms (58.33) and 1557.17 ms (287.02), respectively. The reaction time of the MS group was 41.05% slower than the reaction time of the normative data for the words included in this group. Moreover, there were 81 participants under the cut-off (1220.65 ms) of the normative data for this group of words.

Group C has the largest difference between groups in the reaction time. The MS group had more difficulties retrieving words with a reaction time between 1001 and 1220 ms. Although the words included in Group C are not the ones with the longest reaction time, Group C was the most challenging for the MS participants. In this situation, the slow reaction time of the participants can be considered as a clear indication of increased difficulty in the retrieval processes of people with MS.

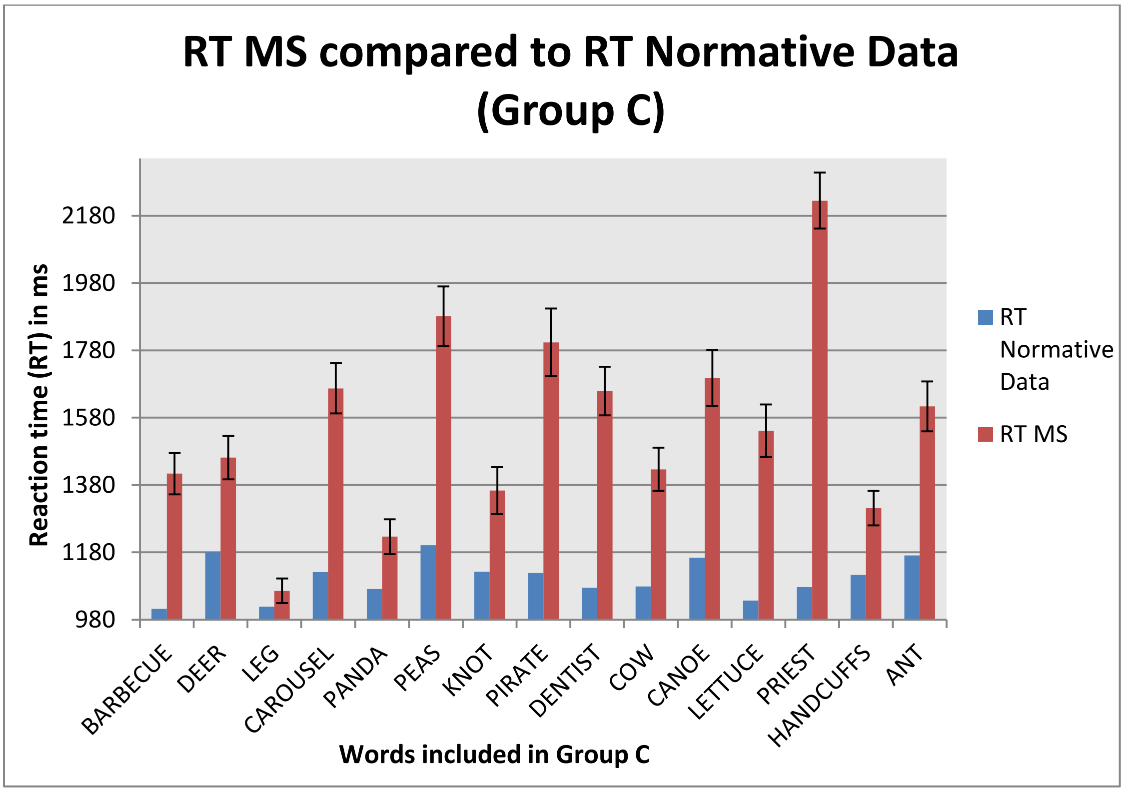


Figure 15- Comparison of reaction time between MS and Normative Data (Group C)

The fourth group (Group D) included words with a reaction time between 1221 and 1500 ms. Table 12 shows the words included in this group and the comparison of the reaction time between both the MS group and the normative data for the words included in this group. Figure 16 shows the differences in reaction time between both the MS group and the normative data for all the words included in Group D.

Table 12- Reaction time of words included in Group D for the MS and Normative Data

Group D (1221-1500 ms)	RT Normative Data (ms)	RT MS group (ms)
TWEEZERS	1328	1512.41
BALCONY	1324	1632.86
TAIL	1383	1916.23
STROLLER	1346	1278.93
BEAVER	1395	1871.85
HINGE	1349	1714.81
WRENCH	1331	1283
TROPHY	1452	1468.96
MOSQUITO	1436	2191.62
SAFETYPIN	1278	1532.21
DRILL	1311	1504.3
SQUIRREL	1234	1373.12
HOE	1346	2357.75
ASPARAGUS	1380	1836.29
LOBSTER	1289	1574.58
AVERAGE RT	**1345.47**	**1669.93**
SD	**57.90**	**314.99**

The average reaction time for both the normative data and the MS group for the words in Group D were 1345.47 ms (57.90) and 1669.93 ms (314.99), respectively. The reaction time of the MS group was 25.78% slower than the reaction time of the normative data for the words included in this group. Moreover, there were 64 participants who scored lower than the cut-off time (1461.28 ms) of the normative data for this group of words.

Surprisingly, although Group D had the longest average reaction time out of the four subgroups of words, this subgroup did not have the largest difference in reaction time between the normative data and the MS group. Group C was the subgroup of words with the biggest difference in reaction time between the normative data and the MS group. Both subgroups had a similar level of accuracy with 75% and 77% of accuracy for Group D and C, respectively, which shows that the reaction time was not affected by accuracy.

Group D did not pose any greater accuracy difficulty to the participants with MS compared with the words included in Group C. However, the words included in Group D were supposed to be more difficult and by extension require a longer reaction time to be named. Moreover, words included in Group D were less frequent and also had a longer length of phonological syllables than the words included in Group C. This surprising finding could have been influenced by other variables such as imageability or number of neighbour words that were not considered when the words were selected.

There were 64% of participants with MS who scored at a lower level than the cut-off time for the task. This reflects a significant difficulty to retrieve the words for the majority of participants with MS.

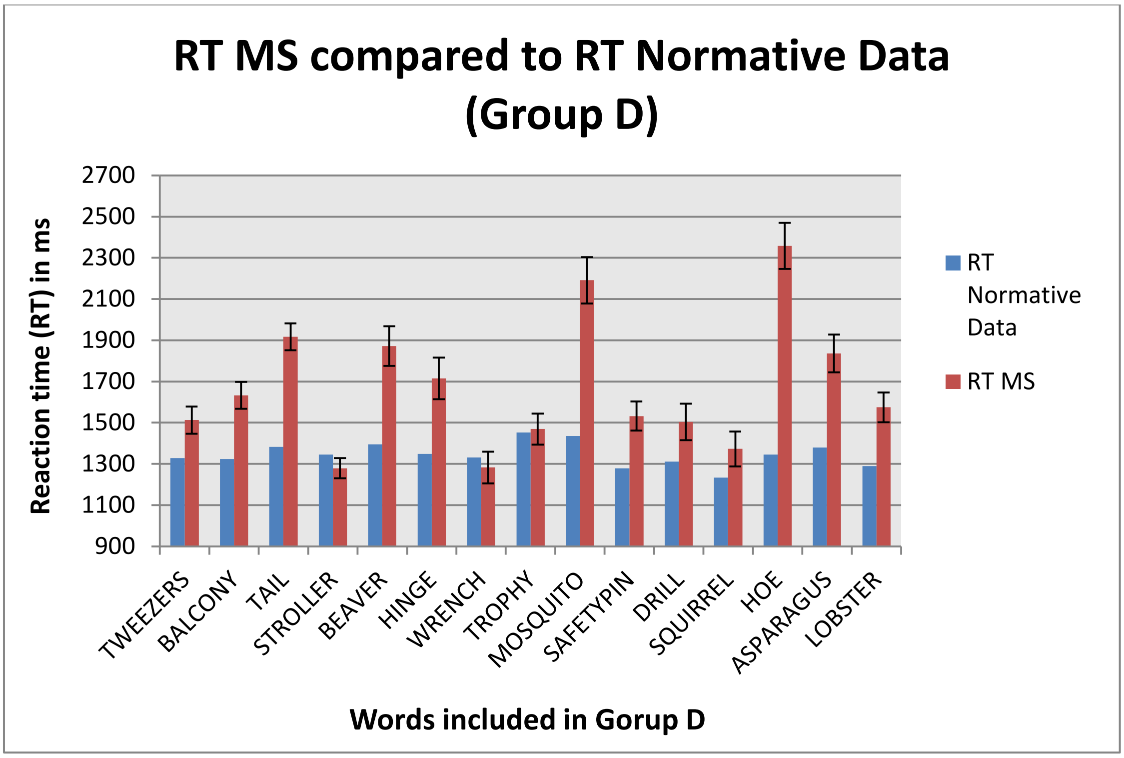


Figure 16- Comparison of reaction time between MS and Normative Data (Group D)

As shown in Figure 16, the participants in the MS group needed a longer reaction time than the participants of the normative data to conduct the task. However, this was not the case for two items included in Group D. There were two words (stroller and wrench) in which the performance of the participants with MS was slightly faster than the cut-off time of the word.

In order to understand whether or not there is a statistically significant difference in the performance of the participants with MS compared to the normative data in the condition of reaction time of the Picture Naming Task, the Mann-Whitney test was conducted. This non-parametric method was selected instead of T-Test because the normality of the distribution of the data collected cannot be assumed. Descriptive statistics showed that for the four subgroups of words (group A, B, C, D) participants with MS required more time to retrieve the words than the normative group.

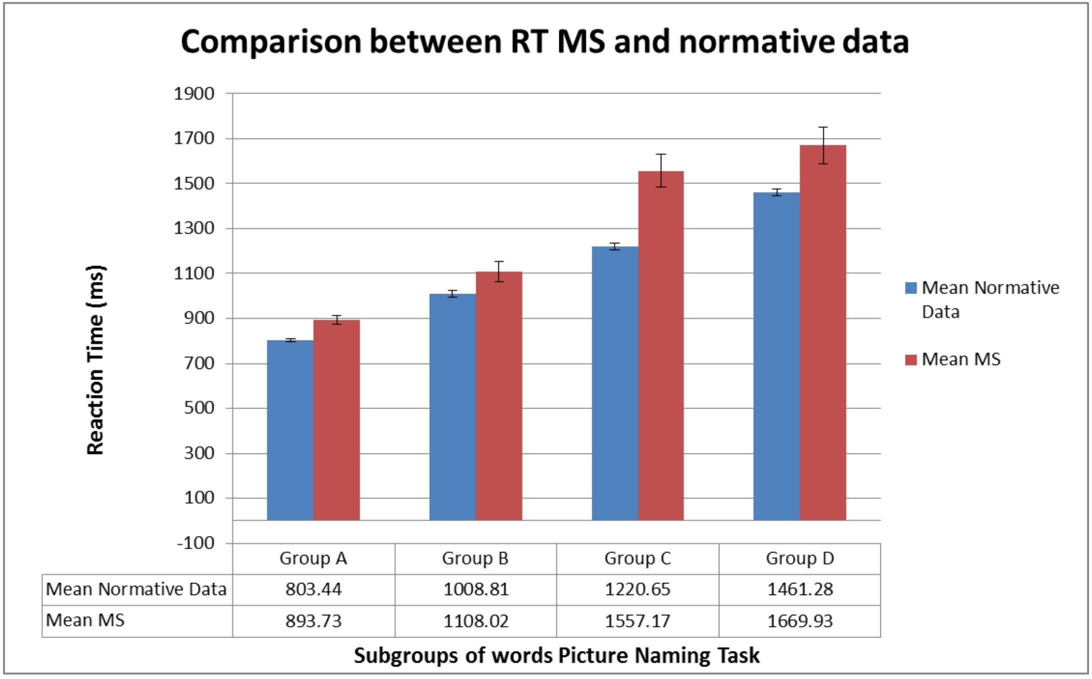
The Mann-Whitney test was first conducted with the RT of both the participants with MS and the RT of the normative data for the subgroup of words A of the Picture Naming Task. The Mann-Whitney Descriptive statistics for group A showed that the RT of participants with MS was higher (median=883.68) than the RT of the normative data (median=746). The Mann-Whitney U was found to be U=4.00,p=,r= .59. This shows that the MS group required more time to retrieve the words included in group A than the normative data.

The Mann-Whitney Descriptive statistics for group B showed that the RT of participants with MS was higher (median=1091.67) than the RT of the normative data (median=894). The Mann-Whitney U was found to be U=34.00, p=.001, r=.76. This shows that the MS group required more time to retrieve the words included in group B than the normative data.

The Mann-Whitney Descriptive statistics for group C showed that the RT of participants with MS was higher (median=1541.51) than the RT of the normative data (median=1113). The Mann-Whitney U was found to be U=12.00, p=.000 r=.76. This shows which shows that the MS group required more time to retrieve the words included in group C than the normative data.

The Mann-Whitney Descriptive statistics for group D showed that the RT of participants with MS was higher (median=1574.58) than the RT of the normative data (median=1346). The Mann-Whitney U was found to be U=31.00, p=.001 r=.61. This shows that the MS group required more time to retrieve the words included in group D than the normative data.

Figure 17 shows a summary of the differences and variability in the reaction time between the normative data and the MS group mentioned so far.



	Group A	Group B	Group C	Group D
Mean Normative Data	803.44	1008.81	1220.65	1461.28
Mean MS	893.73	1108.02	1557.17	1669.93

Figure 17- Comparison of reaction time between normative data and MS group

Z-scores were computed for raw scores in the reaction time of the Picture Naming Task for every subgroup of words. The participants that scored above a z-score of +1.96 were considered as participants with a significantly lower reaction time than the reaction time of the normative data. The reason why a positive z-score above 1.96 reflects deficits in reaction time while retrieving words is because they required a greater time to retrieve the words. On the contrary, a participant with a negative z-score would retrieve words faster than the normative group. The value of the z-score was selected because in a standard normal distribution, the probability of obtaining a score between z= -1.96 and z=1.96 is 95%.

Figure 18 depicts the number of participants in each subgroup of words of the Picture Naming Task whose raw scores represent a z-score higher than 1.96. The number of participants with impairment in RT in every subgroup of words from the Picture Naming Task has not changed from the initial comparison of the cut-off reaction time to the z-score analysis. The reason why this figures have not changed is because the cut-off scores of each subgroup of words were calculated by adding two SD to the average reaction time of the normative data. When calculating z-scores, the same procedure is followed, only participants that are 2SD away from the mean reaction time of the normative data are the ones considered as impaired. By doing so, only participants with a statistically significant difference are selected as impaired.

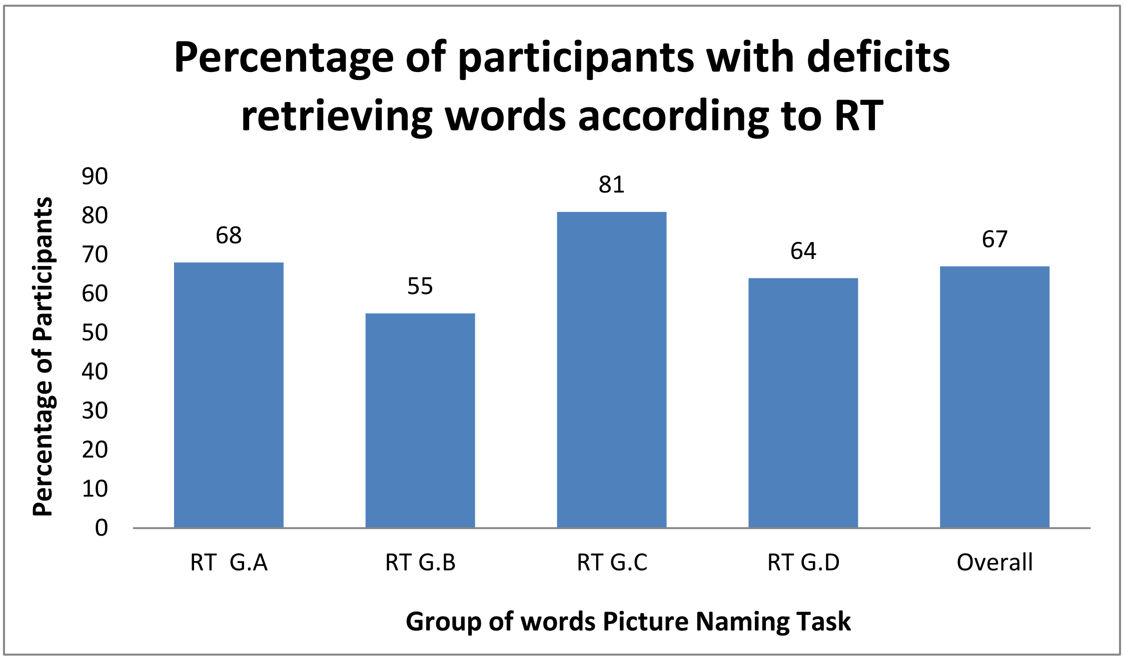


Figure 18- MS participants with deficits retrieving words according to reaction time

Finally, Figure 19 depicts the number of participants with impaired accuracy or reaction time in the Picture Naming Task. This comparison shows how MS produces naming difficulties with a major emphasis in the processing speed (67% of participants under cut-off). This means that participants with MS present a deficit retrieving words.

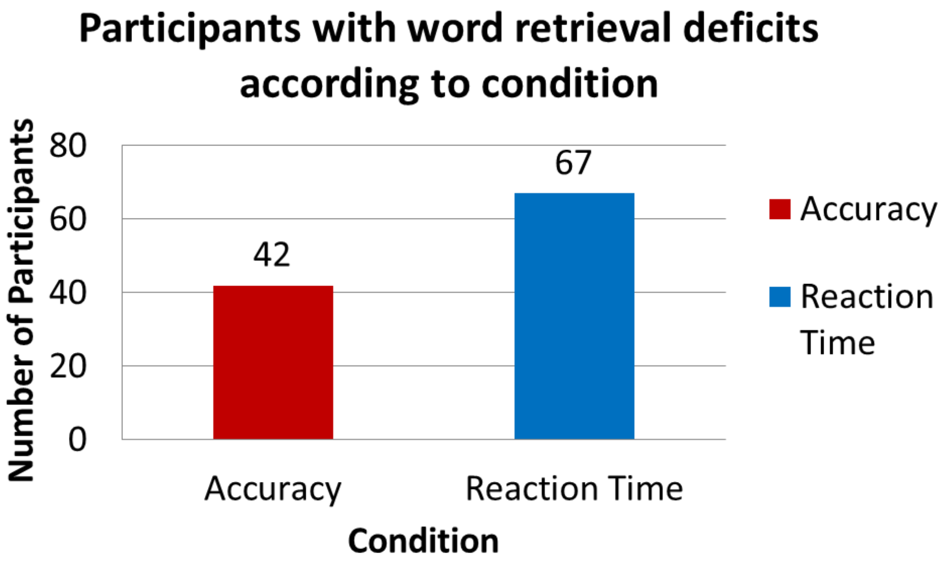


Figure 19- Comparison of participants under cut-off score for the Picture Naming Task according to condition

Problems with accuracy have also been present during the task with 42% of participants. These figures are an indicative of a deficit retrieving words present in the majority of participants. Moreover, within this group of participants, there are participants with deficits in both processing speed and accuracy. These participants not only are inaccurate with their responses, but also require more time to retrieve the words. What this also shows is that there are participants who show deficits in processing speed only, and who appear unimpaired when assessed using a standard accuracy measure. This demonstrates the importance of accessing language deficits using not only accuracy both also reaction time.

These results indicate that there were three types of participant performance within the MS group. The first group included participants with a reaction time equal or faster than the normative data. These participants did not present with naming difficulties and attained a level of naming performance similar to that of a person without MS. These participants obtained the same or higher score than the neuro-typical mean of the tasks. The second group includes participants with a significant difficulty retrieving words that increased substantially their reaction time and reduced their accuracy. The third group includes participants with impairment in one of the conditions (accuracy or reaction time). The average scores of the MS group in both accuracy and reaction time were obtained from the performance of these three types of participants; hence, the mean score of the group reached close to the bottom of the control range.

NART

The NART (Nelson & Willison, 1991) was included in this assessment to detect the presence of dysarthria and as a measure of reading skills in people with MS. As previously mentioned, this task cannot be used to measure premorbid intelligence because MS can produce language deficits (Friend & Grattan, 1998).

Regarding the presence of dysarthria, 67% of participants did not present with any sign of dysarthria, with only 33% of participants presented with mild dysarthric symptoms. The lowest score obtained by a participant was 4 points on a five-point scale where “0” is profound dysarthria and “5” is no dysarthria (Enderby et al., 1997). This is an important finding as it indicates that the naming deficits described above were not the sole result of articulatory motor deficits.

Regarding the performance of the participants with MS in the NART (Nelson & Willison, 1991), the first relevant comparison is between the cut-off score for the normative data and the score of the MS group. The cut-off score of the task is 24 errors and as can be seen in Table 13, the average number of errors for the MS group was 15.59 (8.36) errors.

Table 13- Summary of NART results

	Correct	Error	Accuracy	Error Rate
Mean	34.41	15.59	0.69	0.31
SD		8.36		

Overall, the MS group was more accurate than the normative data. However, within the MS group 11% of participants performed lower than the cut-off score of the task. This means that 11 participants had difficulty reading or articulating words.

Figure 21 shows the variability in the score for the NART (Nelson & Willison, 1991) between participants with MS. The maximum possible score for this task is 50 correct answers, and the maximum score obtained by a participant with MS was 48 correct answers. On the other hand, the lowest score obtained by a participant with MS was 10 correct answers. This difference of 38 points between the participants with the best and the worst performance in the task shows a considerable variability within the MS group in reading aloud.

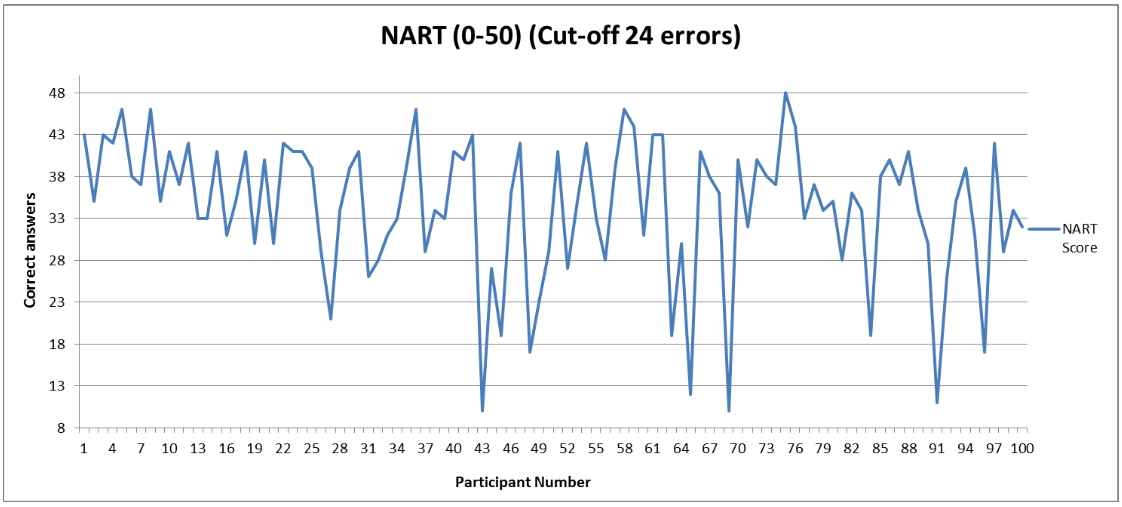


Figure 20- Distribution of participants in NART according to performance

Figure 22 shows the number of correct answers of each participant in rank order. This figure provides a clearer view of the distribution of the participants according to their performance. It is important to keep in mind that Figure 22 shows the number of correct answers of the participants and the cut-off score refers to errors. For this reason, in this figure the participants under 26 correct answers are the participants under the cut-off score.

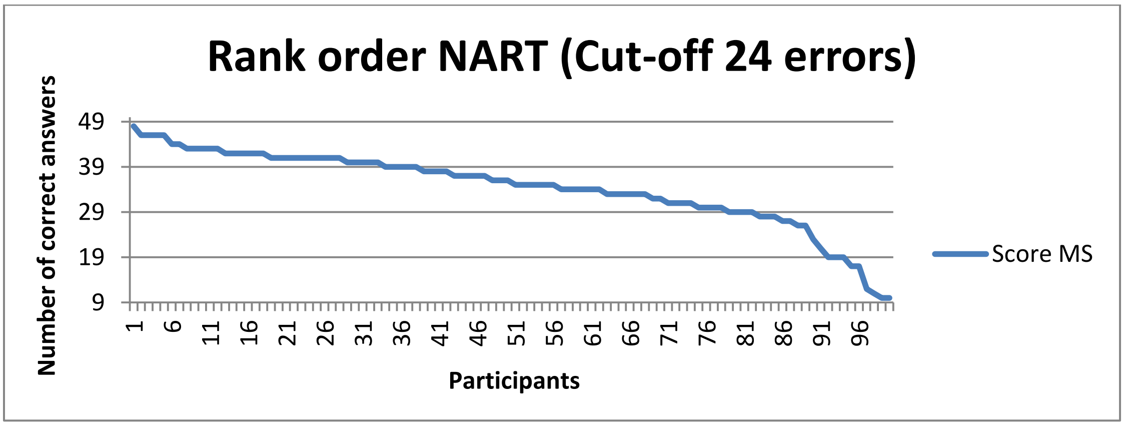


Figure 21- Participants in rank order according to performance in NART

Pyramids and Palm Trees

The Pyramids and Palm Trees (Howard & Patterson, 1992) has a total of 52 items and the cut-off score of this task is 49 correct answers. As can be seen in Table 14, the average number of correct answers for the MS group was 48.91 which is a score very close to the cut-off score of the task, although is below it, indicating some level of mild impairment. Looking at individual participant performance, there were 32 participants under the cut-off of the task. This means that 32% of participants demonstrated semantic problems, specifically accessing or retrieving the meaning of a picture.

Table 14- Summary of Pyramids and Palm Trees results

	Correct	Incorrect	Accuracy	Error Rate
Mean	48.91	3.09	0.94	0.06
SD	2.52			

The reason why the mean of the group is that close to the cut-off is because there was a substantial difference in the performance among the participants with MS in the task. Figure 23 shows an overview of the variability on performance between participants in the task.

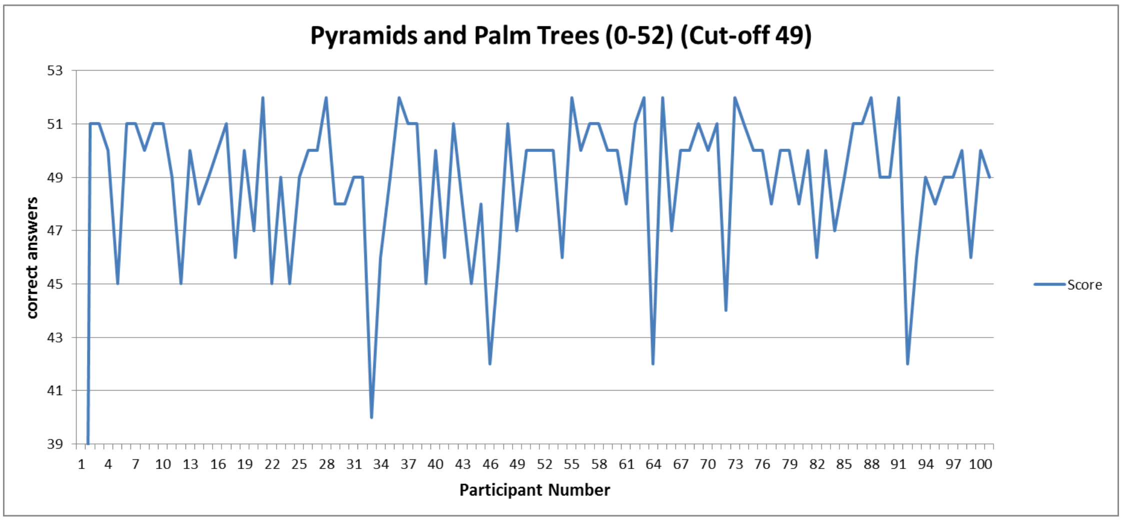


Figure 22- Distribution of participants in Pyramids and Palm Trees according to performance

Figure 24 displays the distribution of performance of the participants in rank order. As can be seen, not only were there 34 participants under the cut-off score of the task, but also this score was substantially low.

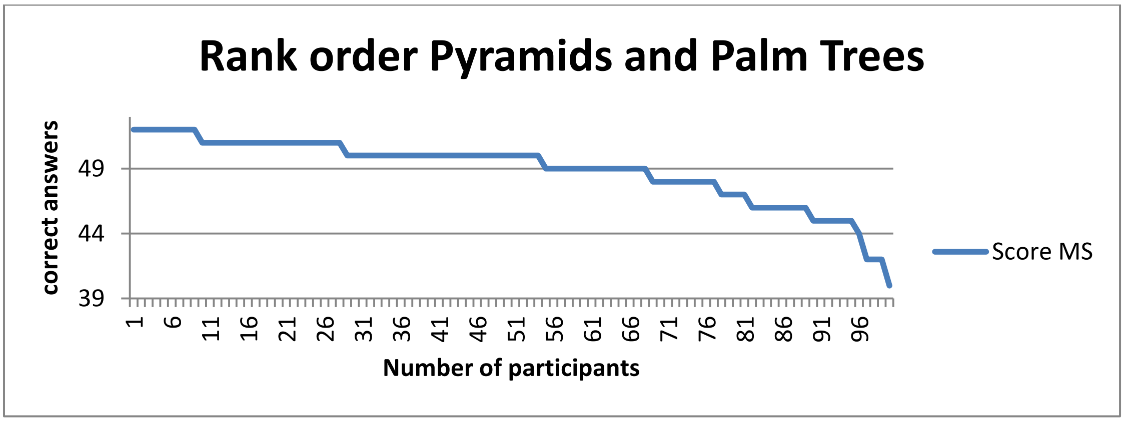


Figure 23- Participants in rank order according to performance in Pyramids and Palm Trees

Amongst the participants with the best performance on the task, there were nine participants that obtained the maximum possible score on the task (52 points). Conversely, there were participants with substantial semantic impairment, obtaining scores considerably lower than the cut-off score of the task. The lowest score obtained by a participant with RRMS was 40 correct answers.

Global assessment results

Figure 25 shows a comparison of the scores between the normative data and the MS group in the main behavioural assessments used in the current study. The value presented for the Picture Naming Task represents average accuracy.

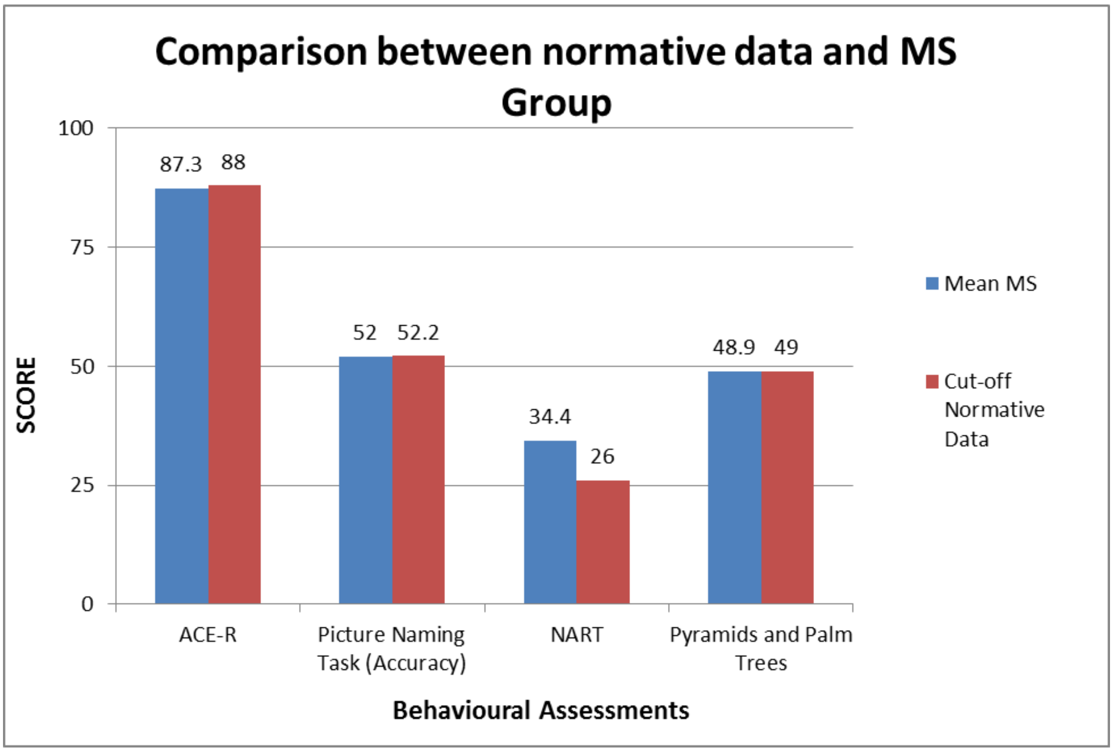


Figure 24- Performance of MS group compared to cut-off scores

The MS group performed at/or just below the cut-off for each task except for the NART (Nelson & Willison, 1991). The participants with MS attained a higher number of correct answers than the cut-off score in the NART (Nelson & Willison, 1991), which reflects that these participants did not present problems reading. Nonetheless, across this and indeed all tasks, the variability within the group was striking.

As can be seen in Figure 26, the participants were presented with considerable challenge in conducting the behavioural assessments selected for the assessment. There were approximately 43% of participants suffering from mark cognitive impairment in more than one cognitive domain. Naming and semantic problems were also present among the group of participants.

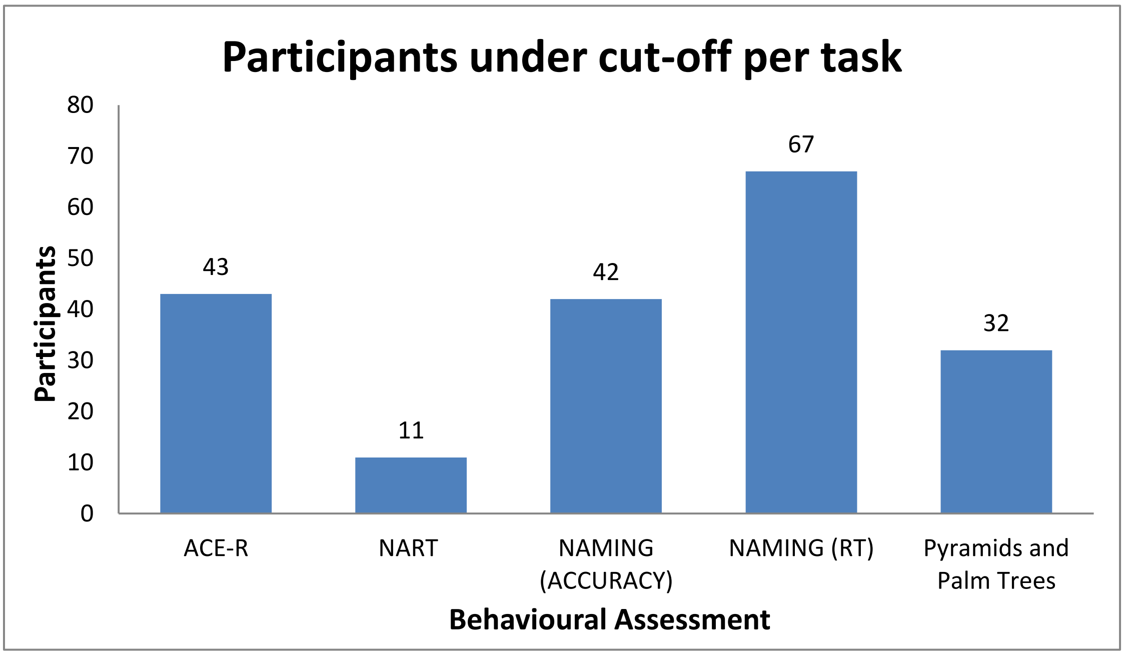


Figure 25- Participants under cut-off in main behavioural assessments

Regarding the presence of dysarthria, it is of note that only 33% of participants presented signs of dysarthric symptoms reading words in isolation. There was no participant with severe dysarthria; there were only signs of mild dysarthria in some participants. However, as can be seen in Table 15, the presence of dysarthria affected the performance of those participants with the impairment, increasing the reaction time of the participants compared to those participants without it.

Table 15- Comparison of RT between MS participants with or without dysarthria

	MS dysarthria	MS no dysarthria
Number of participants	33	67
Mean RT	1415.29	1195.44

A further comparison in the results is to observe the distribution of the participants according to their accuracy across the behavioural assessments. To do so, they have been divided according to the number of tasks with which they demonstrated impairment across the scores for the ACE-R (Mioshi et al., 2006), NART (Nelson & Willison, 1991), Picture Naming Task (accuracy) and Pyramids and Palm Trees (Howard & Patterson, 1992). In this way, participants could have presented with impairment in up to four conditions. Figure 27 shows this distribution.

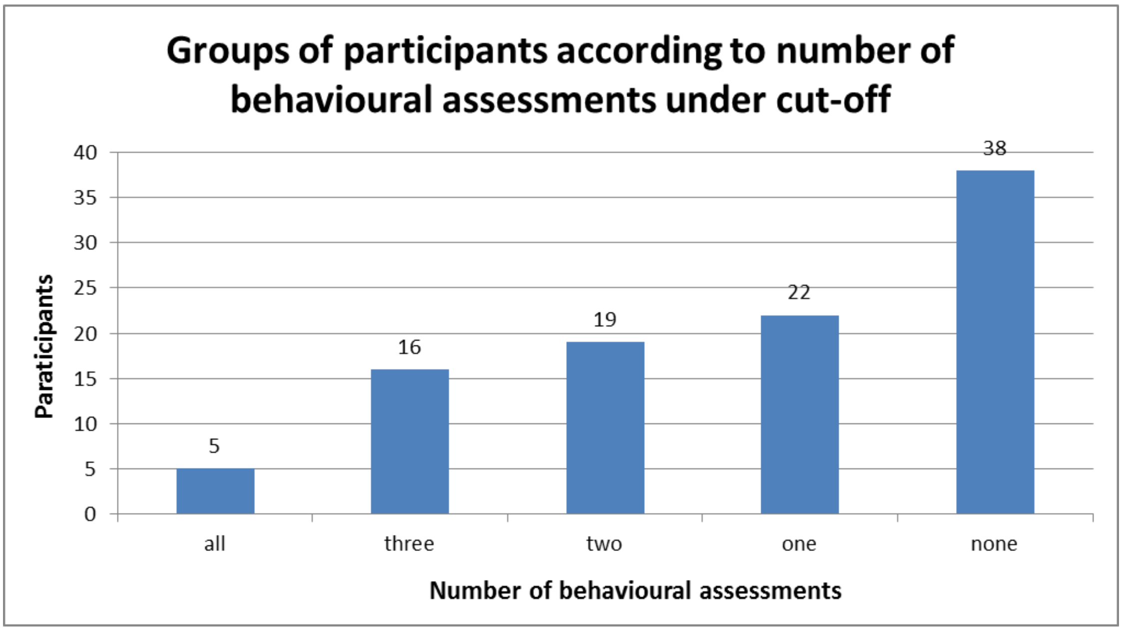


Figure 26- Division of participants according to the number of conditions under cut-off score

Regarding the distribution of these participants according to their performance in each behavioural assessment, 38% of participants did not present any type of significant cognitive dysfunction. Their performance was within the neuro-typical range in all the tasks. At the other extreme, 5% of participants performed lower than the cut-off score on every task. This performance reflects a more generalised and marked cognitive impairment in more than one cognitive domain. This group of participants have seen their cognitive skills greatly affected by MS and would have major limitations in their everyday life.

A large variability in the performance in different behavioural assessments within people with MS has been mentioned throughout the results of this thesis. While some participants did not present any difficulty conducting the assessments, others on the contrary, required more time and presented more difficulties conducting the tasks. In order to better understand this variability among participants, it is useful to analyse the performance of some participants across all tasks. For this reason, five participants were selected according to their performance in the Picture Naming Task and are distributed from no impairment to severe impairment. The differences in the performance between these individual cases show the wide spectrum of performance that can be found in people with MS.

The first participant is a male, 45 years and 8 years with MS. This participant obtained the highest possible score in the Picture Naming Task.

Figure 28 shows the performance of this participant across all the behavioural assessments compared to the cut-off level of each tasks.

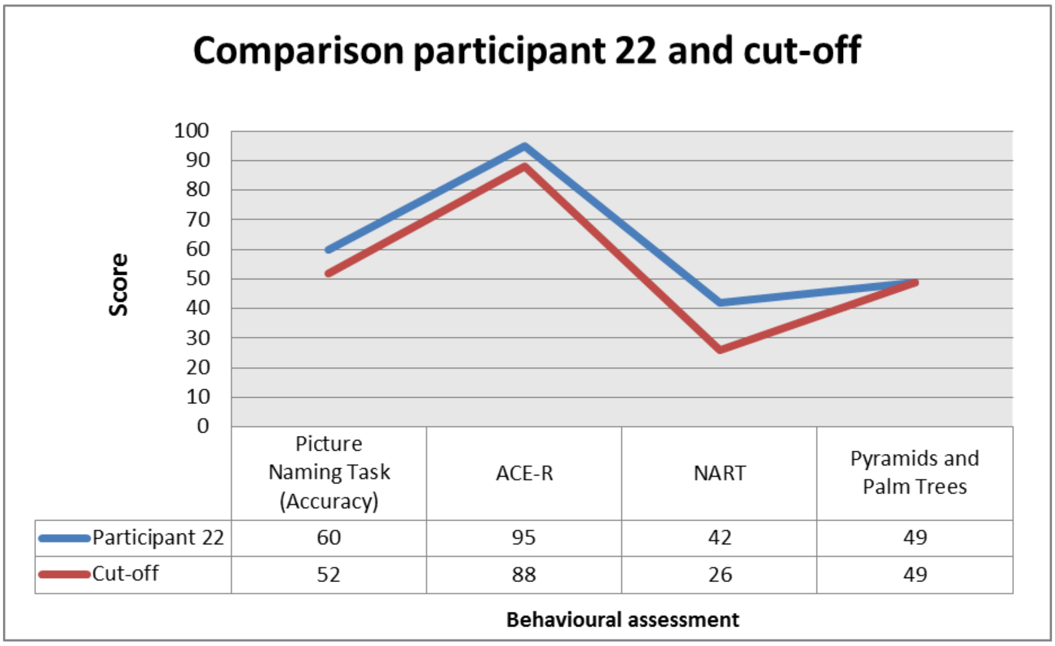


Figure 27- Comparison between score obtained by participant 22 and cut-off across all tasks

This participant did not present any type of anomic symptom and he was capable of naming all the pictures without any difficulty. Moreover, he also performed within neuro-typical limits in the ACE-R (Mioshi et al., 2006), which reflects that his level of cognition has not been significantly affected by MS. His semantic skills were at the lowest level of the normative data, meaning that he did not have semantic deficits, although there may have been some reduction in this skill. Finally, he presented no difficulty conducting the NART (Nelson & Willison, 1991), which reflected good reading skills. Overall, this participant had good performance across all tasks.

The next participant is a male, 47 years and 8 years with MS. This participant represents the profile of participants whose naming skills have been slightly affected, but they do not present word retrieval deficits. This participant obtained a medium-to-high level in the Picture Naming Task compared to the performance of the MS group. He obtained a score at the same level of the cut-off score of the Picture Naming Task (52 points).

Figure 29 shows the performance of this participant across all the behavioural assessments compared to the cut-off level of each tasks.

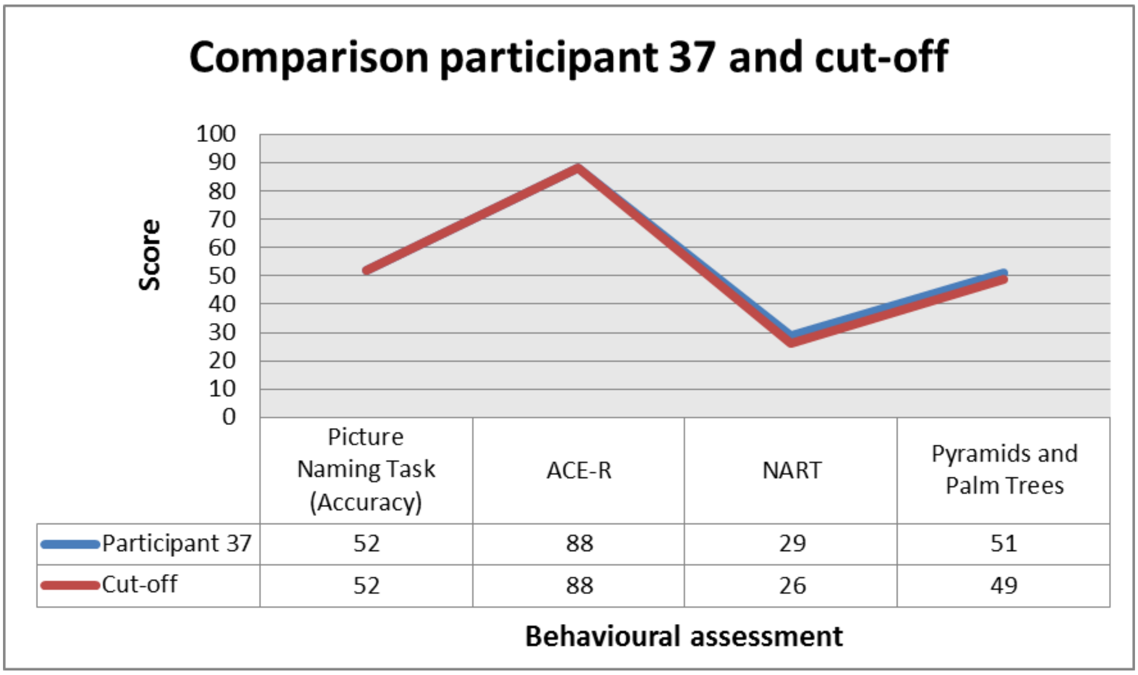


Figure 28- Comparison between score obtained by participant 37 and cut-off across all tasks

This participant performed at the lowest limit within the neuro-typical levels across the four behavioural assessments. His performance in the Picture Naming Task shows that this person presented with some type of difficulty retrieving words which would not be considered as clinical performance. His level of cognition has likely been affected by MS but, as well as with his naming skills, the cognitive deterioration that he presented cannot be considered as clinical. Finally, regarding his reading and semantic skills, both of them were slightly above the cut-off score of the tasks. This shows he did not present with semantic or reading deficits. Overall, this person has likely seen his cognitive skills worsened by MS. None of his cognitive skills can be considered as significantly impaired.

The third participant is a female, 29 years old with 5 years with MS. This participant obtained an average score in the Picture Naming Task compared to the scores of the MS group. However, when comparing her performance with the normative data, this participant presented word retrieval deficits.

Figure 30 shows the performance of this participant across all the behavioural assessments compared to the cut-off level of each tasks.

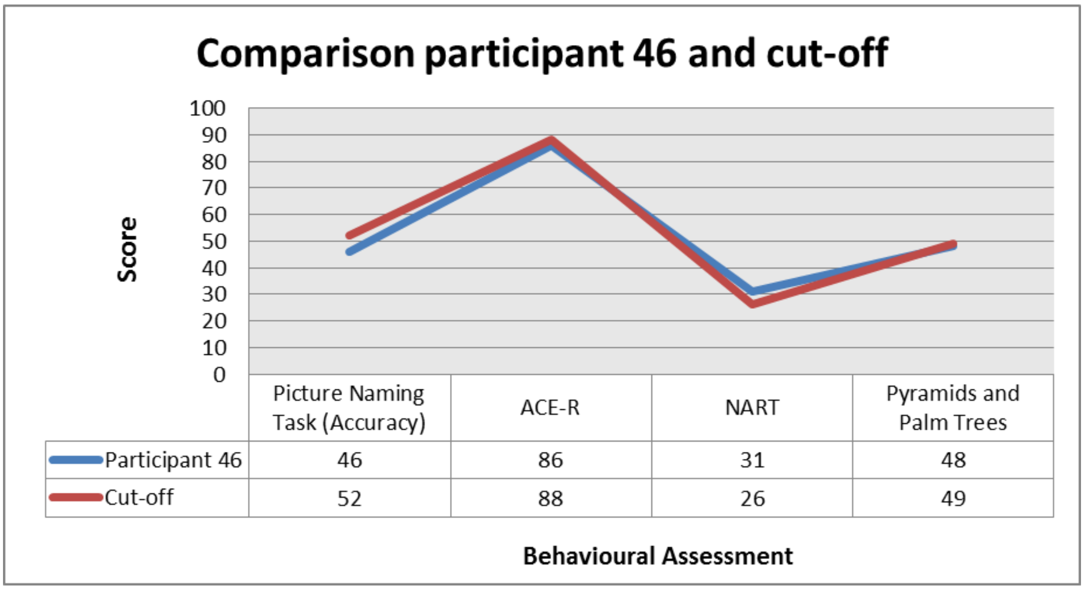


Figure 29- Comparison between score obtained by participant 46 and cut-off across all tasks

This participant had a performance very similar to the previous participant (n.37). The difference in this case is that this participant has performed under the cut-off level of three out of the four tasks. MS has produced a greater impairment in the cognitive skills of this participant than in participant number 37.

Overall, this participant presented with cognitive impairment in more than one cognitive domain. She also presented with word retrieval deficits along with semantic deficits, which seemed to be closely related. Regarding reading skills, they seem not to have been affected in this case.

The next participant is included in the group of participants with a medium-to-low level in naming skills compared to the scores obtained by the MS group. This participant is a male, 51 years old with 14 years with MS. He presents with severe word retrieval deficits and also with generalised cognitive impairment.

Figure 31 shows the performance of this participant across all the behavioural assessments compared to the cut-off level of each tasks.

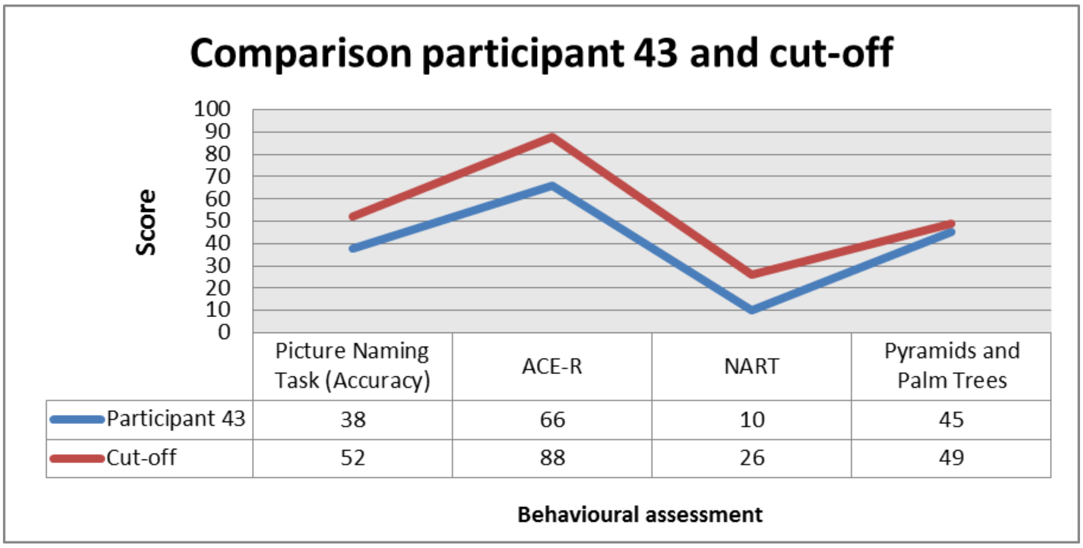


Figure 30- Comparison between score obtained by participant 43 and cut-off across all tasks

This participant performed under the level of the cut-off score in the four behavioural assessments. Clearly, this participant presents with cognitive impairment across more than one cognitive domain. The naming and semantic skills of this participant have been severely impaired. The relationship between impairment in naming and semantic skills has been present in many participants, which may indicate a relationship between these two cognitive skills. Finally, this participant also presented with severe reading deficits which have not been common within the group of participants.

The last participant presented the most impaired naming skills within the group of participants. This participant is a female, 48 years and 5 years with MS. Her performance in the Picture Naming Task was at the bottom of the group with only 35 correct answers out of 60.

Figure 32 shows the performance of this participant across all the behavioural assessments compared to the cut-off level of each tasks.

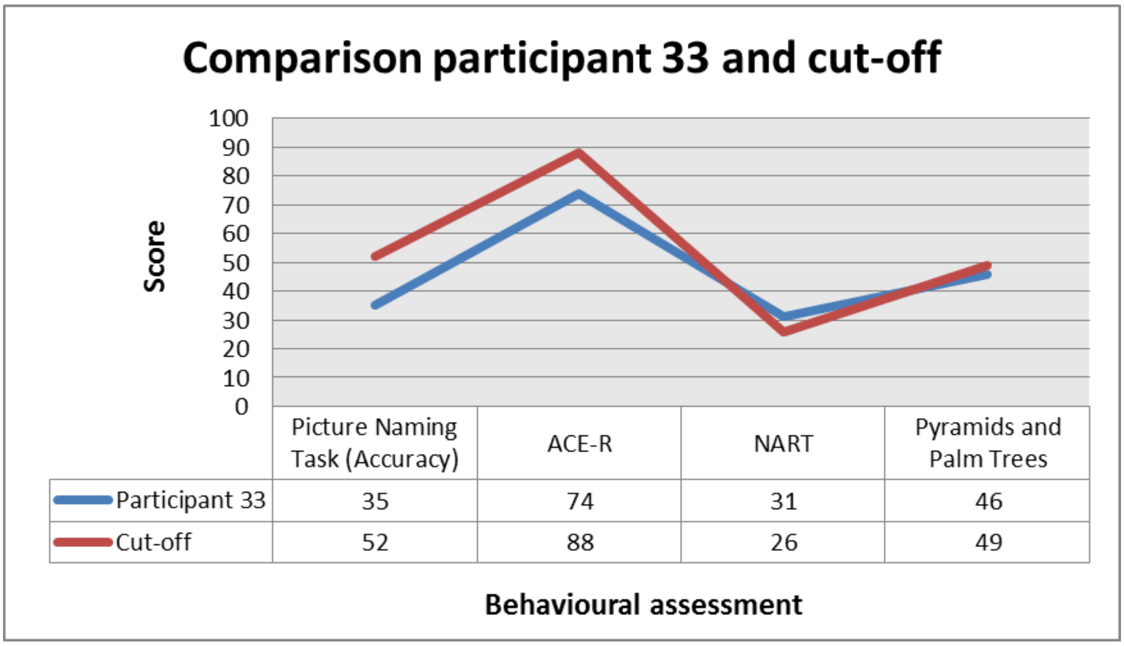


Figure 31- Comparison between score obtained by participant 33 and cut-off across all tasks

This participant performed under the level of the cut-off score in three out of the four behavioural assessments. Cognition, overall, and naming skills seem to be the skills that have been affected the most by MS. Semantic skills are also impaired, although the impairment is not as severe as the one presented in other cognitive skills such as word retrieval. Regarding the reading skills, they have not been affected.

Overall, the difference in the performance of these participants reflects the diversity of cognitive profiles that can be produced by MS. Years with MS do not seem to have an impact in the word retrieval skills of the participants; however, there seem to be other variables affecting this such as semantic skills. After all, naming skills are not a pure deficit and are usually caused by an interaction between several deficits.

Correlation Matrix

A Correlation Matrix between the data from the behavioural assessments was calculated in order to study the degree of relationship between different variables. The correlation analyses were selected and included in the first place to look for initial relationships between different demographic and behavioural variables of the study. After conducting these correlation analyses, a further analysis conducting Multiple Regression analyses was required to understand the way certain behavioural variables (predictor variables) from the assessment were related to the performance on the Picture Naming Task (dependent variable). The correlation analysis does not provide information about the relationship between variables, for this reason was only selected to understand which variables seem to correlate with other variables. On the contrary, multiple regression analysis provides information about the type of relationship between different variables combined together and their impact separately.

Due to the nature of the data (performance across a clinical sample), a non-parametric test of correlation (Spearman's) was conducted to measure the relationship between different groups of variables. This type of non-parametric correlation (Spearman's) was selected because it was not possible to assume a Gaussian distribution of the results.

Correlation matrix between behavioural assessments

Table 16- Nonparametric test of correlation between behavioural assessments

Spearman's Correlation

Behavioural Assessment	1	2	3	4
(1) Picture Naming Task	-			
(2) ACE-R	.498	-		
(3) NART	.463	.658	-	
(4) Pyramids and Palm Trees	.423	.323	.351	-

Non-parametric tests of correlation (Spearman's) were computed among the four behavioural assessments included in the assessment. The sizes of the sample was n=100 for all the tasks. Table 19 shows that there was a significant positive correlation among all the assessments, indicating participants were reasonably consistent in their performance across these tests; some did well in all while others performed less well in all.

As can be seen in Table 16, there was a significant positive correlation between the Picture Naming Task and the score obtained in the ACE- R (Mioshi et al., 2006) (r_s= .489, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak correlation (48.9%) between the two variables.

There was a significant positive correlation between the Picture Naming Task and the score obtained in the NART (Nelson & Willison, 1991) (r_s= .463, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak association (46.3%) between the two variables.

There was a significant positive correlation between the Picture Naming Task and the score obtained in the Pyramids and Palm Trees (Howard & Patterson, 1992) (r_s= .423, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak correlation (42.3%) between the two variables.

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the NART (Nelson & Willison, 1991) (r_s= .658, *N*= 100,

$p <$.0005, two-tailed). The Spearman's correlation shows that there was a positive and strong correlation (65.8%) between the two variables. Figure 33 shows the relationship between these variables.

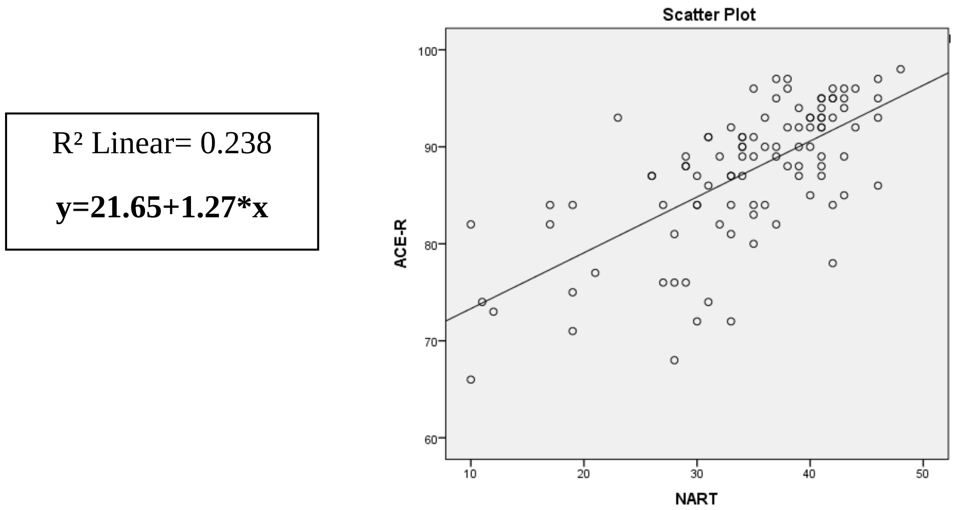


Figure 32- Scatter plot between NART and ACE-R

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the Pyramids and Palm Trees (Howard & Patterson, 1992) (r_s= .323, *N*= 100, $p <$.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak correlation (32.3%) between the two variables.

There was a significant positive correlation between the Pyramids and Palm Trees (Howard & Patterson, 1992) and the score obtained in the NART (Nelson & Willison, 1991) (r_s= .351, *N*= 100, $p <$.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak correlation (35.1%) between the two variables.

Only the nonparametric correlation (Spearman's) between the ACE-R (Mioshi et al., 2006) and the NART (Nelson & Willison, 1991) showed a strong positive correlation (r_s= .658, *N*= 100, $p <$.0005, two-tailed). This result suggests that participants who score higher in the ACE-R (Mioshi et al., 2006) tended to produce fewer errors reading irregular words.

Correlation matrix between ACE-R and subtests

Table 17- Nonparametric correlation between ACE-R and subtests

	Spearman's Correlation					
Behavioural Assessment	1	2	3	4	5	6
(1) ACE-R	-					
(2) Attention	.344	-				
(3) Memory	.798	.174	-			
(4) Verbal Fluency	.632	.037	.313	-		
(5) Language	.658	.174	.357	.317	-	
(6) Visuospatial Skills	.426	.149	.285	.034	.177	-

Non-parametric test of correlation (Spearman's) were computed among the ACE-R (Mioshi et al., 2006) and the five subtests included in this behavioural assessment. This type of correlation (Spearman's) was selected because it was not possible to assume a Gaussian distribution of the results. The sizes of the sample was n=100 for all the subtests. As can be seen in Table 17, although all the subtests had a significant and positive correlation with the ACE-R (Mioshi et al., 2006), there was not a significant correlation among subtests.

Regarding the correlation among the ACE-R (Mioshi et al., 2006) and the subtests, there was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the subtest of attention (r_s= .344, *N*= 100, p <.0005, two-tailed). The Spearman's correlation showed that there was a weak correlation (34.4%) between the two variables. This subtest did not correlate with any other subtest included in the ACE-R (Mioshi et al., 2006).

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the subtest of memory (r_s= .798, *N*= 100, p <.0005, two-tailed). The Spearman's correlation showed that there was a strong correlation (79.8%) between the two variables. The subtest of memory also had a significant and positive correlation with the subtests of verbal fluency (r_s= .313, *N*= 100, p <.002, two-tailed), language (r_s= .357, *N*= 100, p <.0005, two-tailed) and visuospatial skills (r_s= .285, *N*=

100, $p <.004$, two-tailed). While the correlation of memory with the ACE-R (Mioshi et al., 2006) is considerably strong, its correlation was weak with the aforementioned subtests. Figure 34 shows the relationship between the subtests of memory and language.

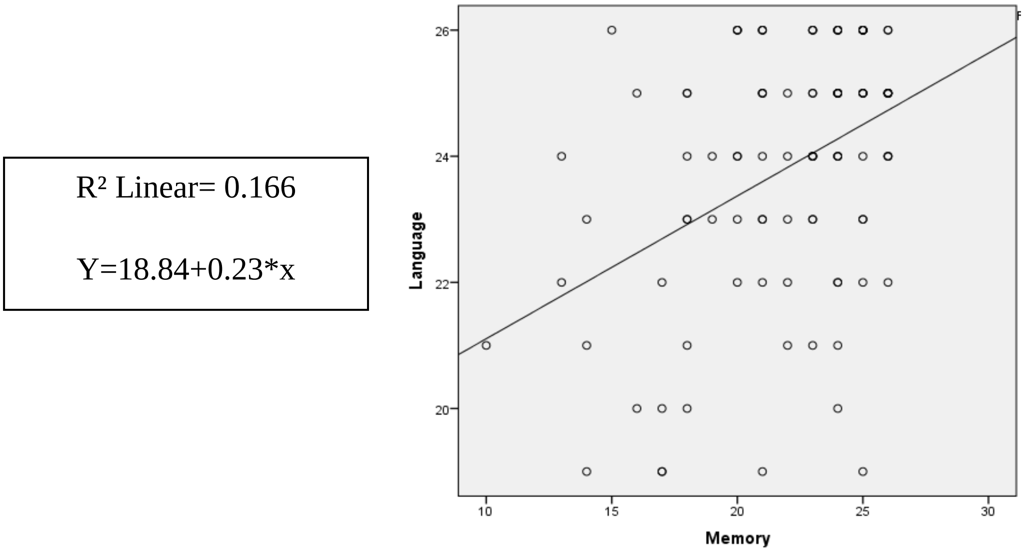


Figure 33- Scatter plot between the subtests of memory and language of the ACE-R

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the subtest of verbal fluency (r_s= .632, *N*= 100, $p <.0005$, two-tailed). The Spearman's correlation shows that there was a positive and strong correlation (63.2%) between the two variables. This subtest had a significant correlation with two other subtests included in the ACE-R (Mioshi et al., 2006). The subtest of verbal fluency had a positive correlation with the subtest of language (r_s= .317, N= 100, $p <.001$, two-tailed). Finally and as has been previously mentioned, the verbal fluency subtest also correlated with the subtests of memory (r_s= .313, N= 100, $p <.002$, two-tailed).

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the subtest of language (r_s= .65.8, *N*= 100, $p <.0005$, two-tailed). The Spearman's correlation showed that there was a positive and strong correlation (65.8%) between the two variables. The subtest of language also had a positive but weak correlation with the subtest of memory (r_s= .357, *N*= 100, $p <.0005$, two-tailed).

There was a significant positive correlation between the ACE-R (Mioshi et al., 2006) and the score obtained in the subtest of visuospatial skills (r_s= .426, *N*= 100, $p <$.0005, two-tailed). The Spearman's correlation showed that there was a weak correlation (42.6%) between the two variables. As previously mentioned, this subtest also had a significant and positive correlation with the subtest of memory (r_s= .258, *N*= 100, $p <$.004, two-tailed).

These results suggest that there was a weak correlation among the subtests included in the ACE-R (Mioshi et al., 2006). However, all the subtests had a stronger correlation with the global ACE-R (Mioshi et al., 2006) scores. The reason these subtests had weak correlations between themselves was because they were created to assess specific distinct cognitive domains. This behavioural assessment consists of five subtests, which assess different cognitive domains. The weak correlations among the subtests helps to better identify impairment in a specific cognitive domain.

Correlation matrix between main tasks and demographic data

Non-parametric tests of correlation (Spearman's) were computed among the four behavioural assessment, the subtests of the ACE-R (Mioshi et al., 2006) and two demographic variables, years with MS and years of education. This type of correlation (Spearman's) was selected because it was not possible to assume a Gaussian distribution of the results. The size of the sample was n=100 for all the tasks and n=99 for the demographic data since there was a missing value in each one of the variables included in the model. The missing values are the years of education for participant 14 and years with MS for participant 56.

Table 18- Correlation matrix between main behavioural assessments and demographic data

Spearman's Correlation											
Variable	1	2	3	4	5	6	7	8	9	10	11
(1) Years with MS	-										
(2) Years Education	-.037	-									
(3) ACE-R	-.140	.178	-								
(4) Attention	-.175	.153	.344	-							
(5) Memory	-.106	.071	.798	.174	-						
(6) Verbal Fluency	0.51	.018	.632	.037	.313	-					
(7) Language	-.213	.283	.658	.174	.357	.317	-				
(8) Visuospatial Skills	-.060	.209	.426	.149	.285	.034	.177	-			
(9) NART	.005	.326	.658	.248	.443	.423	.596	.282	-		
(10) Picture Naming Task	-.156	.105	.489	.023	.275	.417	.521	.205	.463	-	
(11) Pyramids and Palm Trees	-.098	.144	.323	.149	.158	.162	.491	.102	.351	.423	-

As can be seen in Table 18 there was a significant positive correlation between the Picture Naming Task and the score obtained in the subtest of verbal fluency of the

ACE- R (Mioshi et al., 2006) (r_s= .417, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak correlation (41.7%) between the two variables. The Picture Naming Task also had a significant correlation with the subtest of language of the ACE-R (Mioshi et al., 2006) (r_s= .521, N= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and moderate correlation (52.1%) between the two variables.

There was a significant positive correlation between the NART (Nelson & Willison, 1991) and the demographic variable of years of education (r_s= .326, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak association (32.6%) between the two variables. Figure 35 shows the relationship between the score obtained in NART (Nelson & Willison, 1991) and the demographic variable of years of education.

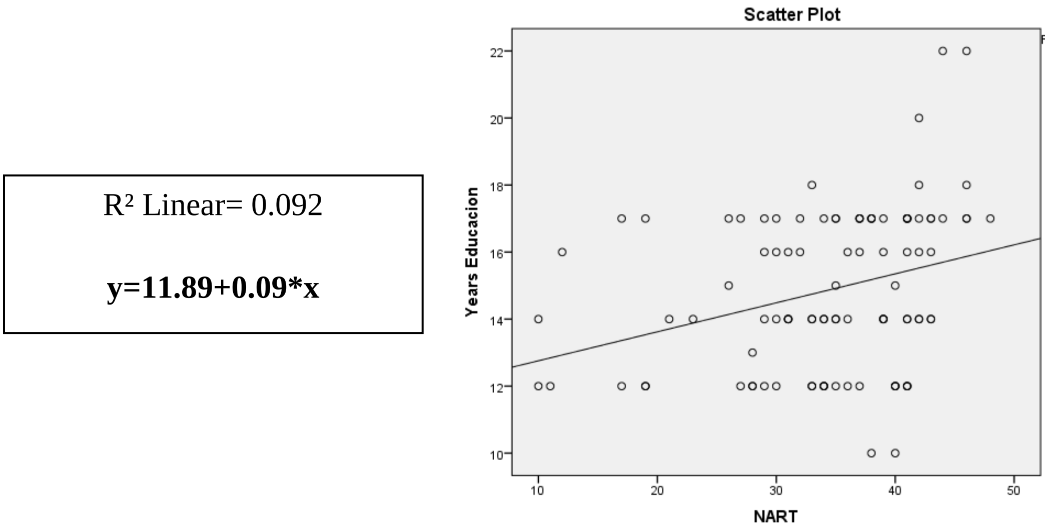


Figure 34- Scatter plot between NART and years of education

There was a significant positive correlation between the NART (Nelson & Willison, 1991) and the subtest of language of the ACE-R (Mioshi et al., 2006) (r_s= .596, *N*= 100, p <.0005, two-tailed). The Spearman's correlation shows that there was a positive and moderate association (59.6%) between the two variables. The NART (Nelson & Willison, 1991) also had a positive correlation with the subtest of verbal fluency of the ACE-R (Mioshi et al., 2006) (r_s= .423, *N*= 100, p <.0005, two-tailed).

The Spearman's correlation shows that there was a positive and weak association (42.3%) between the two variables.

There was a significant positive correlation between the Pyramids and Palm Trees (Howard & Patterson, 1992) and the subtest of language of the ACE-R (Mioshi et al., 2006) (r_s= .491, N= 100, $p <$.0005, two-tailed). The Spearman's correlation shows that there was a positive and weak association (49.1%) between the two variables.

The last significant finding in this correlation is that years with MS do not correlate with performance in the behavioural assessments. This finding is consistent with the current literature about the impact of years with MS has on performance.

Multiple Regression

Multiple Regression analyses were conducted to identify how predictive the score of a participant on a task was according to their performance on other tasks, with a particular focus on the picture naming task, indicative of anomia. The stepwise method was used to explore which variables correlated with each other. This method includes and removes variables in the model according to their relevance in the model.

Multiple regression between tasks

Using the stepwise method, a significant model emerged F (2,97) = 36.418, $p <.0005$. The association between the Picture Naming Task (criterion variable) and the explanatory variables (ACE-R, NART, Pyramids and Palm Trees) is moderately weak (Multiple R= 0.655). Only the Pyramids and Palm Trees (Howard & Patterson, 1992) and the ACE-R (Mioshi et al., 2006) were significant in the model. Together, these explanatory variables (Pyramids and Palm Trees, ACE-R) accounted for 42.9% of the variance (R^2 = .429, p<.000). Both variables positively related to Picture Naming Task score. The regression coefficient for the Pyramids and Palm Trees was 0.89 (95% CI=0.53-1.24); for the ACE-R it was 0.24 (95% CI=0.12-0.37). The confidence limits do not encompass a negative value, therefore, it can be concluded that the population regression coefficients for both the Pyramids and Palm Trees and the ACE-R are positive (Pyramids and Palm Trees – t=4.969; p=<0.00; ACE-R- t=3.878; p=0.00).The standardised regression coefficients show that Pyramids and Palm Trees is a stronger predictor than ACE-R. However, both variables are related to the Picture Naming Task score.

Multiple regression between language related tasks

Using the stepwise method, a significant model emerged F (2,97) = 23.4, $p < .0005$. The association between the Picture Naming Task (criterion variable) and the explanatory variables (subtests of verbal fluency and language) is moderately weak (Multiple R= 0.570). Both explanatory variables were significant in the model. Together, these explanatory variables (subtests of verbal fluency and language) accounted for 32.5% of the variance (R^2 = .325, p<.001). Both variables positively related to Picture Naming Task score. The regression coefficient for the subtest of language was 0.99 (95% CI=0.53-1.45); for the subtest of verbal fluency it was 0.70 (95% CI=0.31-1.10). The confidence limits do not encompass a negative value, therefore, it can be concluded that the population regression coefficients for both the subtests of language and verbal fluency are positive (Language – t=4.299; p=0.00; Verbal Fluency- t=0.00; p=0.00).The standardised regression coefficients show that subtest of language is a stronger predictor than subtest of Verbal Fluency. However, both variables are related to the Picture Naming Task score.

CHAPTER 6: Discussion

The empirical research presented in this thesis set out to gather data from a screening assessment of communication skills in people with MS in order to measure core skills such as word retrieval in the context of broader cognitive-linguistic processing and speech production skills. Prior to implementation of this study, a systematic review on the topic of speech and language skills in people with MS had failed to find a clear consensus as to the nature and extent of speech and language disorders within this population. Rather, a challenging situation to define the variables causing speech and language deficits was found. Language deficits were not originally associated with MS, which reduced the research on the topic since the discovery of the disease. However, later research proved that these deficits may indeed be present at any stage of the disease (Beatty & Monson, 1989; Drake et al., 2002). Nevertheless, the underlying causes of the deficits, anatomical and cognitive, have not always been identified.

The current study conducted to assess language and speech deficits in people with MS included 100 participants with RRMS. The average age of the participants was 41 years old, with an average of 8 years with MS. MS is a disease that affects women predominantly, which is reflected in the current sample of participant which contained 68 women and only 32 men. Participants were recruited into the research study once they met the criteria to participate in the study and were interested to participate. The assessment consisted of an interview and four behavioural assessments, to assess a broad set of cognitive domains assessing language and other related cognitive domains, including picture naming, semantics, attention, and memory. The tasks were audio-recorded to later analyse the presence of dysarthria or reaction time of the participants.

The key findings regarding the presence of speech/language problems in people with RRMS found show that there was a substantial proportion of people with clinical symptoms in one or several of the domains assessed. Although the participants as a group performed at the lower end of the control range, there was a large variability within the participants. These participants presented impairment in both accuracy and speed of processing when retrieving words. The presence of dysarthria had a negative effect on the word retrieval skills of the participants; however, the prevalence of this problem was minimal and does not account for all the word retrieval problems observed. In contrast, a deficit with semantics was found to be related to the word retrieval problems demonstrated by the MS participants assessed, and was the largest contributor to anomic symptoms in people with MS in the current study.

The existing literature regarding communications skills in people with MS fails to describe the nature and extent of anomic deficits in people with MS. The research studies on word retrieval deficits have selected certain approaches to understand this deficit that have been mainly focused on information retrieval deficits caused by memory impairment (Andrade et al., 2003) rather than anomic deficits caused by language impairment (Drake et al., 2002).

MS is a neurodegenerative disease that progressively causes cognitive impairment in different cognitive domains (Rogers & Panegyres, 2007). The location of the plaques and the inflammation determines the extent and nature of the cognitive and physical deficits. Cognitive impairment has been widely found in people with MS and the degree of impairment caused by the deficits MS produces varies according to the clinical course and/or frequency of the outbreaks (Chiaravalloti & DeLuca, 2008). The progressive forms of the disease are known to cause more cognitive impairment than the relapsing forms. The symptoms can be highly disabling for people living with MS. Moreover, although there are some treatments available to reduce the severity of the symptoms, there is not yet definite cure for MS (Merino & Quílez, 2007; Wang, 2005).

Language deficits are usually relatively preserved in people with subcortical dementias. This type of deficit is more common in cortical dementias where areas of the cortical regions of the brain have been damaged (Cummings & Benson, 1988). Although MS is a subcortical dementia, the progression of the disease ultimately affects cortical areas of the brain (Chiaravalloti & DeLuca, 2008). For this reason, MS sufferers present both physical and cognitive deficits. The most common physical problems are muscle weakness, tremors or numbness (Finkelsztejn, 2014). The most common cognitive domains affected by the disease are memory, processing speed and language (Achiron et al., 2013; Amato et al., 2007). Our main interest in this study was to understand cognitive-linguistic deficits causing communication disability in people with MS, especially language deficits.

Language deficits in people with MS have been a controversial topic because of the diversity within participants and assessments used to measure these deficits (Laakso et al., 2000). According to the areas of the brain that have been affected, the language deficits would be different. Moreover, the lack of assessments sensitive enough to detect language deficits underestimates the proportion of people with MS suffering from language deficits.

Language deficits can be present even at the beginning of the disease (Beatty & Monson, 1989). However, the first research studies about language in subcortical dementias, associated this type of deficit with generalised cognitive impairment, more than language deficits as a characteristic of subcortical dementias (Cummings & Benson, 1988).

Usually, people with MS have difficulties in areas such as word retrieval, verbal fluency deficits or semantic deficits (Langdon, 2011). Some of these deficits, such as verbal fluency deficits, have also been found in other subcortical dementias such as Parkinson's disease (Cummings, 1986).

Regarding the presence of word retrieval deficits, there are different cognitive models of lexical processing that explain the presence of this type of deficit. The models provide an explanation about how language is produced and how it is understood (Laine, 2013). Furthermore, they explain the type of errors that people with anomic deficits can make according to the stage of the model of language processing is impaired (Hillis, 2015). The three main cognitive models of lexical access are functional models, local connectionist models and distributed connectionist models (Hillis, 2015; Laine, 2013).

The model that better explains anomic deficits in people with MS is the connectionist model of speech production of Dell (Dell et al., 1999). This model has been used to understand anomic deficits in neurotypical and aphasic population (Dell et al., 1997). Dell's model consists of three nodes or levels of representation through which language is produced (Laine, 2013). Impairment in each level or node (semantic, lexical and phonological) will lead to a different type of anomia as it was described in Chapter 2.

MS can also produce motor-speech deficits. Dysarthria is a common motor-speech deficit present in the majority of people suffering from subcortical dementias and by extension MS (Bodling et al., 2008; Cummings, 1986; Mackenzie & Green, 2009). This deficit has a negative impact in the performance of a person with MS in linguistic tasks; however, there is no information about which aspects of a task can be affected by dysarthria (Bodling et al., 2008).

A systematic review about speech and language disorders in people with MS was conducted to study to what extent anomic deficits have been investigated in people with MS. The review showed a gap in the knowledge about anomic deficits in people with MS. It is a difficult deficit to detect and each research study has had a different approach to understanding these anomic deficits. As has been previously mentioned, according to where the plaques or inflammation are located in the CNS, the deficits and causes of the deficits will be different in each person.

Most of the research in the topic has focused on information retrieval and word retrieval deficits. Both deficits differ in the cognitive domains needed to conduct the task. While in information retrieval tasks, the main cognitive domain assessed is memory. In word retrieval tasks, the main cognitive domain assessed is language. The studies that include word retrieval tasks are the ones that provided useful information for this research study (Beatty & Monson, 1989; Drake et al., 2002; Friend et al., 1999).

Among the research studies investigating the presence of word retrieval deficits in MS there are contradictory findings. These studies have used techniques such as picture naming tasks to measure naming skills in people with MS (Bodling et al., 2008; Jennekens-Schinkel et al., 1990). Although this technique is one of the most accurate techniques to measure this deficit, not all studies have found the same result regarding the presence of anomia in people with MS. The first studies in the topic did not find any sign of anomic symptoms in people suffering from MS (Rao, 1986). However, research later on found that people with MS may indeed suffer from anomic deficits and this deficit can be present at any point in time in the disease (Beatty & Monson, 1989; Drake et al., 2002). A limitation of the research studies in this area is that the samples of participants in the studies have been considerably small. For this reason, despite the fact that some studies have found anomic deficits, there is still little known about the nature and intensity of anomia in people with MS.

There is some previous evidence that people with MS may suffer from deficits in many aspects of language. Verbal fluency deficits and problems with complex language are characteristic of the neuropsychological profile of people with MS (Tallberg & Bergendal, 2009). However, while there is some evidence that MS does produce language impairment in different aspects of language, due to the complexity of the disease it is highly difficult to study the intensity and prevalence of these deficits.

Another characteristic about MS found in the systematic review was the relevance of the interaction between variables (Beatty, 2004; Feenaughty et al., 2013; Jennekens-Schinkel et al., 1990). Cognitive deficits such as memory loss or processing speed deficits have been the main focus of research in MS (Bodling et al., 2008). However, there is little research studying the interaction between cognitive (and physical) deficits. The fact that impairment in different cognitive domains can increase or produce other deficits should always be taken into consideration. When studying the nature of some cognitive deficits, especially language, previous studies have commonly attributed these to be the result of other deficits because the underlying cause may be difficult to detect. Due to the neurodegenerative character of MS, it can be considerably challenging to understand what is causing every cognitive deficit. However, an in-depth evaluation of the cognitive skills of these people can be useful to obtain an idea of which deficits are interacting with each other.

For the above reasons, the current study was interested in furthering the understanding of anomic problems in people with RRMS. It is necessary to clarify the prevalence and characteristics of anomia since it can limit the lives of people suffering from it. Moreover, the study also aimed to examine the relationship between anomic deficits and impairment in other cognitive domains that could act to intensify the presence of this deficit. MS produces cognitive deficits in many cognitive domains and the interaction between different impaired domains can increase the severity of the deficits people with MS suffer from.

The results showed that the participants with RRMS do indeed suffer from anomic deficits, with over half of those assessed demonstrating reduced accuracy or slower reaction time to recognise an object in a Picture Naming Task. In this study, the participants with RRMS presented difficulties in both accuracy and reaction time. The most common characteristic of the word retrieval of these participants was an increased reaction time naming pictures of objects, with more participants showing difficulties in the time taken to name the items rather than accuracy. This impairment in reaction time shows that MS hampers the process to access words. Since the participants have a major difficulty in accessing a target word, they need more time to name the object. This impairment in reaction time is a common deficit in people with MS since impairments such as axonal loss caused by MS hamper the transmission of information increasing the time to answer in a task.

Regarding accuracy, a reduced naming accuracy was also present for a substantial portion of the MS participants. Additionally, a number of participants with MS also presented deficits in both reaction time and accuracy at the same time. The results show these participants not only needed more time to retrieve the name of the pictures, but also failed in retrieving the target word. This group of participants have seen their naming skills considerably impaired because of MS.

Only a few previous research studies focused on understanding naming skills in people with MS have measured the reaction time required to name an object (Beatty & Monson, 1989). These studies have failed to analyse the critical variable of processing speed (Pijpers-Kooiman et al., 1995), which was found to affect the naming performance of a number of participants in the current study. Generally people with MS are less accurate than the control group retrieving words (Drake et al., 2002); however, the naming difficulties presented in people with MS can be better seen in the time they need to retrieve a word. In the current study, there was a larger difference between the control and MS group in reaction time rather than accuracy. For this reason, to measure the reaction time is of major importance when studying naming skills in people with MS. Only one previous study focused on understanding retrieving skills in people with MS examined this factor, and consistent with the current study found that approximately 40% of people with MS present with this deficit (Beatty & Monson, 1989). In this case, the anomic problems where present regardless of the years with the disease. This fact supports the idea that years with MS does not completely correlate with performance in behavioural assessments. This topic will be argued later on the discussion.

In addition to naming difficulties, semantic deficits were also found to be widely present in the current sample of participants. Over 40% of participants had deficits accessing or retrieving the meaning of pictures. Most of the participants who presented with naming difficulties also presented with semantic impairment. This reflects a relationship between these two skills. According to Dell's model of lexical processing, to retrieve a word, there is a competition of activation between words that have similar levels of activation. The words with a higher level of activation are the ones that activate more single elements in the semantic, lexical and phonological stages of word retrieval. In naming an object, a person needs to be able to access the knowledge about that object (semantic knowledge). It seems possible that people with MS may present with deficits in the first stage of lexical processing (semantic features of the word), increasing the severity of the anomic symptoms. In order to empirically test the levels of semantic breakdown in these participants with MS, further and more fine-grained assessment of semantic processing will need to be conducted in future research.

Consistent with the current findings, there has been previous research supporting the fact that people with MS usually present with semantic deficits (Lethlean & Murdoch, 1994). Generally, people suffering from MS make more semantic errors than other type of errors (Lethlean & Murdoch, 1994). The impairment of semantic skills in people with MS can be caused due to the interruption of the connection between subcortical pathways. This interruption of the subcortical pathways also hampers the transmission of information (Langdon, 2011), leading again to an increase of the severity of anomic symptoms.

Overall, the MS participants assessed in the current study seemed to present with two different types of anomic problems when retrieving words. In many instances participants appeared to have a rich semantic representations of a given object in that they were fully aware of its function and appearance but they were unable to generate sufficiently precise semantic information to stimulate the required lexical node. This reflects the presence of word form anomia in which the semantic information of the word is preserved but the access to the word has been hampered (Laine, 2013). This type of deficit is closely linked to impairment in the lexical stage of Dell's model. On the other hand, some participants did not appear to have a conceptual understanding of some objects in that they did not discern their function therefore were not capable of naming them either. This pattern is more characteristic of semantic anomia (Laine, 2013) in which the impairment is in the first level of lexical processing from Dell's model. Hence, the participant suffers from deficits accessing the semantic features of the concept and this impedes the word retrieval process.

One deficit which could affect naming skills is dysarthria, a problem in the motor processes involved in articulation and speech (Connick et al., 2012). However, the current study did not find a high prevalence of this deficit, and did not find any evidence for the presence of severe dysarthria in the current group of participants. This is inconsistent with the literature, which suggests that approximately 40% of people with MS suffer from this motor-speech deficit (Sorensen, Brown, Logemann, Wilson, & Herndon, 1994). This inconsistency may have resulted from the fact that most of the participants in the current sample did not present with severe physical disability. The impact of MS in these participants has had a major influence in their cognition rather than in their physical skills.

It is of note that, although the participants with dysarthria only presented mild dysarthria, this deficit did appear to impact on their reaction time on the Picture Naming Task. Overall, the participants that presented mild dysarthria needed more time to retrieve the names of objects than those without any sign of dysarthria. The increase in naming reaction time found may have been caused by the greater time required to articulate words in the presence of motor speech deficits. However, these participants only presented with mild dysarthria, so it may have been the case that dysarthria was also an indicator of more generalised cognitive and physical impairments that caused the increase in reaction time. Regardless of cause, it is interesting to note that even a mild motor-speech deficit can have an observable impact on naming performance.

Previous research studies which have examined the effect dysarthria has on performance in other tasks have recognised that dysarthria has a negative impact in the performance of participants. Other studies however, have excluded participants that presented with dysarthria to eliminate the impact it has on performance (Tallberg & Bergendal, 2009). Nevertheless, there is no evidence of which aspects of performance can be hampered. This research study has found that dysarthria has a clear impact in increasing the reaction time of participants in the naming task. This underlines the interactive effect of multiple symptoms which makes the clinical presentation of MS complicated to study and understand. Moreover, the increase in reaction time caused by the presence of dysarthria also highlights the fact that the nature of anomic deficits is often caused by the interaction of different factors. It has been previously mentioned that the presence of semantic deficits increases the probability of presenting word retrieval deficits. Now dysarthria can be also included in the list of deficits that cause or intensify word retrieval deficits in MS.

Regarding the overall cognitive status of the participants in the current study, marked cognitive impairment in more than one cognitive domain was highly present in the sample of participants. More than 40% of participants performed under neuro-typical levels in the ACE-R (Mioshi et al., 2006). This assessment involves a range of subtests examining different cognitive domains, and as such, those that showed overall impairment on the assessment presented cognitive impairments in more than one cognitive domain. MS is widely known for producing cognitive impairment since it produces damage in both white and grey matter of the brain (Chiaravalloti & DeLuca, 2008). The lesion caused by the disease can be located in multiple different areas of the brain, causing deficits in several cognitive domains. In addition, these deficits will interact with each other, intensifying the deficits. This characteristic of MS should always be considered when understanding a deficit in people with MS. In the majority of cases, the nature of a deficit in MS will be caused (or at the very least, intensified) by other deficits. For this reason, we should never try to justify a deficit for impairment in only one cognitive domain.

Overall, MS is known to cause cognitive impairment in 40-60% of MS sufferers from all clinical courses (Rogers & Panegyres, 2007). However, the presence of cognitive impairment in clinical courses such as PPMS is much higher and intense than in other clinical courses. Participants in the current study all suffered from the RRMS subtype. This subtype is known to produce less severe cognitive impairment than other clinical courses, and so the high percentage of people suffering from marked cognitive impairment found in the current sample of participants is higher than might be expected. This suggests that the current assessment battery, and examination of both accuracy and reaction time, was sensitive enough to reveal even subtle deficits.

The finding of a high rate of multiple cognitive impairments can help to understand the fact that the majority of participants presented word retrieval deficits. The significant number of participants with cognitive impairment in more than one cognitive domain shows that generalised cognitive impairment was common in the sample of participants. Word retrieval deficits are known to occur because of the interaction of cognitive impairment in several cognitive domains. In this research study, the finding from both tasks supports again the idea of the interaction between deficits as cause of word retrieval deficits.

One interesting finding regarding the course of the disease and the consequence on cognition was the finding that years with MS did not have a direct relationship with performance on the behavioural assessments. This relationship has been controversial because in the majority of neurodegenerative diseases the longer the years with the disease the greater the cognitive impairment. Furthermore, previous research studies on the topic have found different contradictory results. While some studies did not find a relationship between these variables (Denney et al., 2005; Mackenzie & Green, 2009; Rogers & Panegyres, 2007), others have found a clearer link between years with MS and performance in different tasks (Achiron et al., 2013). The current study adds to this debate, in providing additional evidence from a large sample of participants with RRMS that there is not a relationship between the level attained by a participant in a task and years with MS. The reason why this relationship has not been found in this research study might be because MS can produce cognitive deficits even at the beginning of the disease (Beatty & Monson, 1989). The degree of cognitive impairment varies according to the location of the inflammation and plaques throughout the central nervous system. It is possible to find a case in which a person with MS only suffers from mild outbreaks of the disease and this person does not present severe deterioration of the parenchyma. On the contrary, another person with MS can suffer from severe outbreaks that affect larger areas of the brain. Even if these two people have been suffering from MS for the same length of time, the level of cognitive impairment is not going to be the same in both cases. It is true that in some situations both variables can go hand by hand. Nonetheless, the current results show that the lack of relationship is more characteristic of the nature of MS.

The current study examined performance for both the MS group as a whole as well as looking at performance at an individual level. Overall, it was found that there is a significant variability within the current sample of participants in the presence, nature, and severity of cognitive impairment. Almost one-third of participants performed within the neuro-typical levels in all of the tasks. For these participants, MS has not yet affected their cognitive skills and they have not yet seen their everyday life affected by cognitive difficulties. On the other hand, there is another group of participants who were found to suffer from a generalised cognitive impairment affecting multiple domains. This variability within the participants is the reason why when studying cognitive impairment or physical deficits in MS, the findings are usually controversial. When performing group studies in MS, there is a great difficulty in creating groups within the population because there are no specific variables to cluster the participants common to all.

When performing group studies, the best way to cluster people suffering from MS may be by the areas of the brain in which they present plaques or inflammation. The problem with this approach is that due to the fact that lesion may be present in multiple areas; there are not two MS sufferers with lesions in exactly the same brain areas. However, this way of clustering participants would be interesting to use in order to understand anomic problems. First the participants are assessed to measure their naming skills and then using neuroimaging techniques, the areas of the brain in which they present plaques or inflammation are detected. This technique would help to understand if anomic problems are caused by damage in a particular area or areas of the brain. Another way to cluster participants may be by clinical course. Although there are many variables affecting the performance of people with MS in a task, people with the same clinical course could be thought to present with similar deficits. However, the current results suggest that caution should be taken in using this approach, and that a high degree of heterogeneity may be present in the behavioural performance of individuals with MS even within the same disease subtype.

In summary, the results of the current study strongly show that MS does produce language deficits. While only a minority of the participants presented severe anomic problems, a substantial proportion were found to suffer from at least mild to moderate anomic deficits. These word retrieval deficits are likely to have strongly impacted those affected, and anecdotally, a number of participants in the study did report suffering from anomic deficits in their everyday lives. It is difficult to estimate the percentage of the population with MS that suffers from language deficits and more specifically naming problems, however, these difficulties have been found to be widely present in the current large sample of participants.

Regarding the nature of anomia in people with RRMS, deficits in the first stage of lexical processing from Dell's model (access to semantic features), seemed to have substantially contribute to the presence of anomic deficits. Generally, the participants that presented the most severe semantic deficits also had greater anomic deficits. It is true that some participants presented deficits similar to semantic anomia, since they did not even know the use of some objects. However, semantic deficits are not the only cause of anomic problems. Deficits with processing speed or problems with attention can also play a relevant role in the development of anomic deficits. As has been previously mentioned, the role of the interaction between impairment in different cognitive domains plays a relevant role in the performance of a participant in a task.

Limitations of the current study

Although naming difficulties in people with MS have been found in this research study, it is important to state that there are certain limitations to the current study.

The main limitation of this study is that although the sample of participants has a considerable size (n=100), it would be necessary in future work to include in the study participants from all clinical courses. All participants included in this study presented RRMS. MS is a disease with four main clinical courses; each one of these clinical courses produces different levels of disability, and the recovery after every outbreak of the disease is also different. By assessing participants from all the clinical courses, the information regarding naming skills in people with MS would be more representative of the population with MS. In order to include participants from all four clinical courses, the size of the sample would also need to be increased to provide more accurate information. An enlargement of the sample of participants could provide not only the possibility of understanding the naming skills of the population with MS, but also which clinical course presents major naming difficulties. Participants presenting a different clinical course, also have different patterns of cognition. Research in MS has always tried to compare the differences in the performance of people with MS according to their clinical course. However, the samples of participants in the studies have not always been big enough or have not always had the possibility of including participants from the four different clinical courses. Most of the time, these studies have included participants from only two different clinical courses. An examination of the cognitive profiles across the clinical course would provide important information regarding the nature and prevalence of cognitive deficits, such as anomia, in MS, as well as helping to understand how the underlying anatomical damage results in these deficits.

Another limitation of the current study is the time used to assess each participant. The behavioural assessments included in this research study were selected in order to avoid fatigue in the participants. For this reason, the assessment was approximately 45 minutes. Furthermore, the participants were only available during a one hour treatment session. By increasing the time of the assessment, it would be possible to include other behavioural assessments that provide more accurate or specific information about the cognitive status of these participants. The more information that is obtained about the cognitive skills of people with MS, the easier it will become to understand the underlying causes of their anomic deficits and other linguistic or cognitive deficits that can be also present.

Related to the time constraints and screening nature of the current assessment battery is the limited amount of information about the interaction between variables the can be gleaned from the behavioural results obtained. This interaction is a very challenging characteristic of MS that could hamper the understanding of the nature and cause of deficits presented in people with MS, and the presence of cognitive impairment in different cognitive domains and its interaction can be difficult to understand. It would have been interesting to more fully examine the relationship between impairments in the different cognitive domains. While a range of domains were assessed, and a relationship between naming and semantic skills was found, many other variables may be affecting the performance of these participants in the naming tasks. However, the time available for the assessment and the behavioural assessments included were not sensitive enough to provide this information. One way to improve this limitation could be to first understand the relationship between two variables (i.e., memory and attention). After analysing the interaction of two variables, other variables could be included in the model to create a net of knowledge about how different deficits affect each other. For example, a relationship between anomic problems and semantic deficits has been found in this research study. Information about the impact other deficits such as verbal fluency deficits could be added to this knowledge to better understand the interaction between cognitive deficits in MS.

The next limitation of the current study relates to the Picture Naming Task used. To create this task, variables such us frequency, age of acquisition, reaction time and length of phonological syllables were taken into account to select the words used. These words were then divided into subgroups to create four groups of words with similar characteristics in all variables except for reaction time, which was the main variable used to group the words in the task. There are many variables that can have an impact in the performance of a participant in a Picture Naming Task. For this reason, it would be useful to improve the accuracy of the results by equally matching all the subgroups in variables such as length of phonological syllables and age of acquisition. In this research study, the length of phonological syllables was the same in three subgroups and the fourth subgroup had a longer average length of phonological syllables. The value of the age of acquisition increased as the reaction time of the subgroup increased. If these variables were perfectly matched, all subgroups will have similar characteristics and these variables will not interfere as much in the results of the task.

The number of items included in the Picture Naming Task can be considered as a limitation of the current research study. An increase in the number of items could provide more accurate evidence of the naming skills of these participants. This could be done by adding pictures of verbs in the task in addition to the pictures of objects used. The human brain processes both verbs and nouns in a different way and verbs are usually more difficult to process than objects. Since this study only included objects in the Picture Naming Task, the results obtained might not be fully representative of the naming skills of people with MS.

The last limitation of this research study refers to the lack of information about the level of physical disability of the participants. It will be important to measure this variable to see if it correlates with other variables such as type of MS or performance in certain tasks. Since MS is a subcortical disease, physical disability is reported to be one of the main characteristics present in people suffering from MS. Moreover, previous research studies have considered this variable and have found that although there is no relationship between physical disability and cognitive impairment, sometimes physical disability can overshadow cognitive deficits. Cognitive impairment appears to have had a greater impact in the lives of the participants included in this research study than physical impairment. Nonetheless, some participants did present physical problems to a certain extent. These problems did not interfere in their performance in the behavioural assessments, but the level of physical disability could be a relevant variable to cluster participants.

Future research

The current research study points to a number of avenues for future research in the examination of language and other cognitive deficits in MS. This future research needs to be focused on developing an efficient and reliable way to detect the presence of anomic problems in people with MS. Anomic deficits can significantly reduce the quality of life of people suffering from them. The relevance of detecting anomic deficits in people with MS has a great social value since these sufferers see their life limited because of the deficit. As such, the development of assessments aimed at identifying these anomic deficits is of vital importance for the future. In addition to detecting this deficit, it would also be of importance to develop a therapy to improve word retrieval in individuals with MS, and reduce the restrictions anomic problems produce. This would allow people suffering from anomic deficits to continue with their social and professional life.

In order to create more accurate assessment techniques and treatments for anomic problems, there are some aspects of the knowledge about MS that should be studied further. As has been previously mentioned in this discussion, there was no relationship between years with MS and cognitive impairment. However, there is a clearer relationship between cognitive impairment and the area of parenchyma affected by MS. The larger the areas of parenchyma affected by MS, the greater the cognitive impairment. For this reason, the use of techniques such as Magnetic Resonance Imaging (MRI) can help to understand the underlying deficits that these participants present. The performance of these participants in every task responds to damage in specific areas or subcortical pathways of the brain. If it were possible to study the behaviour of people with MS in a task along with the knowledge of the areas of the brain that have been affected by MS, it would be easier to understand not only the nature of the anomic deficits, but also the nature of other cognitive deficits.

One of the most characteristic deficits of MS is the presence of processing speed deficits. This deficit has been largely reported in people with MS, and in the current study people with MS had longer reaction times in the Picture Naming Task, showing some type of processing speed deficit. In this research study, this processing speed ability was only measured in one task. For future studies, it would be interesting to include timed tasks to understand the effect processing speed deficits have in people with MS, and their effect on overall performance in different tasks. Processing speed might not be relevant for all cognitive tasks; however, there are some that are highly influenced by this ability. The results of some tasks, such as Picture Naming Tasks, where participants have a limited time to answer can be greatly affected by unnoticed processing speed deficits, meaning that some deficits could be caused or magnified by processing speed deficits. For this reason, therapies to speed up the reaction time of people with MS could also be very beneficial. The creation of therapies to reduce the negative impact anomic deficits have in people with MS could in the future be tackled using speed therapies (Sotiropoulou, Conroy, & Ralph, 2015). This type of therapy focuses on decreasing the reaction time a person needs to retrieve a word. For a number of people with MS, the increased difficulty to access words was associated with increases in the reaction time of these participants. If speed therapies are implemented in these people, they may be greatly benefited by the potential reduction of their anomic symptoms to the extent that an underling deficit in processing speed is related to their problems in naming. The effect of the therapy could be extended to their everyday tasks and the sufferers of anomic deficits may not see their lives as limited.

Regarding everyday care of people with MS, the current study suggests that it would be beneficial to start including regular neuropsychological evaluations to monitor the cognitive status of people with MS (Hutchinson, 2016). This idea has been largely considered because of the relevance of these evaluations; however, due to its cost, have never been implemented. Another factor that hampers the implementation of these evaluations is the time required to assess all patients. Each evaluation could require approximately three hours per person. Considering that a hospital can have hundreds of patients with MS, the implementation of regular neuropsychological evaluations can be a time consuming method. Nonetheless, while we cannot forget that despite the time required to conduct the assessment, the current study revealed that it may be possible to design and implement briefer screening batteries to reduce the time required to assess patients. Such screening assessments, followed by more comprehensive assessments when initial deficits are identified, may be a useful method to detect cognitive deficits when they appear. The sooner a cognitive deficit is detected, the better for the patient since techniques to tackle the problem can be implemented earlier when the problem is not as severe.

CHAPTER 7: Conclusion

The variable nature and neurodegenerative presentation of MS both pose considerable challenges to our understanding the cognitive and physical deficits that MS produces. The cognitive research on MS has been mainly focused on the most common cognitive deficits such as memory or attentional problems because they are easier to detect. Other complex deficits, such as language, that can be clouded by these ‘primary’ deficits have gone relatively unnoticed in the research regarding cognition and MS. Moreover, when such deficits have been studied, it has not been possible to understand what is causing the deficits. This is because not all the variables that affect the development of a deficit can be easily identified.

The current research study aimed to understand language in people suffering from MS, specifically focusing on deficits such as anomia and dysarthria. The research presented furthers our knowledge of language in people with RRMS, a topic that has been relatively neglected in the current literature of MS.

It was found that the presence of dysarthria in the participants was very subtle, with participants presenting mild dysarthria at most. Moreover, the majority of participants did not present any sign of dysarthria. In contrast, the results regarding the presence of anomic symptoms in people with RRMS showed that MS does indeed produce anomic deficits in a substantial proportion of individuals. It has been seen that people suffering from MS have a greater difficulty retrieving words, reflected in an increased time to name objects, as well as demonstrating reduced accuracy.

The main difficulty found in the naming performance of the current sample of participants with RRMS was an increase in the time required to name objects. The fact that people with MS need more time to name the objects might indicate that the information about the objects has not been lost yet. In fact, in some occasions they were capable of retrieving a synonym, which reflects that they still have information about the object. Instead, it seems that one of the principle underlying difficulties may be in the speed at which this information is able to be retrieved. In a cognitive task, such as language, which requires information to be retrieved within very short time frames; such a deficit could have a substantial impact on the language and communication skills of these individuals in everyday life.

Due to the complex interrelationship between deficits, it has not been possible to fully understand the exact nature of the word retrieval deficits found in the current study. However, there is evidence that seems to indicate that semantic deficits may influence the presence of anomic deficits in these individuals. There might be other variables affecting the naming skills of people with MS that have not been addressed in this research. For this reason, future research about naming skills in people with MS should conduct an in-depth evaluation to further this knowledge.

Regarding the extent of anomic problems, they do indeed appear, on the basis of this evidence, to be present in the majority of people suffering from RRMS. The difference is in the degree of impairment. While some participants have severe anomic deficits others present only mild symptoms. The fact that the majority of participants presented only mild to moderate anomic deficits hampers the detection of anomia, since those symptoms may go unnoticed. The development of techniques to detect anomic deficits in people with MS would be useful to avoid underestimating the percentage of the population with MS suffering from anomic deficits.

Overall, it is clear from the current research study of a large sample of individuals with RRMS that MS does produce anomic deficits. Nonetheless, there is still a great deal of research to be conducted to understand anomic problems in people with MS. This deficit needs to be detected and treated before its impact significantly reduces the quality of life of the people suffering from anomia.

References

Achiron, & Barak. (2006). Cognitive changes in early MS: a call for a common framework. *Journal of the neurological sciences, 245*(1), 47-51.

Achiron, Chapman, J., Magalashvili, D., Dolev, M., Lavie, M., Bercovich, E., . . . Khilkevich, O. (2013). Modeling of cognitive impairment by disease duration in multiple sclerosis: a cross-sectional study. *PloS one*, *8*(8), e71058.

Achiron, Polliack, Rao, Barak, Lavie, Appelboim, & Harel. (2005). Cognitive patterns and progression in multiple sclerosis: construction and validation of percentile curves. *Journal of Neurology, Neurosurgery & Psychiatry, 76*(5), 744-749.

Amato, M. P., Langdon, D., Montalban, X., Benedict, R. H., DeLuca, J., Krupp, L. B., . . . Comi, G. (2013). Treatment of cognitive impairment in multiple sclerosis: position paper. *Journal of neurology, 260*(6), 1452-1468.

Amato, M. P., Portaccio, E., Goretti, B., Zipoli, V., Battaglini, M., Bartolozzi, M. L., . . . Sorbi, S. (2007). Association of neocortical volume changes with cognitive deterioration in relapsing-remitting multiple sclerosis. *Archives of Neurology, 64*(8), 1157-1161.

Amato, M. P., Zipoli, V., Goretti, B., Portaccio, E., De Caro, M. F., Ricchiuti, L., . . . Trojano, M. (2006). Benign multiple sclerosis. *Journal of neurology, 253*(8), 1054-1059.

Andrade, V. M., Oliveira, M. G. M., Miranda, M. C., Oliveira, A. S., Oliveira, E. M., & Bueno, O. F. (2003). Semantic relations and repetition of items enhance the free recall of words by multiple sclerosis patients. *Journal of clinical and experimental neuropsychology, 25*(8), 1070-1078.

Armstrong, C., Onishi, K., Robinson, K., D'Esposito, M., Thompson, H., Rostami, A., & Grossman, M. (1996). Serial position and temporal cue effects in multiple sclerosis: two subtypes of defective memory mechanisms. *Neuropsychologia, 34*(9), 853-862.

Bagert, B., Camplair, P., & Bourdette, D. (2002). Cognitive dysfunction in multiple sclerosis. *CNS drugs, 16*(7), 445-455.

Bates, E., Andonova, E., D'amico, S., Jacobsen, T., Kohnert, K., Lu, C., . . . Herron, D. (2000). Introducing the CRL international picture-naming project (CRL-IPNP). *Center for Research in Language Newsletter, 12*(1), 12-11.

Batista, S., Zivadinov, R., Hoogs, M., Bergsland, N., Heininen-Brown, M., Dwyer, M. G., . . . Benedict, R. H. (2012). Basal ganglia, thalamus and neocortical atrophy predicting slowed cognitive processing in multiple sclerosis. *Journal of neurology, 259*(1), 139-146.

Bayles, K. A., & Tomoeda, C. K. (1983). Confrontation naming impairment in dementia. *Brain and language, 19*(1), 98-114.

Baylor, C., Yorkston, K., Bamer, A., Britton, D., & Amtmann, D. (2010). Variables associated with communicative participation in people with multiple sclerosis: A regression analysis. *American Journal of Speech-Language Pathology, 19*(2), 143-153.

Beatty, W. W. (2004). RBANS analysis of verbal memory in multiple sclerosis. *Archives of Clinical Neuropsychology*, *19*(6), 825-834.

Beatty, W. W., & Monson, N. (1989). Lexical processing in Parkinson's disease and multiple sclerosis. *Journal of Geriatric Psychiatry and Neurology, 2*(3), 145-152.

Benedict, R. H., & Zivadinov, R. (2011). Risk factors for and management of cognitive dysfunction in multiple sclerosis. *Nature Reviews Neurology, 7*(6), 332-342.

Bodling, A. M., Denney, D. R., & Lynch, S. G. (2008). Rapid serial processing in patients with multiple sclerosis: The role of peripheral deficits. *Journal of the International Neuropsychological Society, 14*(04), 646-650.

Bringfelt, P.-A., Hartelius, L., & Runmarker, B. (2006). Communication problems in multiple sclerosis: 9-year follow-up. *International Journal of MS Care, 8*(4), 130-140.

Brissart, H., Morele, E., Baumann, C., & Debouverie, M. (2012). Verbal episodic memory in 426 multiple sclerosis patients: impairment in encoding, retrieval or both? *Neurological sciences, 33*(5), 1117-1123.

Bruce, W. B. D. H. C., & Gatehouse, C. (1997). Cueing the words: A single case study of treatments for anomia. *Neuropsychological Rehabilitation, 7*(2), 105-141.

Burke, D. M., MacKay, D. G., Worthley, J. S., & Wade, E. (1991). On the tip of the tongue: What causes word finding failures in young and older adults? *Journal of memory and language, 30*(5), 542-579.

Calabrese, M., De Stefano, N., Atzori, M., Bernardi, V., Mattisi, I., Barachino, L., . . . Perini, P. (2007). Detection of cortical inflammatory lesions by double inversion recovery magnetic resonance imaging in patients with multiple sclerosis. *Archives of Neurology, 64*(10), 1416-1422.

Chiaravalloti, N. D., & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *The Lancet Neurology, 7*(12), 1139-1151.

Connick, P., Chandran, S., & Bak, T. H. (2013). Patterns of cognitive dysfunction in progressive MS. *Behavioural neurology, 27*(3), 259-265.

Connick, P., Kolappan, M., Bak, T. H., & Chandran, S. (2012). Verbal fluency as a rapid screening test for cognitive impairment in progressive multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry, 83*(3), 346-347.

Coolidge, F. L., Middleton, P. A., Griego, J. A., & Schmidt, M. M. (1996). The effects of interference on verbal learning in multiple sclerosis. *Archives of Clinical Neuropsychology, 11*(7), 605-611.

Cox, D., & Julian, L. (2005). Cognitive Dysfunction in Multiple Sclerosis *Multiple Sclerosis* (pp. 91-102): Springer.

Cummings, J. L. (1986). Subcortical dementia. Neuropsychology, neuropsychiatry, and pathophysiology. *The British Journal of Psychiatry, 149*(6), 682-697.

Cummings, J. L., & Benson, D. F. (1988). Psychological dysfunction accompanying subcortical dementias. *Annual review of medicine, 39*(1), 53-61.

Da Silva, A. M., Cavaco, S., Moreira, I., Bettencourt, A., Santos, E., Pinto, C., . . . Dias, C. C. (2015). Cognitive reserve in multiple sclerosis: Protective effects of education. *Multiple Sclerosis Journal*, 1352458515581874.

Damasio, A. R., & Tranel, D. (1993). Nouns and verbs are retrieved with differently distributed neural systems. *Proceedings of the National Academy of Sciences, 90*(11), 4957-4960.

Dell, G. S., Chang, F., & Griffin, Z. M. (1999). Connectionist models of language production: Lexical access and grammatical encoding. *Cognitive Science, 23*(4), 517-542.

Dell, G. S., Schwartz, M. F., Martin, N., Saffran, E. M., & Gagnon, D. A. (1997). Lexical access in aphasic and nonaphasic speakers. *Psychological review, 104*(4), 801.

DeLuca, C, G., Yates, R. L., Beale, H., & Morrow, S. A. (2015). Cognitive impairment in multiple sclerosis: clinical, radiologic and pathologic insights. *Brain Pathology, 25*(1), 79-98.

DeLuca, Gaudino, E., Diamond, B., Christodoulou, C., & Engel, R. (1998). Acquisition and storage deficits in multiple sclerosis. *Journal of clinical and experimental neuropsychology, 20*(3), 376-390.

DeLuca, Leavitt, V. M., Chiaravalloti, N., & Wylie, G. (2013). Memory impairment in multiple sclerosis is due to a core deficit in initial learning. *Journal of neurology, 260*(10), 2491-2496.

Denney, D. R., Sworowski, L. A., & Lynch, S. G. (2005). Cognitive impairment in three subtypes of multiple sclerosis. *Archives of Clinical Neuropsychology, 20*(8), 967-981.

Drake, M., Allegri, R., & Carra, A. (2002). [Language abnormalities in patients with multiple sclerosis]. *Neurologia (Barcelona, Spain), 17*(1), 12-16.

Duffy, J. R. (2013). *Motor speech disorders: Substrates, differential diagnosis, and management*: Elsevier Health Sciences.

Enderby, P., John, A., & Petheram, B. (1997). Therapy outcome measures. *Singular, San Diego*.

Feenaughty, L., Tjaden, K., Benedict, R. H., & Weinstock-Guttman, B. (2013). Speech and pause characteristics in multiple sclerosis: A preliminary study of speakers with high and low neuropsychological test performance. *Clinical linguistics & phonetics, 27*(2), 134-151.

Feinstein, A., Freeman, J., & Lo, A. C. (2015). Treatment of progressive multiple sclerosis: what works, what does not, and what is needed. *The Lancet Neurology, 14*(2), 194-207.

Ferreira, M. L. B. (2010). Cognitive deficits in multiple sclerosis: a systematic review. *Arquivos de neuro-psiquiatria, 68*(4), 632-641.

Filippi, M., & Rocca, M. (2010). MRI and cognition in multiple sclerosis. *Neurological sciences, 31*(2), 231-234.

Finkelsztejn, A. (2014). Multiple Sclerosis: Overview of Disease-Modifying Agents. *Perspectives in medicinal chemistry, 6*, 65.

Fridriksson, J., Kjartansson, O., Morgan, P. S., Hjaltason, H., Magnusdottir, S., Bonilha, L., & Rorden, C. (2010). Impaired speech repetition and left parietal lobe damage. *The Journal of Neuroscience, 30*(33), 11057-11061.

Friend, K. B., & Grattan, L. (1998). Use of the North American Adult Reading Test to estimate premorbid intellectual function in patients with multiple sclerosis. *Journal of clinical and experimental neuropsychology, 20*(6), 846-851.

Friend, K. B., Rabin, B. M., Groninger, L., Deluty, R. H., Bever, C., & Grattan, L. (1999). Language functions in patients with multiple sclerosis. *The Clinical Neuropsychologist, 13*(1), 78-94.

Gaudino, E. A., Chiaravalloti, N. D., DeLuca, J., & Diamond, B. J. (2001). A comparison of memory performance in relapsing–remitting, primary progressive and secondary progressive, multiple sclerosis. *Cognitive and Behavioral Neurology, 14*(1), 32-44.

Godoy, J., Perez, M., Sanchez-Barrera, M., Muela, J., Mari-Beffa, P., & Puente, A. (1996). Recency effect in multiple sclerosis. *Applied neuropsychology, 3*(2), 93-96.

Gregory, S. G., Schmidt, S., Seth, P., Oksenberg, J. R., Hart, J., Prokop, A., . . . Barcellos, L. F. (2007). Interleukin 7 receptor α chain (IL7R) shows allelic and functional association with multiple sclerosis. *Nature genetics, 39*(9), 1083-1091.

Hamilton, F., Rochester, L., Paul, L., Rafferty, D., O'Leary, C., & Evans, J. (2009). Walking and talking: an investigation of cognitive–motor dual tasking in multiple sclerosis. *Multiple Sclerosis*.

Hartelius, L., Burge, Å., Johansson, A., Ljungsfors, A., Mattsson, A., Winkworth, A., & Andersen, O. (2004). How does fatigue affect communication? The influence of fatigue on cognitive, physical, psychosocial and communicative ability in individuals with multiple sclerosis. *International Journal of MS Care, 6*(2), 39-51.

Hartley, L. L. (1995). *Cognitive-communicative abilities following brain injury: A functional approach*: Singular.

Henry, J. D., & Beatty, W. W. (2006). Verbal fluency deficits in multiple sclerosis. *Neuropsychologia, 44*(7), 1166-1174.

Hillis, A. E. (2015). *The handbook of adult language disorders*: Psychology Press.

Hodgson, L. (1993). Drug effects on speech. *The Australian Communication Quarterly*, 12

Houtchens, M., Benedict, R., Killiany, R., Sharma, J., Jaisani, Z., Singh, B., . . . Bakshi, R. (2007). Thalamic atrophy and cognition in multiple sclerosis. *Neurology, 69*(12), 1213-1223.

Howard, D., & Patterson, K. E. (1992). *The Pyramids and Palm Trees Test: A test of semantic access from words and pictures*: Thames Valley Test Company.

Huijbregts, S., Kalkers, N., De Sonneville, L., De Groot, V., Reuling, I., & Polman, C. (2004). Differences in cognitive impairment of relapsing remitting, secondary, and primary progressive MS. *Neurology, 63*(2), 335-339.

Hutchinson, M. (2016). A useful annual review of cognition in relapsing MS is beyond most neurologists-Commentary. *Multiple sclerosis (Houndmills, Basingstoke, England)*.

Jennekens-Schinkel, A., Lanser, J., Van der Velde, E., & Sanders, E. (1990). Performances of multiple sclerosis patients in tasks requiring language and visuoconstruction: Assessment of outpatients in quiescent disease stages. *Journal of the neurological sciences, 95*(1), 89-103.

Jønsson, A., Korfitzen, E., Heltberg, A., Ravnborg, M., & Byskov-Ottosen, E. (1993). Effects of neuropsychological treatment in patients with multiple sclerosis. *Acta Neurologica Scandinavica, 88*(6), 394-400.

Kaplan, E., Goodglass, H., Weintraub, S., Segal, O., & van Loon-Vervoorn, A. (2001). *Boston naming test*: Pro-ed.

Klugman, T. M., & Ross, E. (2002). Perceptions of the impact of speech, language, swallowing, and hearing difficulties on quality of life of a group of South African persons with multiple sclerosis. *Folia Phoniatrica et Logopaedica, 54*(4), 201-221.

Kujala, P., Portin, R., & Ruutiainen, J. (1996). Language functions in incipient cognitive decline in multiple sclerosis. *Journal of the neurological sciences, 141*(1), 79-86.

Kuljic-Obradovic, D. (2003). Subcortical aphasia: three different language disorder syndromes? *European journal of neurology, 10*(4), 445-448.

Laakso, K., Brunnegård, K., Hartelius, L., & Ahlsén, E. (2000). Assessing high-level language in individuals with multiple sclerosis: a pilot study. *Clinical linguistics & phonetics, 14*(5), 329-349.

Laine, M. (2013). *Anomia: Theoretical and clinical aspects*: Psychology Press.

Langdon, D. W. (2011). Cognition in multiple sclerosis. *Current opinion in neurology, 24*(3), 244-249.

Le Dorze, G., & Nespoulous, J.-L. (1989). Anomia in moderate aphasia: Problems in accessing the lexical representation. *Brain and language, 37*(3), 381-400.

Lethlean, J. B., & Murdoch, B. E. (1994). Naming errors in multiple sclerosis: Support for a combined semantic/perceptual deficit. *Journal of neurolinguistics, 8*(3), 207-223.

Lethlean, J. B., & Murdoch, B. E. (1997). Performance of subjects with multiple sclerosis on tests of high-level language. *Aphasiology, 11*(1), 39-57.

Lin, R., Charlesworth, J., Van Der Mei, I., & Taylor, B. V. (2012). The genetics of multiple sclerosis. *Practical neurology, 12*(5), 279-288.

Lublin, F. D., Reingold, S. C., Cohen, J. A., Cutter, G. R., Sørensen, P. S., Thompson, A. J., . . . Barkhof, F. (2014). Defining the clinical course of multiple sclerosis The 2013 revisions. *Neurology, 83*(3), 278-286.

Mackenzie, C., & Green, J. (2009). Cognitive–linguistic deficit and speech intelligibility in chronic progressive multiple sclerosis. *International Journal of Language & Communication Disorders, 44*(4), 401-420.

Merino, J. A. G., & Quílez, M. R. B. (2007). Tratamiento farmacológico de la esclerosis múltiple. *Información Terapéutica del Sistema Nacional de Salud, 31*(4), 111-117.

Mesulam, M.-M. (2003). Primary progressive aphasia—a language-based dementia. *New England Journal of Medicine, 349*(16), 1535-1542.

Milo, R., & Miller, A. (2014). Revised diagnostic criteria of multiple sclerosis. *Autoimmunity reviews, 13*(4), 518-524.

Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *International journal of geriatric psychiatry, 21*(11), 1078-1085.

Moreno, M. J. G., García, M. C., Marasescu, R., González, A. P., & Benito, Y. A. (2013). Neuropsychological syndromes in multiple sclerosis. *Psicothema, 25*(4), 452-460.

Murdoch, B. E., & Theodoros, D. G. (2000). *Speech and language disorders in multiple sclerosis*: Whurr.

Nelson, H. E., & Willison, J. (1991). *National Adult Reading Test (NART)*: Nfer-Nelson.

Nicholas, L. E., Brookshire, R. H., Maclennan, D. L., Schumacher, J. G., & Porrazzo, S. A. (1989). Revised administration and scoring procedures for the Boston Naming Test and norms for non-brain-damaged adults. *Aphasiology, 3*(6), 569-580.

Pijpers-Kooiman, M., van der Velde, E., & Jennekens-Schinkel, A. (1995). Retrieval from semantic memory may be normal in multiple sclerosis patients: a study of free word association. *Journal of the neurological sciences, 132*(1), 65-70.

Pinter, D., Sumowski, J., DeLuca, J., Fazekas, F., Pichler, A., Khalil, M., . . . Enzinger, C. (2014). Higher education moderates the effect of T2 lesion load and third ventricle width on cognition in multiple sclerosis. *PloS one, 9*(1).

Potagas, C., Giogkaraki, E., Koutsis, G., Mandellos, D., Tsirempolou, E., Sfagos, C., & Vassilopoulos, D. (2008). Cognitive impairment in different MS subtypes and clinically isolated syndromes. *Journal of the neurological sciences, 267*(1), 100-106.

Rao, S. M. (1986). Neuropsychology of multiple sclerosis: a critical review. *Journal of clinical and experimental neuropsychology, 8*(5), 503-542.

Rao, S. M., Leo, G. J., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology, 41*(5), 685-691.

Rogers, J. M., & Panegyres, P. K. (2007). Cognitive impairment in multiple sclerosis: evidence-based analysis and recommendations. *Journal of Clinical Neuroscience, 14*(10), 919-927.

Rossi, F., Giorgio, A., Battaglini, M., Stromillo, M. L., Portaccio, E., Goretti, B., . . . De Stefano, N. (2012). Relevance of brain lesion location to cognition in relapsing multiple sclerosis. *PloS one,* 7(11), e44826.

Rosti-Otajärvi, E. M., & Hämäläinen, P. I. (2011). Neuropsychological rehabilitation for multiple sclerosis. *Cochrane Database Syst Rev, 11*.

Savage, C. R. (1997). Neuropsychology of subcortical dementias. *Psychiatric Clinics of North America, 20*(4), 911-931.

Sepulcre, J., Peraita, H., Goñi, J., Arrondo, G., Martincorena, I., Duque, B., . . . Villoslada, P. (2011). Lexical access changes in patients with multiple sclerosis: A two-year follow-up study. *Journal of clinical and experimental neuropsychology, 33*(2), 169-175.

Sicotte, N., Kern, K., Giesser, B., Arshanapalli, A., Schultz, A., Montag, M., . . . Bookheimer, S. (2008). Regional hippocampal atrophy in multiple sclerosis. *Brain, 131*(4), 1134-1141.

Smith, M. M., & Arnett, P. A. (2007). Dysarthria predicts poorer performance on cognitive tasks requiring a speeded oral response in an MS population. *Journal of clinical and experimental neuropsychology, 29*(8), 804-812.

Snodgrass, J. G. (1984). Concepts and their surface representations. *Journal of Verbal Learning and Verbal Behavior, 23*(1), 3-22.

Sorensen, P., Brown, S., Logemann, J., Wilson, K., & Herndon, R. (1994). Communication disorders and dysphagia. *Neurorehabilitation and Neural Repair, 8*(3), 137-143.

Sotiropoulou, C., Conroy, P., & Ralph, L. M. (2015). *The impact of accuracy-focused and speed-focused therapy on word retrieval in picture naming and composite picture descriptions in post-stroke aphasia.* Paper presented at the INTERNATIONAL JOURNAL OF STROKE.

Stemberger, J. P. (2004). Neighbourhood effects on error rates in speech production. *Brain and language, 90*(1), 413-422.

Sumowski, J. F., Chiaravalloti, N., & DeLuca, J. (2009). Cognitive reserve protects against cognitive dysfunction in multiple sclerosis. *Journal of clinical and experimental neuropsychology, 31*(8), 913-926.

Tallberg, I., & Bergendal, G. (2009). Strategies of lexical substitution and retrieval in multiple sclerosis. *Aphasiology, 23*(9), 1184-1195.

Velázquez-Cardoso, J., Marosi-Holczberger, E., Rodríguez-Agudelo, Y., Yañez-Tellez, G., & Chávez-Oliveros, M. (2014). Recall strategies for the verbal fluency test in patients with multiple sclerosis. *Neurología (English Edition), 29*(3), 139-145.

Viterbo, R., Iaffaldano, P., & Trojano, M. (2013). Verbal fluency deficits in clinically isolated syndrome suggestive of multiple sclerosis. *Journal of the neurological sciences, 330*(1), 56-60.

Vlaar, A., & Wade, D. (2003). Verbal fluency assessment of patients with multiple sclerosis: test–retest and inter-observer reliability. *Clinical rehabilitation, 17*(7), 756-764.

Wang, N. (2005). Treatment of Progressive Multiple Sclerosis *Multiple Sclerosis* (pp. 161-170): Springer.

Yorkston, K., Klasner, E., Bowen, J., Ehde, D., Gibbons, L., Johnson, K., & Kraft, G. (2003). Characteristics of multiple sclerosis as a function of the severity of speech disorders. *Journal of Medical Speech-Language Pathology, 11*(2), 73-84.

Zakzanis, K. K. (2000). Distinct neurocognitive profiles in multiple sclerosis subtypes. *Archives of Clinical Neuropsychology, 15*(2), 115-136.

Appendices

Appendix A: Table systematic review

Study	Participants with MS	Cognitive deficits	Specific description of cognitive deficits	Assessment measure	Actual assessment measures
(Andrade et al., 2003)	25	Presence of memory impairments in different types of memory in MS (e.g.: long-term memory, working memory)	MS patients present deficient immediate and delayed free recall. Encoding and retrieval skills are not impaired	30 word lists	MS participants perform under the level of the control group
(Armstrong et al., 1996)	67	MS produces long-term memory deficits	MS patients present impairment in retrieval processes from long-term memory	Rey Auditory Verbal Learning Test	**Mean (SD)** 0.66 (0.12)

					Mean (SD)
(Beatty, 2004)	58	Memory problems in MS can be produced due to problems retrieving or encoding information	The nature of memory problems in MS is not clear because of the wide range of variables involved in the development of cognitive impairment in MS	RBANS MMSE CMDI-Mood CMDI-Evaluative CMDI-Vegetative	88.8 (16.3) 26.6 (1.15) 59.7 (14.85) 63.9 (20.55) 69.6 (14.85)
					Mean (SD)
(Beatty & Monson, 1989)	34	Naming deficits are believed to be present only in the last stages of MS	New evidence proves that naming skills in people with MS can be impaired even when cognitive impairment is not severe	BNT FAS-Letter FAS-Category Responsive Naming Test Visual Rhyming Semantic Test Semantic Field Test	49.2 (4.4) 31.93 (8.33) 48.26 (10.1) 42.8 (1.6) 36.2 (4.33) 54.56 (3.33)
					Mean (SD)
(Bodling et al., 2008)	63	MS can produce deficits in processing speed of information	Deficits in processing speed are common in MS. Dysarthria and oculomotor deficits hamper the performance of people with MS in cognitive evaluations	Stroop WR Stroop CN Stroop CWN Stroop CWN-CN PNT (centred-repeated) PNT (centred-novel) PNT (distributed-repeated) PNT (distributed-novel)	82.5 (12.7) 68.4 (11.1) 47.5 (10.3) 20.9 (6.6) 68.3 (8.9) 48.8 (9.2) 61.9 (10.0) 46.4 (9.5)

(Brissart et al., 2012)	426	MS can produce impairment in verbal episodic memory	Impairment in verbal episodic memory in people with MS can be produced due to retrieval problems	RL-RI 16 task	**% of MS patients impaired** 65.95% low impairment 37.2% moderate impairment 13.6% severe impairment
(Connick et al., 2013)	88	People with MS may present language and visuospatial deficits.	An interaction between physical disability, reduced processing speed, dysarthria and fatigue, can be causing language and visuospatial deficits in people with MS	ACE-R MSIS-29 BDI-II EDSS PASAT	**Mean (SD)** 90.9 (8.3) 85 (21.5) 14.9 (12.7) 5.8 (1.3) 37.8 (12.7)
(Coolidge et al., 1996)	30	People with MS have problems retrieving information	Memory impairment in people with MS can hamper the ability to recall words	ILT Recall Consistency ILT Semantic Clustering ILT Serial clustering	**Mean (SD)** 73.9 (14.2) 51.8 (23.6) 11.2 (11.2)
(DeLuca et al., 1998)	40	Visual and verbal memory are generally impaired in people	Deficits retrieving information in people with MS are caused because of	SR 7/24 Visual memory test AT-SAT	**Mean (SD)** 7.1 (2.52) 6.5 (3.79) 2930.3 (1,014.9)

		with MS	deficits acquiring information	WAIS-R (Vocabulary) WCST-Categories COWAT CCSE JLO IDD SAI	50.6 (10.74) 5.8 (4.42) 36.3 (12.64) 27.4 (2.52) 24.4 (5.05) 12.2 (11.37) 33.7 (9.48)	
					% of variance	
(DeLuca et al., 2013)	44	MS causes memory deficits, learning and retrieving information	The greater the atrophy in the brain, the worst the initial learning. This can cause deficits recalling information in people with MS.	SRT Total learning SRT 30 mins recall	24% 30%	
					Mean (SD)	
(Drake et al., 2002)	30	Research studies about language problems in MS provide controversial findings	MS produces naming impairment. The main causes of this problem are difficulties accessing to the lexicon and perceptual problems	BNT Semantic verbal fluency Phonological verbal fluency	46.9 (6.5) 15.9 (5.7) 13.1 (4.6)	
					MS high Z-score (SD)	**MS low z-score (SD)**
(Feenaughty et al., 2013)	20	People with MS suffer from speech and	People with MS and cognitive impairment usually			

		reading difficulties	produce a slower speech compared to healthy participants. This happens regardless of level of cognitive impairment	D-KEFS PASAT3-SDMT SIT	0.20 (0.30) -0.18 (0.52) 96.5 (1.51)	-2.17 (0.31) -2.09 (0.46)
					Mean (SD)	
(Friend et al., 1999)	68	People with MS perform worse than healthy participants on language tests	MS can produce deficits in naming, verbal memory, language comprehension and verbal fluency	MAE Visual Naming Test MAE Token Test Category Fluency Test Digit Span (Backward) Digit Span (Forward) Stroop Test RAVLT WAIS-R (information subtest) NART-R	27.62 (3.22) 41.31 (5.51) 55.03 (16.61) 4.69 (1.27) 6.62 (1.35) 27.73 (8.46) 5.06 (1.87) 10.45 (3.27) 24.6 (11.4)	
					Mean (SD)	
(Gaudino et al., 2001)	64	MS can produce deficits in acquisition and retrieval of information	Memory problems in people with MS are produced due to problems acquiring information.	WAIS-R Vocabulary CCSE JLO SR:CLRT SR:LTS	48.9 (11.06) 27.33 (2.23) 24.56 (4.93) 6.56 (2.06) 8.33 (1.09)	

				7/24	6.83 (4.33)
(Godoy et al., 1996)	10	MS can produce problems retrieving and acquiring information	MS produces more deficits recovering information than acquiring information	Rey Auditory-Verbal Test: First trial Delayed recall	**Number of words** 58 87
(Hamilton et al., 2009)	18	Cognitive and physical deficits produced by MS interact with each other leading to an increased difficulty to conduct tasks	MS produces difficulties conducting two activities at the same time. This happens because of the increment in the working memory demand required to conduct both tasks at the same time	WTAR ACE-R HADS-Anxiety HADS-Depression MFIS Walking Fixed digit Titrated digit task Walking + fixed digit task Walking + titrated digit task	**Mean (SD)** 105.22 (14.4) 91.17 (6.49) 8.28 (3.79) 6.50 (2-9) 53.5 (43-62) 108.76 (15.75) 46.11 (29.14) 64.89 (22.78) 99.57 (16.10) /50.50 (27.94) 97.35 (16.98) /29.28 (26.57)
(Henry & Beatty, 2006)	2339	A poor performance in verbal fluency tests can be a sign of cognitive impairment in MS	In MS, impairment in working memory or executive functions can be detected by performance on verbal fluency tests	Phonetic fluency: -WCST CC -WCST PE -BNT -SDMT	**Effect sizes** .25 (.12) .25 (-) .22 (.04) .48 (.10)

				-VIQ Semantic fluency: -WCST CC -WCST PE -BNT -SDMT	.18 (.10) .29 (.11) .28 (-) .27 (.08) .41 (.12)
					Mean (SD)
(Huijbregts et al., 2004)	234	Each clinical course of MS produces different cognitive deficits according to their clinical characteristics	Although all clinical courses produce cognitive impairment, secondary progressive MS produces the most severe cognitive impairment	SRT-LTS SRT-CLTR 10/36 SRT 10/36 SRT Delay SDMT PASAT_3 PASAT_2 WLG	45.86 (1.53) 35.86 (1.76) 19.86 (0.46) 7.3 (0.26) 49.06 (1.6) 41.2 (1.76) 30.9 (1.73) 26.7 (0.83)
					Mean (SD)
(Jennekens-Schinkel et al., 1990)	39	MS does not produce linguistic deficit; however it affects copying tasks and reduces speed reading	Physical problems in MS are usually more responsible for the lower results obtained in assessments by patients, than cognitive impairment	Picture naming Controlled word generation Hundred words reading Stroop reading Stroop colour naming Stroop interference-	29.2 (1.7) 46.2 (16.5) 85.9 (12.7) 51.5 (12.3) 68.6 (15.7) 111.5 (46.0) 43.0 (39.1)

				reading Stroop interference time Writing-to-dictation of standard sentences (errors)	1.39 (-)
(Kujala et al., 1996)	45	MS produces language impairment	The level of language deterioration in patients with MS depends on the level of cognitive decline	Stroop Colour-Word Test BNT Colour naming BDAE-Comprehension Writing to dictation Writing name and date	**Mean (SD)** 88.35 (20) 53.75 (4.55) 44.15 (15.2) 3.5 (0.83) 4.7 (0.7) 2.9 (0.3)
(Lethlean & Murdoch, 1997)	60	MS patients can present high-level language difficulties	High-level language deficits involve problems in the highest levels of language processing	TLC UAS MI RS UME TWT	**Mean (SD)** 137.87 (23.81) 24.49 (7.51) 26.51 (5.14) 58.8 (13.41) 25.81 (5.44) 73.025 (11.22)
(Mackenzie & Green, 2009)	24	MS produces dysarthria and cognitive-linguistic deficits	MS patients have impaired both expression and comprehension of language	ABCD AIDS MBADLI	**Mean (SD)** 14.55 (3.09) 134.46 (79.16) 8.92 (7.14)

(Pijpers-Kooiman et al., 1995)	33	There is a possibility that MS produces difficulties retrieving words	The results show that word retrieval problems are not present in all patients with MS	Free word association	No differences between patients and control group were found
(Sicotte et al., 2008)	23	MS can produce loss of hippocampal volume in the *Cornu Ammonis (CA1)* leading to memory problems	Hippocampal deterioration in MS produces retrieval and verbal learning problems	PASAT Word-pair learning task	**Mean (SD)** 49.25 (3.15) 6.7 (0.66)
(Smith & Arnett, 2007)	97	MS can cause dysarthria	Oral-motor responses are affected in MS patients and are involved in the deficient performance of this patients in some tasks	60s-COWAT 15s-COWAT VE SDMT	**Z-score (SD)** -0.53 (0.93) -0.09 (1.17) -0.85 (1.72) -1.20 (1.31)
(Tallberg & Bergendal, 2009)	25	Impaired language functions can be found in MS patients	Impaired naming, semantic skills and problems retrieving words are among the language deficits that MS produces	BNT FAS	**Mean (SD)** 48.0 (7.4) 31.7 (11.6)

					Mean (SD)
(Vlaar & Wade, 2003)	35	There is evidence of verbal fluency impairment in MS	Semantic and phonological verbal fluency are impaired in MS. However, there is only a moderate relationship between them	Short orientation-Memory-Concentration Test ADL Phonological Fluency Semantic Fluency	19.2 (8.9) 4.5 (4.3) 21.9 (12.1) 26.0 (10.8)
					% patients with speech problems
(Yorkston et al., 2003)	739	MS patients are aware of their speech problems	Speech disorders in MS usually appear along with physical and cognitive problems	SURVEY	31% (n=229) mild 9% (n=67) moderate/severe

ABCD= The Arizona Battery for Communication Disorders of Dementia, **ACE-R**= Addenbrooke's Cognitive Examination-Revised, **ADL**= Barthel Activities of Daily Living, **AIDS**= The Assessment of Intelligibility of Dysarthric Speech, **AT-SAT**= Auditory Threshold-Serial Addition Test, **BDAE**= The Boston Diagnostic Aphasia Examination, **BDI**= Beck Depression Inventory, **BDI-II**= Beck Depression Inventory (II), **BNT**= The Boston Naming Test, **BRB-N**= Brief Repeatable Battery of Neuropsychological Tests, **CCSE**= Cognitive Capacity Screening Examination, **CES-D**= Centre for Epidemiological Studies-Depression Scale, **CLTR**= Consistent Long-Term Retrieval, **CMDI**= The Chicago Multiscale Depression Inventory, **COWAT**= Controlled Oral Word, **EDSS**= Expanded Disability Status Scale, **FAS** = Letter Word Fluency Test, **FIM**= Functional Independence Measure, **HADS**= Hospital Anxiety and Depression Scale, **IDD**= Interview to Diagnose Depression,

ILT= Interference Learning Test, **JLO**= The Judgment of Line Orientation test, **K-DEFS**= Delis-Kaplan Executive Function System Sorting Test, **LTS**= Long-Term Storage, **MBADLI**= Modified Barthel Activities of Daily Living Index, **MFIS**= Modified Fatigue Impact Scale, **MI=** Making Inferences, **MMSE**= Mini Mental State Examination, **MSIS-29**= The Multiple Sclerosis Impact Scale-29, **NART-R**= North American Adult Reading Test, **PASAT**= Paced Auditory Serial Additions Test, **RAVLT**= Rey Auditory-Verbal Learning Test, **RBANS**= Repeatable Battery for the Assessment of Neuropsychological Status Update, **RL-RI 16 task**= Rappel Libre/Rappel Indice 16 Task, **RS=** Re-creating Sentences, **SAI**= State Anxiety Index, **SD=** Standard Deviation, **SDMT**= Symbol Digit Modalities Test, **SEM**= Standard Deviation of the Mean, **SIT**= Sentence Intelligibility Testing, **SR**= Selective Reminding test, **SRT**= The Burshke Verbal Selective Reminding Test, **STAI**= State-Trait Anxiety Inventory, **Stroop CN**= Stroop Colour Naming, **Stroop CWN**= Stroop Colour-Word Naming, **Stroop CWN-CN**= Stroop Interference, **Stroop WR**= Stroop Word Reading, **TLC**= Test of Language Competence, **TWT=** The Word Test, **UAS=** Understanding Ambiguous Sentences, **UME=** Understanding Metaphoric Expressions, **VE**= Visual Elevator, **VIQ**= Verbal Intelligence, **WAIS-R**= the Wechsler Adult Intelligence Scale-Revised, **WCST**= Wisconsin Card Scoring, **WLG**= Word List Generation, **WTAR**= Wechsler Test of Adult Reading, **10/36 SRT**= 10/36 Spatial Recall Test, **10/36 SRT Delay**= 10/36 Spatial Recall Test Delay.

Appendix B: Ethics: Testing protocol

Communication Skills in People with Multiple Sclerosis: Establishing the range and nature of symptoms in the context of the clinical course of the condition.

Background

Communication disability has not been extensively researched in MS, given the dominance of physical disability in terms of research and clinical treatment. However, communication disability can have a devastating impact on social participation and quality of life. This small project is part of a wider collaboration and attempt to begin a programme of research examining the nature of communication disability in MS and critically, its treatment so as to recognise the extent and impact of communication problems and minimise their effects on MS sufferers through enhancements in clinical care. This project will inform our understanding of the extent and nature of communication disability in MS, i.e. who tends to suffer from these symptoms and how they relate to other symptoms associated with MS.

MS is a degenerative disease that results in a loss of the myelin sheaths in the central nervous system (CNS). This demyelination triggers a neuronal degeneration that produces disabling symptoms in people affected by the disease (DeLuca et al., 2015). MS is a degenerative disease that has four different clinical courses, depending on how the exacerbations of the disease are distributed. The clinical courses are:

- Relapsing-Remitting MS (RRMS), which is very common at the beginning of the disease.

- Secondary Progressive MS (SPMS), variant of the MS which comes from the clinical course of RRMS. It involves a relapsing-remitting progress at the beginning and then a progressive development of the disease.
- Primary Progressive MS (PPMS) involves a continued progress of the disease.
- Progressive Relapsing MS (PRMS), this is a rare event of MS. It is characterized by a progressive course with exacerbations in which there is not a complete recovery of the damage (Milo & Miller, 2014).

Each of these clinical courses leads to different symptoms depending on the recovery after the exacerbations or the speed in which the disease is developed. As well as marked physical disability, MS can lead to subcortical dementia, which involves damage in the white matter of the brain. Nevertheless recent research, have also found lesions in the grey matter in people with MS.

Motor speech impairments can commonly occur in MS, particularly for people with marked physical disability. Additionally, cognitive impairments affecting communication have also been noted, with evidence of aphasic, apraxic and agnosic symptoms. However, these symptoms are usually linked to cortical dementias due to the localization of the lesions in the brain.

Cognitive impairment in people with MS has only been recently studied. Moreover, only a limited amount of research has been focused on disordered language skills in people with MS. There has been a lack of sensitive techniques to assess subtle language problems which can occur with MS (Laakso et al., 2000; Mackenzie & Green, 2009).

Anomia involves delays or inaccuracies in word retrieval and can often occur in MS in the context of wider cognitive dysfunction in the domains of memory and attentional skills. Cognitive deficits in MS have not been researched as thoroughly as physical symptoms, although there is increasing recognition that cognitive change directly detracts from vocational roles, social participation and quality of life.

It is also important to take into account that MS is the prevalent neurological disease in adults with an age between 20 and 40 years in areas like Europe or America. This can aid in understanding the importance to study the progress of the disease and what impairments are created by MS in order to mitigate or delay the effects of the disease (Finkelsztejn, 2014).

Research questions in the current project

The first aim of this research project will be to examine the nature (dysarthria and/or anomia) and severity of communication disability in people with MS. The second aim is to understand these symptoms in the context of the clinical course of the MS and/or the degree of physical disability. A further aim will be to understand the nature of anomia in MS, i.e. whether word retrieval impairments are caused by linguistic (e.g. loss of word meaning) or non-linguistic (e.g. memory/attentional) deficits in thinking skills. Achieving these aims will inform a wider research collaboration which aims to devise treatments to minimise the effects of communication disability for people with MS.

Practical methods - location of patient contact and assessment

Patients with MS will be recruited from the Neurology out-patient caseload of Salford Royal Foundation Trust, specifically Dr Rog's clinic. Inclusion criteria include: a diagnosis of MS and be able to give informed consent; also, participants must be over 18 years old and have English as a first language. Dr Rog and colleagues will explain to patients about the study and for those who are interested, the researcher Ms Blanca De Dios, will provide information verbally and in writing. For those who give informed consent to Ms De Dios, they will take part in a 1:1 communication testing session in a room within Neurology which consists of audio-recorded tasks to obtain information pertaining to the speech and language skills of the participants. Aside from testing data, participants will also be asked their name, age, number of years diagnosed with MS, number of years education, gender and whether they feel MS has affected their communication skills (ability to talk, remember words, produce sentences, and to understand others in conversation). Information will also be obtained from patient medical notes, such as corroboration of number of years since diagnosis, and measures of physical disability.

Data Management

Data will immediately be anonymised (according too number of participant recruited: no.1, 2, 3…) and held in written and audio-recording format, pending data analysis. Analysis of audio-data will take several weeks and hence need to be stored on a password protected computer at the University of Manchester. Written anonymised data will be stored for 5 years after publication of any data results on a password protected computer at the University of Manchester. It will be accessible only to the Research Team listed at the top of this document.

Behavioural testing: 30-45 minutes per participant.

Test	**Description of test**
Naming Test	50 objects taken from the International Picture Naming Project http://crl.ucsd.edu/experiments/ipnp/ Participant responses will be audio-recorded and scored for naming accuracy and speed. Naming speed can be judged against neuro-typical data for these stimuli. The picture stimuli will be presented on a laptop computer controlled by the researcher.
ADDENBROOKE'S COGNITIVE EXAMINATION – ACE-III English Version A (2012)	This is a pen and paper screen of cognitive function which screens several domains of cognition: memory, attention, language and visuospatial skills.
Pyramids & Palm Trees Test	This is a paper-based task, in which participants point to pictures which have a semantic (meaning-based) link (e.g. pyramid and palm tree in the sense of being found in hot climates etc.). This is a widely used test to detect deficits in semantic processing related to neurological disease.
Audio-recording of verbal responses to allow scoring of	The Chief Investigator (an experienced Speech and Language Therapist) will score

dysarthria severity.	all participants the Therapy Outcome Measure for dysarthria (TOMS; Enderby & John, 2015) which allows for scores of severity (from no dysarthria to total dysarthria across a five point scale).

Description of tests

1) *Naming Test 60 objects taken from the International Picture Naming Project*

Participant responses will be audio-recorded and scored for naming accuracy and speed. Naming speed can be judged against neuro-typical data for these stimuli. The picture stimuli will be presented on a laptop computer controlled by the researcher.

2) *Addenbrooke's Cognitive Examination – ACE-III (English Version A, 2012)*

This is a pen and paper screen of cognitive function which screens several domains of cognition: memory, attention, language and visuospatial skills. Verbal responses of the participants will be audio-recorded to allow scoring of dysarthria severity. Two experienced Speech and Language Therapists will score all participants the Therapy Outcome Measure for dysarthria (TOMS). This allows for scores of severity (from no dysarthria to total dysarthria across a five point scale).

All of these tests are widely-used in clinical and academic practice and have good psychometric properties with regard to test reliability and validity. We anticipate a good (e.g. >50% of those asked) response rate given the convenience of taking part after an out-patient appointment and the time commitment being relatively limited and non-intrusive.

Obtaining up to 100 sets of participant data will allow as to conduct correlational and regression analyses with regard to the relationship between measures of dysarthric and anomic symptoms and of physical disability and number of years with MS.

A sample size above 40 for anomia will allow us to conduct similar correlational and regression analysis with regard to linguistic or non-linguistic cognitive factor contributing to anomia severity.

Appendix C: Words included in Picture Naming Task

Tables 19, 20, 21 and 22 shows the words included in each subgroup of words of the Picture Naming Task and information about their frequency, age of acquisition and length of phonological syllables. As previously mentioned, this information was obtained from the IPNP (Bates et al., 2000).

Table 19- Words included in Group A (<800 ms)

Group A (<800)	Frequency	Age of acquisition	Phonological syllables
Airplane	1.95	1	2
Arrow	2.77	3	2
Baby	5.56	1	2
Balloon	1.95	1	2
Bicycle	1.79	1	3
Butterfly	2.40	1	3
Car	5.87	1	1
Clock	3.69	1	1
Eye	6.26	1	1
Fish	5.10	1	1
Foot	5.79	1	1
Giraffe	1.10	1	2
Hat	4.23	1	1
Mushroom	2.64	3	2
Scissors	1.61	1	2
MEAN	3.51	1.27	1.73
SD	1.80	0.71	0.71

Table 20- Words included in Group B (801-1000 ms)

Group B (801-1000)	Frequency	Age of acquisition	Phonological syllables
Apple	3.43	1	2
Ball	4.72	1	1
Banana	2.20	1	3
Cactus	1.39	3	2
Can	2.30	2	1
Cheese	3.47	1	1
Dolphin	1.39	3	2
Elephant	3.22	1	3
Fan	2.89	3	1
Feather	3.09	3	2
Fountain	2.56	3	2
Helmet	2.64	3	2
Horse	4.89	1	1
Igloo	0.69	3	2
King	4.60	3	1
MEAN	2.90	2.13	1.73
SD	1.24	0.99	0.71

Table 21- Words included in Group C (1001-1220 ms)

Group C (1001-1220)	Frequency	Age of acquisition	Phonological syllables
Ant	2.56	2	1
Barbecue	1.10	3	3
Canoe	1.95	3	2
Carousel	0.69	3	3
Cow	3.71	1	1
Deer	2.56	1	2
Dentist	2.30	3	2
Handcuffs	1.10	3	2
Knot	2.71	3	1
Leg	5.17	1	1
Lettuce	2.08	3	2
Panda	0.69	3	2
Peas	0.00	1	1
Pirate	1.79	3	2
Priest	3.91	3	1
MEAN	2.16	2.4	1.73
SD	1.38	0.91	0.70

Table 22- Words included in Group D (1221-1500 ms)

Object (1221-1500)	Frequency	Age of acquisition	Phonological syllables
Asparagus	1.099	3	4
Balcony	2.639	3	3
Beaver	1.386	3	2
Drill	2.197	3	1
Hinge	1.609	3	1
Hoe	1.386	3	1
Lobster	1.386	3	2
Mosquito	1.792	3	3
Safety-pin	0.693	3	3
Squirrel	1.946	1	2
Stroller	0.693	1	2
Tail	3.611	3	1
Trophy	1.609	3	2
Tweezers	1.099	3	2
Wrench	1.386	3	1
MEAN	1.63	2.73	2
SD	0.75	0.70	0.93

Appendix D: List of responses accepted in Picture Naming Task

Table 23 shows a list of the answers provided by the participants in the Picture Naming Task and a list of the answers accepted as correct. The list of target words is presented in the same order as the words were presented to the participants.

Table 23- List of answers accepted as correct answers in Picture Naming Task

Target	Responses Accepted
BELL	Bell
BOOK	Book
HAND	Hand
BABY	Baby
AIRPLANE	Airplane, plane
FAN	Fan, hot fan
TWEEZERS	Tweezers, forceps, clip, peg, needle, pen, clippers, tuning fork
BARBECUE	Barbecue
CAN	Can, tin, tin can,
DEER	Deer, stag, reindeer,
CLOCK	clock
BALCONY	Balcony, patio, veranda, terrace
HORSE	Horse
LEG	Leg

IGLOO	Igloo
MUSHROOM	Mushroom
TAIL	Tail, pony tail, horse’s tail
BANANA	Banana
CACTUS	Cactus, cacti
APPLE	Apple
STROLLER	Stroller, pushchair, pram
BEAVER	Beaver
ARROW	Arrow
HINGE	Hinge, door hinge
CAROUSEL	Carousel, merry-go-around
PANDA	Panda
SCISSORS	Scissors, pair of scissors
WRENCH	Wrench, spanner
PEAS	Peas, peas in a pod, pea pod
EYE	Eye
KING	King
KNOT	Knot
FISH	Fish
HELMET	Helmet
PIRATE	Pirate
TROPHY	Trophy, cup
BALL	Ball

MOSQUITO	Mosquito, daddy longlegs
DENTIST	Dentist
FEATHER	Feather, quill
BUTTERFLY	Butterfly
DOLPHIN	Dolphin
SAFETYPIN	Safety pin, pin
COW	Cow
BALLOON	Balloon
DRILL	Drill, electric drill
CANOE	Canoe, kayak
BICYCLE	Bicycle, bike
SQUIRREL	Squirrel
FOOT	Foot
LETTUCE	Lettuce, cabbage
FOUNTAIN	Fountain, water fountain
HAT	Hat
ELEPHANT	Elephant
PRIEST	Priest, vicar, parson
HOE	Hoe, rake
GIRAFFE	Giraffe
CHEESE	Cheese, bloc of cheese, piece of cheese
HANDCUFFS	Handcuffs
ASPARAGUS	Asparagus

CAR	Car
ANT	Ant
LOBSTER	Lobster

Appendix E: Participants information sheet

PIS

Version 4 8th Jan 2016

Participant Information Sheet (PIS)

COMMUNICATION SKILLS IN PEOPLE WITH MULTIPLE SCLEROSIS (MS).

This information sheet provides some information about our study which is investigating communication skills in people with Multiple Sclerosis (MS). This study is part of a Master's degree being undertaken by Ms Blanca De Dios Perez at the School of Psychological Sciences, University of Manchester.

In this document you will find information about what the study is about and what it involves. It is important for you to understand this information before you decide to participate in the research. Please read the following information carefully, ask any questions you like and take the time to decide whether or not you wish to take part, which is entirely voluntary.

What is the purpose of the study?

The study aims to examine the types of communication problems people with MS may experience. This could be a muscular problem to do with producing speech easily and clearly (dysarthria) OR a problem remembering and saying everyday words (anomia). We are interested in how often these problems occur across a large number of people with MS, and how obvious these problems are.

Why have I been invited to take part in this study?

You have been invited to join our project because you have MS.

Do I have to take part?

No, you do not have to take part in the study if you do not want to. Taking part in the research is voluntary; this means it is completely up to you to decide whether or not to join the study. Your decision to participate in this study will not be connected to the care you are receiving now or in the future. If you decide to take part and sign the consent form but change your mind later, you are free to withdraw at any point during the study without giving a reason and without any consequence to your current or future treatment.

What will participation involve?

This study involves an interview with a researcher and carrying out some pen and paper tasks which involve thinking skills (memory, attention, generating a list of words). There will also be a picture naming task using a laptop in which you name objects which appear on the screen. This will take between 30 and 45 minutes and only happens once. The researcher will write down your responses and also take a sound recording of what you say, for later analysis.

What are the possible disadvantages and risks of taking part?

There may be a risk for some people of becoming bored or frustrated by taking part.

What are the possible benefits of taking part?

Some people may find taking part in the research interesting and enjoyable. There may be come satisfaction from the sense of helping us understand communication in MS more fully. We will send all participants a lay summary of the study results.

Will my taking part in the study be kept confidential?

Yes, the information you provide will be anonymised (so no one could identify you) according to a number. All information collected will be kept confidential and only available to the approved research team. All data will be stored securely at the University of Manchester. Records will be destroyed at the end of the study. Direct quotes may be used in the write-up of the study, but will be used in such a way so as not to reveal the identity of individuals. Data from the study will be kept for a minimum of 5 years after the date of any publication which is based upon it, to follow recommended good practice guidelines for research. Staff from the University of Manchester will also need access to the data/information for the purpose of audits.

What will happen if I do not want to carry on with the study?

You can withdraw from the study completely at any time without giving a reason and without any consequence to your current or future treatment. No further data will be collected from the moment you withdraw.

What if there is a problem?

It is unlikely that anything will go wrong. However, if you have a concern about any aspect of this study, you should ask to speak to the project supervisor:

Dr Paul Conroy, Zochonis Building, School of Psychological Sciences, University of Manchester, Manchester M13 9PL, Tel: 0161 2752693.

Dr Conroy will do his best to answer your questions.

If we are unable to resolve your concern or you wish to make a formal complaint regarding the study, please contact the Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk - telephone 0161 275 2674 or 275 2046.

What will happen to the results of the research study?

The findings will be published as part of a Master's degree. But it is part of a wider effort to understand and offer better treatment for communication problems experienced by people with MS.

Who has reviewed the study?

All research which involves NHS patients has to be reviewed by the National Health Service Research Ethics Committee (REC). This study has been reviewed by North of Scotland Ethics Committee.

Who can I contact for further information?

The Chief Investigator is Dr Paul Conroy, Zochonis Building, School of Psychological Sciences, University of Manchester, Manchester M13 9PL,

Tel: 0161 2752693.

Appendix F: Inform consent

MANCHESTER 1824

The University of Manchester

V4 30th Nov 2015

Salford Royal NHS

NHS Foundation Trust

Participant Consent Form

RESEARCH STUDY: COMMUNICATION SKILLS IN PEOPLE WITH MULTIPLE SCLEROSIS (MS).

Participant Identification Number:

Name of Researchers: Dr Paul Conroy Chief Investigator, Ms Blanca De Dios Perez Researcher.

1. I confirm that I have read the information sheet dated 16th November 2015 (version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities (University of Manchester or from the NHS Trust), where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I understand that my responses in participating will be audio-recorded.

5. I agree to take part in the above study.

____________________	____________________	____________________
Name of Participant	Date	Signature

Name of Person taking consent	Date	Signature

Appendix G: Results

Table 24 shows the results obtained for each participant in the four behavioural assessments. The maximum possible score and the cut-off per task are also provided.

Table 24- Global results

Participant	ACE-R (0-100) Cut-off 88	NART (0-50) Cut-off 26 (Errors)		Picture Naming Task (0-60) Cut-off 52		Pyramids and Palm Tree (0-52) Cut-off 49	
		Correct	Incorrect	Correct	Incorrect	Correct	Incorrect
1	94	42	4	54	6	51	1
2	80	34	14	53	7	51	1
3	89	43	7	59	1	50	2
4	78	42	8	51	9	45	7
5	86	46	4	53	7	51	1
6	92	38	12	53	7	51	1
7	97	37	13	53	7	50	2
8	93	46	4	57	3	51	1
9	84	35	15	51	9	51	1
10	93	41	9	51	9	49	3
11	95	37	13	55	5	45	7
12	96	41	7	57	3	50	2
13	87	33	17	52	8	48	4
14	84	33	17	40	20	49	3
15	93	41	9	59	1	50	2
16	91	31	19	53	7	51	1
17	89	35	15	49	11	46	6
18	95	41	9	56	4	50	2
19	84	30	20	55	5	47	5
20	92	40	10	51	9	52	0
21	72	30	20	42	18	45	7
22	95	42	8	60	0	49	3
23	87	41	9	48	12	45	7
24	88	41	9	56	4	49	3
25	88	39	11	53	7	50	2
26	89	29	21	55	5	50	2
27	77	21	29	52	8	52	0
28	90	34	16	53	7	48	4
29	94	39	11	55	5	48	4

30	92	41	9	57	3	49	3
31	87	26	24	49	11	49	3
32	68	28	22	42	18	40	12
33	74	31	19	35	25	46	6
34	87	33	17	54	6	49	3
35	92	39	11	58	2	52	0
36	96	48	4	55	5	51	1
37	88	31	21	52	8	51	1
38	91	36	16	37	23	45	7
39	72	33	17	51	9	50	2
40	92	41	9	51	9	46	6
41	85	40	10	54	6	51	1
42	85	43	7	56	4	48	4
43	66	10	40	38	22	45	7
44	76	27	23	54	6	48	4
45	84	19	31	42	18	42	10
46	84	36	14	56	4	46	6
47	84	42	8	54	6	51	1
48	84	17	33	46	14	47	5
49	93	23	27	51	9	50	2
50	88	29	21	55	5	50	2
51	94	41	9	55	5	50	2
52	84	27	23	57	3	50	2
53	91	35	15	46	14	46	6
54	95	42	8	53	7	52	0
55	81	33	17	48	12	50	2
56	76	28	22	57	3	51	1
57	90	39	11	46	14	51	1
58	97	46	4	56	4	50	2
59	92	44	6	55	5	50	2
60	86	31	19	46	14	48	4
61	96	43	7	57	3	51	1
62	95	43	7	57	3	52	0
63	71	19	31	45	15	42	10
64	87	30	20	55	5	52	0
65	73	12	38	52	8	47	5
66	89	41	9	53	7	50	2
67	96	38	12	51	9	50	2
68	90	36	14	54	6	51	1
69	82	10	40	56	4	50	2
70	93	40	10	56	4	51	1
71	89	32	18	46	14	44	8
72	90	40	10	55	5	52	0
73	97	38	12	51	9	51	1

74	90	37	13	54	6	50	2
75	98	48	2	58	2	50	2
76	96	44	6	56	4	48	4
77	92	33	17	59	1	50	2
78	82	37	13	53	7	50	2
79	89	34	16	56	4	48	4
80	83	35	15	49	11	50	2
81	81	28	22	51	9	46	6
82	93	36	14	52	8	50	2
83	90	34	16	56	4	47	5
84	75	19	31	51	9	49	3
85	88	38	12	53	7	51	1
86	93	40	10	56	4	51	1
87	89	37	13	54	6	52	0
88	95	41	9	58	2	49	3
89	91	34	16	51	9	49	3
90	84	30	20	57	3	52	0
91	74	11	39	38	22	42	10
92	87	26	24	51	9	46	6
93	96	35	15	55	5	49	3
94	87	39	11	48	12	48	4
95	91	31	19	57	3	49	3
96	82	17	33	49	11	49	3
97	93	42	8	54	6	50	2
98	76	29	21	49	11	46	6
99	87	34	16	43	17	50	2
100	82	32	18	44	16	49	3
MEAN	**87.37**	**34.41**	**15.59**	**52.02**	**7.98**	**48.91**	**3.09**
SD	**7.17**	**8.36**		**5.21**		**2.52**	

Table 25 shows the score obtained for each participant for the ACE-R (Mioshi et al., 2006). The score is presented showing both the global score for the task and the score for each subtest (attention and orientation, memory, verbal fluency, language and visuospatial skills). The table also provides information about the maximum possible score in the global task and each subtest.

Table 25- ACE-R results

Participant	Global score (0-100)	Attention and orientation (0-18)	Memory (0-26)	Verbal fluency (0-14)	Language (0-26)	Visuospatial (0-16)
1	94	16	24	14	26	14
2	80	16	17	12	22	13
3	89	15	21	12	25	16
4	78	18	18	6	20	16
5	86	18	20	6	26	16
6	92	17	26	7	26	16
7	97	16	25	14	26	16
8	93	15	23	13	26	16
9	84	17	18	12	23	14
10	93	17	26	11	25	14
11	95	18	25	13	23	16
12	96	16	25	13	26	16
13	87	17	24	10	20	16
14	84	16	20	11	23	14
15	93	17	24	12	26	14
16	91	17	21	11	26	16
17	89	17	20	12	24	16
18	95	15	24	14	26	16
19	84	14	21	11	24	14
20	92	15	25	10	26	16
21	72	11	22	7	23	9
22	95	17	26	11	25	16
23	87	16	23	11	21	16
24	88	18	21	10	23	16
25	88	17	22	9	24	16
26	89	16	23	11	23	16
27	77	16	21	8	19	13
28	90	15	25	13	23	14
29	94	16	26	13	25	14
30	92	15	24	12	25	16

31	87	17	23	12	24	11
32	68	12	18	5	25	8
33	74	17	14	6	23	14
34	87	15	20	14	24	14
35	92	12	26	14	24	16
36	95	17	25	11	26	17
37	88	17	21	10	25	15
38	91	18	24	13	22	14
39	72	13	17	7	19	16
40	92	16	26	12	22	16
41	85	16	23	10	23	13
42	85	16	20	10	26	13
43	66	11	14	7	21	13
44	76	15	19	5	24	13
45	84	17	25	7	19	16
46	84	15	21	13	22	13
47	84	16	20	8	26	14
48	84	17	22	8	21	16
49	93	17	26	9	25	16
50	88	16	25	11	22	14
51	94	17	25	11	25	16
52	84	16	16	13	25	14
53	91	18	24	9	24	16
54	95	17	25	13	26	14
55	81	16	18	10	21	16
56	76	17	13	7	24	15
57	90	18	24	9	25	14
58	97	17	26	13	25	16
59	92	18	21	14	26	13
60	86	16	24	10	22	14
61	96	17	26	14	25	14
62	95	18	23	12	26	16
63	71	15	10	9	21	16
64	87	17	21	9	25	15
65	73	16	14	9	19	15
66	89	15	23	12	25	14
67	96	17	24	14	25	16
68	90	18	25	9	24	14
69	82	16	19	11	23	13
70	93	16	21	14	26	16
71	89	17	23	11	24	14
72	90	17	24	8	25	16
73	97	18	26	13	24	16
74	90	16	25	11	26	12

75	98	17	26	13	26	16
76	96	18	25	12	25	16
77	92	17	26	11	24	14
78	82	16	18	9	23	16
79	89	14	24	11	24	16
80	83	18	18	10	24	13
81	81	17	17	14	20	13
82	93	16	23	12	26	16
83	90	16	25	10	25	14
84	75	15	16	11	20	13
85	88	15	24	11	24	14
86	93	16	23	13	25	16
87	89	17	21	13	23	15
88	95	17	24	12	26	16
89	91	16	25	9	25	16
90	84	17	15	10	26	16
91	74	15	17	8	19	15
92	87	16	22	11	22	16
93	96	17	24	14	25	16
94	87	18	18	12	25	14
95	91	18	22	10	25	16
96	82	17	20	9	22	14
97	93	18	23	14	24	14
98	76	15	13	11	22	15
99	87	17	23	10	24	13
100	82	15	24	6	21	16
MEAN	**87.37**	**16.25**	**21.85**	**10.72**	**23.79**	**14.77**
SD	**7.17**					

Table 26 shows the score of each participant for the Picture Naming Task, the average reaction time of each participant per word and the level of dysarthria. The average reaction time of each participant was obtained from the reaction time of their correct answers.

Table 26- Picture Naming Task results

Participant	Picture Naming Task (0-60)		Average reaction time (ms)	Dysarthria score
	Correct	Incorrect		
1	54	6	1392.54	5
2	53	7	1841.75	5
3	59	1	1113.66	5
4	51	9	1578.1	5
5	53	7	1296.89	5
6	53	7	1041.77	5
7	53	7	847.91	5
8	57	3	893.88	5
9	51	9	1334.41	4.5
10	51	9	1154.55	5
11	55	5	1028.53	5
12	57	3	1278.77	5
13	52	8	1614.92	5
14	40	20	1574.68	4.5
15	59	1	1294.71	5
16	53	7	1183.81	5
17	49	11	1393.41	4
18	56	4	1144.38	5
19	55	5	1162.51	5
20	51	9	908.45	5
21	42	18	1730.1	5
22	60	0	1062	5
23	48	12	1385.79	4.5
24	56	4	1406.43	4.5
25	53	7	1326.11	5
26	55	5	1101.49	4
27	52	8	1268.35	4
28	53	7	1160.26	5
29	55	5	1253.65	5

30	57	3	1128.11	5
31	49	11	1933.04	4.5
32	42	18	1711.26	4
33	35	25	2442.89	4
34	54	6	1618.28	5
35	58	2	1247.07	5
36	55	5	1327.67	5
37	52	8	1286.52	5
38	37	23	1620.22	4.5
39	51	9	1243.88	5
40	51	9	1152.33	5
41	54	6	1358.33	4.5
42	56	4	1586.21	5
43	38	22	1733.11	4
44	54	6	1082.83	5
45	42	18	1883.1	4
46	56	4	1071.34	4.5
47	54	6	1119.44	4.5
48	46	14	1585.48	4
49	51	9	1315.67	5
50	55	5	1418.2	4
51	55	5	1164.53	4
52	57	3	1069.74	5
53	46	14	1261.09	5
54	53	7	1199.26	5
55	48	12	1198.98	4.5
56	57	3	1637.61	4.5
57	46	14	1206.8	5
58	56	4	1278.52	5
59	55	5	1356.27	5
60	46	14	1480.39	5
61	57	3	981.02	5
62	57	3	1042.33	5
63	45	15	1738.2	4.5
64	55	5	1309.02	5
65	52	8	1406.27	5
66	53	7	1326.74	5
67	51	9	1257.39	5
68	54	6	1188.19	4.5
69	56	4	1208.55	5

70	56	4	1127.13	5
71	46	14	1339.24	5
72	55	5	1375.78	5
73	51	9	1272.49	5
74	54	6	1156.5	5
75	58	2	1268.6	5
76	56	4	1105.04	5
77	59	1	935.68	5
78	53	7	1242.19	4
79	56	4	1260.14	4.5
80	49	11	1530.94	5
81	51	9	1338	4.5
82	52	8	1145.87	5
83	56	4	973.64	5
84	51	9	1357.53	5
85	53	7	1140.55	4
86	56	4	1103.39	4.5
87	54	6	1272.39	5
88	58	2	1028.95	5
89	51	9	993.8	4.5
90	57	3	1068.39	5
91	38	22	1678.92	4.5
92	51	9	2273.75	4
93	55	5	1057.64	5
94	48	12	1405.5	5
95	57	3	996.53	5
96	49	11	1101.59	5
97	54	6	959.41	5
98	49	11	1418.53	4
99	43	17	1664.81	5
100	44	16	1650.66	4
MEAN	**52.02**	**7.98**	**1311.93**	**4.76**
SD	**5.21**			

Table 27 shows the scores of each participant in the NART (Nelson & Willison, 1991). The maximum possible score for the task is 50 correct answers. This table also provides information about the accuracy and error rate of each participant for the task.

Table 27- NART results

National Adult Reading Test (0-50) Cut-off				
Participant	**Correct**	**Incorrect**	**Accuracy**	**Error**
1	43	7	0.86	0.14
2	35	15	0.7	0.3
3	43	7	0.86	0.14
4	42	8	0.84	0.16
5	46	4	0.92	0.08
6	38	12	0.76	0.24
7	37	13	0.74	0.26
8	46	4	0.92	0.08
9	35	15	0.7	0.3
10	41	9	0.82	0.18
11	37	13	0.74	0.26
12	42	8	0.84	0.16
13	33	17	0.66	0.34
14	33	17	0.66	0.34
15	41	9	0.82	0.18
16	31	19	0.62	0.38
17	35	15	0.7	0.3
18	41	9	0.82	0.18
19	30	20	0.6	0.4
20	40	10	0.8	0.2
21	30	20	0.6	0.4
22	42	8	0.84	0.16
23	41	9	0.82	0.18
24	41	9	0.82	0.18
25	39	11	0.78	0.22
26	29	21	0.58	0.42
27	21	29	0.42	0.58
28	34	16	0.68	0.32
29	39	11	0.78	0.22

30	41	9	0.82	0.18
31	26	24	0.52	0.48
32	28	22	0.56	0.44
33	31	19	0.62	0.38
34	33	17	0.66	0.34
35	39	11	0.78	0.22
36	48	4	0.96	0.08
37	31	21	0.62	0.42
38	36	16	0.72	0.32
39	33	17	0.66	0.34
40	41	9	0.82	0.18
41	40	10	0.8	0.2
42	43	7	0.86	0.14
43	10	40	0.2	0.8
44	27	23	0.54	0.46
45	19	31	0.38	0.62
46	36	14	0.72	0.28
47	42	8	0.84	0.16
48	17	33	0.34	0.66
49	23	27	0.46	0.54
50	29	21	0.58	0.42
51	41	9	0.82	0.18
52	27	23	0.54	0.46
53	35	15	0.7	0.3
54	42	8	0.84	0.16
55	33	17	0.66	0.34
56	28	22	0.56	0.44
57	39	11	0.78	0.22
58	46	4	0.92	0.08
59	44	6	0.88	0.12
60	31	19	0.62	0.38
61	43	7	0.86	0.14
62	43	7	0.86	0.14
63	19	31	0.38	0.62
64	30	20	0.6	0.4
65	12	38	0.24	0.76
66	41	9	0.82	0.18
67	38	12	0.76	0.24
68	36	14	0.72	0.28

69	10	40	0.2	0.8
70	40	10	0.8	0.2
71	32	18	0.64	0.36
72	40	10	0.8	0.2
73	38	12	0.76	0.24
74	37	13	0.74	0.26
75	48	2	0.96	0.04
76	44	6	0.88	0.12
77	33	17	0.66	0.34
78	37	13	0.74	0.26
79	34	16	0.68	0.32
80	35	15	0.7	0.3
81	28	22	0.56	0.44
82	36	14	0.72	0.28
83	34	16	0.68	0.32
84	19	31	0.38	0.62
85	38	12	0.76	0.24
86	40	10	0.8	0.2
87	37	13	0.74	0.26
88	41	9	0.82	0.18
89	34	16	0.68	0.32
90	30	20	0.6	0.4
91	11	39	0.22	0.78
92	26	24	0.52	0.48
93	35	15	0.7	0.3
94	39	11	0.78	0.22
95	31	19	0.62	0.38
96	17	33	0.34	0.66
97	42	8	0.84	0.16
98	29	21	0.58	0.42
99	34	16	0.68	0.32
100	32	18	0.64	0.36
MEAN	**34.41**	**15.59**	**0.69**	**0.31**
SD	**8.36**			

Table 28 shows the individual score of the participants for the Pyramids and Palm Trees (Howard & Patterson, 1992). The maximum possible score for the task is 52 correct answers. As well as in the table of the results from the NART (Nelson & Willison, 1991), this table provides information about the accuracy and error rate of the participants in the task.

Table 28- Pyramids and Palm Trees results

Pyramids and Palm Trees (Max punt. 52) (Cut-off 49)				
Participant	**Correct**	**Incorrect**	**Accuracy**	**Error rate**
1	51	1	0.98	0.02
2	51	1	0.98	0.02
3	50	2	0.96	0.04
4	45	7	0.87	0.13
5	51	1	0.98	0.02
6	51	1	0.98	0.02
7	50	2	0.96	0.04
8	51	1	0.98	0.02
9	51	1	0.98	0.02
10	49	3	0.94	0.06
11	45	7	0.87	0.13
12	50	2	0.96	0.04
13	48	4	0.92	0.08
14	49	3	0.94	0.06
15	50	2	0.96	0.04
16	51	1	0.98	0.02
17	46	6	0.88	0.12
18	50	2	0.96	0.04
19	47	5	0.9	0.1
20	52	0	1	0
21	45	7	0.87	0.13
22	49	3	0.94	0.06
23	45	7	0.87	0.13
24	49	3	0.94	0.06
25	50	2	0.96	0.04
26	50	2	0.96	0.04

27	52	0	1	0
28	48	4	0.92	0.08
29	48	4	0.92	0.08
30	49	3	0.94	0.06
31	49	3	0.94	0.06
32	40	12	0.77	0.23
33	46	6	0.88	0.12
34	49	3	0.94	0.06
35	52	0	1	0
36	51	1	0.98	0.02
37	51	1	0.98	0.02
38	45	7	0.87	0.13
39	50	2	0.96	0.04
40	46	6	0.88	0.12
41	51	1	0.98	0.02
42	48	4	0.92	0.08
43	45	7	0.87	0.13
44	48	4	0.92	0.08
45	42	10	0.81	0.19
46	46	6	0.88	0.12
47	51	1	0.98	0.02
48	47	5	0.9	0.1
49	50	2	0.96	0.04
50	50	2	0.96	0.04
51	50	2	0.96	0.04
52	50	2	0.96	0.04
53	46	6	0.88	0.12
54	52	0	1	0
55	50	2	0.96	0.04
56	51	1	0.98	0.02
57	51	1	0.98	0.02
58	50	2	0.96	0.04
59	50	2	0.96	0.04
60	48	4	0.92	0.08
61	51	1	0.98	0.02
62	52	0	1	0
63	42	10	0.81	0.19
64	52	0	1	0
65	47	5	0.9	0.1
66	50	2	0.96	0.04

67	50	2	0.96	0.04
68	51	1	0.98	0.02
69	50	2	0.96	0.04
70	51	1	0.98	0.02
71	44	8	0.85	0.15
72	52	0	1	0
73	51	1	0.98	0.02
74	50	2	0.96	0.04
75	50	2	0.96	0.04
76	48	4	0.92	0.08
77	50	2	0.96	0.04
78	50	2	0.96	0.04
79	48	4	0.92	0.08
80	50	2	0.96	0.04
81	46	6	0.88	0.12
82	50	2	0.96	0.04
83	47	5	0.9	0.1
84	49	3	0.94	0.06
85	51	1	0.98	0.02
86	51	1	0.98	0.02
87	52	0	1	0
88	49	3	0.94	0.06
89	49	3	0.94	0.06
90	52	0	1	0
91	42	10	0.81	0.19
92	46	6	0.88	0.12
93	49	3	0.94	0.06
94	48	4	0.92	0.08
95	49	3	0.94	0.06
96	49	3	0.94	0.06
97	50	2	0.96	0.04
98	46	6	0.88	0.12
99	50	2	0.96	0.04
100	49	3	0.94	0.06
MEAN	**48.91**	**3.09**	**0.94**	**0.06**
SD	**2.52**			