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The temporal dynamics of visual processing in multiple sclerosis

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ABSTRACT

Although the integrity of the visual system is often affected in multiple sclerosis (MS), the potential relationship between the temporal dynamics of visual processing and performance on neuropsychological tests assessing processing speed (PS) remains relatively unexplored. Here, we test if a PS deficit is related to abnormalities within the visual system, rather than impaired higher-level cognitive function. Two groups of participants with MS (1 group with PS deficits and another without) and a healthy control group, matched for age and education, were included. To explore the temporal dynamics of visual processing, we used 2 psychophysical paradigms: attention enhancement/prioritization and rapid serial visual presentation. Visual PS deficits were associated with a decreased capability to detect visual stimuli and a higher limitation in visual temporal-processing capacity. These results suggest that a latent sensorial temporal limitation of the visual system is significantly associated to PS deficits in MS.

KEYWORDS

Multiple sclerosis; processing speed; visual system

Introduction

Multiple sclerosis (MS) is a disorder of the central nervous system, affecting approximately 2.1 million individuals worldwide (DeLuca & Nocentini, 2011). Processing speed (PS) deficits represent the most prevalent cognitive difficulty in persons with MS (Guimaraes & Sa, 2012) and have been shown to exert a negative impact on other aspects of cognition (e.g., Chiaravalloti, Stojanovic-Radic, & DeLuca, 2013) and quality of life (Glanz et al., 2010). PS can be defined as "the time required to execute a cognitive task or the amount of work that can be completed within a finite period of time" (e.g., DeLuca, 2008, p. 266). Research has demonstrated that when more time is provided to execute a cognitive task, participants with MS are able to achieve similar performance to that of healthy controls (HCs; Leavitt, Lengenfelder, Moore, Chiaravalloti, & DeLuca, 2011; Lengenfelder et al., 2006). The authors conclude that poor performance on such a task is related to the time participants need to execute the task (i.e., PS rather than the inability to perform the task [i.e., working memory]). The interaction between PS and both working memory and learning deficits in MS has been discussed within the Salthouse theory of "limited time mechanism" (Salthouse, 1996). This theory postulates that "the time to perform later operations is greatly restricted when a large proportion of the available time is occupied by the execution of early operations" (Salthouse, 1996, p. 404). This study draws upon this theory in an effort to enhance our scientific knowledge of the etiology of visual processing speed (VPS) deficits in MS by testing our hypothesis that early visual system abnormalities (lesions within areas responsible for the initial stages of visual processing) are the underlying cause of poor performance on VPS tasks (a latter operation measured by response accuracy and/or time to completion).

Abnormalities of the visual systems, such as internuclear ophthalmoplegia or optic neuritis, are quite common during the course of MS (Frohman, Frohman, Zee, McColl, & Galetta, 2005; Frohman, Graves, Balcer, Galetta, & Frohman, 2010; Maxner, 2006; Tilikete et al., 2011). Both the efferent (ocular-motor) and afferent (sensorial) visual systems are vulnerable to MS, leading to abnormal eye movements (Niestroy, Rucker, & Leigh, 2007) and visual functioning impairments (Burton, Greenberg, & Frohman, 2011). Despite the prevalence

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and impact of both PS deficits and visual abnormalities in MS, few studies to date have examined the relationship between vision and cognition in MS (White & Fielding, 2012). This is a critically important question due to the fact that our standard, widely accepted measures of PS used in MS are mostly visually based (for example, Symbol Digit Modalities Test [SDMT], Stroop test, etc.). Nevertheless, few studies controlled for or even examined the impact of visual problems on the execution of these tasks.

Three previous studies have shown a significant interaction between the visual system and cognition in MS. In all three studies, middle visual acuity problems were found to be associated with poor performances on neuropsychological tests (Bruce, Bruce, & Arnett, 2007; Davis, Hertza, Williams, Gupta, & Ohly, 2009; Feaster & Bruce, 2011). While previous studies have explored the relation between visual acuity and cognition, the present study aims to explore the temporal dynamics of visual processing as a cause for poor performance on the SDMT. It is well known that recognition of a visual stimulus becomes severely impaired at fast presentation rates, suggesting a limitation in the temporal-processing capacity of the visual system (McKeeff, Remus, & Tong, 2007).

The present study examines the hypothesis that PS deficits, as measured with the SDMT, are associated with putative sensorial visual system abnormalities (a higher temporal limitation of the visual system to process fast visual information). Our hypotheses were as follows: (a) Poor performance on the SDMT is not related to poor ability to execute the test. That is, participants are able to perform the cognitive task (match symbols with numbers accurately). (b) Individuals with PS deficits, as evaluated by the SDMT, show a significantly higher temporal limitation of the visual system. That is, their visual system is not able to process visual information as fast as that of HC and individuals with MS without PS deficits.

Materials and methods

Participants

Participants consisted of 18 individuals with clinically definite relapse-remitting MS (McDonald et al., 2001) and 9 HCs. The MS group was composed of 16 women and 2 men, and the HC group was composed of 7 women and 2 men. Before enrollment in the study, all participants signed a consent form approved by the Institutional Review Board of the Kessler Foundation. All participants were aged 25 to 55 years old. Individuals were excluded from the study if they reported a history of medical or psychiatric disorders that could substantially influence cognitive function. All participants with MS had at least 4 weeks since their most recent exacerbation and use of steroids, benzodiazepines, or neuroleptics.

Participants with MS were divided into two groups according to their performance on the oral version of the SDMT (Smith, 1982). Participants with MS who scored 1.5 standard deviations or more below the mean of the HC sample (Parmenter, Testa, Schretlen, Weinstock-Guttman, & Benedict, 2010) were included in the PS-impaired group ($N = 9$), whereas participants with MS performing within 1.5 standard deviations of the mean of the HCs were included in the unimpaired group (–PS intact; $N = 9$). As expected, performance on the SDMT for the three groups was statistically different, $F(2, 24) = 21.03$, $p < .001$. Individuals in the PS-impaired group performed worse than those in the PS-intact group (mean for the PS of the PS-impaired group = −2.61, SEM = 0.31; mean for the PS-intact group = −0.25, SEM = 0.26; $p < .001$) and the HCs (M = −0.07, SEM = 0.35; $p < .001$). Similar performance was observed on the SDMT for the MS PS-intact and HC groups (*ns*). The three groups did not differ on number of incorrect responses on the SDMT, $F(1, 25) = 0.51$, *ns*.

Demographic data are presented in Table 1. There were no statistically significant differences between the three groups for age, $F(2, 24) = 1.65$, *ns*; years of education, $F(2, 24) = 0.84$, *ns*; or estimated overall intelligence (as assessed by the Wechsler Test of Adult Reading-Third Edition), $F(2, 24) = 2.82$, *ns*. The two MS groups were not significantly different in the number of months since diagnosis, $t(16) = -0.3$, *ns*.

The Snellen High Contrast Vision Chart test revealed no significant differences between the groups for visual contrast sensitivity in either eye: right eye, $F(2, 23) = 1.206$, *ns*; left eye, $F(2, 23) = 1.839$, *ns*. Furthermore, the three groups did not differ in their capacity to perform basic visual-spatial orientation (Judgment Line Orientation Test; Benton, Sivan, Hamsher, Varney, & Spreen, 1994)), $F(2, 24) = 0.93$, *ns*. However, all participants in the PS-impaired group reported having had episodes of visual disturbances since their MS diagnosis, whereas only 33.33% (3) of the participants in the PS-intact group did so. Important to note, based on participant reports, none was suffering from a clinical significant visual disturbance during study participation. The participants from the HC group did not report any history of visual disturbances.

Experiment 1: Temporal order judgment task

A temporal order judgment task (Rorden, Mattingley, Karnath, & Driver, 1997) was used to assess whether

Table 1. Demographic information for participants.

	VPS-impaired ($N = 9$)	VPS-intact ($N = 9$)	Healthy controls ($N = 9$)	
	Mean (SE)	Mean (SE)	Mean (SE)	F
SDMT	−2.61 (0.31)	−0.25 (0.26)	−0.07 (0.35)	$F(2, 24) = 21.03$***
JLO	0.28 (0.34)	0.83 (0.23)	0.37 (0.33)	$F(2, 24) = 0.93$
WTAR-III	98 (5.87)	102.44 (3.24)	111.78 (2.77)	$F(2, 24) = 2.8$
Age (years)	39.33 (3.80)	45.44 (2.33)	38.56 (2.46)	$F(2, 24) = 1.65$
Years of education	14.78 (0.88)	14.56 (0.60)	15.78 (0.62)	$F(2, 24) = 0.84$
Acuity, left eye	47.78/20 (19.15)	30/20 (4)	22.5/20 (1.89)	$F(2, 23) = 1.839$
Acuity, right eye	26.67/20 (1.44)	35/20 (5.34)	26.88/20 (2.3)	$F(2, 23) = 1.206$

Note. The z scores are presented for the SDMT and JLO. VPS = visual processing speed; SDMT = Symbol Digit Modalities Test; JLO = Judgment of Line Orientation Test; WRAT-III = Wechsler Test of Adult Reading-Third Edition. *$p < .05$. **$p < .01$. ***$p < .001$.

abnormalities in the ability to process visual stimuli in the appropriate order (that is, correctly identify, from two stimuli, which came first) are related to PS deficits.

Apparatus and procedures

In this task (see Figure 1 for details), participants were presented with two black bars (one to the left and one to the right side of fixation at an identical eccentricity) on a white background. The bars were presented simultaneously or asynchronously, and participants were asked to report which bar appeared first (left or right) using a motor response as soon as the second bar appeared on the screen. The bars remained on the screen until a response was obtained to overcome potential motor slowness problems. The temporal lag (the stimulus onset asynchrony [SOA]) between the presentations of the two bars was manipulated so that the bars could be presented simultaneously or asynchronously. SOA varied between 0 ms and 250 ms, in temporal steps of 0 ms, 20 ms, 30 ms, 50 ms, 120 ms, 180 ms, and 250 ms (the refresh rate of the monitor was 100 Hz). By manipulating the lag between the two bars, we were able to control the amount of time available to process visual information. We sought to understand if individuals with MS with PS deficits require more time between visual stimuli to achieve the same accuracy as the other two groups, which would indicate that they need more time to process the visual stimulus.

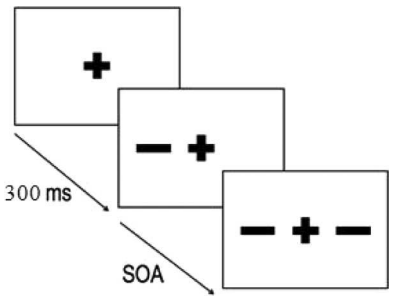

Figure 1. Temporal Order Judgment Task. A baseline fixation cross of 30 ms duration started at each run. The first bar then appeared, on the left or right side of the fixation cross, followed by the second bar. *Note*. SOA = stimulus onset asynchrony.

The experiment consisted of two blocks of 260 trials. Each block was composed of 20 repetitions of six right-bar-first SOAs and six left-bar-first SOAs, in addition to 20 trials with zero SOA (i.e., both stimuli are presented simultaneously). A break was provided between blocks. Participants were instructed to guess when uncertain, and although their responses were not timed, they were advised to respond as quickly as possible while maintaining maximum accuracy.

If PS deficits are associated with an abnormal capability to detect and process visual information, as we hypothesized, participants with PS deficits (PS-impaired group) will be impaired at judging the temporal order of two visual stimuli (accurately identifying which bar comes first) in contrast to HCs and persons with MS with intact PS (PS-intact group), as a function of time available between stimuli.

Data analyses

All statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) for Mac (Version 20) and Kaleidagraph 4.0 (Synergy Software). Accuracy was measured as a function of the percentage of correct responses by SOA for each participant and was collapsed across right and left SOAs. We calculated the SOA required for each participant to achieve 75% accuracy by fitting a probit function to the accuracy scores. The threshold (75%) in this study was obtained as a midway value between chance (50%) and maximal performance (100%). Finally, we calculated the slope of the fitted psychometric curve for each individual.

We performed one-way analyses of variance (ANOVAs) to analyze threshold and slope scores and test the ability of the three groups to detect and process visual information. As such, we contrasted the three groups on the SOA needed to achieve 75% accuracy and on the values of the slopes of the fitted psychometric curves. When significant results were found in the omnibus ANOVA test, post-hoc analyses using the LSD test were performed.

Results

Curve-fitting analysis. The psychometric curve (Figure 2) demonstrated a good fit to the data (PS-impaired group, $r = .92$, SEM = 0.03; PS-intact group, $r = .98$, SEM = 0.01; HC, $r = .98$, SEM = 0.01). A significant main effect of group was found for the 75% threshold, $F(2, 24) = 6.12$, $p < .01$. Post-hoc analyses revealed that the PS-impaired group needed a significantly higher SOA to achieve a 75% correct performance level ($M = 149.53$ ms, SEM = 25.56) in contrast with the other two groups (PS-intact group, $M = 80.9$ ms, SEM = 13.21, $p < .01$; and HC, $M = 71.83$ ms, SEM = 7.53, $p < .01$). No significant difference was noted between the PS-intact and HC groups (*ns*). Additionally, we found a significant negative correlation between performance on the SDMT and the 75% threshold ($r = -.75$, $p < .001$), which indicates that participants with poor performance on the SDMT needed higher SOA to achieve 75% correct responses on the temporal order judgment.

A significant main effect of group was noted for the slope of the psychometric curve, $F(2, 24) = 4.34$, $p < .03$. The slope was less steep for the PS-impaired group ($M = 0.01$ correct/ms, SEM = 0.02) compared with the HC group ($M = 0.02$ correct/ms, SEM = 0.005; $p < .01$), but not in contrast with PS-intact group ($M = 0.02$ correct/ms, SEM = 0.002; *ns*). The psychometric slopes for the PS-intact and HC groups were not significantly different, $t(24) = 1.65$, *ns*.

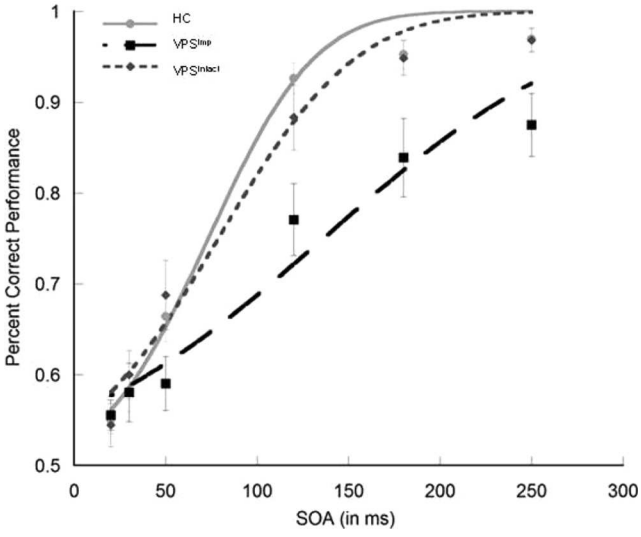

Figure 2. Temporal Order Judgment Task. Percent correct performance is plotted as a function of stimulus onset asynchrony (SOA). Lines correspond to fitted data using the probit function for each group. The solid line corresponds to fitted data from participants in the healthy control (HC) group. The short dashed line corresponds to fitted data from the participants in the visual processing speed-intact (VPS^{intact}) group. The large dashed line corresponds to fitted data from participants in the VPS-impaired (VPS^{imp}) group. Actual data from the HC, VPS^{imp}, and VPS^{intact} groups are presented as a circle (●), a square (■), and a diamond (◆),respectively.

Discussion for experiment 1

Participants with MS with PS deficits (PS-impaired group) performed significantly worse on the temporal order judgments task compared with HCs and the MS group without PS deficits (PS-intact group). The PS-impaired group required longer SOAs to achieve comparable accuracy levels to those of the other groups. Differences were also observed for the slope of the psychometric curve. The HC group presented steeper slopes when compared with the PS-impaired group, suggesting that HC participants required larger steps of SOA to achieve higher accuracy levels than those of the participants with MS with PS deficits. These results likely reflect compromise in the ability to detect and/or temporally process visual information by the PS-impaired group. The present data confirm our hypothesis that individuals with MS with PS deficits are impaired in their ability to judge the temporal order of two visual stimuli. Thus, individuals with MS with PS deficits need more time to process visual information, in contrast to individuals with MS without PS deficits and HCs.

Experiment 2: rapid serial visual presentation

Humans can quickly and accurately recognize briefly flashed stimuli (Thorpe, Fize, & Marlot, 1996). Nevertheless, temporal-processing capacity is limited, and visual recognition can become severely compromised at fast presentation rates (McKeeff et al., 2007). Behavioral studies using the rapid serial visual presentation (RSVP) paradigm within populations of healthy adults with normal or corrected-to-normal visual acuity consistently reveal that visual recognition begins to fail at presentations of 8 items to 10 items per second and declines sharply at faster presentation rates (McKeeff et al., 2007; McMains & Somers, 2004; Potter, 1975). In this paradigm, sequences of pictures are presented at different temporal rates (e.g., as defined by the number of items presented per second) and participants are required to detect a particular target.

In Experiment 2, we used an RSVP task (McKeeff et al., 2007) to investigate the temporal-processing capacity in MS. More specifically, we sought to understand whether potential limitations in visual temporal-processing capacity (which is the amount of time a person needs to accurately perceive a visual stimulus) might be related to PS deficits.

Apparatus and procedures

An RSVP paradigm was adapted from McKeeff et al. (2007). In each experimental trial (see Figure 3), participants viewed stimulus sequences of faces and houses presented at varying temporal rates of 52 ms, 104 ms, 156 ms, 208 ms, and 390 ms per image (19.23 Hz, 9.62 Hz, 4.8 Hz, 2.56 Hz, and 0.16 Hz, respectively; monitor frame rate used was 75 Hz). No blank period or visual mask was presented between the successive images.

The trial sequence began with a fixation-baseline period of 500 ms. Then two target images (a face and a house) were presented, one on each side of fixation, for 5,000 ms, followed by the presentation of the sequence of visual stimuli. Each trial finished when the participants provided a response. The sequence of visual stimuli consisted of a randomly generated sequence of distractor images, selected from the two semantic categories (houses and faces). One of the target images (the face stimulus on 50% of trials and the house stimulus on the other 50% of trials) was introduced at a random position within the sequence provided that it was not presented in the first position or the last position. At the end of each trial, participants were asked to report which of the two target images appeared in the sequence by pressing one of two keys on the computer keyboard. The experiment consisted of three blocks of 50 trials each (five repetitions of each combination of stimulus type and temporal rate). The order of the presentation rate and target identity were counterbalanced across blocks.

We hypothesized that the PS-impaired group would show greater PS limitations—namely, worse performance in the ability to recognize a visual stimulus (accurately identify which image was presented in sequence) as a function of the presentation rate—compared with the participants in the PS-intact and HC groups.

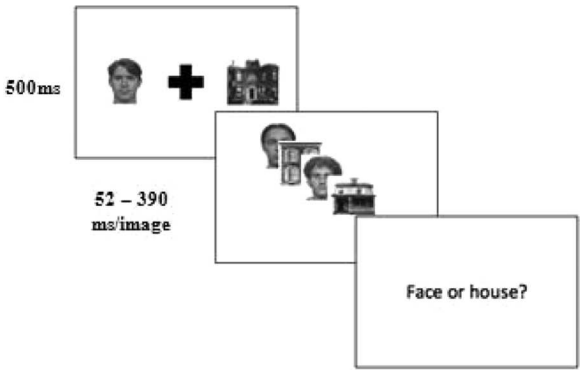

Figure 3. Rapid serial visual presentation procedure. Each run started with a fixation-baseline period, followed by 5,000 ms of the two-target image presentation. The stimulus block consisted of a randomly generated distractor image sequence, presented with variable temporal rates. Each run ended with a question where participants reported the target image that appeared in the stimulus sequence.

Results

In total, five participants (one HC, three from the PS-impaired group, and one from the PS-intact group) were excluded from the analyses because they did not achieve levels of accuracy greater than 65% even for the slowest presentation rate. The data were analyzed as in Experiment 1.

Curve-fitting analysis. The psychometric curves obtained demonstrated a satisfactory fit to the data (PS-impaired group, $r = .89$, SEM = 0.2; PS-intact group, $r = .78$, SEM = 0.05; and HC group, $r = .79$, SEM = .05). A significant main effect of group was found for the 75% threshold, $F(2, 19) = 4.1$, $p = .03$. Post-hoc analyses demonstrated that the PS-impaired group required significantly higher SOAs and hence slower temporal rates to achieve a 75% correct performance ($M = 304.99$ ms/image, SEM = 45.43) when compared with the PS-intact group ($M = 140.40$ ms/image, SEM = 45.95; $p = .02$) and HC group ($M = 156.05$ ms/image, SEM = 35.51; $p = .03$). Furthermore, the PS-intact and HC groups did not differ in the temporal rate required to achieve a 75% threshold (*ns*; Figure 4). No significant main effect of group was found for the slope of the psychometric curve (*ns*). Furthermore, poor performances on the SDMT were correlated with higher SOAs to achieve a performance of 75% correct responses on the RSVP ($r = -.57$, $p = .01$).

Discussion for experiment 2

In the present study, the recognition performance for both the HC and PS-intact groups began to decline, on average, at 156 ms/image and 140 ms/image, respectively, and at rates similar to that observed by others (McKeeff et al., 2007). In contrast, accuracy levels for the PS-impaired group were compromised, with threshold performance occurring at a far slower presentation rate (305 ms/image). This was significantly different from what was obtained for the two remaining groups. The results are consistent with our hypothesis and suggest that PS deficits are associated with a higher limitation in the temporal-processing capacity of the visual system. Because participants are still able to achieve high levels of performance, albeit at longer SOAs, the difficulty participants with MS have with the task appears to be related to a temporal limitation of the visual system to process a briefly presented stimulus, rather than with an impaired capacity to perform a recognition task or process visual information.

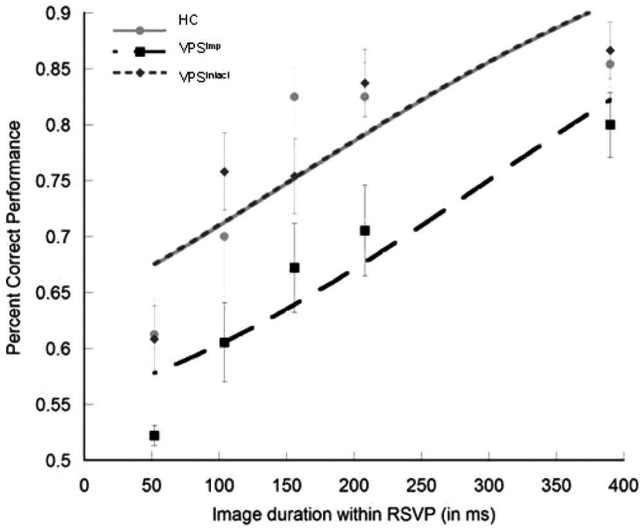

Figure 4. Rapid serial visual presentation (RSVP). Percent correct performance is plotted as a function of stimulus onset asynchrony. Lines correspond to fitted data using the probit function for each group. The solid line corresponds to fitted data from participants in the healthy control (HC) group. The short dashed line corresponds to fitted data from participants in the visual processing speed-intact (VPS^{intact}) group. The large dashed line corresponds to fitted data from participants in the VPS-impaired (VPS^{imp}) group. Actual data from the HC, VPS^{imp}, and VPS^{intact} groups are presented as a circle (●), a square (■), and a diamond (◆), respectively.

General discussion

The present study demonstrates that poor performance on the SDMT, commonly categorized as a PS deficit, in MS is associated with a temporal-processing limitation in the (sensory) visual system. As hypothesized, poor performance on the SDMT (i.e., PS) was associated with a higher temporal limitation of the visual system rather than a higher-level cognitive deficit.

In Experiment 1, we used the temporal order judgment task and showed that participants with MS with PS deficits demonstrated a significant decrease in the sensitivity to detect and process temporal visual information. Participants with MS with PS deficits (as assessed with the SDMT) demonstrated significantly poorer task performance compared with individuals with MS without PS deficits and HCs. Previous studies, using neuropsychological tasks measuring simple reaction times (Reicker, Tombaugh, Walker, & Freedman, 2007) and attentional processes (Kavcic & Scheid, 2011) among populations with MS, have shown that PS deficits are related to abnormalities in the capacity to detect visual information. The findings of the present study are consistent with these results and go further, supporting the notion that the abnormal capacity to detect visual stimuli could be the result of a sensorial visual processing deficit and not due to other nonsensorial factors, such as deterioration in motor performance or a cognitive deficit. The temporal order judgment task had, as a major strength, the capacity to provide a direct index of the potential delays of the visual system generated without the regular confounds resulting from the more motoric processes involved in masking a speeded response. The present study shows an association between poor performance on the SDMT and a delay of the visual system, with preserve ability to execute the task, as shown by an equal number of incorrect responses on the SDMT between the three groups.

In Experiment 2, the RSVP method was used. It was shown that participants with MS with VPS deficits require significantly slower presentation rates to perform as accurately as the other two groups. Once again, the problem seems not to be an impaired capacity to perform the task, because participants were able to perform the recognition task at higher SOAs, but rather, poor performance appears to be due to a greater limitation of the visual system to process visual information quickly.

Together, our experiments provide evidence that individuals with MS and PS deficits are able to accurately perform cognitive tasks; however, they do need more time to reach the same level of performance as HCs or individuals with MS with intact PS abilities. Our results directly associate this delay in individuals with PS deficits to a higher temporal limitation of the visual system.

The present results are in line with previous studies (Chiaravalloti et al., 2013; Genova et al., 2012; Leavitt et al., 2011; Lengenfelder et al., 2006) in demonstrating that individuals with PS deficits are able to perform recognition tasks or process visual information. No differences were found between groups on total number of incorrect responses on the SDMT or performance on the Judgment of Line Orientation Test. Thus, execution of the task is intact. However the PS-impaired group was significantly slower in response time. It is important to note that results do not seem to be related to abnormal visual acuities (i.e., Snell test). The present study furthers our understanding of PS deficits in MS by demonstrating an association between poor performance on a VPS task and an impaired temporal-processing dynamic of the visual system.

In summary, individuals with poor performance on the SDMT, often characterized as having a PS deficit, showed a higher temporal limitation of the visual system; in other words, the visual system needed more time to process the stimulus. Therefore, if more time is needed to execute an initial operation of information processing (process the stimulus), less time is left to execute the cognitive task (pair symbols with numbers), resulting in

poor performance on VPS tasks, such as the SDMT. The results support our hypothesis that PS deficits in MS are related to visual system compromises, instead of a high-order cognitive dysfunction. The present results highlight the need for future research to explore the integrity of the visual system as a potential cause of poor performance on VPS tasks, such as the SDMT. Recently supporting the idea that visual system integrity is important for the performance of visual tasks, Toledo et al. (2008) demonstrated that poor performance on the SDMT was associated with decreases in the retinal nerve fiber layer in MS. Laatu, Revonsuo, Hamalainen, Ojanen, and Ruutiainen (2001) similarly demonstrated that individuals suffering from MS with cognitive deficits also present abnormalities at early stages of visual and semantic processing. Although vulnerability of the visual system in MS is generally accepted in the MS literature, effects on the performance of visual neuropsychological tests remain poorly understood. Important to note, while the present study and previous research performed by others have shown an association between the integrity of the afferent visual system and performance on the SDMT, the impact of efferent visual system disturbances on the performance of the SDMT is unknown. In future studies, researchers should try to understand how different visual system disturbances impact performance on the SDMT.

Although the current study represents a significant advance in our understanding of PS deficits in persons with MS, it suffers from some methodological limitations that limit the conclusions that can be drawn. First, it is important to note that we have a small sample size. The current study should be replicated with larger sample sizes to test the stability of the findings and increase the generalizability of the results. Second, the PS measures utilized were solely visual measures, and we were therefore unable to examine the observed effect across sensorial domains. For future studies, it would be of major importance to include auditory measures of PS to understand differences between sensorial domains. Third, the SDMT has a strong ocular motor component that should, in future studies, be studied or controlled. Future studies should include VPS tasks with a lower ocular motor component. Despite these limitations, the current study represents a major advance in our understanding of the possible etiology of PS deficits in MS. Future research is necessary to further delineate this relationship and identify potential treatments for this very common deficit in persons with MS.

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