

A New Approach to Visuospatial Dysfunction in Multiple Sclerosis

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Abstract

Multiple Sclerosis (MS) is said to result in visuospatial (VS) dysfunction. However, it may be that tests normally used to assess VS function require support of other processes, such as executive functions (EF). Therefore, poor performance on these tests does not necessarily reflect VS dysfunction in MS. This study attempted a preliminary investigation into physical, cognitive, and affective factors prevalent in MS that may confound VS task performance. Six MS participants were compared with six posterior right hemisphere (RH) stroke patients (known to primarily experience VS deficits), and six healthy controls (HC) on relevant VS measures. It was hypothesized that (1) RH participants would perform statistically significantly more poorly than HC on all VS tasks, while MS participants would only produce significantly weaker results on more complex tests; (2) MS participants would perform poorly on Judgement of Line Orientation, NEPSY Block Construction, Rey-Osterrieth Complex Figure, and Stick Test, and not on Benton's Facial Recognition Test; and (3) MS participants would produce significantly weaker scores on these tests for confounding reasons. Group performance on VS tasks was compared using one-way analysis of variance. Results from this South African sample demonstrated that RH participants produced significantly poorer results than HC on all VS measures, while MS participants were only significantly weaker on 3/5 measures (JLO, BC and ST). In light of the small sample size, trends pertaining to the confounding variables were analysed by way of descriptive statistics. These results should be interpreted with caution, but appear to tentatively suggest that VS performance of the MS group was affected by impaired EF, while the RH group may have been influenced by visual deficits. Further research with larger samples should explore the potentially erroneous attribution of MS patients' poor performance on VS tasks to primary VS impairment.

Keywords: Multiple Sclerosis; visuospatial dysfunction; executive function; neuropsychology

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A New Approach to Visuospatial Dysfunction in Multiple Sclerosis

The presence of cognitive deficits in multiple sclerosis (MS) has been documented extensively over many years. Specifically, the claim that visuospatial dysfunction is common in MS has been made repeatedly. However, this may misrepresent the nature of cognitive impairment in MS, with significant implications.

Multiple Sclerosis

MS is a chronic, inflammatory disease in which an autoimmune response is thought to attack the central nervous system, resulting in demyelination of white matter (Romano, Caltagirone, & Nocentini, 2012b). Recent studies indicate this neurodegenerative disorder also affects grey matter and venules (Hurley, Taber, Zhang, & Hayman, 2009; Romano et al., 2012b). However, reduction of the myelin sheath, resulting axonal damage, and formation of white matter plaques are still regarded as the primary features of MS (Romano et al., 2012b).

The course and symptoms of MS are highly variable (Romano, Caltagirone, & Nocentini, 2012a) as the disease affects a range of central nervous system structures such as the cerebral cortex, cerebral white matter, optic nerve, subcortical structures, and spinal cord (Diaz-Olavarrieta, Cummings, Velazquez, & de al Cadena, 1999). Thus, people with MS experience a variety of (1) physical symptoms, such as weakness, sensory disturbance, pain, fatigue, incontinence, ataxia, tremors, and visual impairment (Koch, Mostert, Heersema, & De Keyser, 2007; Romano et al., 2012a); (2) neuropsychiatric disorders, such as depression and bipolar mood disorder (Nocentini, Romano, & Caltagirone, 2012b); and (3) cognitive deficits (Diaz-Olavarrieta et al., 1999; Gilad, Sadeh, Boaz, & Lampl, 2006; Leavitt et al., 2014; Nocentini, Romano, & Caltagirone, 2012a; Sartori & Edan, 2006). Primary features of cognitive dysfunction are said to be attention, speed of information processing, memory, learning, executive function (EF), and visuospatial (VS) function (Nocentini et al., 2012a). This study questions the latter claim.

Visuospatial Function

The domain of VS function encompasses a multitude of processes involving both visual and spatial abilities, rather than operating as a single cognitive function (Banich & Compton, 2011) and includes *inter alia* constructional skills, object and facial recognition, spatial integration, spatial orientation, localising objects in space, understanding spatial relations and angles, and organising visuospatial material (Banich & Compton, 2011; Halpern & Collaer, 2005; Zillmer, Spiers, & Culbertson, 2008). Execution of these processes requires multiple

neural networks, including areas of the occipital, temporal, and parietal lobes, especially posterior right-hemisphere structures (Nobre et al., 1997; Zillmer et al., 2008).

Despite numerous neural mechanisms supporting VS ability, two neural pathways are crucial (Tversky, 2005; Zillmer et al., 2008). These are conceptualised as the ventral visual system, broadly pertaining to visual aspects of VS functioning, and the dorsal visual system, broadly responsible for spatial elements (Banich & Compton, 2011; Zillmer et al., 2008). The ventral system is concerned with higher aspects of visual cognition such as recognition and discrimination between objects, and is thought to course from the primary visual cortex in an antero-ventral direction, encompassing multiple regions of the occipital and temporal lobes (Banich & Compton, 2011; Zillmer et al., 2008). From the primary visual cortex, as well as the somatosensory cortex and vestibular system, visual information is also propagated to the posterior parietal cortex, which has connections with frontal regions, and this is known as the dorsal visual system (Banich & Compton, 2011). This system is associated with localising objects in space, understanding spatial relations, and coordinating movement with this information (Zillmer et al., 2008). These VS processes are primarily governed by the right hemisphere of the brain, but are assisted by the left hemisphere (Banich & Compton, 2011; Nobre et al., 1997). The importance of these two visual systems can be illustrated by the variety of visuospatial deficits that arise as a result of damage to the different mechanisms.

Visuospatial Dysfunction in Multiple Sclerosis

VS disturbance is frequently reported in MS (see, for instance, Amato, Zipoli, & Portaccio, 2008; Gilad et al., 2006; Longoni et al., 2015; Nocentini et al., 2012a; Saxena et al., 2013; Smerbeck et al., 2011; Wishart & Sharpe, 1997), although functions traditionally associated with the left hemisphere (such as language) are rarely disturbed (Nocentini et al., 2012a), despite the fact that there is no evidence to suggest MS preferentially affects the right hemisphere. A seminal study with stringent exclusionary criteria found that patterns of VS deficits in MS patients are common, diverse, highly variable between patients, and may result in profound impact on everyday functioning (Vleugels et al., 2000). In other words, there is no unitary VS variable resulting in a single pattern of impairment, but rather, myriad deficits may arise in multiple combinations in the VS domain (Vleugels et al., 2000).

An imperative element to consider when interpreting these studies, however, is that many tasks used for VS assessment may rely on the integrity of other cognitive processes. In light of this, it is important to consider which tests are appropriate to assess VS dysfunction

in MS patients. A number of confounding variables frequently associated with MS may thus have bearing on tests designed to assess VS dysfunction. For instance, depression has been found to affect MS patients at a higher rate than the general population (Nocentini et al., 2012b), and this neuropsychiatric condition has been associated with global declines in cognitive abilities (Auning et al., 2015), which may therefore act as a confound when assessing cognitive function in MS patients. Another factor potentially exerting a widespread suppressive effect over test performance is attentional deficits, which are commonly documented in MS (Nocentini et al., 2012a). Impairment in this domain may undermine the sustained attention required to complete a test battery, and lead to poor performance on VS tasks. Additionally, speed of information processing, commonly affected during the course of MS (Genova, DeLuca, Chiaravalloti, & Wylie, 2013), may influence performance on time-based VS tasks. Furthermore, physical symptoms associated with MS, such as visual difficulties and motor deficits (Koch et al., 2013a; Romano et al. 2012a), may hinder VS assessment tasks, which assume integrity of these functions.

In addition to this, a number of studies (see, for instance, Longoni et al., 2015; Sartori & Edan, 2006; Vleugels et al., 2000) claim their results indicate diminished VS functioning in the MS population, but use tests such as the Wechsler Abbreviated Scale of Intelligence (WASI) Block Design Test, Rey-Osterrieth Complex Figure (ROCF), and Matrix Reasoning Test, which all require, and indeed are often used to test, EF (Jefferson et al., 2006; Zillmer et al., 2008). In addition, although not used as a test of EF, EF has also been implicated in the JLO, which is commonly used to assess VS dysfunction in MS (Ehler, 2012). It has been suggested that intact visual and spatial abilities are necessary, but not sufficient for certain VS tasks, thus requiring the support of EF (Logie & Della Salla, 2005), which are also impaired in MS (Genova et al., 2013; Leavitt et al., 2014; Pepping, Brunings, & Goldberg, 2013; Phillips et al., 2014; Preston, Hammersley, & Gallagher, 2013). EF can be conceptualised as the necessary abilities for directing, controlling, managing, and guiding behaviour; they include initiating behaviour, generating and maintaining goals, set-shifting, inhibition, abstraction and conceptual thought, inferring and following rules, cognitive flexibility, judgement and decision-making, generativity, and planning (Banich & Compton, 2011; Zillmer et al., 2008). A number of these skills may be essential for adequate performance on tests intended to measure VS function. It is the association between confounding factors and VS performance that requires special investigation.

Given the above, it is possible that participants perform poorly on VS tests for two reasons: either (1) diminished VS abilities result in poor performance on these tasks despite other functions remaining intact, and participants obtain low scores due to primary VS impairment; or (2) deficits in EF (or other confounding domains) in the absence of VS deficits may result in similarly poor performances, which cannot be attributed to primary VS dysfunction.

A paucity of data regarding the relationship between potential confounding factors (such as EF) and VS dysfunction in MS patients is available in neuropsychological literature. It is essential that these domains be considered when interpreting the results of VS tests. Only then will it be possible to determine whether MS specifically results in VS dysfunction.

Rationale, Aims, and Hypotheses

Despite consensus in the literature purporting MS patients experience VS dysfunction, there is a scarcity of research investigating the precise basis of this claim. This study investigated three hypotheses. Due to the fact that posterior right-hemisphere stroke (RH) pathology is typically associated with relatively pure VS deficits that include both perceptual and constructional impairment (Zillmer et al., 2008), the first hypothesis was that RH participants would perform poorly on all VS measures, while MS participants would perform poorly only on complex tests of VS function. Secondly, it was predicted that MS participants would perform poorly on the JLO, ROCF, Developmental NEUROPSYCHOLOGICAL Assessment (NEPSY) Block Construction (BC), and Stick Test (ST). Finally, it was hypothesized that MS participants would perform more poorly on these tests due to confounding influences of impairments in EF (JLO and ROCF) and other functions such as motor dexterity (BC, ST, and ROCF). This was investigated through a comparison of a various test results of a group of MS patients to those of posterior RH patients and healthy controls (HC).

This research, which forms part of a larger study investigating cognitive and affective sequelae of MS, is significant, as potential effects of confounding variables on VS testing in MS has not previously been explored. This is the first study of its kind to provide even a preliminary investigation of the potentially misconstrued deficits of MS patients. The contributions this study will make include the potential to stimulate research regarding the neurodegenerative process and cognitive profile of MS, which may lead to practical applications, such as the ability to inform clinical management and rehabilitation of MS.

Methods

Design

A quasi-experimental design was employed to collect quantitative data from participants with pre-existing neurological conditions (Cozby & Bates, 2012). In order to compare scores across MS, RH, and HC participants, each participant was only tested at one time, using a cross-sectional design. This design was chosen to examine currently existing deficits, as opposed to investigating changes over time (Cozby & Bates, 2012).

Sample

As this research investigates certain patient populations, namely MS and RH, non-probability sampling techniques such as purposive sampling were required (Cozby & Bates, 2012). The ongoing and new research required English-speaking South African participants. MS and HC groups had already been recruited for the aforementioned larger study. Due to time constraints, this research made use of data previously collected from these groups and compared it to a RH sample recruited specifically for this investigation. The final sample size was 18, with six participants in each group. All groups were matched on the basis of age, gender, race, and a socio-economic status (SES) composite of highest level of education and income. This was implemented because EF (one of the focal issues of this research) varies according to factors such as age and highest level of education obtained (Dorbath, Hasselhorn, & Titz, 2013).

MS group. Participants for this group were recruited via Multiple Sclerosis South Africa (MSSA) and from neurologists in private practice in the Western Cape. Subjects required a confirmed MS diagnosis, personally verified by their neurologist. From 60 participants previously collected for the larger study, six eligible participants were selected through matching to the RH group on the aforementioned criteria. Ideally, exclusion on the basis of other medical conditions would have been applied, but due to scarcity of eligible participants, this was not viable. However, none of the selected six participants had a medical history of any conditions that may impact cognition, such as additional autoimmune diseases or neurological conditions (i.e. lupus erythematosus, epilepsy, HIV, brain tumour, dementia diagnosis).

HC group. A limitation in neuropsychological testing in South Africa is the lack of norms for this population. The use of an HC group in this study was an attempt to control for the lack of relevant norms, and provide a benchmark against which patient samples could be measured. HCs were initially recruited to match the larger MS group through convenience

sampling; primarily snowball sampling via other participants. Six participants from this larger sample were selected to match MS and RH groups on the aforementioned factors in order to confidently attribute differences to the criterion being measured. In addition to this, eligibility required participants had no medical conditions that could affect cognitive function.

RH group. RH participants were recruited through various avenues in South Africa, such as neurologists, neuro-occupational therapists, physiotherapists, and neuropsychologists in private practice, as well as from Groote Schuur Hospital (GSH), Headway, and personal contacts.

Participants were excluded if they were left handed; experienced a stroke in fewer than three months prior to testing; or if they had neural pathology affecting areas other than the posterior right hemisphere. The final sample size for this group was six (see Limitations section for a discussion of other avenues pursued in attempts to increase this sample size). As with the MS group, factors pertaining to medical history were noted, and no participants were affected by prior medical conditions that may have bearing on cognitive function.

Procedures

Relevant professionals were contacted to enquire whether they had treated any RH patients who may be eligible for this study. If so, they were contacted by their practitioner and asked if they would consent to being contacted for the study. Patients were contacted via telephone or e-mail to provide them with information regarding the research and an invitation to participate. For patients where there was no provision for a practitioner to contact the patient (for example, from GSH), either the researcher or supervisor contacted them and invited them to take part. If they agreed, an interview was scheduled.

Most interviews were conducted in the participants' homes, or in a quiet room provided by their practitioner/organisation, at their convenience. Upon arrival, RH participants completed a demographic information questionnaire (see Appendix A). Participants were required to sign an informed consent form (see Appendix B), indicating voluntary participation in the research. This form was read to participants, and an extra copy was provided for them to keep. Participants completed 10 standardised tests during the interview. These were administered to each participant in the same order, in an attempt to standardise the procedure as much as possible. The order of the tests was selected in such a way that EF and VS measures were intermingled, so as to avoid sequence effects such as fatigue biasing the results towards the cognitive domain first tested.

Following testing, participants took part in a short debriefing session, were thanked and given the opportunity to ask any questions, and were given a pamphlet with information about common neuropsychological symptoms following RH strokes (see Appendix C). Each test was scored according to respective scoring instructions at a later stage (i.e. not in the participant's presence). Scores were analysed upon completion of all clinical interviews.

Measures

The nature of this study required particular measures allowing for examination of VS and confounding factors. For this reason, it was decided to reject the use of a full battery of tests in favour of selecting a number of specific tests. In addition to the aforementioned questionnaire detailing participant characteristics and potential exclusionary conditions, the following measures were used:

Visuospatial Measures. Five standardised tests were used to assess VS functioning of each subject. With regards to the research hypotheses, the only test used to assess simple VS skills was Benton's Facial Recognition Test (BFRT). More complex tasks that may be influenced by confounding factors were also included, some of which are frequently used to test VS function in MS.

Benton's Facial Recognition Test (BFRT). The BFRT (Benton, Sivan, Hamsher, Varney, & Spreen, 1994a) is used to measure the ability to recognise faces from multiple viewpoints. Each trial depicts a real human face, which must be matched to one of a sample of faces. The test becomes more complex as participants proceed to matching the exemplar to three faces from the sample, which show faces at different angles. Performance was measured by total correct facial matches. The test has been found to have a one-year retest correlation of .60 (Lezak, Howieson, Bigler, & Tranel, 2012).

The Developmental NEUROPSYCHOLOGICAL Assessment (NEPSY) Block Construction (BC). The BC is a subtest of the NEPSY test battery (Korkman, Kirk, & Kemp, 2007), which has been praised for impressive scores of reliability in both internal and test-retest categories, as well as concurrent validity (Brooks, Sherman, & Strauss, 2009). The BC assesses VS and visuomotor ability through the building of structures from blocks that must match a two-dimensional representation of the target structure. Performance was measured by total correctly constructed models within the time limits.

Judgement of Line Orientation Test (JLO). The JLO (Benton, Sivan, Hamsher, Varney, & Spreen, 1994b) assesses VS perception through matching the orientation and angles of two lines in space to eleven numbered lines that form a semicircle on an adjacent

page. Total score was calculated from the amount of correctly matched lines. The JLO possesses high levels of internal and re-test reliability (Lezak et al, 2012).

Rey-Osterrieth Complex Figure (ROCF). The ROCF (Rey, 1941; Osterrieth, 1944) assesses various neuropsychological functions. To assess participants' constructional ability, participants are required to copy a geometric figure, which provides evidence of perceptual disturbances such as neglect or visuoconstructional impairment. Interrater reliability for this test boasts a value of .91 (Lezak et al., 2012). The number of correctly drawn elements measures 'constructional ability', as per Canham, Smith, & Tyrrell (2000)'s scoring method. In order to provide a reliable score, the researcher and two other raters independently scored each participant's ROCF drawing and the mean score was used. Intraclass correlation analyses demonstrated a correlation coefficient of $> .90$, indicating excellent interrater reliability in this study.

Stick Test. In the rotation trial of this test (Butters & Barton, 1970), the subject is required to mentally rotate and construct a pattern of sticks made by the interviewer, assessing visuospatial judgement, constructional, and rotational abilities. This test was scored by total correctly rotated patterns. The copy trial, in which the participant directly copies the pattern of sticks, was administered as a baseline condition. Unfortunately, data regarding the reliability and validity of this test is not available, despite extensive use of this test in clinical practice.

Confound Measures. A series of tests was administered to assess confounding variables that may influence participants' performance on VS tasks. Although attention and speed have been identified as potential factors that may affect MS functioning, measures for these domains were not included. This decision was made on the basis of a lack of significant differences between MS and HC participants in the larger study on these factors, (attention: $t(81) = 1.576$; $p = .119$; and speed: $t(93) = -1.862$; $p = .066$) in conjunction with the attempt to reduce the amount of variables for consideration in light of the small sample size and the necessity to limit the scope of this study.

Motor Dexterity. Motor functioning was assessed through observation of participants, and personal enquiry as to whether participants felt they had deficits in motor skills, including paralysis, tremors, sensory deficits, and muscle weakness. Participants were scored on one of three levels (i.e. no motor impairment; some motor impairment, such as tremors or weakness; or major motor impairment, such as hemiparesis). As no participants demonstrated minor motor impairment, scoring was reduced to a dichotomous classification

of either demonstrating a motor deficit or not being affected by motor impairment.

Depression. The Beck Depression Inventory Fast-Screen II (BDI-FS; see Appendix D) (Beck, Steer, & Brown, 2000) consists of seven Likert-type questions ranging from zero to three and was administered to determine potential depressive mood in participants. This test has been found appropriate for patient populations with physical illnesses (Smarr & Keefer, 2011). Participants indicated their score based on their mood in the two weeks prior to the interview, and these scores were totaled to measure depression.

Visual Acuity. The Rosenbaum Pocket Screener (RPS; never published), a test of near vision, was used to assess visual acuity of participants. Participants covered one eye and were asked to read a series of number sets decreasing in size. Each of these number sets corresponded with a level of vision (i.e. 20/20, 20/40, etc.), and the value for the smallest number set correctly read (i.e. best visual acuity) was recorded for each participant. This was repeated with the other eye. On the recommendation of an optometrist, the score of the vision of the strongest eye was used, as this works as a compensatory mechanism for the weaker eye (S. Moodley, personal communication, September 22, 2015). The denominator of each visual acuity score was used to code this data, and it should be noted that a higher denominator denotes weaker vision.

EF composite. Four tests were used to assess different elements of EF. Standardised results from these tests were used to create an EF composite.

Controlled Oral Word Association Test (COWAT). The COWAT (Benton & Hamsher, 1989) tests generative ability and verbal fluency. Participants provided as many words as possible beginning with an indicated letter within one minute without using proper nouns, numbers, and the same word with a different suffix. The test has been found to have high levels of test-retest reliability (0.84) and excellent interrater reliability, as well as adequate levels of construct validity (Lezak et al., 2012; Spreen, 1991). Performance was measured through total number of suitable words generated across three letter conditions (letters “F”, “A”, and “S”).

Delis-Kaplan Executive Function System (D-KEFS). Two subtests of the D-KEFS battery (Delis, Kaplan, & Kramer, 2001) were used to assess different domains of EF. The Colour Word Interference Test (CWIT), a measure of inhibition and set shifting, consists of words of colours, printed in different colour ink. Participants completed two baseline conditions by naming coloured blocks and reading words printed in black ink. They then (third condition) stated the ink colour of each word (instead of reading the word), and (fourth

condition) switched between naming the ink colour of the printed words and reading words encased by a block, which are interspersed throughout this condition. This is reported to have test-retest reliability values of .90, .83, and .91 for each part of the test (Spreeen, 1991). An inhibition score was derived from the time-based score where the colour-naming task was taken into account. A set-shifting score was derived from the time-based score where the two baseline trials were taken into account. A measurement of error score was also included for the inhibition and set-shifting trials. All scores were converted to age-appropriate scaled scores as per the D-KEFS manual.

The second subtest, the Sorting Test (ST), assesses abstraction through the ability to sort six cards (of different colours and shapes, with different words printed on them) into categories, forming two groups of three cards per group. The participant must explain why they have divided the cutouts in such a way, and must develop as many grouping methods as possible. Only the self-initiated trial was used; thus excluding the recognition condition of the test. The D-KEFS has been highly rated on measures of construct validity and test sensitivity of EF (Delis, Kramer, Kaplan, & Holdnack, 2004). An age-appropriate scaled-score equivalent was calculated from the raw number of correct sorts across the two trials.

Rey-Osterrieth Complex Figure (ROCF). The ROCF (Rey, 1941; Osterrieth, 1944) copy trial was also used to assess the planning ability of participants, via the scoring method outlined by Anderson, Anderson and Garth (2001). Planning ability was scored from levels of one to seven, with seven denoting excellent planning abilities. As previously mentioned, the researcher and two other people rated this task, which also produced an intraclass correlation of $> .90$.

Statistical Analyses

The statistics-based programme G-Power (Faul, Erdfelder, Lang, & Buchner, 2007) was used to analyse the statistical power yielded by the sample size. As previously mentioned, this limited sample is problematic when attempting to detect effect sizes. Power calculations revealed a sample size of 18 would allow for the detection of a medium effect size ($d = 0.5$) with a statistical power of 0.386. Thus, results from this study should be interpreted with caution, as this small power does not allow for generalization to the entire MS population. However, as this is an exploratory study investigating potential confounding variables, the research remains relevant in order to stimulate further research with larger sample sizes.

Descriptive statistics for all data were produced and specific data were analysed with the statistical software programme SPSS (version 22.0). Due to the limited sample size, the

decision was made to run inferential statistics on the fewest possible variables. For this reason, a composite variable was created for socio-economic status (SES), derived from the standardised z-scores of household monthly income and highest level of education. The same procedure was applied to generate an EF composite from EF measures. One-way analysis of variance (ANOVA) and chi-squared analyses were performed on continuous and categorical data respectively, to confirm no pre-existing between-groups differences of participant characteristics existed. A second ANOVA was used to examine between-groups differences on the five VS measures. Tukey's post-hoc analyses were used to determine from where significant differences arose. In the event that Levene's test of homogeneity of variance was significant, the Welch correction was used to obtain the degrees of freedom, F-statistic, and p-value of variables, and the Games-Howell correction was used for post-hoc analyses. A significance level of $\alpha = .05$ was used, in order to avoid the possibility of making type II errors and potentially overlooking effects due to the small sample. In light of the limited sample, and the use of a less stringent alpha, trends in the raw data of confounding variables and descriptive statistics were analysed instead of running further ANOVAs. Although using the ANOVA Bonferroni correction for confounding variables was considered, this was rejected due to criticisms of Bonferroni corrections reducing statistical power (Nakagawa, 2004). However, caution should be used when interpreting these results, as a result of the small sample size and implicit limitations in statistical power.

Ethical Considerations

Approval was granted in 2012 by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee for the larger study this research informs, and reviewed and granted again in 2014 (see Appendices E and F). Amendments for inclusion of this research using posterior RH patients were submitted and approved in March 2015 (see Appendix G).

Costs and benefits. The only identifiable costs in partaking in this research were matters of time and potential fatigue on the part of the patients. Clinical interviews generally lasted one and a half to two hours, so it was possible mild mental fatigue may have occurred. However, it was clearly stated that the subject was permitted to take breaks if they wished to do so.

As this study did not have funding to supply monetary compensation, benefits of participation existed in the form of information. Participants (i.e. the RH group) received pamphlets regarding right-hemisphere strokes, symptoms they may experience, and tips to

manage these symptoms (see Appendix C). Subjects were made aware of the purpose of this research and how their participation benefits the scientific community. Participants were also provided with contact details of the researchers to allow them to make enquiries at a later stage, if they wished to do so.

Results

Descriptive statistics and results of statistical analyses of participant characteristics are presented below.

Table 1
Characteristics of MS, RH, and HC Participants

Variable	MS (N = 6)	RH (N = 6)	HC (N = 6)
Gender – male : female	1 : 5	3 : 3	1 : 5
Race – Caucasian : mixed race	2 : 4	3 : 3	4 : 2
Age	44.50 (16.18)	60.00 (8.74)	41.67 (20.13)
Education	11.67 (2.25)	12.17 (1.94)	13.67 (1.37)
Income	R11,200.50 (R3,919.18)	R14,817.17 (R14,123.51)	R22,433.83 (R13,164.90)

Note. All categorical data are presented as ratios. All continuous data are presented as means with standard deviations in parentheses. ‘Age’ is measured in years. ‘Education’ represents highest level of education in years, measured from Grade 1; a certificate from tertiary education is considered to be 1 year, a diploma, 2 years, and a degree was capped at 3 years. ‘Income’ represents total household income per month.

Table 2
Chi-squared Correlational Results for Categorical Characteristic Variables of MS, RH, and HC Participants

Variable	X^2	<i>df</i>	<i>p</i>	<i>Cramer's V</i>
Gender	2.22	2	.330	.35
Race	1.33	2	.513	.27

Table 3
ANOVA Results for Continuous Characteristic Variables for MS, RH, and HC Participants

Variable		Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	<i>D</i> ²
Age	Between groups	1,168.78	2	584.39	2.36	.129	0.24
	Within groups	3,718.83	15	247.92			
	Total	4,877.61	17				
SES composite	Between groups	12.36	2	6.18	2.56	.110	0.25
	Within groups	36.19	15	2.41			
	Total	48.54	17				

Note. SES composite is a composite created through z-scores of ‘income’ and ‘education’ variables.

The groups were well matched and no pre-existing group differences in sociodemographics were present. Descriptive statistics and results of statistical analyses of VS test performance are presented below.

Table 4
Visuospatial Performance of MS, RH, and HC Participants

Variable	MS (N = 6)	RH (N = 6)	HC (N = 6)
BFRT	21.83 (1.72)	18.67 (2.07)	24.00 (2.28)
JLO	24.33 (3.44)	18.17 (6.68)	29.67 (0.52)
BC	14.17 (4.58)	8.27 (4.12)	21.67 (3.08)
ROCF Construction	28.75 (3.98)	20.75 (7.75)	33.00 (2.24)
ST	4.33 (3.14)	2.83 (1.72)	8.83 (1.60)

Note. All continuous data are presented as means with standard deviations in parentheses.

Table 5
ANOVA Results for Tests of Visuospatial Functioning for MS, RH, and HC Participants

Variable		Sum of Squares	<i>df</i>	Mean Square	<i>F</i> / Welch's <i>F</i>	<i>p</i>	η^2
BFRT	Between groups	86.33	2	43.17	10.42	.001	0.58
	Within groups	62.17	15	4.14			
	Total	148.50	17				
JLO ^a	Between groups	397.44	2	198.72	14.31	.004	0.58
	Within groups	283.50	7	18.9046			
	Total	680.94	9				
BC	Between groups	549.00	2	274.50	17.37	< .001	0.70
	Within groups	237.00	15	15.80			
	Total	786.00	17				
ROCF	Between groups	464.25	2	232.13	7.90	.011	0.53
Construction ^a	Within groups	404.75	9	26.98			
	Total	869.00	11				
ST ^a	Between groups	117.00	2	58.50	18.97	< .001	0.60
	Within groups	77.00	10	5.13			
	Total	194.00	12				

Note. Statistically significant results are presented in bold.

^a = Levene's test for homogeneity of variances was significant, therefore the Welch and Games-Howell corrections for one-way ANOVA with unequal variances were used.

Statistically significant between-groups differences were found for all visuospatial variables. Post-hoc tests revealed both MS and RH participants performed significantly more poorly than HC participants on JLO ($p = .019$ and $p = .028$ respectively); BC ($p = .014$ and $p < .001$ respectively); and ST ($p = .037$ and $p < .001$ respectively). In addition to this, RH performed significantly more poorly than HC on BFRT ($p = .001$), and ROCF Construction ($p = .024$). MS performance was significantly higher than RH on BFRT ($p = .042$), and BC ($p = 0.48$).

Descriptive statistics of confounding variables are presented below.

Table 6
Confounding Variables in MS, RH and HC Participants

Variable	MS (N = 6)	RH (N = 6)	HC (N = 6)
Motor deficits – absent : present	6 : 0	2 : 4	6 : 0
Visual acuity (RPS)	30.83 (9.70)	42.50 (16.04)	20.00 (0.00)
Depression (BDI-FS)	4.00 (3.10)	3.20 (3.03)	1.17 (0.41)
Executive functioning composite	-3.75 (4.45)	-0.83 (3.38)	4.59 (1.91)

Note. All continuous data are presented as means with standard deviations in parentheses. Executive functioning composite is represented in z-scores.

Discussion

This research investigated three hypotheses. Firstly, it was hypothesized that MS participants would demonstrate poorer results than HCs on some complex VS tests. Conversely, RH participants were predicted to demonstrate poor performance all VS tasks. The second hypothesis predicted that MS participants would not produce significantly low scores for BFRT, but would perform poorly on JLO, BC, ROCF, and ST. Finally, the third hypothesis predicted that MS participants would perform in this way due to confounding factors that may be necessary for adequate execution of these tests. It was hypothesized that EF may be necessary for ROCF Construction, and perhaps JLO; and motor dexterity possibly required for BC, ROCF Construction, and perhaps ST; while depression and visual acuity would be more likely to affect performance on all tests. Hypotheses were addressed through a comparison of VS test performance between MS, RH, and HC participants, and a consideration of potential differences in confounding variables between these groups.

As the sample size and statistical power of the study were limited, it is possible that type II errors may have occurred, while setting the alpha level at .05 may have resulted in type I errors. Although every attempt was made to account for the small sample size in this study (see Statistical Analyses section of Methods for a description of data handling), it should be noted that these results must be interpreted with caution. The risk of complications of statistical power and statistical errors remains increased in such a small sample size, and therefore, one must bear in mind that this is preliminary research into a topic requiring studies of a larger sample size to further substantiate present results.

Visuospatial Performance

As predicted, Table 5 shows MS participants scored significantly lower than HC on some complex VS measures (ST, BC, and JLO), whereas RH participants performed significantly lower than HC on all VS measures. As RH participants have pathology commonly resulting in VS deficits (Zillmer et al., 2008), one would expect these participants to perform poorly on all tests measuring VS abilities. Furthermore, these results demonstrate these tasks are indeed sensitive to VS capabilities, as participants expected to have deficits in VS functioning performed significantly worse on these measures than HC. If it were true that people with MS suffer impaired VS functioning, it would be expected that these participants would obtain statistically significantly inferior scores than HC on all VS tests. However, this was not observed in this sample. This suggests that the first null hypothesis should be rejected, as MS participants in this sample did perform poorly on some complex measures of VS ability, while the RH group demonstrated significant impairment on all VS measures. These provisional results appear to suggest that factors other than primary VS deficit may contribute to substandard performance of MS participants on some VS tests. However, it is possible that the general MS population differs from this small sample.

Predicted Measures

It should be reiterated that the groups were well matched. Thus, sociodemographic variables cannot account for variance in test performance between groups. For aforementioned reasons pertaining to sample size, trends will be discussed with reference to raw scores (see Appendix H).

It was predicted that MS participants would be likely to perform poorly on the JLO, ROCF Construction, BC, and ST, due to potential impairments in EF and motor dexterity. Results demonstrate that in this sample, MS participants did obtain significantly inferior results to HC on JLO, designed to assess VS perception (Benton et al., 1994b); BC, designed to assess VS constructional and visuomotor ability for three-dimensional object representation (Korkman et al., 2007); as well as ST, designed to measure mental rotation ability and spatial judgement (Butters & Barton, 1970). Furthermore, it was predicted that the MS participants would not perform poorly on the BFRT, as it has been found to be a rudimentary measure of primary VS abilities through assessing the capacity to recognise and match objects from different perspectives (Benton et al., 1994a). MS participants demonstrated no significant difference in BFRT scores to HC, and, moreover, were significantly more able than RH participants on this test. Thus, the second hypothesis

concerning the predictions of certain tests is predominantly supported, as MS participants did not obtain significantly different BFRT scores to HC, but did perform significantly more poorly on JLO, BC, and ST, as predicted. In contrast to initial predictions, MS participants did not demonstrate significant differences to HC on ROCF Construction.

Confounding Variables

Since MS participants performed poorly on predicted complex tests involving additional domains, and not on the more rudimentary BFRT, the need to examine confounding influences that may affect MS patients' performance on VS tests is illuminated. Results from this sample suggest that MS participants may not be predominantly impaired in VS domains, but rather perform significantly below the HC mean on particular VS tasks for other reasons.

In order to examine the contributions of potential confounding variables to seemingly diminished VS capacity, additional deficits frequently observed in people with MS were examined. Physical, cognitive, and affective domains, all of which are commonly affected in the course of MS (Koch et al., 2007; Nocentini et al., 2012b; Nocentini et al., 2012a), were considered. Potential confounds, such as motor deficits, visual acuity, depression, and EF, were investigated in both the MS and RH groups in an attempt to determine whether these could have influenced the performance of this sample. As previously mentioned, the decision was made to exclude measures of attention and speed, in light of the lack of a significant difference between MS and HC groups on these variables in the larger study, in conjunction with attempting to reduce the amount of variables examined in this small sample and limit the scope of the study. Despite this, one should be cognizant of these factors when using tasks that may rely on them when testing patient populations that could struggle with attention or speed of processing.

Motor deficits. Motor deficits are manifestations of physical effects of MS, and can include tremors, weakness, and paralysis (Koch et al., 2007; Romano et al., 2012a). Any of these deficits could affect performance in tasks that require the participant to write, draw, or manipulate objects. Tasks of this nature were included in this study, such as ST, BC, and ROCF. However, in this sample, no motor deficits of any kind were observed in or reported by MS participants, and therefore, it is highly improbable that this influenced their performance.

While inferential statistics were not employed for this data, it is clear from the descriptive statistics that 100% of the variance on this factor occurred within the RH group,

with hemiparesis affecting four of the six RH participants (RH3-6), with no participants from other groups experiencing motor impairment. However, an examination of the data and the aforementioned tests suggests that in this sample there is no clear pattern demonstrating an impact of hemiparesis on RH participant performance. Although it is possible to complete these tasks with left hemiparesis, the constructive nature of these tests may put those with only one functional hand at a disadvantage to those who are able to use both hands. Of the four participants with hemiparesis, three scored >3 standard deviations (SD) below HC mean on ST; >4 SD below on BC; and >8 SD below for ROCF Construction; tests which have elements of motor functioning. The same three participants also scored >10 SD below HC mean on JLO and >2 SD below on BFRT, both of which are not dependent on motor dexterity. In addition to this, RH4 (with hemiparesis) only performed approximately 2 SD below HC mean for BC; 1.75 SD below for ST; and <1 SD below for ROCF Construction. In contrast, RH4 performed >3 SD below HC mean for JLO, and >2 SD below for BFRT. Thus, despite having hemiparesis, participants also obtained poor results on tests with no motor component. Furthermore, one of the participants with hemiparesis performed worse on tests with no motor components than tests requiring motor functioning.

Of the two participants in the RH group without hemiparesis, RH1 and RH 2 scored >2 SD and >1 SD respectively below HC mean for BFRT; and >5 SD and >3 SD below for JLO. Comparatively, RH1 and RH2 performed >5 SD and >1 SD respectively below HC mean for ROCF; >4 SD and >3 SD below on BC; and >3 SD and >4 SD below for ST, all of which are tests dependent on motor functioning. Thus, participants with no hemiparesis appeared to demonstrate weaker execution of tests dependent on motor ability than on the other tests. Collectively, these findings suggest that motor dysfunction did not appear to play an influential role in VS test performance of either patient group. With reference to the third hypothesis, it is likely that participants performing poorly on the ST, BC, and ROCF did so for reasons other than motor difficulties, such as VS deficits or an alternate confounding variable.

Depression. Mood disorders have been found to affect MS patients at a higher rate than healthy populations, with emphasis on depression (Nocentini et al., 2012b). Although depression can be associated with general decline in cognitive function (Auning et al., 2015), and would therefore likely affect all cognitive domains rather than contributing to the specific picture seen in MS patients, an examination of its potential influence on test performance is necessary as its prevalence is high in this population.

A comparison of descriptive statistics displays that the MS group had the highest mean score of depression ($M = 4$; $SD = 3.10$); the RH group demonstrated a slightly lower mean score ($M = 3.20$; $SD = 3.03$), and the HC group exhibited the lowest group score ($M = 1.17$; $SD = 0.41$). While it is unclear whether or not this difference was significant, it should be noted that the MS group mean represented the point at which people are considered to demonstrate a mild level of depression in terms of the BDI-FS (Whiston & Eder, 2003). Thus, the MS group, on average, may be considered to be at least mildly depressed. However, it is likely that in the event of depression acting as a confounding variable, a global suppression effect would be evident across the battery of cognitive tests (Auning et al., 2015). When examining these trends in conjunction with VS performance across groups, it appears that depression is unlikely to be a seminal confounding factor: the MS group did not perform significantly below the HC mean on the majority of VS tests, while the RH group did perform significantly more poorly across all measures of VS functioning. However, the RH group depression score did not meet the criteria for even mild depression, and only one participant (RH4) scored above the cut-off point of 4. Thus, this may suggest that in this sample, it is unlikely that depression accounted for the VS performance of MS or RH participants.

Visual acuity. MS is frequently associated with demyelination of the optic tract, which can result in an array of visual difficulties (Diaz-Olavarrieta et al., 1999; Romano et al., 2012a). Due to visually presented material in these tasks, it is important to consider the potential influence of deficits in primary vision in this sample. Impaired vision would also be considered to broadly affect performance on this test battery, as every VS test (while purportedly assessing higher visual functions) operates through the medium of lower visual function.

An examination of group means reveals that the RH group demonstrated the worst visual acuity in their strongest eye ($M = 42.50$; $SD = 16.04$), the MS group showed middling scores ($M = 30.83$; $SD = 9.70$), and the HC group, the best visual acuity ($M = 20$; $SD = 0$). Since all six HCs demonstrated 20/20 vision, one might consider any variance within other groups to be noteworthy. However, it is important to note that the cut-off point for poor vision (using the RPS) is considered to be 20/40 (Ladden, 2012). The MS group produced scores far better than this cut-off point, with only one participant scoring below this point (MS5: 20/50). In contrast, the RH group mean was below this cut-off point, with four participants (RH1, RH3, RH5, and RH6) producing poor scores (20/70, 20/40, 20/50, and

20/40, respectively). When one considers that visual acuity would be likely to globally suppress performance across the test battery, and that the MS group produced visual acuity scores stronger than the RH group but still performed significantly more poorly than HC on three of the five VS tests, it is unlikely that vision exerted a substantial influence over MS performance on VS tasks.

The RH group, however, did perform significantly more poorly than the HC group on all VS measures and, on average, demonstrated poorer visual acuity. Furthermore, RH2 and RH4 produced visual acuity scores of 20/30 or better, as well as the highest raw scores across the majority of VS tasks. Conversely, the remaining four RH participants demonstrated visual acuity of 20/40 or weaker, along with the lowest raw scores across the majority of tests. However, posterior RH strokes are known to potentially involve primary visual impairment due to the anatomical lesion site (Banich & Compton, 2011), and therefore, this may be a symptom that co-occurs alongside with, rather than causes, higher VS deficits, or may at least be intricately tied up with the deficit. As more sophisticated statistical analyses such as analysis of covariance were not possible in this limited sample, comments on the possibility of sustained VS dysfunction while controlling for visual impairment cannot be made. However, the focus of this study pertains to MS participant performance on VS tasks, and one is able to infer that primary vision did not appear to play an obviously influential role in the MS sample.

Executive Functioning. EF impairment is a cognitive symptom frequently exhibited in MS. These difficulties are particularly in the realms of planning, abstraction, and problem-solving (Genova et al., 2013; Leavitt et al., 2014; Pepping et al., 2013; Phillips et al., 2014; Preston et al., 2013). It is possible that dysfunction in this system could influence the manner in which these MS participants completed VS tests. The JLO may necessitate abstract representation and non-verbal reasoning; and has been found to be influenced by education, a feature commonly associated with EF rather than pure VS ability (Dorbath et al., 2013; Ehrlert, 2012), while ROCF requires an element of planning.

Observation of descriptive statistics reveals that RH group performance on the EF composite was quite considerably lower than that of the HC group (<2.5 SD below HC mean), and that the MS group was even lower than that (>4 SD below). Although one cannot judge whether the differences between these groups are statistically significant, the raw scores appear to suggest that although both the MS and RH groups seemed to be affected by executive dysfunction to some extent, the MS group was substantially more impaired.

It was predicted that MS participants would perform poorly on ROCF, and possibly JLO, due to test complexity and the need for EF capacity to complete the tests successfully. For instance, the construction element of ROCF cannot be readily separated from the planning aspect of the test, and JLO necessitates the ability to create an abstract representation from incomplete lines in order to match the appropriate lines in the diagram, which also requires judgement. However, of these predicted tests, MS participants only obtained significantly weaker scores on JLO, a task thought to supposedly assess purely VS abilities and most commonly used to test VS dysfunction in MS (Benton et al., 1994). MS participants did not perform significantly differently to the HC group on ROCF Construction. This partially supports the third hypothesis concerning the nature of poor performance on predicted tests, as it was predicted that EF would influence both JLO and ROCF Construction.

If one considers raw scores of MS participants for JLO and ROCF Construction; apart from MS6, who performed poorly on EF but well on the majority of VS tests, the general trend suggests a positive relationship between scores on the EF composite, and JLO and ROCF Construction performance. MS1 and MS5 had the lowest raw scores for the EF composite, and performed the worst on JLO (> 8 SD below HC mean) and ROCF Construction (>3 SD below), while the remaining participants (MS2, MS3, and MS4) performed similarly to one another on the EF composite, as well as on these two VS tests. It is possible that MS participants displayed this trend of diminished EF being associated with lower scores on the JLO and ROCF Construction, but to a lesser degree on ROCF Construction, resulting in non-significance in this sample. Nonetheless, this suggests that EF may impact both JLO and ROCF performance. When considering the remaining tests, a similar picture emerges for BC and ST, for which MS participants performed significantly worse than HC. MS1 and MS5, who yielded the poorest scores on the EF composite, again performed among the worst of MS participants on these tests (>3 SD and >4 SD below HC means for the respective tests). Once again, MS3, and MS4, with similar EF composite scores, performed similarly to one another on BC and ST, and produced higher scores than MS1 and MS5. Thus, it appears that EF may be implicated in not only JLO and (although not significant) ROCF Construction, but also in BC and ST. This is qualitatively different to the predictions of the third hypothesis, which suggested that BC and ST may be influenced by motor dexterity, but further substantiates the possible influence of EF dysfunction on VS tests in MS participants.

In contrast, on the BFRT, neither of the two participants with severely impaired EF composite scores produced the lowest scores of the MS sample. MS2, with one of the highest EF composite scores, produced the weakest score in this group on the BFRT, and MS3, with a similar EF composite score to MS2, performed comparably to MS1 and MS5. The range of scores for this test was also more restricted than that of other tests, despite a wide range of EF composite scores. Although definitive inferences cannot be made from this small sample, these results suggest this test does not require intact EF for adequate completion.

These trends suggest JLO, ROCF Construction, BC, and ST may load on EF components, and may offer a tentative explanation for the association between the majority of these participants demonstrating commonly weak scores. The constructional aspects of the ROCF, BC, and ST necessitate intact planning abilities to draw, build, and rotate structures, with particular reference to BC in order to avoid the collapse of the block structure. As disorganization of planning capability is implicated in MS (Pepping et al., 2013; Preston et al., 2013), it is possible that difficulties with this EF prevented participants from performing adequately on these supposed VS measures. Furthermore, it is possible that three of these common tests may require some measure of abstraction, a cognitive ability frequently disturbed in the course of MS (Preston et al., 2013). As JLO, BC, and ST necessitate the ability to create an abstract representation of the image presented, with JLO requiring judgement to match this representation to another line; BC demanding a three-dimensional construction of this representation, and ST entailing mental manipulation of this abstract representation in order to construct a rotated figure, it is quite possible that EF impairment hindered participants in these VS tasks.

With regards to RH participants, despite RH5, who produced a strong EF composite score but demonstrated some of the lowest scores across VS tests, those with the weakest EF composite scores (RH1, RH3, and RH6) demonstrated the lowest raw scores on all VS tasks. In addition, participants with middling EF composite scores (RH2 and RH4) produced comparatively moderate VS scores. Therefore, it would appear that EF might also be implicated in this group. However, it should be noted that raw scores of RH participants across all VS tasks were generally lower than MS participants', while RH EF scores were generally better. If EF impairment alone were responsible for performance on these tests, the RH group, with a higher mean EF composite score than the MS group, should demonstrate superior VS test scores. This is not the case. Despite higher EF composite scores on

average, the RH group demonstrated consistently weaker performance on VS tests than the MS group. A tentative explanation for these trends may be offered in suggesting that EF dysfunction might have contributed to diminished VS performance of RH participants in this sample, but that this poor performance probably does not hinge on this confound alone. Conversely, EF dysfunction may have played a crucial role in the performance of MS participants on VS tasks.

Although all confounding variables identified as potentially influential factors have now been discussed, a critical evaluation of potential interactions between confounding variables is also necessary.

Interactions

As motor deficits and depression did not appear to obviously affect VS task performance in this sample, potential interactions involving these variables will not be included in this discussion. As visual acuity and EF appeared to possibly influence test performance, interactive effects of these variables should be considered.

In the RH group, apart from RH5 (with the second weakest vision), the three participants with the poorest vision (RH1, RH3, and RH6) also demonstrated the weakest EF composite scores. Here, attention should be drawn to the fact that three of the four tests that comprised the EF composite were presented through a visual medium. As previously stated, deficits in visual acuity would likely produce impairment in any test based on vision, and this would therefore affect RH performance on EF tests as much as it may have affected their performance on VS tests. Thus, it may be vision, rather than EF, that impacted RH performance across all tests administered.

In terms of the MS group, those with the poorest vision (MS1, MS5, and MS6) also produced the lowest EF composite scores. However, as previously mentioned, MS scores of visual acuity were stronger than RH scores (and were not weak enough to be considered impaired), although their EF composite scores were weaker than those of the RH group. If visual acuity were the sole predictor of EF, the RH group should have performed more poorly on the EF composite than the MS group. The combination of MS visual acuity scores being better than those of RH participants, poorer EF scores of MS participants, and significantly superior MS performance to RH on BFRT; could indicate that EF impairment, rather than primary VS dysfunction, may be the principal reason for poor VS task performance by MS participants in this sample.

These results suggest that the third and final null hypothesis, concerning the cause of poor MS scores on VS performance, should be rejected for this sample. However, upon exploration of the data, the confounds associated with potential influence over certain tests differ from predictions. MS participants did perform poorly on expected tests, but it appears that EF may have had an influence over more of these tests than previously predicted. As predicted, it appears as though JLO and ROCF may have been influenced by EF in this sample; while BC and ST appeared not to have been affected by motor functioning as predicted, but may have been influenced by EF.

Implications

Despite the provisional nature of these results and the necessity for further exploration with larger samples, these findings may have significant bearing on the manner in which MS is perceived, and thus, on clinical practice and rehabilitation. This study tentatively suggests that although MS patients are commonly regarded as having VS impairment, they may perform poorly on these tests for reasons other than VS dysfunction. This would imply that this population may not have primary VS impairment, and may explain why right hemisphere deficits are observed more frequently in MS than symptoms associated with the left hemisphere (as language tests may be less complex, thus not requiring EF support), as well as offering a potential explanation for poor performance on VS tests without evidence of MS preferentially affecting the right hemisphere. Furthermore, these results suggest that the manner in which the relationship between MS pathology and cognition is understood may need to be re-evaluated, and that tests currently used to assess VS abilities may need reviewing. In order to gain a true understanding of VS deficits, the difficult task of selecting tests that evaluate VS functioning alone must be undertaken, in order to provide an accurate reflection of impairment patterns. Finally, this study suggests that patients with EF difficulties may struggle with a range of problems in addition to expected difficulties with abstraction, planning, and problem-solving; and this should be considered for tasks in which these domains are not explicitly tested, but are necessary for adequate execution. Further exploration of these avenues with larger samples will allow for informed practical applications in treating MS.

Conclusions

Cumulatively, the results reveal an interesting depiction of the nature of purported VS dysfunction in MS participants. While the results of RH group performance displayed significant impairment on all VS tasks that did not discriminate in terms of different tests, or

on the basis of potentially confounding variables (except, perhaps, vision), a similar trend was not observed in MS participant performance. MS participants did not perform significantly worse than HC on all VS tasks, as one may expect with primary VS impairment.

Trend analyses suggested MS participants in this sample were not substantially influenced by motor deficits, visual acuity, or depression. In this sample, the only apparent difference that could be observed with regards to MS participants was the EF composite. While it is possible that interaction effects may have taken place between impaired EF and other confounds, the results from this small sample suggest that EF is a central confounding factor underlying VS test performance in MS participants.

Limitations and Future Research

As indicated, the sample size of this study substantially limits the generalisability of results as well as the ability to perform inferential statistics. Due to time constraints and inherent difficulties with sampling from a clinical population, only 16 RH patients agreed to take part in this research. 10 of these patients did not meet criteria for inclusion in this study, which curtailed the sample to six eligible participants. Due to statistical complications that would arise from using groups of highly unequal sizes (MS $n = 60$, HC $n = 35$, and RH $n = 6$), the decision was made to use matching for equal group sizes.

A number of avenues were explored from April 2015 when attempting to identify eligible RH participants. These included Groote Schuur Hospital, Vincent Palotti, Constantiaberg Medi-Clinic, Gatesville Medical Centre, The Stroke Survivors Foundation, Headway (branches in Johannesburg, Pretoria, and Durban), Western Cape Life Rehab Centre, a support group held at the Father's House church in Mitchell's Plain, and personal contacts. Although the sample narrows the generalisability of the study, the results of this exploratory investigation suggest further research should be conducted with larger sample sizes, which would yield greater power of results and reduce the risk of sampling error. Furthermore, more sophisticated inferential statistical analyses would be suitable for larger sample sizes, as further analyses of confounding variables were not viable in this study, and thus, it is not possible to know whether or not these differences are statistically significant.

Secondly, motor deficits were not assessed through objective measures. Participants were asked whether or not they had difficulties with motor functioning and gross motor impairment was objectively observed, but it is possible that minor impairments were not conveyed. This may impact on the reported prevalence of motor deficits in the sample, and potentially influence the results with regards to the impact of motor functioning on VS tests.

Although not all tests required intact motor functioning, certain results may be affected, as not all tasks are appropriate for participants with only one functional hand. The potential impact of the use of only one hand should be considered when selecting VS tasks for patient populations that may be impaired on motor dexterity, and further studies should include an objective measure of motor dexterity in order to further assess this.

Thirdly, attention and speed were not included as confounds. Although these were not included due to this and aforementioned reasons pertaining to scope, sample size and non-significance in the larger study, deficits in these realms have been observed in MS, and thus, should be considered in future studies.

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