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Processing speed interacts with working memory efficiency in multiple sclerosis

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Abstract

Information processing speed was assessed using the visual threshold serial addition test (VT-SAT), a computerized modification of the PASAT designed to assess processing speed by controlling for performance accuracy. Persons with MS ($N = 43$) and healthy individuals ($N = 32$) were administered the VT-SAT varying working memory loads (1-back versus 2-back). Results indicated that at the lower working memory load (1-back) all individuals with MS were able to achieve a working memory performance level equivalent to healthy individuals, but required significantly more processing time to do so. In contrast, at the higher working memory load (2-back), about 70% of MS participants were able to achieve a performance level equivalent to healthy individuals, but again required significantly more processing time. The results are discussed in the context of the dynamic nature of the relationship between processing speed and working memory performance, emphasizing the dependence of this relationship on other cognitive and disease-related factors.
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Keywords: Working memory; Multiple sclerosis; Processing speed

1. Slowed processing speed affects working memory performance in multiple sclerosis

Two of the most frequently documented cognitive difficulties in individuals with multiple sclerosis (MS) are working memory and information processing speed (Archibald & Fisk, 2000; D'Esposito et al., 1996; Demaree, DeLuca, Guadino, & Diamond, 1999; Diamond, DeLuca, Kim, & Kelley, 1997; Foong et al., 1999; Kail, 1998; Kujala, Portin, Revonsuo, & Ruutiainen, 1995; Lengenfelder, Chiaravalloti, & DeLuca, 2003; Litvan, Grafman, Vendrell, & Martinez, 1988; Litvan, Grafman, Vendrell, Martinez, Junque et al., 1988; Ruchkin et al., 1994; Wishart & Sharpe, 1997). One of the most popular and well-referenced theories of working memory was proposed by Baddeley (1992). Baddeley conceptualized that working memory is comprised of a central executive system which coordinates, controls and manipulates information processing and two "slave systems", the phonological loop and visuospatial sketchpad, which maintain and temporarily store verbal and visual information. Impairments in both the central executive and slave systems within working memory have been documented in persons with MS. For instance, several investigators have reported deficits in the phonological loop (Litvan, Grafman, Vendrell, & Martinez, 1988; Litvan, Grafman,

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Vendrell, Martinez, Junque et al., 1988; Rao et al., 1993; Ruchkin et al., 1994). Compared to healthy individuals, MS participants demonstrated a limited capacity of the articulatory rehearsal mechanism to rehearse longer words as compared to shorter words. Other researchers have reported deficits in the central executive system, particularly on allocating attentional resources and manipulating information (Grigsby, Ayarbe, Kravcisin, & Busenbark, 1994; Grigsby, Busenbark, Kravcisin, Kennedy, & Taylor, 1994). For example, when compared with healthy participants, individuals with MS demonstrated difficulty on two competing tasks at the same time (i.e., dual-tasks) with differing levels of difficulty (D'Esposito et al., 1996) and on tasks requiring manipulating stored information including Digit Span Backwards, Brown–Peterson task, Symbol Digit Modalities Test and the Paced Auditory Serial Addition Task (PASAT; Grigsby, Ayarbe et al., 1994; Grigsby, Busenbark et al., 1994). Taken together, it is clear that persons with MS experience deficits in working memory tasks.

Impairments in information processing speed have also been documented in persons with MS (Rao, St. Aubin-Faubert, & Leo, 1989) such as on the PASAT (DeLuca, Barbieri-Berger, & Johnson, 1994; Diamond et al., 1997; Johnson, DeLuca, Diamond, & Natelson, 1996) and the Sternberg Memory Scanning Test (Rao et al., 1989). Several investigators found that while accuracy of MS participants responding was similar to healthy individuals, individuals with MS demonstrated disproportionately slower response rates. They concluded that individuals with MS may have slower information processing independent of their level of accuracy. Furthermore, many of these authors have reported that impaired processing speed is a primary determinant for impaired working memory performance, which then decreases the ability to acquire new information (DeLuca et al., 1994; DeLuca, Gaudino, Diamond, Christodoulou, & Engel, 1998). This decreased efficiency thus affects the ability of persons with MS to learn new information and to perform higher level cognitive functions (DeLuca et al., 1994; Gaudino, Donofrio, DeLuca, & Diamond, 2001; Kail, 1998; Litvan, Grafman, Vendrell, & Martinez, 1988; Litvan, Grafman, Vendrell, Martinez, Junque et al., 1988; Thornton & Raz, 1997).

Many of the previous studies have employed methodology that incorporates a "speed versus accuracy confound" (D'Esposito et al., 1996; Grigsby, Ayarbe et al., 1994; Litvan, Grafman, Vendrell, & Martinez, 1988; Litvan, Grafman, Vendrell, Martinez, Junque et al., 1988; Rao et al., 1993). The basis of this confound is that accuracy in performance generally decreases as the speed needed to process information increases (Davies, 1973; Jarvella & Herman, 1973; Pike, McFarland, & Dalgleish, 1974). This confound in the measurement of speed versus accuracy makes it extremely difficult to attribute whether individuals with MS have problems in working memory, speed, or both (e.g., an interaction). Demaree et al. (1999) attempted to address this "speed versus accuracy confound" by controlling accuracy of performance in working memory to examine speed using both auditory and visual threshold serial addition tests, the AT-SAT and VT-SAT, respectively (Diamond, DeLuca, Kelley, & Gross, 1998). These authors demonstrated that individuals with MS were able to achieve accuracy comparable to healthy individuals, but required a significantly longer time to process the information. That is, stimuli had to be presented at a slower rate in order for MS participants to perform well enough to generate an equivalent number of correct responses as healthy participants. These results suggest that when working memory load is "low" increasing the amount of time necessary to process the task can significantly improve performance (even to "normal" levels). However, what is not clear is whether compensating for speed problems could still improve accuracy when there are increasing demands in working memory load. Addressing this issue is a major aim of the present study.

One way to better understand this relationship between working memory accuracy and speed is to examine accuracy at different working memory loads and then determine whether a problem in processing speed is still present. Specifically, if speed is the primary problem in MS, equating individuals for processing speed should result in the absence of significant group differences on accuracy. However, if working memory accuracy plays a significant role in, or interacts with speed, we would expect to see a group difference on accuracy in addition to speed as the working memory load increases.

To do this, the present study used a modified version of the PASAT, the Visual Threshold Serial Addition test (VT-SAT). The VT-SAT is a visual computerized task not only similar to the PASAT but also includes the modulation of an inter-stimulus interval. It employs a method of limits procedure to find the inter-stimulus interval (or threshold speed) necessary to hold accuracy constant at 50% correct across participants in both the MS and healthy groups. As such, the threshold speed is a direct measure of processing speed, uncontaminated by accuracy. While the original PASAT is essentially a "1-back" task, the VT-SAT also employs a more difficult derivative of the 1-back, known as the 2-back, to modulate level of difficulty. This design allowed us to examine the influence of working memory difficulty (i.e., 1-back versus 2-back) on processing speed, to examine if processing speed interacts with task difficulty.

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To equate participants on processing speed, each participant's threshold speed required to achieve 50% correct on the 1-back is used to perform the 2-back task. In this way, if processing speed is the primary problem, equating for processing speed should result in the absence of significant group differences on 2-back accuracy. However, if working memory accuracy plays a significant role in, or interacts with speed, a group difference on 2-back accuracy would be expected.

2. Method

2.1. Participants

The sample consisted of 43 persons with clinically definite MS, as diagnosed by board-certified neurologists with a specialization in MS (Poser et al., 1983), and 32 matched healthy individuals. MS participants were subdivided based on their accuracy on the 2-back task. Consistent with methods used in previous MS studies (DeLuca, Chelune et al. 2004; Rao, Leo, Bernardin, & Unverzagt, 1991), the 5th percentile of the healthy participants' scores on the 2-back trial was used as the cut-off for determining impairment in accuracy. The individuals with MS who performed below the 5th percentile were termed "non-achievers" while individuals with MS who performed at and above the 5th percentile were termed "achievers". Seventy percent ($N = 30$) of individuals with MS were classified as "achievers" while 30% ($N = 13$) were classified as "non-achievers". All participants were screened for prior neurological or psychiatric history, learning disabilities, and history of substance abuse. All participants signed a consent form approved by an institutional review board at the beginning of the testing session. Participants in the MS group were referred from the Bernard Gimbel MS Center in Teaneck, New Jersey and healthy individuals were recruited from the community.

Demographic data for study participants are shown in Table 1. MS and healthy groups did not differ in age or years of education. A difference was found between the groups in intelligence as assessed using the Wide Range Achievement Test-3 Reading Subtest (Wilkinson, 1993; F [2,71] = 8.76, $p < .001$). Although there was no significance difference between groups in the years of education, the MS "non-achievers" did differ on a measure of academic achievement from both the "achievers" ($p < .01$) and healthy individuals ($p < .01$).

Not unexpectedly, MS participants did produce significantly higher scores on the Beck Depression Inventory (BDI; Beck, 1987) compared to the healthy individuals (F [2,69] = 12.60, $p < .001$). Also as expected, the individuals with MS also produced significantly higher scores on the general fatigue index of the Multidimensional Fatigue Inventory (MFI; Smets, Garssen, Bonke, & De Haes, 1995) than the healthy individuals (F [2,72] = 28.54, $p < .001$). Importantly, the two MS groups did not differ in disease-related factors such as months since symptom onset, months since last exacerbation, or functional impairment as assessed using the Expanded Disability Status Scale (Kurtzke, 1983).

3. Materials and procedure

Participants were screened for inclusion criteria, and signed an IRB-approved consent form. The testing session included the administration of standard neuropsychological measures as well as the VT-SAT computerized task. The

Table 1
Demographic information for participants; mean (standard deviation)

	Individuals with MS		Healthy individuals ($N = 32$)
	Non-achievers ($N = 13$)	Achievers ($N = 30$)	
Age	44.15 (10.25)	46.30 (8.80)	44.00 (11.20)
Years of education	14.39 (2.06)	14.40 (2.09)	14.78 (2.01)
WRAT-3	91.83 (13.51)[a]	102.93 (9.29)	104.88 (7.40)
Depression—BDI	10.92 (5.53)	9.00 (6.55)	3.29 (3.86)[b]
Fatigue—MFI	13.80 (4.17)	13.69 (3.79)	7.43 (2.84)[b]
Years since diagnosis	10.18 (8.92)	10.42 (7.91)	
Months since last exacerbation	30.70 (28.09)	21.74 (22.45)	
EDSS	4.18 (2.23)	3.75 (2.48)	

[a] MS non-achievers differed from both MS achievers and HC.
[b] HC differed from both MS groups, which did not differ from each other.

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battery was presented in a fixed order with all subjects receiving the same tests in the same order. All participants were administered the VT-SAT in accordance with previously published procedures (Demaree et al., 1999). The VT-SAT presents a series of 50 digits sequentially on a computer monitor. Similar to the PASAT, participants were instructed to add each single digit number presented (ranging from 1 to 9) to the number immediately preceding it and report the sum aloud. The numbers were presented centrally on the computer monitor and were 5 mm in height.

The VT-SAT uses a method of limits procedure to determine the rate of stimulus presentation needed for each participant to achieve an approximate 50% success rate. This inter-stimulus interval, referred to as threshold, represents an index of processing speed that is achieved while controlling for performance accuracy. Patterns of performance can change over the course of a protocol and so only an approximation of the "true" threshold can be computed. However, in order to generate a representative individual threshold the program does evaluate the entire pattern of an individual's performance using algorithms that respond differently to changes in performance and the point at which these changes occur. The standard VT-SAT administration is a "1-back task", in which participants are instructed to add each number presented to the number presented immediately before it and report the sum out loud, repeating the operation consecutively.

In order to increase the working memory load on the VT-SAT in the current study, a second trial was administered immediately following the 1-back trial. This second trial was a 2-back task, in which participants were instructed to add each number presented to the number presented 2-back and report the sum out loud. The 2-back VT-SAT trial allowed us to determine to what extent manipulations in speed alone were sufficient to sustain performance accuracy at desired levels, even with an increased memory load.

Finally, a third VT-SAT trial was conducted. In the previous 1-back and 2-back trials participants' accuracy was examined by using a method of limits procedure to determine the rate of stimulus presentation needed for each participant to achieve a 50% accuracy rate at which point speed could then be quantified. In the third trial, the reverse was done, that is, participants were equated for speed of processing to then quantify accuracy of performance. To equate participants on speed for the third trial, each participant performed the 2-back version of the VT-SAT a second time, but this time, using their optimum threshold speed from the 1-back condition. If processing speed is the primary cognitive problem, then equating processing speed should not result in differences in accuracy on the 2-back across MS and healthy groups. However, if working memory accuracy plays a significant role or interacts with speed, we would expect to see group difference on 2-back accuracy on trial 3 when speed is equated.

The measures of interest for each VT-SAT trial were overall performance *accuracy*, defined as the proportion of correct answers produced during the trial, and *processing speed*, defined as the item presentation speed at which participants performed at 50% accuracy during the trial.

4. Results

4.1. Trial 1: 1-back

The results of the 1-back version of the VT-SAT replicated our initial results in persons with MS (Demaree et al., 1999). Both the MS and healthy groups were able to achieve comparable accuracy levels on the 1-back task (MS non-achievers = 52%, MS achievers = 53%, and HC = 54%; see Fig. 1). Both MS groups required significantly longer threshold scores (reflecting slower processing speed) to achieve a similar level of accuracy as controls (F [2,72] = 40.10, $p < .001$; see Fig. 2). Additionally, post hoc Tukey HSD test revealed that the MS non-achievers required significantly longer threshold speeds when compared to MS achievers ($p < .001$).

4.2. Trial 2: 2-back

A one-way ANOVA showed a significant difference in processing speed between the three groups on the 2-back condition (F [2,72] = 77.53, $p < .001$). Specifically, post hoc Tukey HSD test revealed that the MS non-achievers group required significantly longer threshold times than both the MS achievers ($p < .001$) and the healthy individuals ($p < .001$) on the 2-back VT-SAT (see Fig. 2). The MS achievers also had longer threshold times compared to the healthy individuals ($p < .001$). Importantly, the MS non-achievers had threshold times (mean = 1028 Ms) almost twice as high as the threshold times of the MS achievers (mean = 535 Ms).

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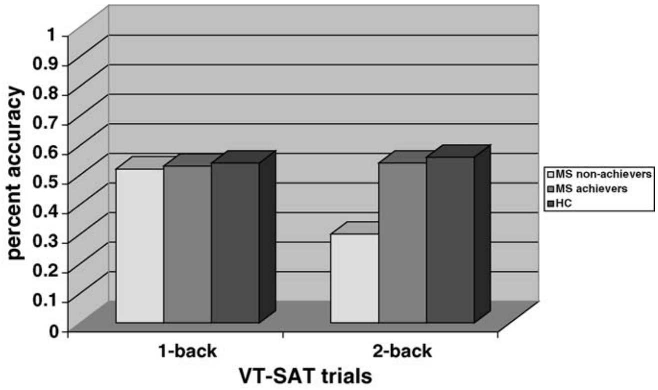

Fig. 1. Percent accuracy on VT-SAT trials for MS non-achievers, achievers, and HC groups.

4.3. Trial 3: 2-back at 1-back threshold

In this analysis participants' were equated on speed to examine accuracy of performance. Each participant performed the 2-back version of the VT-SAT this time using their optimal speed they achieved on the 1-back condition.

When accuracy of performance was observed on the 2-back with processing speed held constant, a one-way ANOVA revealed differences in the number of correct responses among the three groups ($F\,[2,72] = 7.39$, $p < .001$). Specifically, Tukey HSD tests showed that the MS non-achievers had significantly lower accuracy compared with MS achievers ($p < .05$) and the healthy individuals ($p < .001$; see Fig. 3). The MS achievers and healthy individuals' accuracy did not differ from each other.

4.4. Neuropsychological measures

Additional analyses were undertaken to determine if a pattern of neuropsychological performance might differentiate the two MS groups (see Table 2). A significance level of $p < .01$ was adopted as a cut-off in an attempt to control for Type I error and Bonferroni corrections were used to adjust for the numerous comparisons. Post hoc analyses revealed that the non-achievers demonstrated poorer performance on a speeded measure that did not contain a high working memory load component, the Symbol Digit Modalities Test (SDMT). Interestingly, the two MS groups did not differ on tests of working memory (i.e., Letter Number Sequence, Digit Span). The non-achievers group had significantly lower total correct scores on both the PASAT 3″ and 2″ (Brittain, La Marche, Reeder, Roth, & Boll, 1991) than the achievers. The non-achievers also demonstrated poorer performance in executive functioning as measured by the Wisconsin Card Sorting Test (WCST). Finally, the two MS groups differed with respect to verbal learning and memory (SRT # of trials

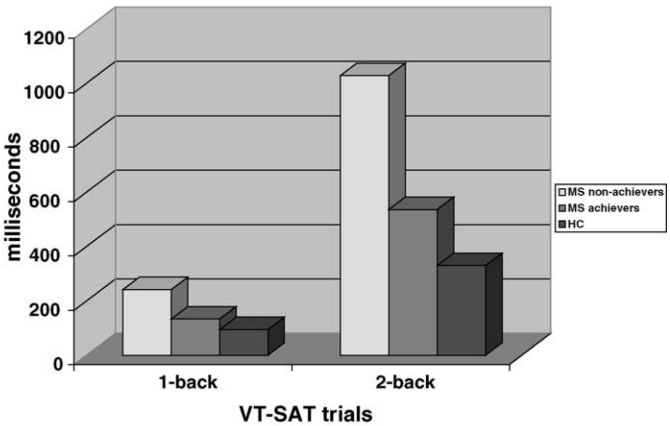

Fig. 2. Processing speed on VT-SAT trials for MS non-achievers, achievers, and HC.

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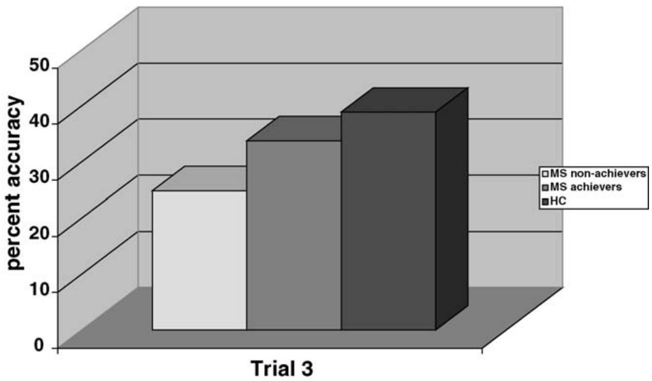

Fig. 3. Percent accuracy on VT-SAT Trial 3: 2-back condition using individual's own optimal threshold speed.

Table 2
Differences in performance on neuropsychological measures

	MS non-achievers	MS achievers	Healthy individuals	p
7/24 # of trials to reach criterion	8.69	4.13	3.97	<.001[a]
7/24 recall 30 min	5.31	6.67	6.34	<.01[a]
7/24 recall 90 min	5.77	6.70	6.50	ns
CFL	35.46	42.33	42.42	ns
Digit span backward	5.38	7.00	8.66	<.001[b]
Digit span forward	7.69	8.40	10.47	<.001[b]
Letter comparison	10.38	11.47	13.19	ns
Letter number sequencing	9.00	10.93	12.52	<.001[b]
PASAT 2 s	22.23	35.00	41.41	<.001[a]
PASAT 3 s	30.15	44.35	52.19	<.001[a]
Pattern comparison	14.81	17.19	20.90	<.001[b]
SDMT	39.00	53.69	64.06	<.001[a]
SRT # of trials to reach criterion	11.77	8.27	6.72	<.001[a]
SRT recall 30 min	8.62	9.33	9.72	<.01[b]
SRT recall 90 min	8.54	9.10	9.16	ns
WAIS-R similarities	18.92	19.40	20.19	ns
WCST # of trials	108.77	90.57	82.26	<.001[a]
WCST categories	4.77	5.33	5.97	<.01[b]
WCST failure to maintain set	0.92	0.63	0.32	ns
WCST perseverative responses	24.92	11.67	8.39	<.001[a]
WCST total errors	36.31	21.70	14.48	<.001[a]

[a] MS non-achievers different from MS achievers and HC.
[b] MS non-achievers different from HC only.

to criterion, 30 min recall) and visual learning (7/24 # of trials to criterion) with the non-achievers group requiring a greater number of trials to learn the list of words and patterns.

5. Discussion

The results of the present study indicate that speed, not accuracy, is the primary information-processing problem in individuals with MS. The results for the 1-back condition indicate that at a lower working memory load, all MS participants perform as accurately as healthy individuals, although they require a significantly greater amount of time to do so. These results support previous research indicating that individuals with MS experience deficits in processing speed when compared to healthy individuals (Demaree et al., 1999; Diamond et al., 1997).

The results of the 2-back condition indicate that when the central executive system is sufficiently taxed at a higher working memory load there is an interaction between processing speed and working memory such that a subgroup of

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individuals with MS who demonstrate working memory difficulties in addition to speed problems emerges. Specifically, 70% of the individuals with MS ("achievers") were able to perform as accurately as healthy individuals in the 2-back condition, although they required a greater amount of time to do so. For this group, speed, not working memory accuracy, is the primary information-processing problem. In contrast, 30% of the individuals with MS ("non-achievers") could not reach the necessary level of accuracy regardless of the amount of information processing time allowed to perform the task. The non-achievers demonstrated an interaction of impairments in both processing speed and working memory. For this group, impairments in working memory emerge with the additional central executive requirement of the 2-back condition.

Taken together, the combined results of the 1-back and 2-back conditions support the hypothesis that deficits in speed of information processing are present in individuals with MS when requirements to the central executive system are not maximized (e.g., 1-back condition). Deficits in working memory ability become apparent in only a subset of the individuals with MS when the central executive is increasingly taxed (e.g., 2-back condition). These results support previous findings that when the central executive is minimally or slightly challenged working memory is generally efficient, however when greater central executive involvement is required differential working memory performance between two groups of MS participants emerges (Lengenfelder et al., 2003).

Previous research has found that deficits in working memory ability performance were more pronounced in individuals with MS as the disease progressed or those with greater overall cognitive impairment (Archibald and Fisk, 2000; DeLuca, Chelune, Tulsky, Lengenfelder, & Chiaravalloti, 2004; Lengenfelder et al., 2003). In order to further understand what differentiated those individuals with MS who demonstrated working memory impairments on the 2-back condition (non-achievers) from those without working memory impairments (achievers), performance on additional neuropsychological measures were examined. Individuals who had impairments in both accuracy and processing speed on the 2-back condition (i.e., non-achievers) had poorer performance on tasks that involved both working memory and speed components (PASAT, SDMT) but not on tasks that involve either primarily speed (PC, LC) or primarily working memory (Digit Span, LNS). This interaction of speed and working memory suggests that, although speed of processing appears to be the primary deficit, either increasing the requirement of speed or higher working memory load demands could disrupt performance in this impaired subgroup.

Additionally, the non-achievers who had both impairments in accuracy and processing speed on the 2-back condition also differed from the other MS participants on tasks of verbal and visual learning. Specifically, the non-achievers required a greater number of trials to reach the learning criterion on the SRT and 7/27 compared to the other two groups. Differences between the two MS groups were also noted on visual memory. Others have previously described a relationship between speed and/or working memory and learning in MS suggesting that working memory may contribute to deficits in learning and long term episodic memory (DeLuca et al., 1994; Gaudino et al., 2001; Thornton and Raz, 1997).

There are at least three potential explanations for the differences in processing speed and working memory among individuals with MS demonstrated in this study. The first, termed the Relative Consequence Model (DeLuca et al., 2004) is that persons with MS have a primary problem in processing speed which in turn results in difficulties in other cognitive processes (e.g., working memory). Therefore, the greater the impairment in processing speed the more effects there will be on other cognitive processes. Thus, this hypothesis predicts that inefficiencies in other cognitive processes are a by-product of slower cognitive processing. When both processing speed and working memory are required for a task such as in the 2-back condition, the group with greater processing speed deficits will demonstrate difficulties in working memory as well. This is in fact what was observed in the non-achievers on the 2-back condition when compared to the MS achievers. This idea of processing speed problems resulting in other cognitive deficits has received support in the aging literature where an age-related deficit in processing speed has been shown to be one of the major causes of variability on working memory tasks (Salthouse, 1996). Support for the notion that impairments in processing speed influence other aspects of cognition in the MS literature is growing (Donders, Tulsky, & Zhu, 2001; Kail, 1998). Further, the fact that the two MS groups did not differ on tests of working memory but did on at least some tests of processing lends support to the Relative Consequence Model.

The second potential explanation, termed the Independent Consequence Model (DeLuca et al., 2004) is that deficits in processing speed could be independent to deficits in working memory. In this case, the MS achievers could have deficits in processing speed only whereas the non-achievers could have deficits in both processing speed and working memory. Since MS as a disease is relatively heterogeneous in lesion location, pattern, severity, etc., these factors may contribute to additional cognitive deficits (i.e., working memory deficits) in some individuals with MS that are

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not present in other individuals with MS. According to this model, early in the course of disease, speed may be the primary deficit but as the disease progresses and develops into a secondary progressive phase, specific areas of cerebral involvement may increase leading to additional problems in other cognitive functions such as working memory (Archibald & Fisk, 2000; DeLuca et al., 2004). In this case, the non-achievers may have both processing speed and working memory deficits that are independent of each other, perhaps due to individual disease factors such as lesion location, so no matter how much extra time these participants are provided (i.e., to improve a processing speed deficit), they are simply unable to perform the complex working memory task.

Finally, a third potential explanation to account for the difference in performance between the two groups of MS participants may have to do with cognitive reserve theory. Cognitive reserve, also called cerebral reserve or functional reserve, is defined as "the ability to optimize or maximize performance through differential recruitment of brain networks, which perhaps reflect the use of alternate cognitive strategies." (Stern, 2002). The reserve model suggests that when task difficulty is increased, additional cognitive resources are recruited such that those with greater cognitive reserve will use additional or alternate networks in an easier and more efficient way than those with less cognitive reserve. Following this model, cognitively impaired individuals then would use up available resources earlier than non-impaired individuals and therefore, performance under conditions of maximum cognitive load would decrease at a differentially greater rate in impaired individuals relative to non-impaired individuals. In the present study, it is possible that the individuals in the achievers group possessed greater cognitive reserve compared to the non-achievers and this may be responsible for the difference in performance evidenced in the 2-back condition. Much of the work on cognitive reserve comes from the aging and dementia literature where studies on cognitive reserve have demonstrated differences in cognitive functioning despite similarities in brain structure (Bigio, Hynan, Sontag, Satumtia, & White, 2002; Meguro et al., 2001; Satz, 1993). Models addressing the cognitive reserve hypothesis have attempted to examine whether possessing more of a reserve factor (i.e., brain size before disease onset, education, and occupation) would protect an individual from cognitive decline due to aging or disease. While we cannot directly test this hypothesis in the current study the achievers and non-achievers groups did show a difference on the WRAT-3, a measure of academic achievement which is used to estimate intelligence (Wilkinson, 1993). Despite having no difference in educational levels, the non-achievers performed significantly lower on the WRAT-3 than both the achievers and healthy individuals which could suggest that the non-achievers may have less cognitive reserve than the achievers. Other indirect evidence from recent functional neuroimaging work suggests that individuals with MS require more cerebral resources than healthy individuals to complete working memory tasks (Chiaravalloti et al., 2005). This might suggest that persons with MS are more reliant on their cognitive reserve to achieve performance similar to that of healthy individuals. The role of cognitive reserve in cognitive processing in MS awaits further research.

While the VT-SAT 1-back has generally been effective in measuring processing speed while controlling for performance accuracy, not everyone with MS in the current study could meet accuracy criteria on the 2-back trial. Therefore, establishing threshold speeds for all subjects at the higher WM load (i.e., 2-back) was not possible. In the 2-back task, working memory, attention/concentration and the operation of the central executive were increasingly taxed. Even under these conditions, 70% of the individuals with MS did achieve levels of accuracy on the 2-back that did not functionally differ from that of healthy controls and the MS-MET group. As the VT-SAT was designed to continue to search for an optimal threshold speed until the very last trial, it can be reasonably concluded that in the 30% of the MS sample that did not meet the established accuracy criterion, no degree of speed manipulation was sufficient to raise their level of performance in the VT-SAT 2-back task. The results should be replicated and extended using measures that assess performance issues integral to this type of task, in addition to speed-related factors.

If processing speed represents the primary deficit in information processing in MS, it is possible that remediation techniques designed to provide additional processing time may be beneficial for individuals with MS. In fact, such work is already underway in our laboratory. Rehabilitation efforts can be focusing on helping persons with MS utilize additional time when confronted with tasks that challenge working memory. Alternatively, if increasing information processing time improves working memory accuracy only at certain levels of task difficulty, persons with MS may be taught how to determine which everyday working memory tasks may be improved by the utilization of additional time. Improved working memory accuracy as a result of optimizing information processing time may enhance stimulus acquisition abilities in MS, thus improving learning. Consequently, by functionally restoring impaired skills or providing compensatory strategies to enhance learning, cognitive rehabilitation can help persons with MS perform tasks and activities that are critical to daily living.

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