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The relationship between neuropsychological measures and the Timed Instrumental Activities of Daily Living task in multiple sclerosis

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Multiple sclerosis (MS) can result in cognitive deficits and a loss of functional independence. To date, little research has linked the observed cognitive and behavioral deficits in MS, especially those in the processing speed domain, to performance on tasks of everyday functioning. The present study examined the relationship between neuropsychological test performance and performance on the Timed Instrumental Activities of Daily Living task (TIADL) in individuals with MS, and in healthy controls (HCs). The TIADL is a functional measure, which assesses both accuracy and speed in one's performance of everyday activities. The MS group performed significantly worse on the TIADL relative to the HC group. Additionally, TIADL scores of individuals with MS were significantly correlated with neuropsychological measures of processing speed. TIADL scores were not, however, correlated with neuropsychological measures of verbal episodic memory or working memory. These results indicate that the impairments in processing speed may contribute to impairments in activities of everyday living in persons with MS. *Multiple Sclerosis* 2007; **13**: 636–644. http://msj.sagepub.com

Key words: cognitive functions; instrumental activities of daily living; multiple sclerosis; neuropsychological measures; processing speed; rehabilitation

Introduction

In many clinical and research settings, rehabilitation professionals seek assessment tools that can provide information about an individual's everyday life functioning and performance during instrumental activities of daily living (IADL) [1,2]. IADL are activities considered to be of a higher order than basic ADL, such as eating or bathing, as IADL involve the operation of a tool or instrument, and require more steps for successful completion [3]. Evaluating the ability to live independently is important in rehabilitation because it affects the quality of life of an individual, as well as emotional health and re-entrance into the community. Understanding the relationship between neuropsychological test performance and everyday task performance in individuals with multiple sclerosis (MS) may provide a greater understanding of the capacities underlying day-to-day activities.

MS is one of the most common forms of neurologic compromise in middle-aged adults in the US [4], often resulting in cognitive deficits, emotional instability, and loss of functional independence [5–7]. It is now well recognised that individuals with MS have significant impairments in information processing speed [8–10], and that such impairments may underlie other cognitive deficits common to MS [11–13]. However, to date, little research has linked processing speed deficits with performance of everyday activities in persons with MS. The goal of the present study was to examine the relationship between various neuropsychological measures (including processing

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speed) and a measure of everyday competency, which was designed to be sensitive to processing speed abilities.

Performance on measures of processing speed includes components of central processing or cognitive speed, as well as peripheral or motor speed. Speed of information processing refers to either the time required to execute a cognitive task or the amount of work that can be completed within a finite period of time. Although typically referred to as a singular construct, processing speed is likely multidimensional [11]. For instance, based on factor analysis, Chiaravalloti *et al*. [11], showed that 'simple' processing speed indices, such as reaction time, can be differentiated from 'complex' processing speed with little shared variance between the two. Further, only 'complex' processing speed was associated with variance in performance on tasks of learning and memory [11].

Processing speed deficits are common in a number of different neurological and psychiatric populations, including individuals with Alzheimer's disease [14], Huntington's disease [15], chronic fatigue syndrome [16], aging [17–19], schizophrenia [20], stroke [21], traumatic brain injury (TBI) [22], as well as MS [12]. Salthouse [23], postulates that if processing speed deficits exist in older adults, higher order cognitive processes may also be impaired because there is not enough time to complete such processes. A similar hypothesis has been suggested in MS, with results suggesting that processing speed deficits in MS may underlie other MS-related cognitive deficits, such as long-term memory and working memory impairments [8,13]. Specifically, it has been shown that individuals with MS require more time to perform complex cognitive tasks, and when give more time to complete the task, behavioral performance is comparable to healthy adults [12,24]. Furthermore, decreased processing speed affects the ability of individuals with MS to learn new information and to execute higher-level cognitive functions [13,25–27]. Given the broad effect of processing speed on higher-level cognitive processes, it is reasonable to hypothesise that speed of information processing is a primary contributor to everyday life functional activities.

The relationship between performance on IADL and processing speed has been observed in elderly adults [28–31] and in individuals with closed head injury [32]. It has been argued that processing speed difficulties may underlie performance of IADL in aging, especially those which require higher order cognitive processes [33], including managing finances, taking medications and driving [29–31]. In individuals with MS, only two studies have reported that processing speed is associated with driving [34] and quality of life [35]. In the driving study, however, researchers used two instruments to assess driving-related skills, but not actual driving. In the second, quality of life was assessed via a self-report measure. Thus, neither study assessed actual performance of IADL.

The current study examined how processing speed and other cognitive constructs (ie, working memory, episodic memory) affect IADL activity in persons with MS. The study used the Timed Instrumental Activities of Daily Living test (TIADL) [28,33], which is a performance-based assessment of IADL, with a component of speed against which task performance can be measured. The TIADL has been used previously in studies examining aging [28,29,33]. It was hypothesised that individuals with MS will perform significantly worse (ie, take more time to complete) on the TIADL relative to healthy controls (HCs). Also, we hypothesised that everyday functional abilities, as measured by the TIADL, will be significantly correlated with neuropsychological measures of processing speed.

Methods

Participants

Participants consisted of 17 healthy control participants (HCs), between 22 and 55 years of age (mean = 35.7, SD = 12.0), without any reported medical disabilities, and 18 participants diagnosed with clinically definite MS, according to the criteria of Poser *et al*., between 23 and 55 years of age (mean = 40.4, SD = 7.7). Demographic characteristics of the sample are presented in Table 1. There were significantly more females in the MS sample ($n = 15$) relative to the HC group. All MS participants were at least one-month post most recent exacerbation, if any, and were free of corticosteroid use at the time of testing. Some 83.3% of the MS sample were on disease modifying treatment at the time of this study. With regard to disease course, 77.8% ($n = 14$) of the participants with MS had a

Table 1 Characteristics of the two groups (mean ± standard deviation)

	MS ($n = 18$)	Healthy adults ($n = 17$)	*P*
Age	40.4 ± 7.7	35.7 ± 12.0	0.17
Education	15.2 ± 1.8	15.9 ± 2.3	0.30
Female (%)	76.2	37.5	0.01
Time since illness onset (years)	5.4 ± 5.3	N/A	N/A
WRAT-3	48.0 ± 5.2	51.5 ± 4.4	0.10
Disease type		–	
Relapsing remitting	77.8%	–	
Primary progressive	16.7%	–	
Secondary progressive	5.6%	–	

relapsing remitting course, 16.7% ($n = 3$) of the participants had primary progressive type of MS, and 5.6% ($n = 1$) had secondary progressive MS. Participants in both groups were similar in their estimated level of pre-morbid general intelligence, as assessed by the Wide Range Achievement Test 3, Reading Subtest (WRAT-3) [36]. Participants were excluded from the study if they had a previous admission to an alcohol/drug treatment program or if they were previously diagnosed with a neurological disorder other than MS (eg, stroke, seizure disorder), or reported major psychiatric illness.

Measures

Activities of daily living

Timed Instrumental Activity of Daily Living (TIADL) [28,33]. The TIADL is an evaluation tool, consisting of five tasks sampling common instrumental activities of daily living-(1) communication: finding a number in a phone book; (2) finance: counting change; (3) nutrition: locating and reading ingredients from a can of food; (4) shopping: locating items on a shelf filled with food items; and (5) medicine: locating and reading directions from a medicine bottle. All tasks utilise actual everyday objects (eg, coins, cans of food, medicine bottles, etc.), rather than simulated, enlarged stimuli or pictures of stimuli. To minimise memory load, provision of standard instructions ensured that the participant knew what the target item was before beginning the task. For example, on the task requiring the participant to locate a telephone number in a phone book, the investigator provided the name of the person to be located, and then requested that the participant repeat the name before beginning the search through the phone book. To minimise the effects of motor deficits on performance, stimulus materials were placed in the participant's hand immediately before the task began. For example, when the participant needed to count change, the coins were placed in their non-dominant hand and not on the table. The tasks used in the TIADL required very simple motor ability (eg, reading ingredients on a can of food or instructions on medicine bottles).

General instructions to the participants were:

> Now I want you to perform five different tasks for me. These are similar to tasks you might do in your everyday activities ... I will be timing you in each of these activities, so please stay focused on the task.

Each task had a preset maximum time limit of 2 minutes, with the exception of the telephone task, which had a time limit of 3 minutes. If participants did not complete a task within this time limit, the task was terminated, and maximum time was assigned to this task. Time required to complete each task was recorded in seconds.

The TIADL was administered in accordance with standard published instructions [28,33]. Scoring of task performance was determined by both accuracy and time to completion. Task accuracy was scored according to one of three choices: (1) the task was completed without any errors, within the time limit; (2) the task was completed within the time limit, but with a minor error; (3) the task was not completed within the time limit and/or it had a major error. Minor errors were defined as a small change or deviation from the expected response (eg, a small reading error, such as reading the word 'beef' instead of 'beets'). Major errors were defined as a failure of the participant to perform the task correctly (eg, if a participant was asked to read ingredients from a can of food, and instead, he or she read another section from the label). Participants who had a major error were assigned the maximum time allotted on the item. For the tasks completed with minor errors, a time penalty was added to completion time. This added time penalty for the minor errors is equal to 1 standard deviation from the mean of each task, based upon the data from HC and MS participants who completed the same item without error [28,33]. The final dependent measure used in this study was the total raw score (average time it took to complete all five tasks).

Speed of information processing

Symbol Digit Modalities Test (SDMT) – oral version [37]. The SDMT involves a set of nine meaningless geometric figures, each corresponding to a different number (1–9). In this study, the participants were given a key, presented at the top of the page, indicating which number corresponded to each symbol. Participants were then presented only with the geometric figures and asked to quickly state the number associated with each figure. The dependent measure was the total number of correctly completed numbers in 90 seconds. The SDMT has been found to be a sensitive measure of processing speed in persons with MS [38–40].

Letter and Symbol Cancellation tasks (Cancel H) [41]. The Cancel H task is composed of different alphabetic letters. The test consists of 105 targeted letters and 56 non-targets scattered on letter-sized paper. The participants were required to scan the page and to cross out a target letter 'H' with their pencil. The participants were asked to put the pencil down when they were done. The total time to finish this task was recorded and served as the dependent variable.

Trail-Making Test (TMT) A and B [42]. The TMT consists of two parts, A and B. Part A consists of 25 consecutive, encircled, numbers randomly arranged on a piece of paper. The participants were asked to connect the numbers in the proper ascending order using a pencil. Part B is a more complex task, in which a series of 13 consecutive encircled numbers (1–13) and letters (A–L) are randomly arranged on a sheet of paper. The participants were asked to connect them with pencil lines in alternating order (number-letter-number-letter) until the 25th circle was reached as quickly as possible. The TMT yielded two measures: (a) 'TMT B-A' dependent variable: the difference between the time taken to complete part A from the time taken to complete part B (Part B (seconds) minus Part A (seconds)). The subtraction of parts A from B was carried out to obtain a 'pure' score of speed, and to control for the motor time necessary to perform this task [43]. The second variable was (b) 'TMT A' the time in seconds taken to complete part A of the test. This score provided a measure of 'pure' motor speed, used to control for motor speed differences caused by MS.

Paced Auditory and Serial Addition Task (PASAT) [44]. Participants were presented with a series of single-digit numbers via audiocassette tape. Participants were instructed to add each pre-recorded number to the number immediately preceding it, and to say the sum aloud, repeating the operation consecutively. There were four trials, each with 50 numbers presented to the participants, which required 49 responses. With each trial, the rate at which each number was presented increased (ie, 2.4, 2.0, 1.6 and 1.2 seconds). The dependent measure was the number of correct responses across the four trials.

General intelligence

Wide Range Achievement Test 3, Reading Subtest (WRAT-3) [36]. This task involves the oral reading of a 42-word list. The test is discontinued after 10 pronunciation failures. The dependent measure was the number of correctly pronounced words.

Working memory

Digit Span subtest (WAIS-R) [45]. Each trial of this test (forward and backwards) consists of orally presented strings of random number sequences. In the digit span forward trial, the participants were instructed to repeat the string of digits in the same order in which they were presented by the examiner. In the digit span backwards trial, the participants were instructed to repeat the string of digits in the reverse order from which they were presented. The dependent measure was the number of the correct responses for each trial.

Episodic learning and memory

Hopkins Verbal Learning Task (HVLT) [46]. The HVLT is an auditory verbal memory test, where the experimenter orally presented a list of 12 words, each belonging to one of three semantic categories. The word list was repeated over three trials. After each trial, participants were asked to repeat as many words from the list as they could remember. Following a 20-minute delay from the third trial, participants were asked again to recall as many words from the list as they could remember. Following the delay, recognition was assessed by participants identifying the original 12 words from among 24 words read aloud. The dependent measure used was the total number of correct responses across the three trials.

Procedure

All participants were recruited by flyers posted at the University of Medicine and Dentistry of New Jersey (UMDNJ)/New Jersey Medical School, within the Kessler Medical Rehabilitation Research and Education Corporation (KMRREC), and throughout the local community. All recruitment and procedures were approved by the Institutional Review Board (IRB) and HIPAA compliance boards. Each participant signed an informed consent form approved by the IRB's of both KMRREC and UMDNJ prior to study participation. Each participant was tested individually in an environment free from distractions. The total time for each examination was approximately 60 minutes. All participants were paid for their participation.

Data analysis

Data analysis was completed in three stages: (1) descriptive analyses were performed to examine the TIADL performance scores, and the neuropsychological tests scores; (2) one-way analysis of covariance (ANCOVA) comparing TIADL and the neuropsychological tests between the two groups, with gender as a covariance, was performed;

(3) Pearson correlation coefficients were used to examine relationships between performance on the neuropsychological measures and performance of the TIADL in the MS group.

Results

Mean performance on the neuropsychological battery for both the MS and HC groups are presented in Table 2. The two groups differed significantly in performance on the SDMT ($F(2,31) = 10.07$; $P = 0.004$), and PASAT ($F(2,29) = 5.6$; $P = 0.02$), with the MS group showing significantly lower scores than the HC group (while controlling for group differences in gender via ANCOVA). No other group differences in neuropsychological performance and motor performance speed (TMT A) were significant.

Means and standard deviations on the TIADL and its subtests across the two groups are presented in Table 3. The total TIADL raw score for the MS group (mean = 27.4, SD = 15.7) was significantly greater than that of healthy participants (mean = 15.6, SD = 12.1) ($F(1,35) = 4.9$, $P = 0.03$). On the locating and reading ingredients on food cans (nutrition task), the MS group took significantly more time (with errors included as penalty) (mean = 12.1, SD = 8.7) to complete the task than the HC group (mean = 6.1, SD = 3.3) ($F(1,35) = 5.5$, $P = 0.02$). On the locating and reading instructions from a medicine bottle task, the HC group performed significantly faster (mean = 8.6, SD = 3.1) than the MS group (mean = 12.2, SD = 7.5) ($F(1,35) = 4.1$, $P = 0.05$). No significant group differences were observed for finding a phone number, coins – counting change, and locating food items on a shelf, of the TIADL.

A chi-square analysis was conducted to examine the number of errors committed in each group for each of the TIADL subtests. No significant differences were found in the number of errors MS participants made in each of the TIADL subtests in comparison to the HCs. Data for each subtest were-(1) communication: finding a number in a phone book (MS errors = 4; HC errors = 1, $P = 0.18$); (2) finance: counting change (MS errors = 2; HC errors = 1, $P = 0.52$); (3) nutrition: locating and reading ingredients from a can of food (MS errors = 4; HC errors = 1, $P = 0.18$); (4) shopping: locating items on a shelf filled with food items (MS errors = 1; HC errors = 1, $P = 0.74$); and (5) medicine: locating (MS errors = 1; HC errors = 1, $P = 0.74$).

To examine the relationship between TIADL scores and neuropsychological measures of processing speed, working memory and episodic learning and memory, Pearson product moment correlations were calculated between TIADL total raw score and its five subtests and the neuropsychological tests for the MS group. These correlations are presented in Table 4.

Statistically significant correlations were found between TIADL total score and measures of speed of information processing (Cancel H and TMT B-A). Significant correlations were also observed between several TIADL subtests (nutrition-locate and read ingredients on cans of food; shopping-locate food items on a shelf; medicine-locate and read medicine instructions), and scores obtained from speed of information processing tests. Thus, slowed information processing speed was associated with slower times and worse performance on the TIADL.

Discussion

The results of the present study demonstrated that persons with MS who suffer neuropsychological impairments in information processing speed, took significantly more time to complete tasks on

Table 2 Neuropsychological performance means scores by participants group while controlling for gender ($n = 35$)

Domain assessed	MS	Healthy controls	F	Eta2
Speed of information processing				
PASAT	112.7 ($n = 18$)	152.3 ($n = 14$)	10.0**	0.26
Cancel H	111.6 ($n = 18$)	68.4 ($n = 15$)	2.5	0.07
SDMT	50.1 ($n = 17$)	58.8 ($n = 13$)	5.6*	0.23
TMT B-A	58.5 ($n = 18$)	31.9 ($n = 15$)	2.2	0.08
Episodic learning-memory				
HVLT	27.5 ($n = 17$)	28.5 ($n = 15$)	0.39	0.02
Working memory				
Digit span forward	8.2 ($n = 18$)	8.6 ($n = 15$)	0.12	0.01
Digit span backward	6.1 ($n = 18$)	7.2 ($n = 15$)	1.9	0.07
Motor speed				
TMT A	33.0 ($n = 18$)	23.0 ($n = 15$)	2.8	0.09

*$P < 0.05$.
**$P < 0.01$.

Table 3 Analysis of covariance for the TIADL and its subtests score across the two groups with control for gender ($n = 35$)

	MS (mean ± SD) ($n = 18$)	Healthy adults (mean ± SD) ($n = 17$)	F	Eta2
TIADL raw scores	27.4 ± 15.7	15.6 ± 12.1	4.9*	0.20
Communication–finding phone number	80.4 ± 65.0	41.6 ± 40.5	2.1	0.07
Finances–counting change	24.3 ± 36.3	14.5 ± 27.2	2.1	0.12
Nutrition–locate and read ingredients on cans of food	12.1 ± 8.7	6.0 ± 3.1	5.5*	0.15
Shopping–locate food items on a shelf	7.8 ± 3.6	7.7 ± 5.5	1.2	0.10
Medicine–locate and read instructions	12.2 ± 7.5	8.5 ± 2.9	4.1*	0.14

*$P < 0.05$.

the TIADL relative to HCs. The number of errors observed among participants with MS did not differ significantly from HCs, suggesting that the groups' differences is due primarily to impaired processing speed in the MS group, and not a result of the errors they made during task performance. It is now well established that reduced processing speed is a major cognitive deficiency in persons with MS [12,16]. Thus, the present study is the first to show that processing speed may greatly influence deficits observed in actual tasks of everyday functional activities in MS. This finding is similar to that of Barker-Collo [35], who concluded the processing speed ability is related to reported quality of life. It is important to note, however, that Barker-Collo used a self-report measure of health related quality of life (SF-36) [47], and in the current study, an actual performance measure of IADL was used.

The findings of the current study further support the notion that processing speed is a critical variable which predicts functional ability. Salthouse [23], argues that processing speed can account for both: (1) other cognitive deficits, and (2) functional deficits. That is, processing speed is a basic cognitive building block, and can account for a significant amount of the variance accounting for deficits in higher cognitive functions in persons with MS which affect everyday functions and may require different levels of assistance in their daily lives [6,48–50]. Thus, processing speed is not just 'another area of cognition' that predicts functional deficits in MS–it is a fundamental element. Furthermore, these findings suggest that the TIADL is sensitive to functional impairments experienced by individuals with MS that relate to speed of information processing.

The present results showed significant group differences, primarily on two of the TIADL subtasks: nutrition and medicine tasks, indicating that it took the MS group significantly longer to complete these tasks. There are at least two potential explanations for the differential sensitivity of these two subtests on the TIADL. The first could be reading problems in the MS group, resulting potentially from visual acuity impairments. While visual acuity was not assessed in the current study, potential effects of impaired acuity were minimised, since participants who used glasses for reading were required to use them when needed while performing the TIADL tasks. In addition, participants were allowed to hold and manipulate the stimuli, affording them the opportunity to maximise their visual acuity. Lastly, no participant had significant difficulty reading the stimuli. The second possibility lies with the multi-dimensional nature of processing speed itself. It could be argued that the two tasks (nutrition and medicine: locating and reading medicine instructions and can ingredients) are more complex and require a greater number of cognitive domains relative to the other TIADL tasks. There is recent evidence showing that information processing speed may have distinct components related to the degree of cognitive involvement [11]. Stokx and Gaillard [51],

Table 4 The relationship between TIADL total and sub-tests scores with the neuropsychological tests scores for the MS group ($n = 18$)

	TIADL–total	TIADL–communication	TIADL–finances	TIADL–nutrition	TIADL–shopping	TIADL–medicine
PASAT	−0.27	−0.33	0.22	−0.19	−0.26	−0.56*
Cancel H	0.51*	0.31	0.17	0.51*	0.60**	0.93**
SDMT	−0.17	−0.22	0.13	−0.29	0.33	−0.35
TMT B–A	0.49*	0.31	0.13	0.46	0.56*	0.94**
HVLT	0.17	0.16	0.03	−0.06	0.08	0.24
Digit span forward	−0.15	−0.28	0.32	0.31	−0.24	−0.29
Digit span backward	−0.37	−0.36	0.04	−0.48*	−0.15	−0.30

*$P < 0.05$.
**$P < 0.01$.

concluded that slowed processing speed may affect every level of the information processing chain, and it is particularly evident in complex tasks under time pressure [52]. Thus, the extra cognitive effort required for the medicine and nutrition tasks may explain why these tasks were more sensitive to the cognitive deficits in processing speed experienced by the MS participants.

Kalmar *et al*. [53], examined the relationship between performance of an IADL test (executive functions performance test; EFPT) [54,55], and cognitive abilities in MS. These investigators found that processing speed was related to the higher-level cognitively demanding tasks of everyday life functioning (ie, medication management, paying bills and complex cooking task), but not tasks with lower-level cognitive demands (simple cooking task, making a phone call and washing hands). The work of Kalmar *et al*. [53], provides additional support to the findings that processing speed was related to tasks that require more cognitive processes, and the medicine and nutrition tasks may be the tasks most sensitive to processing speed difficulties.

The hypothesis that everyday functional ability in an MS sample can be related with neuropsychological indicators of basic processing speed was supported. Specifically, significant relationships were observed between performance of the TIADL and performance of processing speed tasks, such as the cancel H and TMT B-A. Performances on measures of processing speed typically include components of central processing or cognitive speed, as well as peripheral or motor speed [56]. Importantly, TIADL performance was not associated with cognitive measures related to episodic learning and memory or working memory.

While advancing our understanding of the nature of processing speed in MS and its relationship to IADLs, the present study has several methodological limitations. First, the sample size is small. Using larger samples will allow for statistical analyses which can further assess the relationships between the different cognitive domains/abilities and IADL performance. Second, while potential deficits in fine motor speed were controlled statistically using a test of motor speed (Trails A), and every attempt was made to control for gross motor difficulties, these motor influences during the manual operations required in the TIADL cannot be totally ruled out. By better accounting for fine and gross motor skill, future work may differentiate between motor and cognitive influences on TIADL performance. Likewise, the level of disability (EDSS) in the MS group was not assessed in this study, and it is unclear how overall disability level, like motor impairment, would affect the findings of the study. Third, the cognitive impairment in the current MS sample was limited primarily to deficits in information processing speed and efficiency. It is not clear how MS participants with more severe and a broader range of cognitive impairment would perform on the TIADL. Fourth, level of depressive symptomatology was not assessed in the current study. Earlier research studies have failed to consistently show a clear relationship between depressive symptoms and cognitive impairment in MS [57]. However, some recent work suggests that in MS information processing speed, working memory and executive functioning may be affected in individuals with moderate to severe depression, compared to those with more mild depression [58]. Therefore, future studies on processing speed and everyday life activity should include an assessment of depression. Finally, the TIADL is a functional test, which contains IADL tasks that have a relatively low cognitive load [33], and does not rely on higher level cognitive operations, such as problem solving and/or working memory. As such, the TIADL provides very specific (and easy) tasks related to processing speed *per se*, but may not generalise to other aspects of everyday life. Unfortunately, there are few structured IADL instruments whose construct validity adequately assesses actual (not self-report) real world functional activity [2], and so this criticism is more general than specific to the present study.

Despite limitations, the present study is the first study to relate processing speed impairments with actual performance of everyday life activity in individuals with MS. Considering the current emphasis on processing speed and its effect on outcome in individuals diagnosed with MS, the nature of the relationship of processing speed to outcome must be more clearly elucidated. The present study represents a first step in that direction.

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