### King Devick Test and MoCA can be used in Routine Clinical Visits to Help Detect Cognitive Impairment in Multiple Sclerosis

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### Abstract

**Background:** People with Multiple Sclerosis (MS) can have cognitive impairment affecting daily living. Easy to administer assessment tools, such as the King Devick Test (KD) and the Montreal Cognitive Assessment (MoCA) are easy to use tools to administer to detect cognitive impairment.

**Objective:** This study aimed to determine if the KD test detected cognitive impairement in people with MS in a clinical setting. Furthermore, this study aimed to determine which subscales of cognitive impairment the KD test may be measuring by using the MoCA subtest scores for comparison.

Methods: 77 people with MS completed the KD test, MoCA, and Symbol Digit Modalities Test (SDMT). A T-score ≤ 40 on the SDMT classified participants as impaired.

**Results:** The KD test correlated significantly with the SDMT (r=-0.49; p <0.001) and MoCA (r=-0.38; p=0.001), and the Expanded Disability Status Scale (EDSS; r=0.23; p<0.05). The MoCA correlated significantly with the SDMT (r=0.52; p<0.001) and education (r=0.28; p<0.015). The KD test also significantly classified participants with cognitive impairment, as defined above, with an improved model after adding the EDSS and education variables ( $\chi^2$ increase 34.79, p<0.001). The MoCA also significantly classified participants with cognitive impairment with a full model including EDSS score ( $\chi^2$  17.05, p=0.01).

**Conclusion:** The KD test and MoCA accurately classified participants with MS with cognitive impairment and may be useful in high-volume, fast-paced clinics to assess cognitive function.

Keywords: Multiple sclerosis • Neuropsychology • Cognitive impairment • Screening • Cognition • Saccades • King devick test

### Introduction

People with Multiple Sclerosis (MS) can have visual and oculomotor deficits that manifest through various signs and symptoms, including optic neuritis, internuclear ophthalmoplegia, ocular motor palsies, nystagmus, abnormal suppression of vestibulo-ocular reflex, and saccadic dysmetria [1-2]. Numerous pathways travel from the eyes to the visual cortex with extensive connections to the frontal, parietal, and temporal lobes [3]. The dorsolateral prefrontal cortex, frontal eye fields, supplementary eye fields, posterior parietal cortex, cingulate eye field, and middle temporal areas participate in generating saccadic eye movements [3-7] and some of these regions are also involved in cognitive processes such as attention, language, and information processing speed [3,8-10].

Many people with MS also experience cognitive deficits with information processing speed, memory and visual learning most often affected [11]. These deficits can impact quality of life [12]. Therefore, it is essential to detect cognitive impairment and track its progression over time. A commonly used instrument to measure information processing speed is the Symbol Digit Modalities Test (SDMT). Additional quick and easy tests that help busy clinicians objectively assess cognitive function in people with MS may prove useful.

The King Devick (KD) test is a rapid number naming task, sensitive to detecting performance change in people experiencing concussion [13-16]. The KD test is a simple visual-verbal task that requires saccades and intersaccadic fixation. Previous research has shown that people with MS performed worse on the KD test when compared to healthy controls [17-18] and performance is correlated with SDMT scores [19]. However, this research does not show what cognitive domains are being used while performing these tests.

The Montreal Cognitive Assessment (MoCA) is a brief screening tool for mild cognitive impairment and is commonly used to screen for cognitive impairment in Alzheimer's disease [20-21]. The MoCA has seven subsections that assess several cognitive domains: memory, visuospatial, executive function, attention, language, and orientation [20]. Some research has emerged showing that the MoCA can be used to detect cognitive impairment in MS [22]. Given that the MoCA has subtests that allow different cognitive domains to be assessed, comparing the SDMT and KD tests to the MoCA can help differentiate between which cognitive domains are being measured.

Our study aimed to determine if the KD test detected cognitive impairment in people with MS in a clinical setting. For comparison, we used the SDMT, a well validated measure of information processing speed in MS. The SDMT is a short neuropsychological test that is sensitive to cognitive impairment in MS [23-26]. We also used the MoCA, which has been validated to detect mild cognitive impairment in multiple clinical scenarios and can be divided into meaningful cognitive subscales [20-22]. While research has shown that people with MS have worse KD test scores when compared to controls, the KD test has not been fully validated in MS [17]. Our study sought to validate and compare the KD test to the SDMT and MoCA.

### **Materials and Methods**

#### Participants

A convenience sample of participants with MS was recruited from the LSU Healthcare Network Multispecialty Clinic, a university-based outpatient clinic, and from the general public. We recruited 85 participants who met the 2017 McDonald MS diagnostic criteria [27]. Participants with relapsing remitting, secondary progressive and primary progressive MS were eligible to participate in the study. All participants were 18 years or older. Exclusion criteria included having a history of stroke, epilepsy, or other neurodegenerative disorders. Acute, severe or unstable medical condition such as metastatic or active cancer, hepatic disease, or primary renal disease requiring dialysis was also included in exclusion criteria. Eight participants were unable to complete the KD test or the SDMT and were therefore excluded. The LSU Health Sciences Center-New Orleans Institutional Review Board approved the study, and all participants provided written informed consent to participate.

### Procedure

The demographic and clinical data collected included diseasemodifying medications, type of MS, disease duration from date of diagnosis, and history of optic neuritis in either eye. A study investigator determined the Expanded Disability Status Scale (EDSS) using the Neurostatus © definitions [28]. All participants completed the oral version of the SDMT, the KD, and the MoCA. The SDMT is a neuropsychological assessment tool that measures information processing speed and requires participants to match numbers to abstract symbols as quickly as they can [29]. The test has a nine symbol-number pairs (1-9) key at the top of the page. Participants were asked to verbally say the number that corresponds to its symbol. There were 10 practice items and 110 test items. Participants were given 90 seconds to complete as many test items as they could. Raw scores were based on the total number of correct responses given in 90 seconds. A lower score indicated worse performance. Age and education-normed T-Scores  $\leq$  40 were classified as borderline or impaired for the analyses.

The KD test is a visual scanning test that requires participants to verbally read numbers across a 13-inch iPad screen as quickly as possible. There is one demonstration card at the beginning, which is followed by 3 test card screens that became progressively more difficult due to changes in spacing and vertical crowding of the numbers. Each test card has 40 numbers, presented in rows of five; spacing between each number is different within each row and across rows. The test cards increase in visual demand as the test progresses. The first test card consists of straight lines connecting the numbers, which aids in visual scanning. The next test card only has numbers and the lines connecting the numbers are absent. Finally, the last test card consists of numbers without connecting lines and the spacing between the rows is truncated. Each card increases visual demand and allows interference from other rows as the participant reads across the page. The KD test is shown in Figure 1. Participants were instructed to read each number on the screen aloud from left to right, row by row, with both eyes open and, if needed, corrective lenses. The complete time for all cards was recorded using the King Devick Pro Monitoring software. A higher score indicated worse performance and aged-normed T-Scores  $\leq 40$ were classified as borderline or impaired for the analyses.

The MoCA is a (10-15) minutes cognitive screening instrument with a maximum score of 30 points. A score of 25 or less was considered to be cognitively impaired [20]. To administer the MoCA, a one-hour training and certification must be completed. The MoCA was administered using the published administration guidelines.

### Statistical analysis

We used SPSS software version 26 for the statistical analyses. A Pearson's correlation was used to observe the relationship between the raw SDMT and KD scores. T-scores were calculated based on available normative data for both the SDMT [29] (published test manual) and KD (given by the KD Pro Monitoring software). Next, we conducted group analyses for scores classified as borderline/cognitively impaired or not. A score of  $\ge$  1.0 standard deviation below the published normative data was considered borderline/cognitively impaired (16th percentile). Logistic regression analysis was used to determine the ability of the KD and MoCA to predict borderline/impaired status assigned by SDMT performance. The initial model included only the KD or MoCA test variable as a predictor. A full model sequentially entered additional demographic and clinical variables using SPSS's Stepwise Selection algorithm based on Likelihood Ratios. Additional logistic regressions were used to determine if subtest scores on the MoCA predicted impairment determined by T-scores on the KD and the SDMT. A stepwise linear regression was used to enter all the subtests of the MoCA into the model.

### Results

**Table 1** presents the demographic and clinical characteristics that included 77 participants with a clinical diagnosis of MS (age 47.5  $\pm$  12.3; 81% female). Forty present of participants had a history of optic neuritis, but enough visual acuity to complete the tests with glasses if needed. The majority of participants had relapsing-remitting MS (RRMS; 86%). Fewer participants diagnosed with Primary Progressive MS (PPMS, 8%) and Secondary Progressive MS (SPMS, 6%) were enrolled in the study.

Pearson's correlations were performed to determine the relationship among the variables. The KD test showed a significant correlation with the SDMT (r=-0.49, p <0.001), MoCA (r=-0.38, p=0.001), and EDSS (r=0.23, p=0.047), but not with age, and disease duration (**Table 2**). The MoCA showed a significant correlation with the SDMT (r= 0.51, p<0.001) and education (r= 0.28, p=0.013), but age, disease duration, and EDSS (**Table** 2) did not significantly correlate with MoCA performance. The SDMT showed a significant correlation with education (r=0.26, p=0.02), age (r-0.29, p=0.01), disease duration (r=-0.39, p<0.001), and EDSS (r=-0.42, p<0.001).

### Linear regression analysis of cognitive tests (SDMT, KD, and MoCA) with demographic and clinical predictors

Stepwise linear regression was used to determine which demographic and clinical variables were related to SDMT raw scores. EDSS ( $\beta$ =-1.86, p=0.001), disease duration ( $\beta$ =-0.47, p<0.001), and education ( $\beta$ =1.29, p=0.002) were significantly related to SDMT scores. Analysis for influential points identified 3 cases, but the results did not change when these cases were removed (data not shown) so they were left in the model. Linear regression identified EDSS ( $\beta$ =2.15, p=0.047) as being significantly related to KD raw scores, but this relationship was not present after the removal of 4 influential cases. Consequently, the KD scores were not influenced by demographic or clinical variables. Linear regression identified education



Figure 1: KD Test Cards.

( $\beta$ =0.33, p=0.016) as being significantly related to MoCA raw scores, but this relationship was also not present after the removal of 4 influential cases indicating that the MoCA scores were not influenced by demographic or clinical variables.

# Logistic regression analysis KD, demographic, and clinical predictors of impairment on SDMT

Since the SDMT is well validated in MS, the primary logistic regression analysis determined whether the KD test correctly classified cases as borderline/impaired based on SDMT T-scores  $\leq$  40 (16th percentile). The

Table 1: MS patient characteristics and clinical measures.

•	
MS Cohort	N=77
Age	47.3 ± 12.4
Education (years ± SD)	14.7 ± 2.8
Disease duration (years ± SD) 10.8 ± 9.6	
Se	к (%)
Female	81
Male	19
Rac	e (%)
Caucasian	70
African American	29
American Indian	1
MS sub	otype (%)
PPMS	8
RRMS	86
SPMS	6
EDSS (score ± SD)	4.0 ± 2.2
History of Op	tic Neuritis (%)
Yes	40
No	58
Unknown	2
Cognitive	e Measures
SDMT	47.8 ± 11.9
K-D	67.0 ± 20.7
МоСА	24.4 ± 3.41
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EDSS: Expanded Disability Status Scale; SD: Standard Deviation; SDMT: Symbol Digit Modalities Test; K-D: King Devick Test; MoCA: Montreal Cognitive Assessment

Table 2: Pearson's correlations between cognitive, demographic, and clinical variables.

N=77	KD	SDMT	MoCA
SDMT	-0.49**		
MoCA	-0.38**	0.52**	
EDSS	0.23*	-0.41**	-0.17
Disease Duration	0.08	-0.38**	-0.17
Age	0.03	-0.29*	0.06
Education	-0.11	-0.28*	0.28*

indicates significance  $\leq 0.05$ ; "indicates significance  $\leq 0.001$ , KD: King Devick Test; SDMT: Symbol Digit Modalities Test; MoCA: Montreal Cognitive Assessment; EDSS: Expanded Disability Status Scale

simplified model included only the KD as a predictor. According to the Model chi-square statistic, the overall model was significant at p<.001 level ( $\chi^2$ =11.6). The model accounted for 30% (Nagelkerke R<sup>2</sup>) of the cognitive impairment variance and predicted 65% of the cases correctly (**Table 3**). The Area Under the Curve (AUC) of the receiver operating characteristic curve (ROC) was 0.76 (Figure 2).

The full model included additional theoretically important independent variables: KD, age, education, EDSS, and disease duration as predictors and used forward entry likelihood ratio. Step 1 entered only KD as the predictor. Step 2 entered years of education, significantly improving the model ( $\chi^2$  increase 7.69, p=0.006), accounting for 40% of the variance (Nagelkerke R<sup>2</sup>), and predicting 67% of the cases correctly. Step 3 added the EDSS with further improvement in the model ( $\chi^2$  increase 7.98, p=0.005), accounting for 49% of the variance (Nagelkerke R<sup>2</sup>), and predicting 83% of the cases correctly (**Table 4**). ROC AUC was 0.87 (**Table 3**, **Figure 3**). Four participants had KD scores that were statistical outliers. Susceptibility analyses removing these participants showed no significant change in the results (data not shown).

## Logistic regression analysis MoCA, demographic, and clinical predictors of impairment on SDMT

The logistic regression analysis determined whether the MoCA test correctly classified cases as borderline/impaired based on SDMT T-scores  $\leq$  40. The simplified model included only the MoCA as a predictor (**Table 5**). According to the Model chi-square statistic, the overall model was significant at p=.001 level ( $\chi^2$ =12.85) (**Table 4**). The model accounted for 21% (Nagelkerke R<sup>2</sup>) of the cognitive impairment variance and predicted 69% of the cases correctly. The ROC AUC was 0.72.

The full model included additional theoretically important independent variables: MoCA, age, education, EDSS, and disease duration as predictors and used forward entry likelihood ratio. Step 1 entered only MoCA as the predictor. Step 2 entered EDSS, significantly improving the model ( $\chi^2$  increase 7.95, p=0.005), accounting for 32% of the variance (Nagelkerke R<sup>2</sup>), and predicting 71% of the cases correctly (**Table 4**). The ROC AUC was 0.78. Three participants had MoCA scores that were statistical outliers. Susceptibility analyses removing these participants showed no significant change in the results (data not shown).

### Logistic regression analysis with MoCA subscale scores as predictors

The MoCA subscales scores (visuospatial, attention, language, abstraction, memory, and orientation) were entered as predictors of borderline/impaired status based on KD T-score  $\leq$  40. After stepwise entry, only the memory subscale score remained a significant predictor of impairment on the KD test ( $\chi^2$ =5.30, p=0.02, **Table 5**). With the same MoCA variables entered in the logistic regression, the model was significant ( $\chi^2$ =19.12, p<.001), with the attention and visuospatial subscale scores remaining as predictors of impairment based on SDMT T-score  $\leq$  40 (**Table 5**).

### Discussion

The current study aimed to identify the cognitive domains associated with the KD and measured if these domains were similar to the SDMT. Previous research showed that people with MS had significantly slower KD test scores when compared to controls [17-18]. Our data extended this work by demonstrating not only that the KD test can be used in MS, but also why it is useful. While the SDMT is known as a test of information processing speed, it also identifies impairment in visual, oral motor, and

**Table 3:** Logistic Regression: KD test Predicts Cognitive Impairment based on SDMT T-score  $\leq$  40.

Predictor	β	SE β	W	ald's χ² df	р	OR	95% CI	Sensitivity	Specificity
Simple model								54%	74%
Constant		-0.18	0.23	0.64	1 0.43		0.83		
KD		0.08	0.02	11.6	1 0.001*		1.09 1.04-1.14		
Full Model								80%	85%
Constant		-0.16	0.23	0.47	1 0.49		0.85		
KD		0.1	0.03	10.1	1 0.002*		1.1 1.04-1.17		
Education		-0.3	0.11	6.9	1 0.009*		0.74 0.60-0.93		
EDSS		0.4	0.15	6.9	1 0.009*		1.5 1.11-2.00		
Variables removed fr	rom the e	equation							
Age, Disease Duratio	on								

Dependent variable was cognitive impairment as defined by SDMT T-score. β (b coefficients); SE β: standard error β; KD: King Devick -Test; Education: years of education; EDSS: Expanded Disability Status Scale; OR: odds ratio.





Figure 3: Receiver operating characteristic for logistic regression with cognitive impairment predicted by KD test, EDSS, and education. Area under the curve 0.87.

**Figure 2:** Receiver Operating Characteristic for Logistic Regression with cognitive impairment predicted by KD test. Area under the curve 0.76.

Table 4: Logistic Regression: MoCA predicts cognitive impairment based on SDMT T-score ≤ 40.

Predictor	β	SE β	Wald's χ²	df	р	OR	95% CI	Sensitivity	Specificity
			Si	mple mod	el			57%	79%
Constant	-0.18	0.23	0.64	1	0.43				
MoCA	-0.28	2.15	9.27	1	0.002*	0.76	0.64-0.90		
			I	Full Model				71%	71%
Constant	4.88	2.21	4.85	1	0.03				
MoCA	-0.27	0.09	8.76	1	0.002*	0.77	0.64-0.91		
EDSS	0.35	0.13	6.9	1	0.008*	1.4	1.10-1.84		
ariables remov	ed from the	equation							
lucation, Age, I	Disease Dura	ation							

Dependent variable was cognitive impairment as defined by SDMT T-score. β (b coefficients); SE β: standard error β; KD: MoCA: Montreal Cognitive Assessment; Education: years of education; EDSS: Expanded Disability Status Scale; OR: Odds Ratio

oculo motor functions [17, 23, 30-31]. The KD measures rapid number naming, which makes it a promising assessment for people with MS since visual and oculo motor impairment are widely prevalent in individuals with MS [17, 32-33]. Past research showed that individuals with MS performed worse on the KD than a healthy control group. These studies found that a worse KD score was related to more severe impairment, neurologic disability, and worse vision related quality of life [17-18]. Taken together, the KD and the SDMT should have a close relationship since both tests have a visual, oral motor and oculo motor component. Indeed, Chen et al. reports that the KD significantly predicts performance on the SDMT [19].

We found a similar relationship in our study. Our data showed there was a significant relationship between performance on the SDMT and KD (Table 2). Our study also aimed to understand if KD scores were related to the cognitive subscales of the MoCA. The MoCA is a 15 minute test that assesses multiple cognitive domains and is widely used to screen for cognitive impairment in Alzheimer's disease [20]. Recently, the MoCA proved useful in detecting cognitive impairment in MS [22, 40]. The test evaluates cognitive domains that are commonly affected in MS, such as executive function, visuospatial ability, attention, language, and memory [20, 40-41]. Therefore, comparing the KD test to the MoCA allowed us to understand what domains were being assessed in the KD test. There was a relationship that showed the MoCA subscale of memory was the best predictor of borderline/impaired performance on the KD (Table 2). This differed from the results with the SDMT that showed the MoCA subscales of visuospatial and attentions were predictive of borderline/impaired performance on the SDMT (Table 5).

The current study allowed for a deeper understanding of the KD test. Results showed that the KD significantly predicted cognitive impairment as determined by the SDMT and that adding information about education and EDSS improved the predictive capability of the model. We used the SDMT norms, including corrections for age and education, to determine the T-score, and thus, the borderline/impaired and non-impaired groups. Past research showed that the KD test was associated with visual dysfunction [18]. The results from our study showed that not only did the KD measure visual dysfunction, but was also associated with cognitive dysfunction.

Cognitive abnormalities are prevalent in MS and are independent of the overall disease course [11]. The most common cognitive deficits in MS include attention, executive function, information processing speed, and memory [34-37]. These deficits affect daily living activities for people with MS, such as running a household, maintaining employment, and participating fully in society [12]. Detecting cognitive impairment early in the disease course allows for a better understanding of how cognitive impairment progresses in MS [23, 38]. In addition to cognitive deficits, problems with eye movements are also common in MS [2]. Interestingly, control of eye movements correlates with cognitive functions such as information processing speed, attention, and memory [39]. One likely reason the KD and SDMT provide insight into cognition is because the control of eye movements in complex tasks involves extensive brain networks that also participate in cognition.

Logistic regression also showed that EDSS predicted cognitive impairment on the SDMT. Although we used the oral version, where patients did not have to write their answers, disability was still a predictor of SDMT scores. This finding could be because speech impairment may slow the participants' responses and because higher disability is associated with worse cognitive function. The KD test also correlated with EDSS, but both the KD and SDMT captured a cognitive component independent of physical disability, namely memory for the KD and visuospatial and attention for the SDMT.

Precise and controlled eye movements are required to perform the KD test. The slower KD test times previously measured in people with MS indicated worse control of rapid eye movements [17-18]. Clough et al. (2015) found longer saccade latencies in people with MS than in

 Table 5: Logistic regression analysis with MoCA subscales score predictors of impairment.

Predictor	β	SE β	Wald's χ²	df	р	OR	95% CI	Sensitivity	Specificity
	89%	17%							
Constant	0.79	0.25	10.37	1	0.001*	2.21			
Memory	-0.4	0.18	4.83	1	.028*	0.67	0.47-0.96		
			Va	riables rem	oved from the e	quation			
			Visuospatial,	Attention, L	anguage, Abstra	action, Orient	ation		
		I	mpaired= SDMT T-:	score ≤ 40				67%	79%
Constant	-0.18	0.23	0.64	1	0.43	0.83			
Visuospatial	-0.55	0.29	3.63	1	0.057	0.56	0.33-1.02		
Attention	-0.9	0.33	7.27	1	0.007*	0.41	0.21-0.78		
			Va	riables rem	oved from the e	quation			
			Visuospatial	Language	Abstraction, Me	emory Orienta	tion		

OR: odds ratio.

controls across multiple tasks. They also found that latencies increased as a function of disease duration and argued that saccade latency depended upon the integrity of long-range networks that were susceptible to degradation in people with MS [42-43]. Our results extend this research by exploring other correlated functions such as information processing speed measured by the SDMT. When compared to controls, people with MS have longer inter-saccadic intervals (time between saccades) and generate a larger number of saccades. The inter-saccadic interval consists of the time needed to initiate a saccade and duration of the saccade. These two aspects of saccades also involve cognitive processing [18].

The KD test measures multiple factors, including the generation and control of saccades, maintenance of attention to the stimuli, and the ability to name each number. Moster et al. found that KD performance in people with MS correlated with performance on the Paced Auditory Serial Addition Test (PASAT) [18]. In people with Alzheimer's disease, the KD test correlated strongly with the Trail Making Test, a well-established and validated neuropsychological measure of attention, visual tracking, and information processing speed [44]. Chen et al. recently compared the KD and SDMT test performance in 130 participants with MS and found that the KD had a moderate correlation with the SDMT [19, 45], but education was not a significant predictor of SDMT scores in their study. They showed a correlation between the two tests, but did not provide descriptions of whether or not participants fell into the borderline/impaired range. Our study extended the knowledge by calculating T-scores for the SDMT and KD, showing a strong concordance between the two tests as measurements of cognitive impairment. Our results further extended those of Chen et al. by including people with lower education levels and highlighting the limitations of the SDMT regarding education. Chen et al. interpreted the KD's correlation with the SDMT as oculo motor confounding of the SDMT [19]. Our study did not include direct measures of simple oculo motor function, and thus this component of the relationship could not be separated. However, we hypothesized the KD and the SDMT captured a cognitive impairment component that was not accounted for by simple oculo motor dysfunction. Further studies are needed to clarify this relationship.

Detection of cognitive impairment in neurodegenerative diseases, such as MS, is essential for tracking disease progression. Brief, easily administered measures requiring minimal training are desirable for fastpaced, high patient volume clinics. Although several cognitive assessment tools are available, they have lengthy administration times and demographic variables influence most of them. The current study expands the choice of assessment tools by identifying the KD test as a promising tool to assess cognitive impairment in people with MS. While the MoCA did accurately classify patients as borderline/impaired or not based on SDMT T-scores, it was not as accurate as the KD and takes considerably longer to administer. Both the KD and the SDMT are fast and relatively inexpensive. The KD test is well suited for many clinicians and clinical researchers. Western Psychological Services Company sells the SDMT (https://www. wpspublish.com/sdmt-symbol-digit-modalities-test), and King-Devick Technologies, Inc. sells the KD at (https://kingdevicktest.com) along with the Pro Monitor program. The KD test requires minimal training to administer and interpret as the software automatically presents the instructions at the beginning of each testing trial [18]. The Pro Monitoring Program for the KD test provides age-normed comparisons. The KD can also measure the change serially for an individual over time. The KD test takes two to three minutes to administer, and the SDMT takes five or more minutes to administer and score using normative data, but requires training for proper administration [29]. Previous work that examined the KD time in sports-related concussions demonstrated the KD test's reliable administration by non-medically trained laypersons [46]. The MOCA has not been widely used in studies of people with MS. The MOCA does not fully replace a complete psychometric battery but it does have subscales targeting different cognitive domains. The MOCA is free but needs 1 hour of training to properly administer and since it takes (10-15) minutes it is harder to administer during a busy clinical visit. Thus each of these tests seems useful and clinicians should consider implementing at least one of them.

### Conclusion

There are some limitations to our study. We only examined crosssectional data, so we could not use the KD as a tool for predicting future cognitive decline. However, we are collecting longitudinal data of the KD test in MS and controls to answer this question. In this study, we evaluated motor impairment in MS using the EDSS; however, we did not evaluate if specific motor abnormalities were associated with the worse KD times. Future studies should elucidate the relationship of the KD times to the specific eye movement and neurological exam deficits seen in people with MS. In conclusion, our findings extend the research determining the usefulness of the KD test in MS. The KD test is a rapid and easily administered exam that detects the speed of internally generated saccades.

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### Authors' contributions

M.M., J.L., B.C., L.H., S.M., and D.D. contributed to the study concept, design, and drafting of the manuscripts. All authors contributed to the acquisition, analysis, and interpretation of data. We also like to thank Ashleigh Aubin, Hannah Zachary, Abigail Olinde, Tiana Dimasi, Katherine Henry, and Andrew Amedee for helping with data acquisition. Lastly, we want to thank Gerard Guillot, Ph.D. for assistance with graphics.

### Declaration

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#### References

- 1. Pula, J.H., & Reder, A.T. "Multiple sclerosis. Part I: neuro-ophthalmic manifestations". Curr Opin Ophthalmol 20.6 (2009) 467-475.
- Nerrant, E., & Tilikete, C. "Ocular Motor Manifestations of Multiple Sclerosis". J Neuro-ophthalmol Off J North Am Neuro-Ophthalmol Soc 37.3 (2017): 332-340.
- Pierrot-Deseilligny, C., et al. "Eye movement control by the cerebral cortex". Curr Opin Neurol 17.1 (2004): 17-25.

an cerebral cortex 25 Lónez-Góngora M et

- 4. Yeo, B.T.T., et al. "The organization of the human cerebral cortex estimated by intrinsic functional connectivity". *J Neurophysiol* 106.3 (2011): 1125-1165.
- 5. Ptak, R. "The frontoparietal attention network of the human brain: action, saliency, and a priority map of the environment". *Neurosci Rev J bringing Neurobiol Neurol Psychiatry* 18.5 (2012): 502-515.
- Bruce, C.J., & Goldberg, M.E. "Primate frontal eye fields. I. Single neurons discharging before saccades". *J Neurophysiol* 53.3 (1985): 603-635.
- Luppino, G., et al. "Prefrontal and agranular cingulate projections to the dorsal premotor areas F2 and F7 in the macaque monkey". *Eur J Neurosci* 17.3(2003): 559-578.
- 8. Bisley, J.W., et al. "Activity of neurons in cortical area MT during a memory for motion task". *J Neurophysiol* 91.1 (2004): 286-300.
- 9. Galetta, K.M., et al. "The King-Devick test of rapid number naming for concussion detection: meta-analysis and systematic review of the literature". *Concuss* 1.2 (2016).
- 10. Pierrot-Deseilligny, C., et al. "Cortical control of ocular saccades in humans: a model for motricity". *Prog Brain Res* 142 (2003): 3-17.
- 11. Rao, S.M., et al. "Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction". Neurol 41.5: 685-691.
- Rao, S.M., et al. "Cognitive dysfunction in multiple sclerosis. II. Impact on employment and social functioning". *Neurol* 41.5 (1991): 692-696.
- 13. Galetta, K.M., et al. "The King-Devick test and sports-related concussion: Study of a rapid visual screening tool in a collegiate cohort". *J Neurol Sci* 309,1-2 (2011):34-39.
- Galetta, K.M., et al. "Adding vision to concussion testing: a prospective study of sideline testing in youth and collegiate athletes". J Neuroophthalmology Off J North Am Neuro-Ophthalmology Soc 35.3 (2015): 235-241.
- Galetta, M.S., et al. "Saccades and memory: baseline associations of the King-Devick and SCAT2 SAC tests in professional ice hockey players". J Neurol Sci 328.1-2 (2013): 28-31.
- King, D., et al. "Concussions in amateur rugby union identified with the use of a rapid visual screening tool". *J Neurol Sci* 326.1-2 (2013): 59-63.
- Hainline, C., et al. "Capturing saccades in multiple sclerosis with a digitized test of rapid number naming". J Neurol 264.5 (2017): 989-998.
- Moster, S., et al. "The King-Devick (K-D) test of rapid eye movements: A bedside correlate of disability and quality of life in MS". J Neurol Sci 343.1-2 (2014):105-109.
- 19. Chen, M.H., et al. "Visual and motor confounds on the symbol digit modalities test". *Mult Scler Relat Disord* 45 (2020): 102436.
- Nasreddine, Z.S., et al. "The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment". J Am Geriatr Soc 53.4 (2005): 695-699.
- Pinto, T.C.C., et al. "Is the Montreal Cognitive Assessment (MoCA) screening superior to the Mini-Mental State Examination (MMSE) in the detection of Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) in the elderly?" Int Psychogeriatrics 31.4 (2019): 491-504.
- 22. Dagenais, E., et al. "Value of the MoCA test as a screening instrument in multiple sclerosis". *Can J Neurol Sci Le J Can des Sci Neurol* 40.3 (2013): 410-415.
- Kalb, R., et al. "Recommendations for cognitive screening and management in multiple sclerosis care". Mult Scler J 24.13 (2018): 1665-1680.
- Benedict, R.H.B., et al. "Validity of the symbol digit modalities test as a cognition performance outcome measure for multiple sclerosis". *Ther Adv Vaccines* 9.6 (2018):259-261.

- 25. López-Góngora, M., et al. "A one-year follow-up study of the Symbol Digit Modalities Test (SDMT) and the Paced Auditory Serial Addition Test (PASAT) in relapsing-remitting multiple sclerosis: An appraisal of comparative longitudinal sensitivity". BMC Neurol 15.1 (2015): 2-9.
- Sonder, J.M., et al. "Comparing long-term results of PASAT and SDMT scores in relation to neuropsychological testing in multiple sclerosis". *Mult Scler* 20.4 (2014): 481-488.
- Carroll, W.M. "2017 McDonald MS diagnostic criteria: Evidence-based revisions". *Mult Scler* 24.2 (2018): 92-95.
- Kurtzke, J.F. "Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS)". *Neurol* 33.11 (1983): 1444-1452.
- 29. Smith, A. "Symbol Digits Modalities Test". (2011).
- Benedict, R.H.B., et al. "Neuropsychology of multiple sclerosis: looking back and moving forward". J Int Neuropsychol Soc 23.9-10 (2017): 832-842.
- Benedict, R.H.B., et al. "Validity of the Minimal Assessment Of Cognitive Function In Multiple Sclerosis (MACFIMS)". J Int Neuropsychol Soc 12.4 (2006): 549-558.
- Feaster, H.T., & Bruce, J.M. "Visual acuity is associated with performance on visual and non-visual neuropsychological tests in multiple sclerosis". *Clin Neuropsychol* 25.4 (2011): 640-651.
- 33. Costa, S.L., et al. "Neuro-ophthalmic syndromes and processing speed in multiple sclerosis". *J Neuro Ophthalmol* 36.1 (2016): 23-28.
- Chiaravalloti, N.D., & DeLuca, J. "Cognitive impairment in multiple sclerosis". *Lancet Neurol* 7.12 (2008): 1139-1151.
- 35. Denney, D.R., et al. "Cognitive impairment in three subtypes of multiple sclerosis". Arch Clin Neuropsychol 20.8 (2005): 967-981.
- Drew, M.A., et al. "Examining the link between information processing speed and executive functioning in multiple sclerosis". Arch Clin Neuropsychol Off J Natl Acad Neuropsychol 24.1(2009): 47-58.
- Neuhaus, M., et al. "Decision-Making in multiple sclerosis patients: a systematic review". *Mult Scler Int* (2018):7835952.
- Benedict, R.H.B., et al. "Prediction of neuropsychological impairment in multiple sclerosis". Arch Neurol 61.2 (2004): 226.
- Nguyen, J., et al. "Visual pathway measures are associated with neuropsychological function in multiple sclerosis". *Curr Eye Res* 43.7 (2018): 941-948.
- Charest, K., et al. "Detecting subtle cognitive impairment in multiple sclerosis with the montreal cognitive assessment". *Can J Neurol Sci* 47.5 (2020): 620-626.
- 41. Vogel. S.J., et al. "Concordance of the montreal cognitive assessment with standard neuropsychological measures, alzheimer's dement diagnosis". Assess Dis Monit 1.3 (2015): 289-294.
- Clough, M., et al. "Ocular motor measures of cognitive dysfunction in multiple sclerosis II: working memory". J Neurol 262.5 (2015): 1138-1147.
- Clough, M., et al. "Ocular motor measures of cognitive dysfunction in multiple sclerosis I: inhibitory control". J Neurol 262.5 (2015): 1130-1137.
- Galetta, K.M., et al. "Screening utility of the king-devick test in mild cognitive impairment and alzheimer's disease dementia". Alzheimer Dis Assoc Disord. 21.2 (2017): 152-158.
- Baner, N., et al. "Speeded saccadic eye movement predicts symbol digit modalities test performance in multiple sclerosis". *Neurol* 88 (2017): 330.
- Leong, D.F., et al. "The King-Devick test as a concussion screening tool administered by sports parents". J Sports Med Phy Fitness 54.1 (2014): 70-77.

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