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Running Title: Information Processing Speed and Executive Functioning

Examining the Link between Information Processing Speed and Executive Functioning in Multiple Sclerosis

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Abstract

Slowed information processing speed (IPS) is frequently reported in those with Multiple Sclerosis, and at least 20% are compromised on some aspect of executive functioning also. However, any relationship between these two processes has not been examined. The Sternberg Memory Scanning Test, Processing Speed Index (WAIS-III), Delis Kaplan Executive Function System (D.KEFS) and Working Memory Index (WMS-III) were administered to 90 participants with MS. MS participants' performance on the PSI was significantly below the normative scores but no deficits in memory scanning speed were evident. The initial response speed of the Sternberg and the PSI were most closely related to DKEFs performance particularly in timed tasks with a high cognitive demand (switching tasks). In contrast, memory scanning speed was related to working memory. This study reinforces the link between IPS and working memory in MS, and supports the suggestion that IPS is not a unitary construct.

Keywords: Multiple Sclerosis; Information Processing Speed; Executive Functions; Sternberg Memory Scanning Test; Delis Kaplan Executive Function System; Working Memory; Processing Speed Index (PSI); Response Speed

Multiple Sclerosis (MS) is a demyelinating disease that affects the central nervous system, and in New Zealand approximately 4000 people (~1% of the population) suffer from this debilitating disease. The deficits arising from this disease include sensory and motor symptoms and a significant proportion (65%) of individuals with MS are affected by some degree of cognitive impairment (Rao, Leo, Bernardin & Unverzagt, 1991).

One of the most consistently reported impairments in MS is slowed information processing speed (IPS). Indeed, slowed IPS was included as part of the 'known' rather than as part of what is 'believed' about MS (Fischer et al., 1994), and many authors have demonstrated a significant difference in processing speed between those with MS and healthy controls (e.g., Archibald & Fisk, 2000; Demaree, DeLuca, Guadino & Diamond, 1999; Diamond, Johnson, Kaufman & Graves, 2008; Kail, 1998; Lengenfelder et al., 2006; Rao, St. Aubin-Faubert & Leo, 1989). Deficits and differences in IPS have been documented in several MS subtypes. For example, both chronic progressive and relapsing remitting groups showed significantly slower information processing (scanning) speed, using the Sternberg Memory Scanning Test (Sternberg, 1967) compared to healthy controls but only the chronic progressive groups showed deficits in sensory / motor reaction time (Archibald & Fisk, 2000). Other studies suggest that those with secondary progressive MS show IPS deficits using the Paced Auditory Serial Addition Test (PASAT), compared to those with relapsing remitting MS & healthy controls (DeLuca et al., 2004; Snyder, Cappelleri, Archibald & Fisk, 2001), whilst Denney, Lynch, Parmenter and Horne (2004), demonstrated that the general speed of processing was slower for a sample of those with relapsing remitting MS than for a sample of those with primary progressive MS and both groups were significantly slower compared to healthy controls. A few studies have suggested that IPS deficits were not as apparent in their MS samples (Litvan et al., 1988, Janculjak et al., 1999, Santiago et al., 2007). Of these, Litvan et al., (1988) only found deficits on the two fastest levels of the PASAT, but not on the Sternberg memory scanning speed, whilst Janculjak et al. (1999) used a non standard recording method (the examiner made the response rather than the participant) which may have biased their data. The third study (Santiago et al., 2007) reported no deficits in IPS in their MS sample (assessed using the Stroop test), but deficits in performance on the PASAT were apparent, which was used as a measure of working memory. But taken together, there appears to be a general consensus that impairments in IPS are common in those with MS.

Some researchers have suggested that slowed IPS was one characteristic of the cognitive impairment thought to typify those with MS (Archibald et al., 2004; Mahler & Benson, 1990; Randolph et al., 2005; Rao, 1986; White, Nyenhuis & Sax, 1992). However, others suggested that rather than being a separate deficit, slowed IPS underlies all other cognitive impairment in this population (De Sonneville et al., 2002; Kail, 1998; Kujala, Portin, Revonuo & Ruutianen, 1994; Mohr & Cox, 2001). If this were the case then a relationship between IPS and other cognitive functions would be expected. Indeed, it has been suggested that impaired reasoning and remembering abilities seen in those with MS could well be explained by a general slowing of IPS (Arnett, Higginson & Randolph, 2001; Demaree et al., 1999; Gontkovsky & Beatty, 2006; Kail, 1998). Further, Kujala et al., (1994) found that a cognitively ‘impaired MS’ group were impaired on aspects of IPS, whilst a cognitively ‘unimpaired MS’ group showed only minor IPS deficits. Several studies have also examined (and demonstrated) an association between working memory and IPS in those with MS (Archibald & Fisk, 2000; DeLuca et al., 2004; Demaree et al., 1999; D’Esposito et al., 1996). In particular, IPS deficits in MS are more pronounced in tasks with high working memory demands (Legenfelder et al., 2006).

One other issue which is apparent in the IPS literature is the variety of assessment tools which are used. In MS one of the most common measures of IPS is performance on the PASAT, but others have used simple reaction time, Sternberg Memory Scanning Test, Stroop or the Trail Making Test (Archibald & Fisk, 2000; D’Esposito et al., 1996; Santiago et al., 2007). These tasks differ in their complexity, cognitive demands and also in their reliance upon a motor response, which together suggests that these tasks cannot all measure the same cognitive construct (Chiaravalloti, Christodoulou, Demaree & DeLuca, 2003). Indeed, in a factor analytical study, Chiaravalloti et al., 2003, demonstrated that different measures of IPS load on different factors indicating that IPS is not a unitary construct. This is clearly an issue that needs to be considered when interpreting results from studies using different IPS measures.

Previous research indicates that at least 15% - 20% of those with MS have impaired executive functions (Drew, 2005; Drew, Tippett, Starkey & Isler, 2008; Fischer, 2001; Fischer et al., 1994; Rao et al., 1991). The type of executive dysfunction observed in those with MS varies, with researchers reporting deficits across a range of functions including verbal fluency (Benedict et al., 2006), colour word naming (Denney et al., 2004), reasoning (Benedict et al., 2006), temporal ordering, semantic encoding and planning (Arnett et al., 2001; Arnett et al., 1997), and metamemory (Beatty & Monson, 1991; Scarrabelotti & Caroll, 1999).

Few studies have been conducted which assess the link between IPS and executive function in the MS population. Of those that have, the range of executive functions that have been assessed are limited. However, IPS is reported to correlate with verbal fluency (Barker-Collo, 2006; Diamond, et al., 2008). Similar to the findings with IPS and working memory, it has been suggested that IPS is predictive of performance in executive function tasks that require effortful processing (Diamond et al., 2008) and that IPS slowing is more evident with complex timed tasks, for example attentional set shifting (De Sonneville et al., 2002). Thus, there is preliminary evidence for a relationship between IPS and some executive functions, indicting that more studies assessing a wider range of executive functions is warranted. Indeed, other researchers have suggested that this is an area worthy of further investigation (DeLuca et al., 2004).

The overall aim of the larger project was to assess general ability, memory, executive functions, information processing speed and attention in a community based sample of participants with MS and to examine the relationships between these functions (Drew, 2005; Drew et al, 2008). The current study focused on two of these areas. The first aim was to examine the level of IPS in our participants with MS and secondly to examine the relationships between IPS, executive function and working memory.

1. Method

1.1. Participants

Ninety-five individuals with MS living in the community around the greater Waikato and Bay of Plenty regions of New Zealand participated in this study. Of the 98 interested participants, three were excluded due to an aneurysm, epilepsy and malingering respectively. This sample made up approximately 2.5% of the MS population in New Zealand. Of the remaining 95 participants, 90 completed all of the psychological assessments and the following analyses are based on these participants.

Eighteen (20%) were male and 72 (80%) were female. They were aged between 17 and 78 years (M = 52.5 years, SD = 11.6), and the mean number of years of education was 12.8 (SD = 3.3). The average number of years since the participants detected the first symptoms of MS was 24.2 years (SD = 13.0). In contrast, the average number of years since MS was first diagnosed was only 11.6 years (SD = 10.5). The classification of disease course (self-reported) showed a split that was consistent with the MS literature. Forty six (51.1%) had the relapsing-remitting form of MS, 26 (28.9%) had acute or secondary progressive, with only 15 (16.7%) indicating they were chronic progressive and very few, 3 (3.3%) indicating the benign form. At the time of testing all relapsing-remitting participants self reported that they were in remission. The mean Expanded Disability Status Scale (EDSS, Kurtzke, 1983) score for this sample was 4.8 (SD = 2.0) which is in the 'not severe' range. The mean composite score for the Chicago Multiscale Depression Inventory (CMDI, Nyenhuis et al., 1998) was 55.4 (SD = 13.1), suggesting that the cognitive performance of the sample should not have been significantly influenced by depressive illness.

Seventy four friends or family of the participants acted as a control group for the Sternberg Memory Scanning Test. Thirty (40.5%) were male, and 44 (59.5%) were female. Their ages ranged from 15 to 78 years (M = 51.7, SD = 14.7), and the mean number of years education was 13.0 (SD = 2.7). There was no significant difference between the MS group and control group in relation to age or years of education ($p > .05$), however, a chi squared analysis comparing the gender ratios in each group was significant ($\chi 2 = 8.27$, $p < .01$) with the MS group containing a significantly greater number of females.

1.2. Measures

The results of the larger project are reported elsewhere (Drew, 2005; Drew et al, 2008). This study focused on the data for information processing speed, assessed using the Sternberg Memory Scanning Test (Sternberg, 1967) and the Processing Speed Index (PSI) of the Wechsler Adult Intelligence Scale III (WAIS III; Wechsler, 1997a), executive functions which were assessed using the Delis Kaplan Executive Function System (D.KEFS, Delis, Kaplan, & Kramer, 2001) and working memory function which was determined from scores on the Working Memory Index of the WMS III (Wechsler, 1997b). Further details of these measures are provided below. In addition, ratings of levels of physical disability were obtained using the Expanded Disability Status Scale (EDSS) (Kurtze, 1983), and the Chicago Multiscale Depression Inventory (CMDI) (Nyenhuis et al., 1998) was administered to determine levels of depression (Drew, 2005).

Various tests have been used previously as a measure of information processing speed in MS, including the PASAT (e.g., D'Esposito et al., 1996), the Sternberg Memory Scanning Test (e.g., Archibald & Fisk, 2000), and in some studies, the Stroop Test (e.g., Santiago et al., 2007). Several reports suggest that participants find the PASAT rather stressful, and it has been reported to increases negative mood. Furthermore, in some studies a high proportion of patients refuse to take the test or stop part way through (Lezak, Howieson & Loring, 2004; Strauss, Sherman & Spreen, 2006). Thus, in order to obtain data from a maximum number of participants, and to avoid jeopardising the participants' willingness to complete the neuropsychological assessments for the rest of the study, we chose to use the Sternberg Memory Scanning Test as the primary measure of IPS (Sternberg, 1967).

The Sternberg Test requires participants to memorise a set of 1, 2 or 4 digits and they then have to indicate whether numbers which are subsequently displayed on the computer screen were one of the previously 'remembered' numbers. Thus, this test requires less manipulation of numbers compared to the PASAT, and there is little evidence that participants find this task stressful. The Sternberg Test was administered on a Compaq Presario laptop computer and the test parameters (e.g., stimulus display, negative and positive responses) were based on those used in Sternberg's original publication (1967). For each trial the participant was required to memorise a set of 1, 2 or 4 digits, which were presented together in the center of the computer screen (as used by Rao et al., 1989). There was a maximum time of 2 minutes for this 'memorisation' stage, however the next stage of the trial could be started when the participant indicated they were ready. Previous studies suggest that the length of this memorization phase does not affect the scanning speed results obtained from the test (Sternberg, 1975) and we wanted to minimise any memory confounds, and allow sufficient time for the stimuli to be adequately encoded. The 'test' stimuli consisted of a single digit (from 1 to 9) which was presented in the center of the screen and the participant was asked to press the left l mouse key if the number on the screen was one of those previously remembered, or press the right mouse key if not. There were a total of 12 trials, four for each set size. Each trial comprised the presentation of the target number(s) followed by the 15 test digits, presented individually on the screen in a random order. The 'to be remembered' numbers were different for each trial (to avoid possible 'practise' effects) and there were four positive responses required on each trial. The test was preceded by two practice trials each of which contained a memory set of 3 digits. After each key press response, visual feedback of "correct" or "incorrect" appeared on the screen for 0.5 seconds followed by a ‘+’ sign which remained in the center of the screen for 1 second prior to the presentation of the next digit. The time taken to respond to each of the stimuli was recorded.

The Sternberg Memory Scanning Test provides several measures of interest. Previous studies show that the time taken to respond to the stimuli increases in a positive linear fashion as the size of the remembered set increases (Sternberg, 1967, 1969, 1975). The slope produced when reaction time is plotted against memory set size represents the time taken to compare the test digit with those in memory (memory scanning speed), which is independent of motor function or the initial perception of the stimulus. Thus, a steeper slope is indicative of slower memory scanning speed (see Figure 1). The point at which the slope crosses the y axis, gives a measure of the time taken to encode the test stimulus, make a yes / no decision, and produce a response. Thus, this measure is susceptible to deficits in perception or slowed motor responding and is similar to a simple reaction time (this is termed ‘initial response speed’). In addition to these main measures, accuracy (number correct out of 60 responses) in each of the one, two and four digits conditions was also recorded.

In addition to the Sternberg Test, scores from the WAIS-III (Wechsler, 1997a) Processing Speed Index (comprising Digit Symbol Coding and Symbol Search) are also reported to provide an additional measure of IPS for the MS participants. The full WAIS III results are reported elsewhere (Drew, 2005; Drew, Tippett, Starkey & Isler, 2007). The PSI provides a measure of mental and motor speed associated with solving nonverbal problems. It comprises two subtests, Digit Symbol Coding and Symbol Search. In Digit Symbol Coding, the participant is given a series of numbers each of which is paired with a different symbol. The participant is provided with a grid of numbers, onto which they have to copy the appropriate symbols as quickly as they can. In Symbol Search, the participant has to scan two groups of symbols and then indicate if either of the target stimuli are in the other group. Digit Symbol Coding primarily measures psychomotor speed, whilst Symbol Search provides a measure of mental speed (Kaufman & Lichtenberger, 1999). The PSI has a mean of 100 and a standard deviation of 15 whilst the subtest scores have a mean of 10 and standard deviation of 3.

Executive functioning was assessed using the Delis Kaplan Executive Function System (D.KEFS, Delis, Kaplan, & Kramer, 2001). This is a relatively new assessment battery which assesses a wide range of executive functions. It consists of nine tests, which are adaptations of tests currently used for assessing executive functions. These tests are, Trail Making, Verbal Fluency, Design Fluency, Colour-Word Interference, Card Sorting Test, Twenty Questions, Word Context, Tower Test and Proverbs. For this assessment battery, the standardised, age adjusted scaled scores which are provided for all tests, are based on normative data from a large sample (N = 1750), which is representative of the United States population. For each test the mean standardised score is 10 and the standard deviation is 3. A list of validity studies which have demonstrated the sensitivity of the D.KEFS to executive function deficits in a variety of clinical populations has recently been published by Delis, Kramer, Kaplan and Holdnack (2004). Although reliability coefficients for the D.KEFS tests were generally less than .80, this is comparable with other neuropsychological tests, and it is probable that for these assessments, test complexity underlies performance variability. Twenty primary scores that are generated by the D.KEFS were used as the measures executive functioning. As the object of the current analysis was to determine related levels of performance, detailed categorisation of the nature of any executive dysfunction was not attempted.

Although working memory processes are utilised when performing the D.KEFS tests, working memory is not measured directly (or separately) by this battery. Therefore the age adjusted, scaled Working Memory Index (WMI) score from the Wechsler Memory Scale, Third Edition (WMS-III; Wechsler, 1997b), was used as a measure of these processes. The WMI score (mean = 100, SD = 15) is a composite of two subtests from the WMS-III; Letter Number Sequencing and Spatial Span (mean = 10, SD = 3). In Letter Number Sequencing, participants listen to a series of alternating letters and numbers. They have to repeat these back to the examiner with the numbers in ascending order and the letters in alphabetical order. For the spatial span task, the examiner points to a series of wooden block on a board, the participant has to point to them in the same order. In later trials, the participant has to point to the block in reverse order (Wechsler, 1997b).

1.3. Procedure

Ethical approval was obtained from the Psychology Research and Ethics Committee at the University of Waikato. Individuals with a diagnosis of MS who belonged to the local MS society were sent an information letter and contacted the researcher directly if they were interested in taking part in the research. The same information sheet was sent to MS field officers who covered the outlying areas, and they forwarded the names of those willing to participate. All participants signed a consent form prior to testing.

The assessments for the larger project were carried out over two, three hour sessions. General ability (WAIS-III), memory (WMS-III) and premorbid intelligence (Wechsler Test of Adult Reading: WTAR) were assessed in the first session. The information processing speed assessment (Sternberg Memory Scanning Test) was administered at the beginning of the second session followed by the Delis Kaplan Executive Function System (D.KEFS) battery. The WAIS-III, the WMS-III and the D.KEFS were administered and scored according to the standardized instructions in their respective manuals.

The time between the first and second sessions for the MS participants varied but the average interval was 12 days (SD = 13.8). The control group completed all required assessments in the one session.

1.4. Data Analysis

Data were analysed using SPSS (version 14) and various data analysis approaches were utilised. The first part of the analysis focused on the Sternberg Memory Scanning Test, with both correct and incorrect responses included in the analysis. Initially, pre-analyses data screening was conducted to determine if the ‘yes’ and ‘no’ responses could be pooled and to determine if males and females performed similarly on this task. Then a MANCOVA (with age and number of errors as covariates) was conducted to examine the effects of MS on the measures from the Sternberg. For the Processing Speed Index (PSI) and its subtests, one sample t-tests were carried out to compare the MS participants’ performance to normative data (as control participants did not administered a WAIS III). Subsequently correlations were conducted to examine the relationship between the measures from the Sternberg Test and the PSI and its subtests. Further analysis examined the link between level of disability and processing speed. Finally, correlations and a series of multiple regressions were conducted to examine the relationship between the measures of processing speed, executive function and working memory.

2. Results

2.1. Pre-Analysis Data Screening for the Sternberg Memory Scanning Test

In previous studies, the ‘yes’ and ‘no’ response times increased in a similar linear fashion as the digit number increased (i.e. the memory scanning speed did not differ between ‘yes’ and ‘no’ responses) and thus data from both type of responses had been pooled (e.g., Sternberg, 1975). This was also the case here (‘Yes’ memory scanning speed = 69.62 ms/digit; ‘No’ memory scanning speed = 69.86 ms/digit), suggesting that the data for both responses could be pooled. But first, we needed to determine if the MS and control groups differed in their response time to the ‘yes’ and ‘no’ stimuli. Thus, a 2 (Group: MS vs Control) x 2 (Response type: yes / no) x 3 (number of digits: 1, 2 or 4) mixed ANOVA was conducted on response time. The overall ANOVA indicated significant main effects for number of digits, $F(2,161) = 131.42$, $p < .001$, response type, $F(1,162) =$

15.96, $p < .001$, and group, $F(1,162) = 60.27$, $p < .001$, but no significant interaction effects (all ps > .05). Closer examination of the data confirmed that as described, response time significantly increased as the number of digits in the set increased (ps < .05 in all cases), that the 'yes' responses were significantly faster than 'no' responses and that MS participants' response times were significantly slower than those of the controls. Thus, as the time taken to respond to 'yes' and 'no' stimuli were the same for the MS and control groups, this indicated that data from these responses could be pooled for subsequent analysis. This is in keeping with other studies using the Sternberg Test with MS populations (e.g., Archibald & Fisk, 2000; Rao et al., 1989).

As there was a greater proportion of females in the MS group compared to the control group, the performance of males and females on the two measures of the Sternberg Test were also compared and no significant differences were found ($p > .05$), thus gender was not included as a covariate in subsequent analyses.

2.2. The effects of MS on Performance in the Sternberg Memory Scanning Test

As previous studies have indicated that reaction time is correlated with age (e.g., De Sonneville et al. 2002), this was included as a covariate in the analysis described below. In addition, as both correct and incorrect responses were retained in our data set, accuracy of responding was also included as a covariate. Descriptive data for the MS and control groups can be found in Table 1.

To examine the effect of MS on the performance in the Sternberg Test, a between groups (MS / control) MANCOVA with covariates of age and accuracy was conducted on the two measures of the Sternberg Test; memory scanning speed (slope) and initial response speed (intercept). The overall MANCOVA revealed a significant difference between the MS and control groups, $F(2, 157) = 13.51$, $p < .001$). Subsequent analyses showed that the MS group had a significantly slower initial response speed compared to the control group, $F(1, 158) = 25.81$, $p < .001$ but there was no significant difference in the memory scanning speed, $F(1,158) = .30$, $p > .05$). Figure 1 shows how memory scanning speed increased as the memory set size increased. It can be clearly seen that the initial response speed (intercept) is slower for the MS group compared to the controls but the slope of the lines, which is the measure of memory scanning speed, are very similar.

2.3. The effects of MS on performance on the PSI (from WAIS III).

Control data was only collected for the Sternberg Memory Scanning Test, therefore, to examine performance levels of the MS participants on the WAIS-III measures of processing speed, one sample t tests were conducted using the normative data as a comparison (normative mean = 10, SD = 3). For these measures the MS sample obtained significantly lower scores compared to the normative data; Digit Symbol Coding (M = 8.3, SD = 3.0), $t(84) = 5.14$, $p < .001$; Symbol Search (M = 8.6, SD = 3.4), $t(90) = 3.9$, $p < .001$; PSI (M = 92.6. SD = 15.6), $t(84) = 25.0$, $p < .001$. Closer inspection of these data revealed that approximately a third of participants obtained scores more than 1SD below the normative mean, of these, around 13% obtained scores more than 2 SDs below the norms and only 1 participant obtained scores more than 3 SDs below the normative mean.

2.4. Relations between the Processing Speed Measures.

Persons correlations revealed that the scores on the two Sternberg measures, initial response time (intercept) and memory scanning speed (slope) was low and not significant ($r = -.05$, $p > .05$), suggesting that these two scores assess different processes. In contrast, the scores for Digit Symbol Coding and Symbol Search, correlated quite highly ($r = .77$, $p < .001$), indicating that there may be some similarity in the functions assessed by these two tests.

Pearson's Correlations were also conducted between the Sternberg measures and the WAIS-III PSI measures and are summarized in Table 2. Memory scanning speed was significantly (but weakly) correlated with Digit Symbol Coding and Symbol Search but not with the overall PSI. In contrast, response speed correlated more highly with all PSI measures. Fisher's *r*-to-z transformations indicated that there was a significant difference in the correlations between the two Sternberg measures and Symbol Search ($p < 0.05$) whilst the difference between the correlations for the overall PSI approached significance ($p = 0.07$). This is likely to be reflective of the motor component in both the response speed of the Sternberg test and the subtests of the WAIS-III PSI.

In order to determine if level of disability influenced the processing speed assessments, correlations were also conducted between the EDSS scores and the processing speed measures. EDSS scores correlated significantly with the PSI and its subtests (Digit Symbol Coding, $r = -.39$, $p < .001$; Symbol Search $r = -.33$. $p < .01$; PSI, $r = -.32$, $p < .01$) and the initial response speed of the Sternberg ($r = .43$, $p < .001$). However, the correlation between memory scanning speed and EDSS was small and not statistically significant ($r = .06$, $p > .05$). This is in keeping with the suggestion that only the intercept measure of the Sternberg relates to motor response speed and that the memory scanning measure is relatively free from this confound.

2.5. Executive Function and Working Memory in participants with MS.

As these data have been reported elsewhere they will only be summarised here (Drew, 2005; Drew et al., 2008). On the D.KEFS the mean scores for the MS group were close to the standardized mean of the test. The group mean ranged from a low of 8.5 for Trails (SD = 3.9) to 10.5 for Design Fluency (SD = 3.2), compared to the standardized mean of 10 (SD = 3). Around a third of participants showed no apparent deficits on any of the D.KEFS measures, obtaining scores within 1SD of the mean. However, around 16% of the participants obtained scores more than 1SD below the mean on more than 6 D.KEFS measures, indicating they had widespread executive function difficulties.

Similarly, for the WMI, the group mean was 97 (SD = 15.1), indicating that overall the group showed little evidence of working memory difficulties compared to the standardized mean of 100 (SD = 15). However around a third of participants obtained WMI scores which were significantly lower than that predicted from pre morbid intelligence measures (WTAR). This suggests that for some of the participants there had been a significant decline in working memory ability.

2.6. The Relations between Executive Functions, Working Memory and the Processing Speed Measures.

In order to examine the link between the two processing speed measures, executive functioning and working memory, Pearson's correlations between the Sternberg Memory Scanning Test measures, the twenty primary scores of the D.KEFS tests and the working memory measures from the WMS-III (Working Memory Index (WMI) and its two subtests, Letter Number Sequencing and Spatial Span) were conducted. In addition, correlations were also conducted between these scores and the PSI measures from the WAIS III (overall PSI, Digit Symbol Coding and Symbol Search). The results of these analyses are presented in Table 3.

Overall, it can be seen from this table that those D.KEFS tests which were timed (Trail Making, Fluency and Colour Word Interference), correlated with both measures of the Sternberg test. The measures for the Proverbs and the Letter Numbering Sequencing and the overall WMI measures also showed significant correlations with memory scanning speed. In contrast, all measures except for the Common Proverbs and the Proverbs Accuracy were significantly correlated with initial response speed. Fisher's *r*-to-*z* transformation was used to test for significant differences between the correlation coefficients from the two Sternberg Test measures. This revealed that response speed correlated significantly more highly with Trails ($p < .05$), Twenty Questions total questions ($p < .01$), Twenty Questions total score ($p < .01$) and the Tower Test total score ($p < .01$) compared to memory scanning speed. There were no statistically significant differences between the correlations of the two measures from the Sternberg Test and the other D.KEFS measures.

The PSI and both its subtests showed significant correlations with the D.KEFS and WMI measures. In most cases these measures correlated more highly with the executive function test scores than those obtained from the Sternberg. Particularly high correlations (>.6) were observed between the PSI and D.KEFS tests which incorporated inhibition or switching (Trail Making, Colour Word Interference). Fisher's *r*-to-*z* transformation indicated no significant differences between the correlation coefficients for the three processing speed scores from the WAIS III. However, compared to the Sternberg Memory Scanning Speed measure, the PSI correlated significantly more highly with several of the D.KEFS measures including all of the switching scores (Trail Making, Verbal Fluency, Design Fluency, Colour Word Interference), the Recognition score in the Card Sorting Test, 20 Questions Test and the Tower Test.

To determine the extent to which the IPS measures (Memory Scanning Speed, Response Speed and PSI) accounted for unique variance in each of the D.KEFS scores, stepwise multiple regressions were conducted. Digit Symbol Coding and Symbol Search were not included in the regressions as they were both highly with the overall PSI. As expected, the variable with the highest correlation with the D.KEFS measure was the primary predictor. These are indicated in bold in Table 3.

The PSI was the primary predictor for most of the D.KEFS and WMI scores. In fact, the PSI made a significant contribution to the variance of all measures except for 20 Questions Total, Word Context Total and Tower Test Total scores. For the scores where PSI was the significant primary predictor, Memory Scanning Speed accounted for significant additional variance in Category Fluency (ΔR^2 = .04), Colour Word Interference Switching (ΔR^2 = .04), Total (ΔR^2 = .07) and Common Proverbs (ΔR^2 = .05), and the WMI (ΔR^2 = .07). The Response Speed measure from the Sternberg made a unique and significant contribution to the variance in Trails Switching (ΔR^2 = .07), Category Fluency (ΔR^2 = .06) and Total Questions on the 20 Questions Test (ΔR^2 = .05).

Memory Scanning Speed was the primary predictor for Proverbs Accuracy and Letter Number Sequencing and the PSI score made a significant and unique contribution to the variance for each of these (ΔR^2 Proverbs Accuracy =.04, ΔR^2 Letter Number Sequencing = .08).

The Sternberg Response Speed measure was the primary significant predictor for the 20 Questions Total Score, Word Context Total Score and the Tower Test Total Score. Neither Memory Scanning Speed, nor the PSI made a significant contribution to explaining the variance in these scores.

3. Discussion

The Sternberg Memory Scanning Test revealed no significant difference in memory scanning speed between the participants with MS and the control group. However, MS participants had a significantly slower initial response speed compared to controls.

Our findings differ from several previous studies which list reduced IPS as one factor in the cognitive profile of those with MS (e.g., Archibald et al., 2004; Arnett, 2000; Beatty, 1996; Fischer et al., 1994; Randolph et al., 2005; Rao, 1995, 1996), as well as others which have suggested that reduced IPS seems to be a key factor which possibly underlies all other cognitive impairment in those with MS (e.g., Brassington & Marsh, 1998; Demaree, et al., 1999, Mohr & Cox, 2001). Although different assessment tools and definitions make direct comparisons of results difficult, three previous studies which have used versions of the Sternberg Memory Scanning Test have found evidence of a slowed information processing speed in their MS samples (Archibald et al., 2004; Archibald & Fisk, 2000; Rao et al.,1989) whilst two have not (Janculjak et al., 1999; Litvan et al., 1988).

The scanning speed demonstrated by our MS participants was, on average 74ms / digit, which is relatively fast compared to values reported by others (Archibald & Fisk, 2000; 86.4 ms/digit, Archibald et al., 2004; 67.5 ms/digit, and Rao et al., 1989; 100ms/digit). It is possible that as our large sample was community based rather then accessed via a specialist clinic they has less severe symptoms than those who participated in other studies. Indeed, a limitation of using a community based sample was that diagnosis of MS subtype was by self report which was not verified by a clinician. However, the possibility of our sample showing less sever MS symptoms is in keeping with Kujala, et al. (1994) who found that a cognitively ‘impaired MS’ group were impaired on aspects of IPS, whilst a cognitively ‘unimpaired MS’ group showed only minor IPS deficits. In addition to this, the scanning speed of our control group (64ms/digit) was relatively slow compared to others (Archibald & Fisk, 2002; 47.9 ms/digit, Rao et al, 1989; 68 ms/digit, Sternberg 1967; 36 ms/digit). The control group were relatives / caregivers of the MS participants and there is a possibility that this burden may have led to significant levels of depression / fatigue in this group, however as we did not assess depression in this group we are unable to determine if this was a contributing factor.

One point of difference between the current study and two of the previous studies (e.g., Archibald & Fisk, 2000) was the number of digits in the memory set. While this study used a maximum of 4 digits, other studies have used up to 6. Although these previous studies found no significant differences between their MS sample and a control group on measures of memory, the sample sizes were small and performance levels of those with MS were shown to be consistently lower on the memory measures. Thus it is possible that the additional number of digits that were to be committed to memory may well have slowed the response (or processing) time in previous studies. Given the high level of accuracy in the performance of the MS participants in the Sternberg Scanning Test it seems unlikely that deficits in short term memory can explain the findings.

In contrast other researchers have also found no deficit in the memory scanning measure of the Sternberg test, but observed deficits in the initial response time (Janculjak et al., 1999; Litvan et al., 1988). The methodology of this latter study was somewhat different to other studies, as the researcher rather than the participant recorded the response, but this should have primarily affected the initial response time and not the time increment evident over increasing set sizes. In addition to the

Sternberg Test, Litvan et al., (1988) also administered the Paced Auditory Serial Addition Task (PASAT) and found deficits in the two fastest levels which is indicative of slowed IPS. This indicates that the Sternberg and the PASAT measure different constructs and reflects the suggestion by Chiaravalloti et al., 2003, that IPS is not a unitary construct.

In keeping with this, our data revealed that although the MS participants showed no evidence of memory scanning deficits, performance on the PSI and its subtests was significantly below that of the test norms. Thus, deficits in IPS were apparent with one measure but not the other. One possible explanation is that the Sternberg memory scanning measure reflects an underlying function quite distinct from that assessed by either the initial response speed of the Sternberg Test or the PSI. This is supported by larger correlations between the Sternberg initial response speed measure and the PSI compared to those between the memory scanning speed and the PSI. Furthermore, level of disability was found to correlate with initial response speed and the PSI but not memory scanning speed. Initial response time is a measure similar to simple reaction time and includes motor speed, stimulus recognition time, and other initiating responses such as perceptual analysis and response selection, that remain constant regardless of the number of digits to be processed. The closer relation between the PSI and initial response speed probably reflects the motor component of the PSI subtests. In contrast, the smaller correlations between the Sternberg memory scanning measure and the PSI may be because the stimuli for both subtests of the PSI are constantly displayed and thus limited memory scanning is required. Thus, the difference in demands of the processing speed measures may explain the lack of consistency in our findings.

These findings lend further support to the suggestion by Chiaravalloti et al., 2003, that IPS is not a unitary construct and highlights the need for clear definitions of the functions being assessed by IPS tests. As previously mentioned, measures of IPS have ranged from simple reaction time, to the tasks which make up the Processing Speed Index of the WAIS-III battery (e.g., DeLuca et al., 2004), through to the PASAT, or its variants, which require the manipulation of information, and therefore make greater demands on other cognitive resources than the less complex measures (Demaree et al., 1999, Diamond et al., 1997, Lengenfelder et al., 2006). Thus, the task requirements in the different tests differ substantially.

Not only do measures of IPS differ across studies, the name given to the construct being measured also varies, with the same tasks described as measuring either complex attention, cognitive speed, or processing speed (Chiaravalloti et al., 2003; Demaree et al., 1999, Diamond et al., 1997, Lengenfelder et al., 2006). In order to clarify this issue Chiaravalloti et al., 2003, carried out factor analysis on scores from various processing speed tasks including simple reaction time, choice reaction time and the PASAT. They found that both the simple and choice reaction time (CRT) tasks loaded on the first factor which they labelled simple speed / reaction time, the PASAT loaded on the second factor which was termed complex information processing and working memory tasks loaded on the third and final factor. On closer examination of the tasks involved in the Sternberg and the CRT, there are clear similarities – both require a key press in relation to a decision regarding stimuli presented on the screen, however the task for the Sternberg increases in difficulty, unlike the CRT. It is this increasing difficulty which allows the initial response speed to be dissociated from the memory scanning time. However, even in the 4 digit condition, there is minimal demand on the participant to manipulate information – their task is simply to compare the current stimulus to that held in short term memory. In contrast, the PASAT requires the participant to undertake a substantial amount of information manipulation and it has been suggested that this task draws heavily on the 'central executive' component of working memory proposed by Baddeley and Hitch (1994) (Chiaravalloti et al., 2003). Thus, the cognitive requirements of the Sternberg Memory Scanning Test lie somewhere between that of the CRT and the PASAT, as it is neither a test of simple or choice reaction time, nor of complex information processing speed. Indeed, successful performance on the Sternberg Test will probably rely primarily on one of the working memory slave systems (visuospatial sketchpad), and as the number of digits in the set increases, the central executive may also be engaged. However, the demands on the central executive during the Sternberg Test are likely to be much lower than during the PASAT. Together this suggests that the Sternberg may best be thought of as a test that assesses one of the cognitive constructs (memory scanning speed) that contributes to the larger group of abilities known as 'information processing speed' (Chiaravalloti et al., 2003).

Interestingly, an extension of the CRT test has been developed, the Computerised Test of Information Processing (CTIP) which progressively increases the amount of processing required by the participant (Reicker, Tombaugh, Walker & Freedman, 2007). At its easiest level, the test assesses simple reaction time, the second stage assesses choice reaction time whilst the third stage involves conceptual processing as the participant has to decide if a stimulus belongs to a particular group or not. This test shows remarkable similarities to the Sternberg Memory Scanning Test and has recently been used to demonstrate processing speed deficits in MS patients compared to controls. To provide additional clarification of the relationship between tests purporting to assess processing speed, further factor analytic studies based on performance on the Sternberg Test, the CTIP and the PASAT would be warranted.

As the Sternberg memory scanning measure and the PSI appeared to be measuring quite distinct abilities, their relationship with executive functions and working memory differed. Generally the PSI and the response speed measure from the Sternberg showed the highest correlations with the executive function measures. This is probably partly due to the degree of overlap in the functions assessed by these two measures and may reflect the elementary response initiating factors are common to many of the tasks. There appeared to be some relationship between processing speed, task complexity and time constraints as the PSI explained the greatest amount of variance in timed measures with high cognitive demands (Trails and CW interference switching). Interestingly both of these tasks have been used to assess information processing speed in previous studies (DeLuca et al, 1995; Santiago et al, 2007). The relationship between IPS and timed complex tasks is in keeping with previous studies (De Sonneville et al, 2002; Diamond, Johnson, Kaufman & Graves, 2008).

Thus, these results indicate that memory scanning speed does not appear to underlie successful performance on DKEFs executive function tests. However, as our MS sample showed no significant deficits in memory scanning speed, it is possible that stronger relationship between this measure and executive function may occur in those whose scanning performance shows a greater degree of impairment.

In contrast, memory scanning speed was linked to working memory, in particular performance on the Letter Number Sequencing task. This is in keeping with Cowan (1999), who described memory scanning, as measured by the Sternberg paradigm as a search of currently activated memory and it adds support to the preceding discussion about working memory. The relationship between working memory and IPS has been well described, for example, Mecklinger et al., 2003, revealed that those with a higher working memory capacity exhibit both a faster choice reaction time and a lesser interference cost than those with a lower working memory capacity. Other studies indicate that whilst there is a relationship between working memory and processing speed in the MS population (e.g., Demaree et al., 1999; DeLuca et al., 2004; Lengenfelder et al., 2006; Litvan et al., 1988), it has also been shown that these processes are separate. Thus when participants are given enough time to complete a working memory task, performance generally improves to a level equivalent to that of the control group (Demaree et al., 1999; Lengenfelder, 2006)

Overall, the results of this study support the findings of Cowan (1999) and others who suggest there is some link between memory scanning rate (and therefore an underlying construct of IPS) and working memory. Although there has been suggestion previously that slowed information processing speed underlies all cognitive impairment found in those with MS (e.g., Kail, 1998), this study lends greater support to the idea that if a task does not have a time constraint, there seems to be very little effect of memory scanning speed. The exception to this is the relationship between working memory and memory scanning speed, which may vary depending on the nature and complexity of the tasks.

One final point to note is that this study has highlighted the need to give careful consideration to the tasks used to measure processing speed. In particular it emphasises the need to interpret the findings to reflect the true underlying nature of the cognitive constructs being assessed rather than using the general term ‘information processing speed’ which has been shown not to be a unitary construct (Chiaravalloti et al., 2003)

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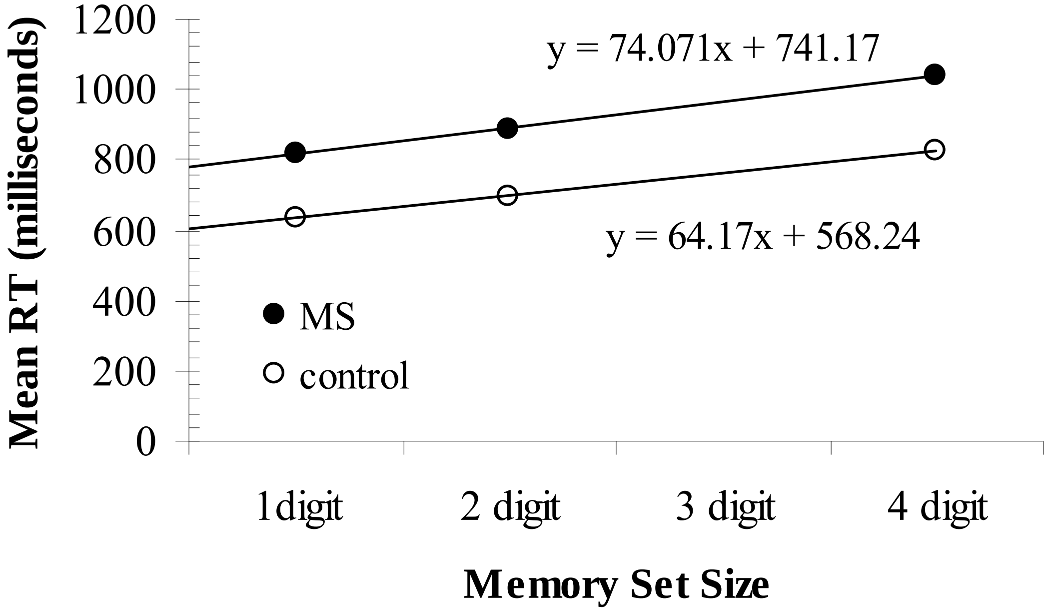

Figure 1. Sternberg Memory Scanning Test: The effect of set size on mean reaction time for participants with MS and controls (positive and negative trials combined). The slope of the line provides a measure of memory scanning speed whilst the intercept provides the initial responses speed.

Table 1

Means and (Standard Deviations) of MS Participants and Controls for Demographic and Sternberg Test Variables

Group	MS N=90	Control N=74
Demographics		
Gender **	M=18 F=72	M=30 F=44
Age	52.5 (11.6)	51.7 (14.7)
Yrs Education	12.8 (3.3)	13.0 (2.7)
Sternberg Measures		
Memory Scanning Speed (ms / digit)	73.8 (67.0)	65.0 (39.6)
Initial Response Speed (ms)**	749.7 (253.7)	569.3 (122.5)
1 digit no correct (from 60)	58.7 (1.70)	59.2 (1.49)
2 digit no correct (from 60)	59.0 (1.41)	59.4 (1.01)
4 digit no correct (from 60)	58.3 (1.74)	58.7 (1.58)

Note: M = Male, F = Female ** p < .01 between the MS and control group on this measure

Table 2

Correlations between the Sternberg Test Measures and the WAIS III Processing Speed Measures in MS participants

	Sternberg Test Measures	
WAIS III Processing Speed Measures	Memory Scanning Speed	Response Speed
Digit Symbol Coding	-.220*	-.435**
Symbol Search	-.217*	-.425**†
Processing Speed Index	-.204	-.454**

Note. *p < .05, ** p < .01 for correlations. † indicates instances where the memory scanning speed and the response speed correlations are significantly different (p < .05). See text for further details.

Table 3

Correlations between the primary scores from the D.KEFS tests, the working memory measures from the WMS-III and the IPS Measures from the Sternberg and WAIS III Processing Speed Index for the MS participants.

	Sternberg IPS Measures		WAIS III IPS Measures		
Test	Memory Scanning Speed	Response Speed	Proc Speed Index	Digit Symbol Coding	Symbol Search
1. Trail Making Switching	-.288**	-.573**†	**.620**††**	.584**†	.665**††
2. Verbal Fluency					
Letters	-.289**	-.409**	**.428****	.385**	.511**
Category	-.304**	-.481**	**.464****	.469**	.514**
Switching	-.231*	-.397**	**.522**†**	.430**	.608**††
3. Design Fluency					
Switching	-.207	-.426**	**.490**†**	.415**	.581**††
4. C-W Interference					
Inhibition	-.360**	-.459**	**.565****	.488**	.648**††
Switching	-.322**	-.375**	**.642**††**	.624**††	.616**†
5. Card Sorting Test					
Correct Sorts	-.196	-.320**	**.332****	.315**	.429**
Description	-.183	-.328**	**.335****	.346**	.410**
Recognition	-.105	-.325**	**.456**††**	.403**†	.505**††
6. 20 Questions					
Abstraction	-.149	-.248*	**.220***	.118	.697**††
Total Questions	-.082	-.463**††	**.433**†**	.429**††	.492**††
Total	-.088	**-.454**††**	.301**	.303**	.423**††
7. Word Context Total	-.168	**-.375****	.228*	.199	.354**
8. Tower Test					
Total	-.006	**-.420**††**	.291*	.263*	.396**††
9. Proverbs					
Total	-.361**	-.263*	**.390****	.358**	.467**
Common	-.263*	-.204	**.309****	.249*	.430**
Uncommon	-.347**	-.282**	**.350****	.346**	.405**
Accuracy	**-.313****	-.173	.268*	.220*	.368**
Abstraction	-.278**	-.357**	**.387****	.371**	.473**
WMS-III					
Letter Numbering Sequencing	**-.409****	-.245*	.363**	.359**	.415**
Spatial Span	-.183	-.342**	**.352****	.242*	.506**††
Work Mem Index	-.357**	-.314**	**.402****	.339**	.502**

Note. *p<.05, ** p < .01 for correlation with the PSI measures. † p < .05, †† p < .01, significantly different to memory scanning speed correlation. **Bold** indicates the measure which was the primary predictor in the multiple regression. See text for further details.