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# Validation of cognitive screening questionnaire for neurological disorders (CSQND) for screening of cognitive complaints among patients with multiple sclerosis

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## Abstract

**Background:** The prevalence of cognitive impairment (CI) can reach up to 65% among multiple sclerosis (MS) patients. Self-administered screening questionnaires can offer a valuable solution for screening MS patients for cognitive complaints. The cognitive screening questionnaire for neurological disorders (CSQND) is an Arabic self-administered questionnaire that has been developed to screen patients with various neurological disorders attending neurology clinics. The aim of this study was to assess cognitive complaints and to validate the CSQND as a screening tool among Egyptian MS patients.

**Results:** Four-hundred MS patients and 400 controls were included in this study. All 400 patients and 400 controls were subjected to the CSQND, only 50 out of the 400 patients and 50 out of the 400 controls retook the CSQND 1 week later to establish test–retest reliability. Fifty patients and 50 controls were assessed by the symbol digit modalities test (SDMT) to establish concurrent validity. Thirty-four percent of patients complained of memory problems, 51% complained of concentration difficulties, 34% complained of language difficulties and 22.5% complained of space and time disorientation. Multiple sclerosis patients had significantly more cognitive complaints ( $12.4 \pm 12.6$ ) compared to controls ( $6.2 \pm 6.8$ ) when screened using the CSQND ( $P < 0.000001$ ). Total scores of CSQND were positively significantly correlated to age at onset, total disease duration, EDSS scores and total number of relapses, ( $r = 0.14$ ;  $0.275$ ;  $0.3$ ;  $0.167$ , respectively),  $P < 0.05$  for all. Agreement was found between CSQND results and the SDMT results, where the line of equality lied within the 95% confidence interval of the mean. A significant positive correlation was found between the CSQND results at the first application and upon retesting both in patients ( $R = 0.9$ ,  $P = 0.0001$ ) and controls ( $R = 0.85$ ,  $P = 0.0001$ ).

**Conclusions:** The CSQND was found to be a simple, valid, and reliable self-administered questionnaire to screen for cognitive complaints in MS patients.

**Keywords:** Multiple sclerosis, Cognition, CSQND, Questionnaire

## Background

The prevalence of cognitive impairment (CI) can reach up to 65% among multiple sclerosis (MS) patients [1]. Cognitive impairment in MS can occur in either an

insidious or a gradual manner and it can start in early stages of the disease or even before a definite diagnosis of MS has been made like in radiologically isolated syndrome (RIS) [2–5].

It is obvious that as the disease progresses, the prevalence of CI gets higher, the prevalence of CI among clinically isolated syndrome (CIS) patients and RIS patients is estimated to be 20–25%, 30–45% among relapsing

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remitting MS (RRMS) patients and 50–75% among secondary progressive MS (SPMS) patients [2].

The assessment of CI among MS patients has always been posing a problem for MS practitioners as it consumes a considerable portion of doctors' and patients' time and requires more resources to implement regularly. Self-administered screening questionnaires can offer a solution for this problem, patients can fill screening questionnaires while waiting to meet their doctors or even questionnaires can be sent to patients to fill them at home prior to visiting the clinic.

The cognitive screening questionnaire for neurological disorders (CSQND) is an Arabic self-administered questionnaire that has been developed to screen patients with various neurological disorders attending neurology clinics. Patients who turn out to have cognitive complaints after taking the CSQND should then undergo a detailed cognitive assessment specific to their cognitive complaints and the neurological condition they have.

The aim of this study was to assess cognitive complaints and to validate the CSQND as a screening tool among Egyptian MS patients.

## Methods

This study included 400 MS patients attending the MS clinic at Cairo university hospital (CUH) and 400 age and sex matched apparently normal healthy controls. Sample size was calculated based on the following equation: sample required ( $n$ ) =  $N/1 + N*d^2$ , where  $N$  = Total population and  $d$  = Margin of error or precision [6]. Around 3500 MS patients attend our clinic. We aimed to work at 95% confidence interval (CI), where margin of error or precision rate decided by researcher is 5%. On applying the fore-mentioned formula: ( $n$ ) =  $3500/1 + 3500*(0.05)^2$ , sample size ( $n$ ) was found to be 358.9. Considering a 10% dropout of study participants, the minimum sample size was set to be 393 (358 + 35). Patients were recruited between February and August 2021. All patients were diagnosed with clinically definite MS (CDMS) according to the 2017 revised McDonald criteria [7]. Patients with known psychiatric disorders, visual impairment that may interfere with performing tests or patients in relapse were excluded.

Besides the routine history taking and clinical assessment, all 400 patients and 400 controls were subjected to the CSQND (Appendix), only 50 out of the 400 patients and 50 out of the 400 controls retook the CSQND 1 week later to establish test–retest reliability. Fifty patients and 50 controls were assessed by the symbol digit modalities test (SDMT) of the Arabic version of brief international cognitive assessment for MS (BICAMS) [8] to establish concurrent validity of the CSQND.

The study protocol was revised and approved by the institutional review board of faculty of medicine—Cairo university (MS-171-2021).

The CSQND is a self-administered questionnaire designed to screen for cognitive complaints in different neurological disorders. The questionnaire is composed of six parts covering different domains of cognitive functions with a total of 40 questions: Memory problems (12 questions), concentration (1 question), space and time orientation (4 questions), cash transactions and arithmetic operations (2 questions), language difficulties (7 questions), executive functions (4 questions) and other cognitive tasks (10 questions).

The 40 questions are short, close ended (Yes/No) questions written in simple language to be easily understood by the patient. The patient is awarded one point for every “Yes” answer and no points for every “No” answer. The total score is simply the sum of all answers with a score range of 0–40.

Face validity of the CSQND was tested on a sample of 50 patients attending the MS clinic of CUH to check that the questionnaire was understood linguistically and relevant to the targeted population. Two expert MS consultants revised the questionnaire to establish content validity.

The Arabic version of BICAMS is a validated well-established tool for assessment of CI in MS patients that can be administered by a neurologist. It is composed of three tests: The symbol digit modalities test (SDMT), the five initial learning trials of the second edition of the California verbal learning test (CVLT-II) and the revised brief visuospatial retention test (BVRT-R). The SDMT is used for assessment of divided attention, visual and motor processing speed. The SDMT presents a series of nine different symbols, corresponding to the numbers 1 through 9 in a key at the top of a standard sheet of paper. Patients are asked to write the correct number under the corresponding symbol as rapidly as possible for 90 s. The number of correct substitutions within the 90 s interval is recorded. [8]

Statistical package for social sciences (SPSS) version 18.0 was used for data management and data analysis. Mean  $\pm$  standard deviation described quantitative variables and median with range when appropriate (distribution did not follow normality). Number and percentages described qualitative data and  $\chi^2$  or Fisher exact tested proportion independence. In addition,  $\chi^2$  test for Goodness of fit was used to test an observed binomial distribution to an expected one. For comparing mean values of 2 independent groups, parametric and nonparametric  $t$  test were used. For comparing means of more than two independent groups one way ANOVA (analysis of variance) and Kruskal Wallis ANOVA were used. For

**Table 1** Demographic characteristics of patients and controls

	Patients (n = 400)	Controls (n = 400)	P value
Age (years)	25.7 ± 11.6	30.9 ± 11.5	0.5
Gender			
Females	285 (71.25%)	270 (67.5%)	0.2
Males	115 (28.75%)	130 (32.25%)	

**Table 2** Clinical characteristics of patients

MS (n = 400)	Median	IQR	Mean ± SD
Age at disease onset (years)	25	19–31.75	24.6 ± 10.5
ARR	0.46	0.22–1.03	0.85 ± 1.15
Disease duration (months)	78.05	31.5–132	91 ± 74
EDSS	2	1–3	2.2 ± 1.6

MS multiple sclerosis; IQR interquartile range; SD standard deviation; ARR annualized relapse rate; EDSS expanded disability status scale

comparing means of 2 dependent groups, paired *t* test and Mann Whitney tests were used.

The construct validity was tested by applying the “Known groups validity” method [9], where the CSQND patients’ results were compared to the results of age and sex matched controls. To establish concurrent validity, Bland–Altman plot was used to test the agreement between the results of the CSQND and the SDMT results [10]. Test–retest reliability was done by Pearson’s correlation coefficient (*r*).

## Results

The mean age for the patients’ group was 25.7 ± 11.6 years, 71.25% of patients were females (*n* = 285) and 28.75% were males (*n* = 115). The control group was age and sex matched. Table 1 shows the demographic characteristics of patients and controls.

Most patients had RRMS (*n* = 349, 87.5%), 8.75% had SPMS (*n* = 35) and 3.75% had primary progressive MS (*n* = 15). Table 2 summarizes the clinical characteristics of patients.

There was a statistically significant difference between patients and controls regarding 31 out of the 40 questions of the CSQND, where patients choose more “Yes” answers than controls. Thirty-four percent of patients complained of memory problems, 51% complained of concentration difficulties, 34% complained of language difficulties and 22.5% complained of space and time disorientation. Table 3 shows patients’ and controls’ responses to the CSQND 40 questions.

Total scores of CSQND were positively significantly correlated to age at onset, total disease duration, EDSS

scores and total number of relapses, (*r* = 0.14; 0.275; 0.3; 0.167, respectively), *P* < 0.05 for all.

Multiple sclerosis patients performed significantly worse on SDMT than controls, the mean SDMT score was 44.5 ± 15.1 for MS patients compared to 52.8 ± 4.8 for controls (*P* 0.0003).

There was a statistically significant difference between patients and controls as regards the CSQND total score, where MS patients had significantly more cognitive complaints (12.4 ± 12.6) compared to controls (6.2 ± 6.8) (*P* < 0.000001), confirming the ability of the questionnaire to distinguish between MS patients and controls, which is considered an indicator of construct validity of CSQND (Known groups validity).

Agreement was found between CSQND results and the SDMT results using the Bland–Altman plot, where the line of equality lied within the 95% confidence interval of the mean establishing concurrent validity of CSQND (Fig. 1).

A significant positive correlation was found between the CSQND results at the first application and upon retesting both in patients (*R* = 0.9, *P* = 0.0001) and controls (*R* = 0.85, *P* = 0.0001) confirming the test–retest reliability of the CSQND.

## Discussion

The aim of this study was to assess cognitive complaints among Egyptian MS patients and to validate the CSQND as a screening tool for cognitive complaints in Egyptian MS patients.

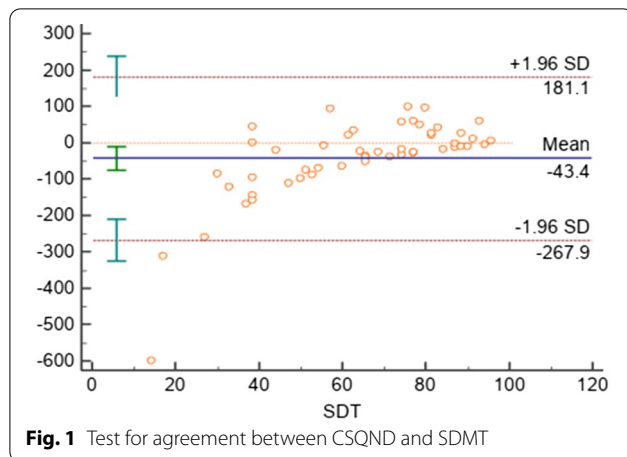
After taking the CSQND questionnaire, 34% of our patients were found to have memory problems, 51% had concentration difficulties, 34% had language difficulties and 22.5% had space and time disorientation. In a multi-center study carried out across Italy, Nocentini et al. found that 33% of MS patients suffered from memory dysfunction, 43% suffered from reduced processing speed, 20% suffered from language difficulties and 23% suffered from visuo-perceptual dysfunction [11]. In a cohort of 291 MS patients, Benedict and colleagues found 51.9% of patients to suffer impaired processing speed and 54.3% to suffer from memory dysfunction. [12] Other cohorts estimate memory problems to exist in up to 65% of MS patients [13], around 12–25% of MS patients suffer from attention difficulties [14], and around 25% of MS patients suffer from visuo-perceptual impairment [15].

Sadigh-Eteghad in a cohort of 115 MS patients, found that similar to this study, EDSS scores and disease duration were positively correlated with severity of CI, while unlike this study, age at disease onset and relapse rate were not correlated. However, in that study all variables except EDSS score significantly predicted CI severity [16]. In another cohort of 125 MS patients,

**Table 3** Patients' and controls' responses to the CSQND 40 questions

	Patients (n = 400)				Controls (n = 400)				P value
	Yes		No		Yes		No		
	n	%	n	%	n	%	n	%	
<b>Memory Problems</b>									
Q 1	226	56.5	174	43.5	172	43	228	57	0.0001
Q 2	141	35.25	259	64.75	139	34.75	261	65.25	0.8
Q 3	89	22.25	311	77.75	61	15.25	339	84.75	0.01
Q 4	139	34.75	261	65.25	94	23.5	306	76.5	0.0005
Q 5	85	21.25	315	78.75	30	7.5	370	92.5	<0.0001
Q 6	125	31.25	274	68.5	110	27.5	290	72.5	0.2
Q 7	109	27.25	291	72.75	124	31	276	69	0.2
Q 8	141	35.25	258	64.5	93	23.25	307	76.75	0.0005
Q 9	145	36.25	252	63	150	37.5	250	62.5	0.5
Q 10	133	33.25	267	66.75	81	20.25	319	79.75	<0.0001
Q 11	160	40	240	60	156	39	244	61	0.7
Q 12	154	38.5	245	61.25	75	18.75	325	81.25	<0.0001
Q 13	208	50.75	192	48	100	25	300	75	<0.0001
Q 14	100	25	300	75	105	26.25	295	73.75	0.6
<b>Concentration</b>									
Q 15	63	15.5	337	84.25	74	11.75	353	88.25	0.17
Q 16	81	19.5	319	79.75	39	9.75	361	90.25	0.0009
Q 17	51	12.75	349	87.25	26	6.5	374	93.5	0.002
Q 18	76	17.5	324	81	54	13.5	346	86.5	0.09
<b>Cash Transactions and Arithmetic Operations</b>									
Q 19	86	21.5	314	77	73	18.25	327	81.75	0.1
Q 20	136	34	264	64.5	87	21.75	313	78.25	0.0002
<b>Language Difficulties</b>									
Q 21	104	25	296	74	39	9.75	361	90.25	<0.0001
Q 22	128	32	272	67	94	23.5	306	76.5	0.0084
Q 23	88	22	311	77.75	31	7.75	369	92.25	<0.0001
Q 24	91	22.5	309	77.25	19	4.75	381	95.25	<0.0001
Q 25	83	20.25	317	79.25	32	8	368	92	<0.0001
Q 26	60	15	340	85	20	5	380	95	<0.0001





a significant association between age at onset, disease duration, and EDSS score and the risk of developing CI was found [17]. Sandi and colleagues in a cohort of 553 CIS and RRMS patients found EDSS score to be significant predictor of CI, but they found no association between age at onset, disease duration and cognitive dysfunction [18]. This can be explained by the different sample sizes and methodologies used in these studies.

In this study patients with MS performed poorly in SDMT, SDMT was affected in about 26% of patients with significant difference between patients and healthy controls. These results are similar to previous reports which found that 31% of Egyptian MS patients performed poorly in SDMT [8]. Different studies showed relatively higher percentages with a range of 28–67% for SDMT total score [19–21], this may be explained by the relatively younger age, shorter disease duration and less disability in our cohort.

A statistically significant difference was found between patients and controls as regards the CSQND total score, where MS patients significantly had more cognitive complaints than controls as expected. This establishes the construct validity of the CSQND through “Known groups validity” which is a form of construct validation in which the validity is determined by the degree to which an instrument can demonstrate different scores for groups known to vary on the variables being measured [9].

The CSQND results were in agreement with results of SDMT of BICAMS establishing the concurrent validity of CSQND. The SDMT has been found to be the most sensitive individual cognitive measure for use in MS due to its predictive validity, high sensitivity and specificity, ease of administration, and patient-friendliness [22]. The agreement of CSQND with SDMT which assesses the cognitive processing speed may suggest that cognitive symptoms in MS patients may be explained by affection

in processing speed rather than true memory or executive dysfunction.

The test–retest reliability of CSQND was confirmed by correlating the CSQND results at the first application and 1 week later upon retesting both in patients and controls and a significantly positive correlation was found.

This study has proven the CSQND to be a valid and reliable tool for screening cognitive complaints of Egyptian MS patients. Limitations in this study were difficulty to assess objectively other masked MS symptoms other than CI which may affect cognition due to lack of resources. Further studies in different cohorts and different disease areas are still needed to establish the validity of CSQND as a screening tool for cognitive complaints in different neurological disorders.

## Conclusions

Multiple sclerosis patients suffer from various cognitive complaints that include memory, concentration, and language among others. The CSQND was found to be a simple, valid, and reliable self-administered questionnaire to screen for cognitive complaints in MS patients.

## Appendix

### Cognitive screening questionnaire for neurological disorders (CSQND)

لا	نعم
	مشاكل في الذاكرة
	1 هل تنسى أين تركت الأشياء (على سبيل المثال ، مفاتيح وغيرها)؟
	2 هل تنسى الأسماء؟
	3 هل تنسى وجوه الناس ؟
	4 هل تنسى ما ينبغي أن تفعله اليوم ؟
	5 هل تنسى أين أنت أو أين أنت ذاهب ؟
	6 هل تنسى المواعيد؟
	7 هل تنسى الأحداث الأخيرة (على سبيل المثال،ماذا أكلت في الفطور)؟
	8 هل تنسى ترتيب الأحداث؟
	9 هل تنسى الأحداث التي وقعت منذ زمن طويل؟
	10 أنا أكثر اعتمادا على الآخرين لتذكيري الأشياء
	11 رغم كثرة النسيان ألا انى اتذكر معظم المعلومات لاحقا
	12 هل يلاحظ الاهل و المعارف وجود مشاكل بذاكرتك ؟
	التركيز
	13 هل يوجد صعوبة في التركيز ؟
	مشاكل التعرف على المكان و الزمان
	14 هل تجد صعوبة في معرفة تاريخ اليوم ؟
	15 هل تجد صعوبة في معرفة الوقت؟
	16 هل تجد صعوبة في معرفة الاماكن؟



لا	نعم
17	هل تجد صعوبة في معرفة مواعيد الصلاة؟
	<b>المعاملات النقدية و العمليات الحسابية</b>
18	هل تجد صعوبة في اجراء المعاملات النقدية عند البيع و الشراء؟
19	هل تجد صعوبة في العمليات الحسابية؟
	<b>صعوبات اللغة</b>
20	هل توجد صعوبة في العثور على الكلمة المناسبة؟
21	هل تجد صعوبة في تسمية الاشياء؟
22	هل تجد صعوبة في التعبير عن الأفكار؟
23	هل تجد صعوبة في فهم ما يقوله الآخر؟
24	هل تجد صعوبة في فهم ما قرأت؟
25	هل تجد صعوبة في الكتابة؟
26	هل تجد صعوبة في القراءة؟
	<b>المهام التنفيذية</b>
27	هل تجد صعوبة في فعل الأشياء بالترتيب الصحيح (التسلسل)؟
28	هل تجد صعوبة في التخطيط لتنفيذ اي عمل؟
29	أعاني من بطء في اتمام المهام المطلوبة
30	هل تجد صعوبة في ايجاد حل للمشاكل و عدم القدرة على ايجاد حلول بديلة؟
	<b>مهام معرفية أخرى</b>
31	هل تجد صعوبة في التعرف على الأشياء؟
32	هل تجد صعوبة في التعرف على الوجوه و الاشخاص؟
33	هل تجد صعوبة في التعرف على الاصوات ؟
34	هل تجد صعوبة في التعرف على أجزاء الجسم؟
35	هل تجد صعوبة في تحديد الاتجاهات؟
36	هل تجد صعوبة في التعرف على الأماكن المألوفة؟
37	هل تجد صعوبة في العوده الى المنزل أو الذهاب الى المناطق المألوفة؟
38	هل تجد صعوبة في عمل المهام المنزلية اليومية (مثل اعداد الطعام و الاهتمام بالمنزل... الخ)؟
39	هل تجد صعوبة في ممارسة العمل اليومي و الواجبات الوظيفية؟
40	هل تجد صعوبة في ارتداء أو خلع الملابس؟

### Abbreviations

CSQND: Cognitive screening questionnaire for neurological disorders; CI: Cognitive impairment; MS: Multiple sclerosis; RIS: Radiologically isolated syndrome; CIS: Clinically isolated syndrome; RRMS: Relapsing remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; CUH: Cairo university hospital; CDMS: Clinically definite multiple sclerosis; SDMT: Symbol digit modalities test; BICAMS: Brief international cognitive assessment for multiple sclerosis; CVLT-II: Second edition of the California verbal learning test; BVRT-R: Revised brief visuospatial retention test; SPSS: Statistical package for social sciences; ANOVA: Analysis of variance; EDSS: Expanded disability status scale.

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### Author contributions

MAN, MF, MIH, AF and AS carried out the work. MAN and MF designed the protocol. MIH, AF and AS shared collected scientific data. MIH was responsible for writing the initial draft of the manuscript. MF, MIH and AF did the statistical analysis. All authors read and approved the final manuscript.

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### Availability of data and materials

The data sets generated and/or analyzed during the current study are not publicly available due to the current Egyptian clinical research legislation but are available from the corresponding author on reasonable request and after institutional approval.

### Declarations

#### Ethics approval and consent to participate

The authors obtained permission to conduct this study that was approved by the Institutional Review Board (IRB), Faculty of Medicine—Cairo University (MS-171-2021). All participants signed an informed consent. The procedures followed were in accordance with our protocol. We recruited 400 patients from the MS clinic of Cairo university hospital.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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