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Computerized Neuropsychological Battery Detects Cognitive Impairment Differences between Relapsing Remitting and Secondary Progressive Multiple Sclerosis Patients

Lambros Messinis, Nikolaos Dimisianos, Athanasios Paphathanasiou, Grigoris Nasios & Panagiotis Paphathanasopoulos

Abstract

CNS Vital Signs (Gualtieri & Johnson, 2006), is a computerized neuropsychological test battery that was developed as a routine clinical instrument. It is comprised of seven cognitive tests: verbal and visual memory, finger tapping, symbol digit coding, the Stroop test, a test of shifting attention and the Continuous performance test. These tests yield 5 cognitive domains: composite memory, psychomotor speed, reaction time, complex attention and cognitive flexibility. In the present study, we compared the cognitive abilities of multiple sclerosis patients with relapsing remitting (RRMS) and secondary progressive (SPMS) subtypes and healthy controls, utilizing the CNS Vital Signs neuropsychological battery. We found differences in frequency and severity of cognitive impairment between RRMS and SPMS patient groups. Further, we demonstrated that the CNS Vital Signs is sensitive in detecting cognitive decline in MS patients and also noted cognitive impairment differences between RRMS and SPMS patients. The observed clinical group differences in the present study reflect the fact that patients with SPMS have more widespread brain damage, specifically, diffuse pathology in normal-appearing white matter and gray matter injury.

Key words: CNS Vital Signs, neuropsychological battery, Cognition, Relapsing Remitting Multiple Sclerosis, Secondary Progressive Multiple Sclerosis

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Introduction

The functional consequences of cognitive impairment in Multiple Sclerosis (MS) patients can be devastating and cognitive impairment has a direct impact on health-related quality of life during all stages of the disease process (Mitchell et al., 2005). MS reduces physical independence and social activities (Rao et al., 1991), competence in daily activities (Goverover et al., 2007), personal and community independence (Amato et al., 1995), medication adherence (Bruce et al., 2010), rehabilitation potential (Langdon & Thompson, 1995) and driving safety (Marcotte et al., 2008). Cognitive impaired MS patients are also more likely to be unemployed, while employed MS patients are more cognitively preserved (Honarmad et al., 2011).

Large studies of MS patients have reported cognitive impairment prevalence rates of between 40 and 70% (Chiaravalloti & De Luca, 2008; Rao et al., 1991). Impairment in cognition has been demonstrated during all stages and in all subtypes of the disease (Clinically Isolated Syndrome - CIS, Relapsing Remitting Multiple Sclerosis – RRMS, Secondary Progressive Multiple Sclerosis - SPMS, Primary Progressive Multiple Sclerosis - PPMS and benign MS) (Potagas et al., 2008. Langdon, 2011), however, more severe cognitive impairment tends to occur in the progressive subtypes (Denney, Sworowski & Lynch, 2005) and especially the primary progressive subtype (Ruet et al., 2013). Although almost all types of cognitive deficits can be observed in MS (Prakash et al., 2008), the typical profile is deficits in information processing speed, memory and often executive function, with relative preservation of language (Messinis et al., 2009; Chiaravalloti & De Luca, 2008).
There is also large interpatient variability in the pattern and severity of cognitive deficits in MS. In an effort to explain this variability, investigators have recently addressed the question of cognitive reserve (CR), which is gained through life experience i.e., intellectually enriching leisure activities and education level. Both years of education and reading level improved predictions of cognitive decline over a five year period (Benedict et al., 2010). It has been suggested that cognitive reserve relies on a default network, involving the anterior and posterior cingulated cortices (Sumowski et al., 2010). Further, brain reserve (BR) which was established by examining the maximal lifetime brain volume (MLBV) of MS patients, protected against cognitive inefficiency (Sumowski et al., 2013).

Another important issue involves MS patients self report of cognitive impairment, which although important clinically, is unlikely to be related to objective cognitive test performance, but rather associated to depression. On the other hand, relative’s reports of patient’s cognitive function are more likely to be reliable (Kinsinger, Lattie & Mohr, 2012).

Cognitive status is typically only partially related to disease duration (Smestad et al., 2010) and physical disability (Amato et al., 2010), although larger studies have shown significant relations (Lynch, Parmenter & Denney, 2005). Cognition can also predict future disease progression as cognitive status at the Clinically Isolated Syndrome (CIS) event stage predicts conversion to MS (Zipoli et al., 2010) and cognitive status at diagnosis of MS predicts accumulation of physical disability (Deloire et al., 2010).

Cognitive impairment is correlated with brain abnormalities as visualized by various MRI techniques. These studies have demonstrated that neuropsychological performance correlates with T2 and T1 weighted white matter lesions as well as lesions
in gray matter visualized by inversion recovery pulse sequences; brain atrophy as measured in whole brain volume, gray matter volume, brain parenchymal fraction, ventricular diameter and callosal area; and microscopic pathology as visualized by magnetization transfer, diffusion tensor and proton spectroscopy in both lesions and normal appearing brain tissue (Fillipi et al., 2010).

Computerized neuropsychological test batteries represent a viable method for rapidly screening cognition and have demonstrated comparable results to traditional neuropsychological batteries in detecting cognitive impairment in various patient groups including mild cognitive impairment (Gualteri & Johnson, 2005), mood disorders (Iverson et al., 2011), pediatric neurologic disorders (Brooks & Sherman, 2012) and multiple sclerosis (Messinis, Anyfantis, Lyros & Paphathanasopoulos, 2009). Further, cognitive decline in relapsing remitting multiple sclerosis patients with low disability status has been detected utilizing a computerized neuropsychological battery (Messinis, Anyfantis, Paschali, & Paphathanasopoulos, 2009).

In the present study we investigated cognitive function in a Greek sample of adult multiple sclerosis patients and further aimed to designate possible differences in the cognitive profile between MS patients with relapsing remitting (RRMS) and secondary progressive (SPMS) subtypes, utilizing a computerized neuropsychological test battery, CNS Vital Signs™, Chapper Hill (Gualtieri & Johnson, 2006). We hypothesized, based on our previous preliminary research, clinical experience with MS patients and the international literature that (a) patients with SPMS would have more extensive cognitive dysfunction than patients with RRMS and (b) both RRMS and SPMS patients would have more severe cognitive decline relative to the demographically matched healthy control participants (c) the overall prevalence of cognitive impairment would be higher in the SPMS group.
Methods

Participants

Fifty eight patients with MS, diagnosed according to the Mc Donald criteria (McDonald et al., 2001), were evaluated at the neuropsychology unit, Department of Neurology, University of Patras Medical School, in Greece. Patients were classified as RRMS (n=36) and SPMS (n=22). Patients with acute relapse during the last three months, on corticosteroids or on other medications that could interfere with cognition, learning disabilities, visual deficits, motor involvement of the upper limb, major psychiatric illness, other neurological diseases and non native Greek speakers were excluded from the study. Expanded Disability Status Scale score (Kurtzke, 1983) was obtained from each patient by thorough neurological examination. In addition, twenty three healthy control participants were recruited. Exclusion criteria for the control sample included non native Greek speakers, visual deficits, learning disabilities, psychiatric or neurological disorder, history of brain injury, cardiovascular illness, medication use that could interfere with cognitive performance, drug and alcohol consumption. MS patients were further assessed with the Beck Depression Inventory Fast screen (BDI-fastscreen) (Beck, Steer, & Brown, 2000) in order to exclude major depression as a concomitant factor that could interfere with cognitive performance. The BDI fast screen is a 7-item self – report case-finding instrument that screens for severity of depression that corresponds to the psychological or nonsomatic criteria for diagnosing major depression disorders as listed in the DSM-IV-TR (APA, 2000) in adults and adolescents. It consists of seven items extracted from the 21-item Beck Depression Inventory – II (Beck, 1996). The administration procedure used was the one
suggested by (Beck et al., 2000) using a Greek translated and adapted version (Messinis & Papathanasopoulos, 2006) with Cronbach’s internal reliability coefficient (a = 0.84)

All participants provided written informed consent to participate in the study, which was approved by the Ethics Committee of the University of Patras. Table 1 shows demographic (age, education, gender distribution) and clinical (EDSS, disease duration, BDI-FS) characteristics of patients and controls.

**Neuropsychological assessment**

CNS Vital Signs (Gualtieri & Johnson, 2006), a recently developed computerized neuropsychological battery which also provides a Greek adapted language version was used to investigate cognitive performance of the MS patients. This battery provides core neuropsychological assessment utilizing seven neuropsychological tests. A brief description of each measure is presented below followed by a description of the primary domain scores.

The first of these tests, the *Verbal Memory Test* involves learning immediate and delayed recognition for 15 words. These words (drawn from a reservoir of 100 words) are presented, individually, on a computer screen every two seconds. For the immediate recognition trial, the participant has to identify those words nested among fifteen new words. Then, after been assessed with the remaining six tests (approximately 30 minutes duration), there is a delayed recognition trial. The same paradigm is followed for the *Visual Memory Test*, which measures recognition memory for figures (immediate and delayed recall), drawn from a reservoir of 45 designs.

For the *Finger Tapping Test*, participants are asked to press or tap the space bar with their index finger (separately for right and left hands) as many times as they can for
a period of 10 seconds, over 3 trials, with a preceding practice trial. The scores produced are the average number of taps for the right and left hands. This test examines psychomotor speed and fine motor control.

The **Symbol Digit Coding Test** assesses information processing - psychomotor speed, complex attention and visuo-perceptual speed. The participant is required to type in numbers that correspond to 8 different symbols presented on the screen (drawn from a reservoir of 32 symbols). Scoring is the number of correct and incorrect responses generated in 2 minutes.

The **Stroop Test** examines executive function, simple and complex reaction time, information processing speed, psychomotor speed and inhibition- disinhibition. It contains 3 parts that involve responding to words and colors. In the *first* part the words RED, YELLOW, BLUE and GREEN (which are written in black color on the computer screen), appear randomly on the screen and the participant presses the space bar as soon as the word is seen. In the *second* part the words appear on the screen printed in color. The participant is asked to press the space bar when the color of the word matches what the word says (e.g., the word RED printed in red ink) but not responding when the color of the word does not match what the word says (e.g., RED printed in blue ink). In the *third* part, the participant is asked to press the space bar when the color of the word does not match what the word says (e.g., RED printed in blue ink) but not responding when the color of the word matches what the word says (e.g., RED printed in RED ink). Scores include simple reaction time (part1), complex reaction time (parts 2 and 3), and a commission error score (part3).

The **Shifting Attention Test** examines executive function, reaction time, psychomotor and information processing speed. It is a measure of the ability to shift from one instruction set to another quickly and accurately. Participants are instructed to
match geometric objects either by shape or by color. The participant is asked to match 1 of 2 bottom figures to a figure at the top of the screen based on 1 of 2 rules that are presented (e.g., “match to shape” or “match to color”). The test continues in this manner for 90 seconds. Shifting Attention Scores include correct matches, errors, and response time.

The Continuous Performance Test is a measure of vigilance and sustained attention. The participant is asked to respond to the target stimulus “B” but not to any other letter while stimuli are presented randomly for 5- minutes. Scoring is correct responses, commission errors, omission errors, and choice reaction time.

The CNS Vital Signs Domain scores which are normed, similar to traditional IQ scores, with a mean standard score (SS) of 100 and a standard deviation (SD) of 15, are derived by combining 18 subtest scores from the 7 measures. Low scores in clinical practice or research can be defined in several ways, such as (a) more than 1 standard deviation (SD) below the mean (i.e., < 85 SS), (b) below the 10th percentile (i.e., < 81 SS), (c) at or below the 5th percentile (i.e., ≤ 76 SS), and (d) more than 2 SDs below the mean (i.e., < 70 SS). Normative data for this battery is provided in Gualtieri & Johnson, (2006), who indicate that random selection of the stimuli used in testing help reduce practice effects on repeated testing. The measures have adequate test – retest reliability, adequate concurrent validity with traditional paper and pencil measures and other computerized tests, and the domain scores have been shown to discriminate between various clinical groups (Iverson et al., 2011).

Correct responses from the verbal and visual memory tests provide Verbal Memory and Visual Memory domains scores, respectively, as well as the Composite Memory domain score. The total of right and left taps from the Finger Tapping Test and the total correct responses on the Symbol Digit Coding Test generates a composite score.
for Psychomotor Speed. Averaging the 2 complex reaction time scores from the Stroop Test generates a domain score for Reaction Time, which can be considered as measuring information – processing speed in a test of executive function. The number of correct responses on the Shifting Attention Test, minus the number of errors on the Shifting Attention Test and the Stroop Test, is used to create a domain score for Cognitive Flexibility. The domain score for Complex Attention is generated by adding the number of errors committed in the Continuous Performance Test, the Shifting Attention Test, and the Stroop Test. The overall summary score, called the Neurocognition Index, is the average of the domain scores.

**Statistical Analyses**

Statistical analyses were performed with the SPSS package (Release 20.0). Group comparisons for demographic and clinical characteristics were analyzed by means of one-way ANOVA (age, education, disease duration, BDI-FS), independent – samples Mann-Whitney U test for rank data (EDSS score) and the Pearson chi square ($X^2$) test was used to compare gender distribution. Between - group differences for neuropsychological variables were analyzed with a series of analyses of covariance (ANCOVAs). Demographic and clinical variables that differed across the groups were included as covariates in all analyses. Bonferroni corrected $p$ values were used to interpret significance when multiple comparisons were performed. We also calculated the proportion of participants impaired on individual CNS Vital signs neuropsychological test domains. We further calculated the Cohen $d$, as a measure of the effect sizes (magnitude of mean differences in SD units). Effect sizes are interpreted either as small ($d =0.2$), medium ($d=0.5$), or large ($d \geq 0.8$) (Cohen, 1988).
Results

Comparison of the demographic and clinical data

Relapsing remitting MS patients were younger and had lower EDSS scores than the SPMS patients. Disease duration was also longer for the SPMS group, compared with RRMS. There were no significant gender distribution differences or differences in years of education between groups. Further, the MS groups did not differ in severity of depression (see Table 1). Due to the significant differences found between the groups on the confounding variables age, EDSS and disease duration these variables were statistically controlled through analysis of covariance (ANCOVAs) in further analyses.

| Table 1: Demographic and clinical characteristics of patients and controls: mean (SD) |
|---------------------------------|-------------------------------|----------------|------------------|
|                                  | RRMS                          | SPMS            | Controls         | Significant differences |
| N                                | 36                            | 22              | 23              |                      |
| Age (years)                      | 40.65 (2.55)                  | 47.80 (5.65)    | 40.25 (10.60)   | RRMS < SPMS          |
| Education (years)                | 12.20 (3.50)                  | 12.65 (3.25)    | 12.80 (1.20)    | ns                   |
| Gender (% M/F)                   | 24.5 / 75.5                   | 28.7 / 71.3     | 40.5 / 59.5     | ns                   |
| EDSS                             | 3.150 (.750)                  | 6.180 (.625)    | -               | RRMS < SPMS          |
| Duration illness                 | 8.60 (3.95)                   | 14.90 (4.85)    | -               | RRMS < SPMS          |
| BDI-FS                           | 7.72 (3.95)                   | 7.84 (3.87)     | -               | ns                   |

RRMS = Relapsing Remitting Multiple Sclerosis; SPMS = Secondary Progressive Multiple Sclerosis; Significant differences determined by one-way ANOVA (age, education, disease duration, BDI-FS) independent – samples Mann-Whitney U test for EDSS; Pearson ($X^2$) test for gender; Significant at the $p < .05$ level
Neuropsychological performance

A series of (ANCOVAs) controlling for age, EDSS and duration of illness were carried out in order to determine whether there were significant differences between the three groups (RRMS, SPMS, Controls) in each cognitive domain of the CNS Vital Signs neuropsychological battery. Table 2 provides mean scores and standard deviations obtained by the groups in each cognitive domain and the significant differences noted in the performance of the multiple “post hoc” comparison tests.

Table 2: Neuropsychological test performance of patients with RRMS, SPMS and healthy controls: mean (SD)

<table>
<thead>
<tr>
<th>Domain</th>
<th>RRMS</th>
<th>SPMS</th>
<th>Control</th>
<th>RRMS vs. SPMS</th>
<th>RRMS vs. Control</th>
<th>SPMS vs. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Memory</td>
<td>90.95 (9.50)</td>
<td>83.40 (9.35)</td>
<td>92.70 (10.85)</td>
<td>.045*</td>
<td>.062</td>
<td>.026*</td>
</tr>
<tr>
<td>Psychomotor Speed</td>
<td>126.55 (25.30)</td>
<td>104.26 (26.84)</td>
<td>142.36 (23.25)</td>
<td>&lt;.001**</td>
<td>.023*</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>Reaction Time</td>
<td>810.42 (160.25)</td>
<td>885.59 (114.76)</td>
<td>710.65 (90.65)</td>
<td>.002*</td>
<td>.017*</td>
<td>.002*</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>18.45 (9.62)</td>
<td>12.25 (6.78)</td>
<td>32.72 (11.70)</td>
<td>.015*</td>
<td>.016*</td>
<td>.004*</td>
</tr>
<tr>
<td>Complex Attention</td>
<td>15.80 (9.57)</td>
<td>18.25 (7.20)</td>
<td>12.62 (5.60)</td>
<td>.020*</td>
<td>.002*</td>
<td>.008*</td>
</tr>
</tbody>
</table>

Values are mean (SD) domain scores for the CNS Vital signs neuropsychological battery; RRMS = Relapsing Remitting Multiple Sclerosis; SPMS = Secondary Progressive Multiple Sclerosis; Significant differences p < .001 **, p < .05 *

For Composite memory, Psychomotor Speed, and Cognitive Flexibility domains, higher scores indicate better performance. For Reaction time and complex attention domains lower scores indicate better performance.
We found a significant main group effect for the *composite memory* domain ($F_{2, 80} = 7.305; p = .0004$). Post hoc multiple comparisons indicated differences between the RRMS and SPMS group, with the progressive subtype having lower performance than the relapsing remitting patients and between the SPMS group and controls, where the healthy participants performed better. On the contrary, the RRMS group did not differ significantly from the controls on this domain. We further found main group effects for the psychomotor speed ($F_{2, 80} = 0.115; p < .0001$), reaction time ($F_{2, 80} = 6.052; p = .0011$), cognitive flexibility ($F_{2, 80} = 9.031; p < .0001$) and complex attention domains ($F_{2, 80} = 16.908; p = .0008$). Post hoc multiple comparisons indicated differences between the SPMS and RRMS groups, the SPMS group and controls and the RRMS group and controls on the *psychomotor speed, reaction time, cognitive flexibility and complex attention* domains. Specifically, the secondary progressive MS patients performed substantially lower than both the RRMS patients and the healthy participants on all previously mentioned domains (see Table 2).

Large effect sizes were present when the SPMS patients were compared to controls on composite memory, psychomotor speed, reaction time and cognitive flexibility and a medium effect size was present for complex attention. When RRMS patients were compared to controls, large effect size were found for reaction time, psychomotor speed and cognitive flexibility, with a small effect size noted for complex attention. Comparison of the two clinical groups indicated large effect sizes only for composite memory, while psychomotor speed and reaction time had medium effect
sizes. Small effect sizes were noted for cognitive flexibility and complex attention between the clinical groups (see Table 3).

Table 3: Effect sizes (Cohen $d$) for differences between MS subgroups and between healthy controls and MS subgroups controlling for (age, EDSS and duration of illness)

<table>
<thead>
<tr>
<th></th>
<th>RRMS vs. SPMS</th>
<th>RRMS vs. Control</th>
<th>SPMS vs. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Memory</td>
<td>.85</td>
<td>-</td>
<td>.85</td>
</tr>
<tr>
<td>Psychomotor Speed</td>
<td>.62</td>
<td>.97</td>
<td>1.52</td>
</tr>
<tr>
<td>Reaction Time</td>
<td>.52</td>
<td>1.05</td>
<td>.96</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.48</td>
<td>.91</td>
<td>.87</td>
</tr>
<tr>
<td>Complex Attention</td>
<td>.30</td>
<td>.38</td>
<td>.59</td>
</tr>
</tbody>
</table>

Effect sizes are interpreted either as small ($d=0.2$), medium ($d=0.5$), or large ($d \geq 0.8$)

Prevalence of cognitive dysfunction

We also recorded the proportion of RRMS and SPMS patients impaired on each specific domain of the CNS vital signs neuropsychological battery. Various studies have used several different impairment criteria, depending on whether the authors were interested in assessing subtle or more severe forms of impairment. In the present study,
we examined the proportion of impairment on specific cognitive domains using as criterion for impairment $1.5$ standard deviations (S.D) below the control group mean. Our overall prevalence rate of cognitive dysfunction was $51.72\%$ (30/58 MS patients). For the proportion of MS patients impaired on specific cognitive domains of the CNS vital signs neuropsychological battery refer to (Table 4).

Table 4: Proportion of MS patients impaired on specific cognitive domains of the CNS vital signs neuropsychological battery

<table>
<thead>
<tr>
<th></th>
<th>RRMS ($n=36$)</th>
<th>SPMS ($n=22$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Memory</td>
<td>6 (16.6%)</td>
<td>9 (40.1%)</td>
</tr>
<tr>
<td>Psychomotor Speed</td>
<td>8 (22.3%)</td>
<td>14 (63.6%)</td>
</tr>
<tr>
<td>Reaction Time</td>
<td>21 (58.3%)</td>
<td>17 (77.4%)</td>
</tr>
<tr>
<td>Complex Attention</td>
<td>9 (25.0%)</td>
<td>8 (36.4%)</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>10 (27.8%)</td>
<td>13 (59.0%)</td>
</tr>
</tbody>
</table>

Discussion

Computerized neuropsychological batteries comprise one option for providing assessment of cognitive abilities and appear to have adequate psychometric properties compared to traditional paper-and-pencil measures. The aim of the present study was to demonstrate performance on the CNS Vital Signs computerized test battery in relapsing remitting and secondary progressive multiple sclerosis patients in a district Greek population of Western Greece. To our knowledge, this is the first study in Greece to demonstrate that CNS Vital Signs has the potential to detect cognitive impairment differences between patients with relapsing remitting and secondary progressive multiple sclerosis. To date, evidence that the CNS Vital Signs can detect cognitive
impairment in Greek MS patients was provided in a preliminary study by Messinis, Anyfantis, Lyros & Papathanasopoulos, (2009), however, this study did not compare relapsing remitting and secondary progressive patients.

The overall prevalence of cognitive dysfunction in our patients was 51.72 %, thus in accordance with the estimated prevalence of previous studies that ranged from 40 to 70% (Chiaravalloti & De Luca, 2008). Our results also confirmed previous data that cognitive deficits are more frequent and pronounced in chronic progressive MS and tend to worsen over time (Denney, et al., 2005; Filippi et al., 2010).

The largest proportion of impaired RRMS patients was found in reaction time (58.3%). We further found lower percentages of impaired RRMS patients in cognitive flexibility (27.8%), psychomotor speed (22.3%) and composite memory (16.6%). It thus appears from this study that the cognitive domain mostly affected in our impaired RRMS patients is processing speed as demonstrated by the significantly low reaction time. With regards the SPMS patients, the highest percentages of cognitive impairment were detected in reaction time (77.4%), psychomotor speed (63.6%) and cognitive flexibility (59.0 %), with lower percentages found in composite memory and complex attention. Thus, secondary progressive MS patients demonstrate significantly low reaction (processing speed) time and psychomotor speed, which is further complicated by cognitive flexibility deficits, in essence, executive dysfunction.

Information processing speed refers to the rate at which cognitive processes can be executed (Krail & Sanan, 1994). Two types of processing speed (PS) have been discussed in the literature. Simple PS is the amount of time needed for simple attentional tasks and complex PS, is the amount of time necessary to process more complicated tasks (Chiaravalloti et al., 2003). There is a clear association between working memory (executive function) and processing speed, suggested by some authors
in the sense that working memory deficits, especially early in the course of multiple sclerosis are mainly due to deficits in processing speed (De Luca et al., 2004). The authors discuss this notion in terms of two models. The Relative Consequence Model suggests that patients' fundamental slowing of PS affects their abilities to perform other cognitive tasks, while The Independent Consequence Model suggests that deficits in working memory-executive function are independent of impaired PS. In another study, authors assess information processing speed mainly by evaluating reaction time (Brett et al., 2007). Traditionally the most widely used tests of processing efficiency and speed in MS are the Paced Auditory Serial Addition Task (PASAT) and the Symbol Digit Modalities Test (SDMT) (Langdon, 2011; Parmenter et al., 2007).

In the present study, we used the CNS Vial Signs computerized battery that utilizes a computerized form of the SDMT, providing our group with the opportunity to accurately and automatically quantify a ‘speed factor’ via multiple parameters such as reaction time, psychomotor speed and processing speed. As noted above, our results indicated that reaction time is the most frequent cognitive deficit in both RRMS and SPMS patients. Further, psychomotor speed deficits were identified in a significant proportion of SPMS patients and although also found in some (22.3%) of RRMS patients, comparison between RRMS and SPMS group revealed significant differences with a medium effect size indicating its prominence in the progressive stages of multiple sclerosis. Similar predominance in SPMS patients, but with a small effect size was found in cognitive flexibility and complex attention, in keeping with previous studies (Piras et al., 2003).

Our findings are in accordance with previous studies suggesting that the most frequently affected cognitive domains in MS patients are that of executive function and
processing speed, followed by episodic memory (verbal and visual) (Potagas et al., 2008; Messinis et al., 2010).

Regarding the utilization of a computerized neuropsychological battery in the present study, some issues need to be raised. Traditional paper-and-pencil neuropsychological test batteries are usually time consuming and often require qualified clinical neuropsychologists to be administered. Furthermore, they need additional time to evaluate the results and lack of alternate forms may minimize practice effects which in turn negatively affect serial testing over time. Further, traditional neuropsychological tests are not ideally suited to detect reduction of psychomotor and information processing speed as well as reaction time (Piras et al., 2003). On the contrary, computerized batteries have demonstrated comparable results to traditional neuropsychological batteries (Wilken et al., 2003; Akbar et al., 2011). The CNS Vital signs neuropsychological battery that utilizes computerized forms of traditional tests such as the Symbol Digit Modalities Test (SDMT) and the Stroop test could provide the non-neuropsychologist clinician with a reliable screening tool for detecting cognitive deficits in RRMS and SPMS patients.

However, cognitive assessment with computerized batteries does have several limitations. First of all there are multiple-choice formats and a definite reliance on the visual modality. There are many potential sources of error in computerized neuropsychological assessment including use of various configurations and operating systems. In addition, there is provision of less qualitative information compared with the traditional pencil-and-paper tests as well as limited assessment of each cognitive domain. Finally the participants must be familiar with computers (Woo, 2008; Cernich et al., 2007).
Future studies utilizing face to face parallel testing by traditional paper and pencil tests versus computerized neuropsychological assessment will be of great interest in order to address the efficacy of computerized neuropsychological tests in detecting cognitive impairment in multiple sclerosis patients.

In conclusion, the main finding of our study is the difference in frequency and severity of cognitive impairment between RRMS and SPMS patient groups. Further, we demonstrated that the CNS Vital Signs computerized neuropsychological battery is sensitive in detecting cognitive decline in multiple sclerosis patients and also noted cognitive impairment differences between RRMS and SPMS patients. The observed clinical group differences in the present study reflect the fact that patients with SPMS have more widespread brain damage, specifically, diffuse pathology in normal-appearing white matter and gray matter injury.

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Λάμπρος Μεσσήνης, Νικόλαος Δημησιάνος, Αθανάσιος Παπαθανασίου, Γρηγόριος Νάσιος & Παναγιώτης Παπαθανασόπουλος

Περίληψη

Η συστοιχία δοκιμασιών CNS Vital Signs (Gualtieri & Johnson, 2006), αποτελεί μια ηλεκτρονική συστοιχία νευροψυχολογικών δοκιμασιών που αναπτύχθηκε για τακτική κλινική χρήση. Αποτελείται από επτά γνωστικές δοκιμασίες: λεκτική και οπτική μνήμη, δοκιμασία ταχών κινήσεων δακτύλου, αντιστοίχηση συμβόλων γραμμάτων, δοκιμασία Stroop, μια δοκιμασία μετατόπισης της προσοχής και μια δοκιμασία συνεχούς προσοχής. Οι δοκιμασίες αυτές διαμορφώνουν 5 γνωστικά πεδία: μνήμη, ψυχοκινητική ταχύτητα, ταχύτητα αντίδρασης, σύνθετη προσοχή και γνωστική ευελιξία. Στην παρούσα μελέτη συγκρίναμε τις γνωστικές λειτουργίες ασθενών με τη υποτροπία και δευτεροπαθή προοδευτική μορφή σκλήρυνση κατά πλάκας και φυσιολογικά άτομα με τη χρήση της συστοιχίας δοκιμασιών CNS Vital Signs. Τα ευρήματα μας ανέδειξαν διαφορές στη συχνότητα και σοβαρότητα των γνωστικών ελλειμμάτων μεταξύ των δύο κλινικών ομάδων. Επιπλέον, από τα δεδομένα μας φάνηκε ότι η συστοιχία δοκιμασιών CNS Vital Signs είναι ευαίσθητη στην ανίχνευση γνωστικών ελλειμμάτων σε ασθενείς με σκλήρυνση κατά πλάκας και στη διάκριση γνωστικών διαλειτουργιών μεταξύ ασθενών με υποτροπία και δευτεροπαθή προοδευτική μορφή σκλήρυνσης κατά πλάκας. Οι παρατηρήσεις αυτές στην παρούσα μελέτη μπορούν να ενσωματωθούν σε ερευνητικές και πειραματικές σειρές με σκοπό να επιλύσουμε τις αναγκαίες ερωτήσεις σχετικά με την διάχυτη παθολογία της λευκής ουσίας και την εφικτότητα προστασίας της στην σκλήρυνση κατά πλάκας.

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Λέξεις ευρετηρίου: CNS Vital Signs, συστοιχία νευροψυχολογικών δοκιμασιών, γνωστικές, υποτροπίζουσα μορφή σκληρύνσης κατά πλάκας, δευτεροπαθής προοδευτική μορφή σκληρύνσης κατά πλάκας