Looking anew at cognitive dysfunction in multiple sclerosis

The gorilla in the room

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ABSTRACT

Objective: Inattention blindness refers to a phenomenon in which individuals fail to notice an object in plain sight. Present in healthy, cognitively intact individuals, it has not been studied in patients with MS in whom it could theoretically act as a marker for real-world cognitive difficulties in those deemed cognitively intact on conventional neuropsychological batteries. Our hypothesis was that difficulty sustaining attention in patients with MS would paradoxically be associated with less inattention blindness.

Methods: A cross-sectional study was undertaken in which a consecutive sample of 68 patients with MS completed neuropsychological testing with the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS) battery. Two additional tests were administered, the Stroop Test and a measure of inattention blindness, i.e., the gorilla in the room paradigm. The gorilla test elicited 2 variables: the ability to detect the gorilla and the number of times a ball was passed between members of one team.

Results: Cognitive dysfunction by MACFIMS criteria was present in 36.8% of subjects. There were no differences between patients with MS and healthy control subjects on the gorilla indices. Similarly, no inattention differences were present between cognitively intact and impaired patients with MS. However, patients with MS who were impaired on the Stroop and 2-second Paced Auditory Serial Addition Test were more likely than their intact counterparts to detect the gorilla ($p = 0.038$ and 0.014 , respectively), with Stroop-impaired patients detecting fewer ball passes ($p = 0.002$).

Conclusions: The results support our hypothesis that less inattention blindness is associated with heightened distractibility. This may explain why some patients with MS deemed cognitively intact on a battery of tests such as the MACFIMS still struggle with real-world challenges such as multitasking and filtering distracting stimuli. *Neurology*® 2012;79:1124-1129

GLOSSARY

ANART = American National Adult Reading Test; **CVLT-II** = California Verbal Learning Test-II; **HADS** = Hospital Anxiety and Depression Scale; **MACFIMS** = Minimal Assessment of Cognitive Function in Multiple Sclerosis; **MS** = multiple sclerosis; **PASAT** = Paced Auditory Serial Addition Test; **SDMT** = Symbol Digit Modalities Test.

Inattention blindness, also called perceptual blindness, refers to the phenomenon whereby individuals fail to notice an object in plain sight. It is thought to arise as a consequence of selective, focused attention in environments overloaded with sensory inputs. Although the phenomenon has been well described and replicated in healthy, intelligent individuals, it has not been studied in patients with neurologic disease associated with cognitive compromise, such as multiple sclerosis (MS).

A number of studies have shown that cognitive dysfunction affects 40%–60% of patients with MS¹ and is linked to greater difficulty finding and sustaining employment, managing relationships, and attending to basic activities of daily living.² Some patients found to be cognitively intact on psychometric testing may nevertheless experience similar difficulties, with depression cited as the most likely reason for their failings. Although the effects of depression

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on subjective³ and objective^{4,5} indices of cognition are well described, it is also possible that neuropsychological batteries recommended for MS research tell only part of the story. Adding an inattentional blindness test to these batteries may therefore widen the scope of cognitive inquiry and in the process provide fresh insights into the nature of problems encountered. Here, an intriguing hypothesis is presented: the real-world deficits of distractibility and impaired vigilance, discernible on a conventional psychometric test such as the Stroop Test, may be associated, paradoxically, with less inattentional blindness. Put another way, lack of attention in patients with MS may allow them to detect extraneous environmental stimuli that their more focused, attention-intact fellow patients miss. This hypothesis forms the subject of the present study.

METHODS Subjects with MS. A consecutive sample of 68 patients between the ages of 18 and 59 attending 2 hospital-based outpatient MS clinics was enrolled. Three subjects had to be excluded because of their familiarity with the Gorilla in the Room Test. All subjects met modified McDonald criteria⁶ for a diagnosis of MS. Standard demographic and disease-related variables (type and course of MS, physical disability according to the Expanded Disability Status Scale⁷) were collected.

Exclusion criteria included the presence of developmental delay, concurrent neurologic disease, enrollment in another study, major psychiatric illness (psychosis or dementia), substance abuse, a history of a traumatic brain injury, and visual acuity less than 20/100 in at least one eye.

Control subjects. Twenty-seven healthy control subjects were recruited and matched as a group to the patients with MS with respect to age, gender, years of education, and premorbid IQ.

Cognitive assessment. Subjects with MS were administered a consensus-derived battery of cognitive tests that has been developed for MS research, namely the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS).⁸ Each test on the MACFIMS comes with published normative data (age-, gender- and education-specific, where appropriate) that are used for scoring purposes. These comprise the following 5 cognitive domains: 1) information processing speed: Paced Auditory Serial Addition test (PASAT) 3- and 2-second versions⁹ and the Symbol Digit Modalities Test (SDMT)^{2,10}; 2) verbal and visual memory: California Verbal Learning Test–II (CVLT-II)¹¹ and the Brief Visuospatial Memory Test^{12,13}; 3) executive function: Delis-Kaplan Executive Function System Sorting Test¹⁴; 4) spatial processing: Judgment of Line Orientation¹⁵; and 5) verbal fluency: Controlled Oral Word Association Test.¹⁶

Failure on each test was defined as a score 1.5 SD below the mean of normative scores. Global impairment on the MACFIMS was defined, by convention, as impairment on 2 or more cognitive measures. After completion of the MACFIMS, subjects were administered 3 further tests:

The American National Adult Reading Test (ANART)¹⁷: This test was used to assess premorbid IQ.

The Stroop Test¹⁸: A computerized version of this classic distracter task was used to measure the ability of subjects to focus attention on one attribute of a compound stimulus while ignoring a competing attribute. We have previously used this version of the Stroop Test to detect differences between subjects with MS and healthy control subjects.^{19,20} Failure on this task was defined as a score below the 5th percentile of total test time obtained from the matched control sample of 27 healthy subjects. The Stroop paradigm was specifically chosen as an additional index of distractibility in keeping with our a priori hypothesis concerning inattentional blindness.

The Gorilla in the Room Test²¹: This cognitive test probes inattentional blindness. Subjects were shown a 30-second film clip in which 3 people wearing white shirts passed a basketball to one another while another 3 people in black shirts passed a different basketball to each other. Subjects were instructed to count the number of passes made by the players wearing white only. As per the test's instructions, the subjects were also told the following, to quote: "...This counting task can be difficult. It requires sustained attention and concentration but most people can do it if they concentrate hard enough." Halfway through the test, a person wearing a gorilla suit wanders into the subjects' field of view, waves her hands, and then leaves. Two performance variables were obtained from this test, i.e., whether the subject did, or did not, see the gorilla and the number of passes of the ball between the players in white. Historically, in the assessment of inattentional blindness, correctly counting the passes has not been considered important, regarded instead as a means to an end.⁶ However, given that we shifted the use of the test from a healthy sample to a MS sample and considering the broader aim of our inquiry, the accuracy of the counting assumed a new and important significance. The results from the Gorilla in the Room Test were compared with those from the 27 matched healthy control subjects.

Finally, depression and anxiety were assessed with the MS-validated Hospital Anxiety and Depression Scale (HADS).^{22,23}

Subjects with MS and healthy control subjects completed the ANART, Stroop Test, Gorilla in the Room Test, and the HADS, but control subjects were not given the MACFIMS.

Statistical analysis. The distribution of all continuous data was checked using the Kolmogorov-Smirnov test. Thereafter, between-group (patients with MS vs control subjects) and subgroup (patients with MS who were cognitively impaired and intact) comparisons were undertaken with *t* tests or the Mann-Whitney *U* test, according to Gaussian distribution. Ordinal comparisons were completed with χ^2 analyses, whereas correlations (Pearson or Spearman rank) were based on data distribution. Statistical significance was set at $p < 0.05$. Given that inattentional indices have not been used before in MS research, we could not perform a sample size calculation based on previous findings.

Standard protocol approvals, registrations, and patient consents. The study received approval from the ethics committees of both Sunnybrook Health Sciences Centre and St. Michael's Hospital. Informed consent was also obtained from all subjects.

RESULTS Demographic data. Demographic data for MS and control subjects and neurologic data for MS subjects are shown in table 1.

Cognitive and behavioral data. The MACFIMS data revealed that 36.8% of the MS sample was cognitively

Table 1 Demographic and disease characteristics of the MS and healthy control samples

	MS sample/frequency (n = 65)	Healthy control sample (N = 27)	t test/ χ^2 test	p Value	95% CI
Age, y, mean (SD)	45.75 (8.86)	42.93 (8.81)	t: 1.392	0.167	−1.202 to 6.842
Female sex, n (%)	44 (67.7)	16 (59.3)	χ^2 0.60	0.439	
Premorbid IQ (ANART), mean (SD)	112.95 (8.19)	115.82 (6.34)	t: −1.491	0.14	−0.958 to 6.690
Education, y, mean (SD)	14.58 (1.98)	15.44 (1.97)	t: 1.921	0.061	−0.04 to 1.775
Duration of MS, y, mean (SD)	9.54 (7.15)				
Disease course, n (%)					
Relapsing-remitting	40 (58.8)				
Primary Progressive	9 (13.2)				
Secondary Progressive	19 (27.9)				
EDSS score, mean (SD)	3.59 (2.59)				

Abbreviations: ANART = American National Adult Reading Test; MS = multiple sclerosis.

impaired. The percentage of patients impaired on the Stroop Test was 17.6%. Compared with the healthy control subjects, patients with MS had higher depression (7.05 [SD 3.71] vs 2.81 [SD 3.6], $z = -4.76$, $p = 0.0001$; Mann-Whitney U test) and anxiety (7.62 [SD 4.74] vs 3.96 [SD = 2.61], $z = -3.44$, $p = 0.001$; Mann-Whitney U test) scores on the HADS.

There were no differences between the patients with MS and the healthy control subjects in counting the number of times the ball was passed (16.43 [SD 1.38] vs 16.59 [SD 1.28], $t = 0.523$, $p = 0.602$) nor in their ability to detect the presence of the gorilla (20% vs 33.3%, $\chi^2 = 1.864$, $p = 0.172$).

Comparisons between cognitively intact and impaired patients with MS with respect to inattentional blindness.

There were no differences between cognitively intact and impaired patients with MS when it came to counting the number of passes nor in the frequency with which they detected the gorilla. However, an analysis of individual cognitive tests revealed some significant differences with patients with MS impaired on the Stroop Test and PASAT_2 more likely to detect the appearance of the gorilla. In addition, patients impaired on the SDMT, the Stroop Test, and the CVLT counted fewer passes (table 2). Similarly, significant correlations were found in the MS group between failure on the Stroop Test and detecting the gorilla ($r = 0.3$, $p = 0.039$, Spearman rank correlation), and time to complete the Stroop Test and number of passes detected ($r = -0.4$, $p =$

Table 2 Comparisons between cognitively intact and impaired subjects with MS^a

	Gorilla detected, %				Passes counted, mean (SD)				
	MS intact	MS impaired	χ^2	p Value	MS intact	MS impaired	t test	p Value	95% CI
Global impairment	17.1	25	0.595	0.441	16.61 (1.43)	16.13 (1.26)	1.376	0.174	−0.22 to 1.19
BVMT delayed recall	20	20	0.0	1.0	16.45 (1.44)	16.30 (1.06)	0.323	0.747	−0.80 to 1.11
BVMT total	18.2	30	0.739	0.390	16.40 (1.46)	16.60 (0.84)	−0.419	0.677	−1.15 to 0.75
CVLT delayed recall	19.6	22.2	0.032	0.857	16.59 (1.3)	15.44 (1.51)	2.393	0.020	0.19 to 2.10
CVLT total	20	20	0.0	1.0	16.42 (1.42)	16.60 (0.89)	−0.283	0.778	−1.48 to 1.11
PASAT_2	15.4	50	6.06	0.014	16.52 (1.36)	15.90 (1.6)	1.279	0.206	−0.35 to 1.59
PASAT_3	18.9	30	0.637	0.425	16.60 (1.2)	15.50 (2.01)	1.678	0.124	−0.36 to 2.56
SDMT	16.7	21.4	0.234	0.628	16.78 (1.07)	15.96 (1.62)	2.411	0.019	0.14 to 1.49
D-KEFS Sorting	19.4	33.3	0.349	0.554	16.50 (1.34)	15.0 (1.73)	1.874	0.066	−0.10 to 3.10
COWAT	12.5	21.1	0.321	0.571	16.44 (1.4)	16.38 (1.3)	0.121	0.904	−0.99 to 1.11
JOL Orientation	21.1	12.5	0.321	0.571	16.51 (1.38)	15.88 (1.36)	1.221	0.227	−0.40 to 1.67
Stroop Test	15.1	41.7	4.318	0.038	16.77 (1.07)	14.92 (1.62)	3.786	0.002	0.80 to 2.91

Abbreviations: BVMT = Brief Visuospatial Memory Test; CVLT = California Verbal Learning Test; JOL = Judgement of Line Orientation Test; COWAT = Controlled Oral Word Association Test; D-KEFS = Delis-Kaplan Executive Function System; MS = multiple sclerosis; PASAT_2 = Paced Auditory Serial Addition Test, 2 second; PASAT_3 = Paced Auditory Serial Addition Test, 3 second; SDMT = Symbol Digit Modality Test.

^a Cognitively intact (n = 41); impaired (n = 24).

0.0001; Pearson correlation). Of note, however, was the fact that the inverse association between detecting the gorilla and the number of passes counted did not reach statistical significance ($r = -0.13$, $p = 0.235$; Spearman rank correlation).

There were no statistically significant differences between the patients with MS who were cognitively intact or impaired with respect to depression (6.71 [SD 3.70] vs 7.63 [SD 3.73], $t = -0.96$, $p = 0.34$) and anxiety (7.32 [SD 4.14] vs 8.13 [SD = 5.67], $t = -0.66$, $p = 0.51$) scores on the HADS.

DISCUSSION The prevalence of cognitive impairment in our sample approximates that found in other studies, whereas the breakdown of our sample according to age, gender, physical disability, and disease course is also typical of that seen in MS clinics. From this we have concluded that our sample is broadly representative of the MS population in general.

What is notable about our data is that when we move away from the tried and tested established cognitive parameters, a slightly different perspective comes into view. By shifting the emphasis of our inquiry, we have used a well-known test of inattention blindness for a different purpose, namely as an objective measure of distractibility. The originators of the Gorilla in the Room Test have made the point that detecting the gorilla is not dependent on IQ or a person's ability to attend to a task.²⁴ However, this well-replicated finding has been derived from healthy samples. Our data, in part, support this too in that patients with MS found to be cognitively intact on the MACFIMS did not differ in their ability to detect the gorilla and count the correct number of passes compared with results from a healthy control group.

Of note too is that the above finding also held up when we compared gorilla detection between patients with MS who were cognitively impaired and intact. At first glance, this result again supports the assumption made by the authors of the seminal gorilla study that inattention blindness is not linked to cognitive ability. However, if one parses the cognitive data more finely some striking differences emerge. The determination of overall cognitive impairment on the MACFIMS is based on a composite score. This battery of tests, recommended by expert consensus, as a sensitive and specific index of cognition in patients with MS, taps into multiple individual aspects of cognition as described earlier. Failure on any 2 or more indices is considered statistically the most robust indicator of overall cognitive compromise, which means that an individual may be rated as impaired even if, in theory, memory and executive functioning, to give but 2 examples, are

intact. Conversely, failure on a single index of information processing speed does not, by itself, qualify as a marker of overall cognitive compromise. Therein can be found one of the limitations of conventional neuropsychological inquiry, namely that group scores can obscure individual psychometric results that may still be of clinical relevance. Neuropsychologist researchers of course know this, and research is replete with examples of how thresholds are shifted (failure on 1 test, 2 tests, 3 tests, and so on), in the search for a statistically significant result (see an editorial comment on this strategy).²⁵

These observations are particularly germane when it comes to the gorilla in the room analysis. The Stroop Test was included with the MACFIMS because it is a classic example of a distracter task with subjects having to suppress one aspect of their cognition while focusing on another. It also taps into a subject's vigilance or sustained attention. We hypothesized, a priori, that the inability of subjects to stay focused could in theory mitigate a degree of inattention blindness, and this was indeed what we found. Stroop-impaired subjects were more likely to see the gorilla, but rather than this detection proving beneficial, the dysfunctional nature of this distractibility was underscored by the Stroop-impaired patients counting statistically fewer ball passes than their intact colleagues. This finding was partly replicated by a finding from one of the MACFIMS tests, i.e., the PASAT, with the result remaining significant even if we took a stricter statistical cutoff ($p < 0.01$) in response to the post hoc nature of the analysis. This paradigm has many similarities with the Stroop Test in that it too is timed, probes sustained attention, and involves a strong distraction component with subjects being asked to serially add numbers while suppressing others. In the more demanding of the two PASATs, i.e., with numbers presented every 2 as opposed to 3 seconds, the PASAT-impaired rather than the intact subjects were again more likely to detect the gorilla. Although they also counted fewer passes, this difference did not reach statistical significance. On no other index of cognition were statistically significant gorilla detection differences apparent.

We have shifted paradigms in devising this study and interpreting the findings. Inattention blindness has not been thought of historically as evidence of cognitive dysfunction in the same way as impaired memory or a dysexecutive syndrome. Numerous studies have shown how 50% or more of healthy individuals including university graduates²⁴ fail to detect the gorilla. To be sure, inattention blindness has been evoked to explain all sorts of day-to-day phenomena with negative consequences, for example, drivers not seeing cyclists or motorists resolutely following GPS commands and driving into danger-

ous situations (floods, rail tracks, and others). It could therefore be argued that any reduction in inattention blindness can potentially confer some real-world benefits, but not if this comes at the cost of less efficiency when having to keep focus on the bigger issue. Improved task performance plus detecting the gorilla is the best combination, but when the latter occurs at the expense of the former, then individuals fail at the task set before them. Detecting the gorilla in the context of impaired cognition may therefore be seen *not* as a plus, but rather as a potential surrogate marker of cognitive failing.

The real-world implications of this hypothesis are readily apparent: workplace inefficiency, distractibility by extraneous stimuli, and inability to multitask. Here we acknowledge a limitation in our study for we do not have independent data from our patients' workplaces or home environments to corroborate these attributions. With this drawback in mind, the results of our study may still be seen as another reminder that patients with MS found to be cognitively intact on conventional, well-validated, and highly touted psychometric batteries such as the MACFIMS may still struggle cognitively if their performance is viewed from a different perspective. Through a paradigm shift, the "invisible" gorilla emerges as an apt metaphor for MS-related cognitive failings that may likewise escape detection.

AUTHOR CONTRIBUTIONS

Anthony Feinstein, as principal investigator on the study was responsible for obtaining funding for the research, completing the literature search, conceptualizing the study, planning the study design, analyzing and interpreting the data, writing and editing the manuscript, and overseeing the general running of the project. Helen Lapshin was responsible for assisting with the literature research, completing the bulk of the data collection, preparing the figures, contributing to data analysis, and interpretation and editing the final manuscript. Paul O'Connor, as collaborator, assisted in data collection, data interpretation, and editing of the final manuscript.

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DISCLOSURE

A. Feinstein has served on scientific advisory boards for Merck Serono and Avanir Pharmaceuticals; has received speaker honoraria from Merck Serono, Teva Pharmaceutical Industries Ltd., Bayer Schering Pharma, and Biogen Idec; chairs the Medical Advisory Committee for the Multiple Sclerosis Society of Canada; conducts neuropsychiatric evaluation, cognitive testing, and brain imaging in neuropsychiatry in his clinical practice; and receives research support from the Canadian Institute of Health Research, the Multiple Sclerosis Society of Canada, and Teva Pharmaceutical Industries Ltd. H. Lapshin receives support from an Ontario Graduate Scholarship grant. P. O'Connor serves on scientific advisory boards for Novartis, sanofi-aventis, Bayer Schering Pharma, Genentech, Inc., and Roche; has received speaker honoraria

from Biogen Idec, Teva Pharmaceutical Industries Ltd., Novartis, and sanofi-aventis; has served as a consultant for Biogen Idec, Actelion Pharmaceuticals Ltd., Bayer Schering Pharma, EMD Serono, Inc., Teva Pharmaceutical Industries Ltd., Genentech Inc., and Warburg Pincus; has received research support from Abbott, Bayer Schering Pharma, Novartis, BioMS Medical, sanofi-aventis, CIS Pharma, Genmab A/S, Cognosci, Inc., Wyeth, Daiichi Sankyo, and Roche; and serves as the National Scientific and Clinical Advisor to the MS Society of Canada. **Go to Neurology.org for full disclosures.**

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