



Cognitive Assessment of Individuals with Multiple Sclerosis in the Arab World: a Systematic Review

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Abstract

The prevalence of multiple sclerosis (MS) is on the rise globally, and recent epidemiological studies have observed increased rates in the Arab world (i.e., countries of North Africa and the Middle East where Arabic is the primary language). However, assessment of cognitive impairment and its relevant covariates (e.g., fatigue and depressive symptomatology) in the Arab world has not been rigorously reviewed. Thus, the objective of the present study was to systematically review the current use of cognitive assessment measures in observational and interventional studies of individuals with MS in the Arab world. A systematic review of studies that assessed cognitive function in adults with MS in the Arab world was conducted using PubMed, PsycINFO, CINAHL, The Cochrane Library, Embase, WHO Global Index Medicus, and Ovid Global Health. Studies that featured at least one objective cognitive measure were included. Eligible studies were reviewed for bias and study quality using the QUADAS-2 and NIH QAT. Study characteristics and findings were extracted by two independent reviewers, with results confirmed by a third reviewer. A total of 13 ($N = 846$) studies met inclusion criteria. Risk of bias and included measures varied across studies. Results demonstrated inconsistent availability and use of MS cognitive assessment tools across the Arab world. An Arabic version of the BICAMS was the only cognitive battery that was evaluated with regard to psychometric properties. The most common individual test included in reviewed studies was the SDMT. However, validation studies are still needed for this and a number of other measures. Other measures are still in the early stages of translation and cultural-linguistic norming. This review of cognitive assessment of individuals with MS in the Arab world was limited by variable study quality and measure selection. The present review provides a summary of the tests most commonly used in this region and recommendations for future investigation.

Keywords Multiple sclerosis · Cognitive assessment · Arabic

Multiple sclerosis (MS) is a chronic central nervous system disorder that leads to significant disability. MS is characterized by inflammation and destruction of the myelin sheath that protects nerve fibers, ultimately leading to axonal loss and neurodegeneration in the brain, spinal cord, and optic nerves (Weinshenker et al., 1989). The disease can take several

subtypes – relapsing-remitting, secondary progressive, or primary progressive – with disability severity ranging from minimal to severe. Although MS is estimated to affect over 2.5 million people worldwide, prevalence rates differ significantly between geographical regions (Makhani et al., 2013; Pugliatti, Sotgiu, & Rosati, 2002).

Historically, epidemiological studies have shown a general trend that higher latitudes confer greater risk for MS (Anderson et al., 1992; Rosati, 2001). However, much of the early research was limited to studies conducted in North American and northern Europe (Weinshenker, 1994), and thus did not account for the significant variability in clinical presentations observed in other regions and populations throughout the world. More recent MS epidemiological research points to highly complex interactions between genetic, environmental, and cultural-behavioral risk factors, especially for diverse regions like the Middle

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East and North Africa (Alonso & Hernán, 2008; Simpson, Blizzard, Otahal, Van der Mei, & Taylor, 2011).

Rates of MS within the Arab world – countries within the Middle East and North Africa in which Arabic is the primary language – are comparable to those of North America (58–95 per 100,000), and are greater than those in parts of southern Europe (Becuş & Popoviciu, 1994; Dean, Aksoy, Akalin, Middleton, & Kyriallis, 1997). Thus, rates of MS in the Arab world do not appear to conform to previous findings of a global latitude gradient. Rates within the Arab world vary significantly, ranging from as low as 0.7 per 100,000 in Jerusalem (Karni et al., 2003), to 55 in Dubai (Bohlega et al., 2013), and 64.4 in Abu Dhabi (Benamer, Ahmed, Al-Din, & Grosset, 2009; Heydarpour, Khoshkish, Abtahi, Moradi-Lakeh, & Sahraian, 2015; Schiess et al., 2016). MS disease type, severity, and clinical characteristics also differ for Arab populations. Compared to geographically proximate Persian populations, Arab populations exhibit higher rates of primary progressive MS (15% vs 5%), motor deficits, and cerebellar dysfunction (Al-Araji & Mohammed, 2005; Saadatnia, Etemadifar, & Maghzi, 2007; Sharafaddinzadeh et al., 2013). With regard to sex differences, men in North America and Europe tend to exhibit greater disease severity than women. However, a study conducted in Lebanon showed the opposite pattern, with women demonstrating greater disease progression (Yamout et al., 2008). Given these findings, additional work is needed to characterize other common features of MS in Arab populations, including cognitive impairment.

Cognitive impairment affects 40–75% of people with MS, and typically manifests in the domains of processing speed, learning efficiency, and working memory (Chiaravalloti & DeLuca, 2008; Rao, Leo, Bernardin, & Unverzagt, 1991). In North America, Europe, and Australia, recommendations for comprehensive MS care encourage routine cognitive assessment (Foley, Benedict, Gromisch, & DeLuca, 2012; Kalb et al., 2018), as well as assessment of fatigue and depressive symptoms, which can negatively affect cognitive function (Rao et al., 1991). Measures that have been validated for use in MS include: (1) cognitive screening tools such as the Montreal Cognitive Assessment (MOCA), (2) assessment batteries such as the Minimal Assessment of Cognitive Function in MS (MACFIMS) or the Brief International Cognitive Assessment for MS (BICAMS), and (3) self-report inventories such as the Fatigue Severity Scale (FSS) and the Patient Health Questionnaire – 9 (PHQ-9) for fatigue and depressive symptoms, respectively (Benedict et al., 2006; Charvet et al., 2015; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989; Sjonnesen et al., 2012). Although most of these measures were developed in English and have been translated to other Indo-European languages (Goretti et al., 2014; Vanotti, Smerbeck, Benedict, & Caceres, 2016), their availability and use in the Arab world has been limited historically (Manee, Nadar, Jassem, & Chavan, 2017). In a recent systematic review of cognitive assessment in

Arab samples, less than half of the measures examined across 384 studies were adequately adapted or validated (Fasfous, Al-Joudi, Puente, & Perez-Garcia, 2017; Manee et al., 2017).

Fortunately, cognitive assessment in the Arab world is becoming more common for a wide range of neurologic conditions (e.g., dementia, epilepsy, Parkinson's disease). The review by Fasfous et al. (2017) found 53 neuropsychological measures that had been adapted and validated in neurologic or healthy samples from 18 of the 22 Arab countries. Although the review included several measures that are commonly used in MS (e.g., MOCA and several tests from MACFIMS and BICAMS batteries), none of those studies featured MS samples. Thus, the objective of the present study was to systematically review the current use of cognitive assessment measures in observational and interventional studies of individuals with MS in the Arab world. Results will help inform recommendations for promoting culturally competent assessment of cognitive impairment in this diverse and under-studied population.

Method

The present review was planned and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). The review protocol was not pre-registered. A PRISMA checklist has been provided as an online supplement (see Supplement 1), and a PRISMA flow diagram is presented in Fig. 1.

Eligibility Criteria

The following inclusion criteria were developed by the study team and refined as needed as questions arose during the search process. For final inclusion, all studies were required to: (1) be published journal articles, poster abstracts, or unpublished theses written in English, Arabic, or French, (2) feature a sample of adults (age 18 or older) with a diagnosis of MS, (3) take place in at least one of the 22 countries of the Arab world, and (4) include at least one objective measure of cognitive function. Studies could also include self-report measures of cognition, fatigue, and mood, though this was not an inclusion criterion. Studies could be observational or experimental in design, provided that at least one objective cognitive measure was administered prior to initiation of an intervention. No restrictions were placed on dates of publication or length of follow-up. Reviews (including meta-analyses) and case studies were excluded.

Search Strategy and Sources

A comprehensive list of search terms was developed by the study team with a help of a clinical informationist (CP) to

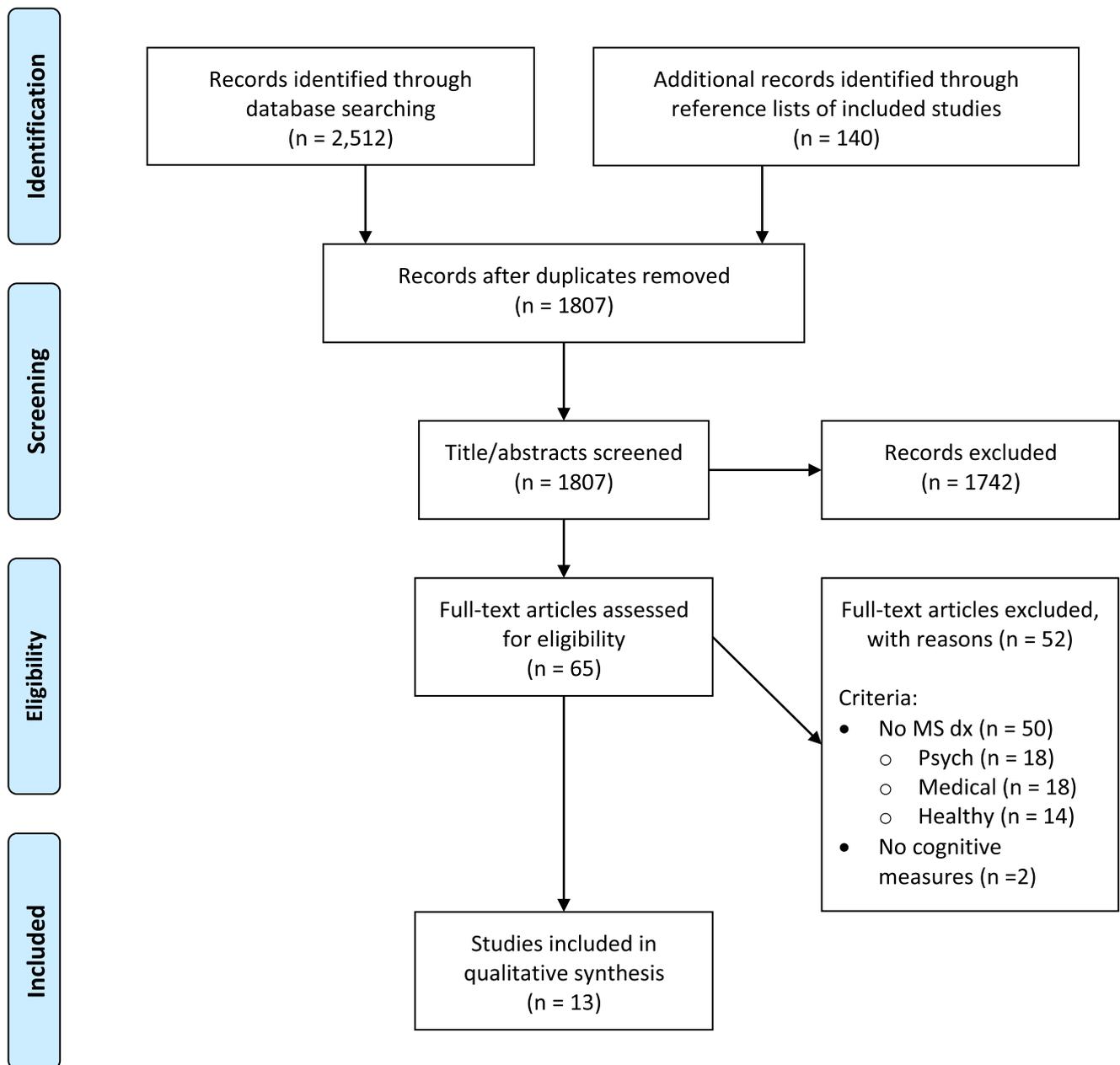


Fig. 1 PRISMA flow diagram

refine search syntax according to unique database requirements (see Supplement 2). Search terms included: (1) “multiple sclerosis” or its variants, and (2) any term that reflected a country (e.g., “Iraq”), region (e.g., “middle east”) or population (e.g., “Arab”) relevant to this study. Searches included Medical Subject Headings (MeSH), text words, and wildcard (*) terms and were conducted in the following databases: PubMed, PsycINFO, CINAHL, The Cochrane Library, Embase, WHO Global Index Medicus, and Ovid Global Health. Additional references were identified via the reference list from a recent systematic review of neuropsychological assessment in the Arab world (Fasfous et al., 2017). All searches took place in

July 2018 and were conducted by the clinical informationist and repeated by the third author (AH).

Study Selection

After removal of duplicate titles, all unique titles and abstracts were independently screened for eligibility by the first two authors (SP and AB). Differences in eligibility determination were resolved by the third author (AH). After removal of ineligible studies, remaining studies underwent full text review by the first two authors (SP and AB). Reviewers exhibited 86% agreement, and discrepancies were resolved by the third author (AH). All remaining eligible studies, as well as a

random selection of 25% of excluded studies, underwent full text review by the third author (AH) to ensure agreement with reasons for exclusion. Study selection took place between July and September 2018.

Data Extraction and Summary Measures

Data extraction and risk of bias assessment took place between September and October 2018. A data extraction form was modified from a previous review of depression assessment in MS (Hind et al., 2016) and included the following items and summary measures (see Tables 1 and 2): (1) study authors, year and country, (2) study type (journal article or published abstract) and design (observational or interventional), (3) sample characteristics (sample size, % female, mean age, MS types, mean MS duration, mean disability score), (4) whether the study controlled for potential covariates such as age or education, (5) whether the study measures were translated (to Arabic), adapted, or evaluated for reliability or validity, (6) objective cognitive tests, (7) self-report measures of fatigue or depressive symptoms, and (8) responses to relevant items from two measure of individual study bias - the Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2; Whiting et al., 2011) and the National Institutes of Health Quality Assessment Tool (NIH QAT; National Institutes of Health, 2014). Using separate forms, two authors (AB and AH) independently extracted data, and results were compared for consistency. Discrepancies were discussed with the team and resolved. Discrepancies were minimal and typically involved confirming whether the study included sample size justification and adequate inclusion criteria.

Risk of Bias

Risk of bias at the individual study was reviewed using the three sample selection bias items from the QUADAS-2, and six relevant study design items from the NIH QAT (see Table 2). The second author (AB) rated all included studies, and all items were checked by the third author (AH). Discrepancies were resolved by discussion among the authors. Bias at the global review level was assessed using the Risk of Bias in Systematic Reviews (ROBIS; Whiting et al., 2016).

Results

Study Selection

Database searches retrieved 2512 articles (see Fig. 1 and Supplement 2). An additional 140 references were retrieved from Fasfous et al.'s systematic review (2017). After removal of duplicate records, 1807 titles and abstracts were independently screened for eligibility. Differences in eligibility

determination were observed for 3% ($n = 51$) of the studies. Following resolution of discrepancies, 65 studies underwent full text review. Fifty-two studies were excluded during full-text review, with reviewers exhibiting 86% agreement. Of note, 50 of those studies were excluded due to the sample not being MS. Reasons for exclusion are presented in the PRISMA flow diagram (Fig. 1). Additionally, a table of the excluded citations, reasons for exclusion, and study populations is provided in an online supplement (Supplement 3). Following resolution of discrepancies, a total of 13 studies ($N = 846$ unique participants with MS) were included in the final review.

Study Characteristics

Study characteristics for the 13 included studies are presented in Table 1. The studies were published between 2004 and 2017, with the majority (69%) published within the past five years (Alosaimi, AlMulhem, & Moscovici, 2017; Ben Aljia et al., 2016; Darwish et al., 2017; El Ayoubi et al., 2016; El Ghoneimy, Hassan, Homos, Farghaly, & Dahshan, 2015; El-Ghoneimy et al., 2009; El-Kholy, Ramadan, El-Sheikh, & Ali, 2012; Hamdy et al., 2013; Kamel, El Kholy, & Hashem, 2004; Khalil et al., 2017; Kishk et al., 2017; Yamout et al., 2010; Yamout et al., 2013). Countries represented in the included studies were Egypt ($n = 6$), Lebanon ($n = 4$), Saudi Arabia ($n = 2$), Tunisia ($n = 1$), and Syria ($n = 1$). Median sample size was 50 (range 10–195). Ten studies were published articles, and three were poster abstracts. Regarding study design, 10 studies were observational (e.g., examining associations between cognitive performance and other MS-related variables), two were randomized controlled trials, and one was a quasi-experimental single-group design. Regarding study objectives, all studies examined cognitive performance in individuals with MS in the Arab world. However, only one study expressly aimed to determine psychometric properties of a cognitive measure. Specifically, that study was a poster abstract that evaluated the reliability of an Arabic version of the BICAMS (Kishk et al., 2017). The remaining 12 studies examined associations between cognitive measures and other MS-relevant variables (e.g., MRI indices), or examined changes in cognitive function following intervention (e.g., vitamin D replacement).

Sample demographic characteristics were reported in 11 of the included studies. Median sample age across studies was 33.5 years, and median percentage of women was 71%. Ten studies reported mean MS duration (median = 6.1 years, range = 2.6 to 20.0) and eight studies reported disability severity based on the Expanded Disability Status Scale (EDSS; median = 2.4, range = 1.2 to 4.0). For studies that reported on MS subtype ($n = 10$), all but one (Yamout et al., 2010) featured samples that were over 50% relapsing-remitting. Only

Table 1 Study characteristics

Citation	Country	Type	Design	N	% female	Age (yrs)	MS Duration (yrs)	MS Type	EDSS	Covariates	Objective Cognitive Tests	Self-Report Measures	TL	AD	Psychometrics
Alosaimi et al., 2017	SA	JA	OBS	195	81%	31.8	6.3	RR, SP, PP	NR	NR	MOCA	PHQ-9	Y	Y	N
Ben Aljia et al., 2016	TN	PA	OBS	86	77%	35.3	NR	NR	NR	NR	PASAT SDMT	BDJ-II MFIS	NR	NR	N
Darwish et al., 2017	LB	PA	QE	88	NR	NR	NR	RR, CIS	NR	NR	BVMT-TL BVMT-DR MOCA SDMT	NR	NR	NR	N
El Ayoubi et al., 2016	LB	JA	OBS	47	77%	31.7	2.6	100% RR	1.2	Age Education MS (yrs)	BVMT-TL BVMT-DR MOCA SDMT Stroop	HSCL	Y	NR	N
El-Ghoneimy et al., 2009	EG	JA	OBS	30	63%	28.9	5.9	50% RR 30% SP 20% PP	3.9	NR	PASAT	FSS	NR	NR	N
El-Ghoneimy et al., 2015	EG	JA	OBS	31	35%	34.4	6.9	74% RR 26% SP	3.9	NR	BICAMS BVMT-TL BVMT-DR COWAT CVLT-TL CVLT-DR MMSE PASAT SDMT	FSS	Y	Y	N
El-Kholy et al., 2012	EG	JA	OBS	50	74%	29.3	4.2	100% RR	2.3	NR	WAIS-DS WCST	NR	NR	NR	N
Hamdy et al., 2013	EG	JA	RCT	30	73%	24.0	3.5	83% RR 17% SP	2.2	NR	BICAMS BVMT-TL BVMT-DR COWAT CVLT-TL CVLT-DR PASAT SDMT WCST	BDJ-II FSS	NR	NR	N
Kamel et al., 2004	EG	JA	OBS	24	42%	36.5	5.2	100% RR	4.0	NR	COWAT MMSE	NR	Y	Y	N
Khalil et al., 2017	SA	JA	OBS	70	71%	34.3	7.8	100% RR	2.3	Age BDI-II Education MFIS Sex	MOCA SDMT	BDJ-II MFIS	Y	Y	N

Table 1 (continued)

Citation	Country	Type	Design	N	% female	Age (yrs)	MS Duration (yrs)	MS Type	EDSS	Covariates	Objective Cognitive Tests	Self-Report Measures	TL	AD	Psychometrics
Kishk et al., 2017	EG	PA	OBS	58	NR	NR	NR	84% RR, 12% SP, 2% PP, 2% CIS	NR	Age Education Sex	BICAMS BVM-TL BVM-T-DR CVLT-TL CVLT-DR SDMT	NR	Y	Y	Reliability
Yamout et al., 2010	LB	JA	RCT	10	60%	42.8	20.0	10% RR, 90% SP	4.0 to 7.5	NR	PASAT	NR	NR	NR	N
Yamout et al., 2013	LB/SY	JA	OBS	127	63%	39.0	9.2	75% RR, 11% SP, 4% PP, 10% CIS	2.4	NR	SDMT	FSS HDRS	NR	Y	N

Abbreviations: AD, adapted; AR, Arabic; BDI – II, Beck Depression Inventory – II; BVM-T-DR, Brief Visuospatial Memory Test – Revised Delayed Recall Trial; BVM-T-TL, Brief Visuospatial Memory Test – Revised Total Learning Trials; CIS, clinically isolated syndrome; COWAT, Controlled Oral Word Association Test; CVLT – DR, California Verbal Learning Test – II Delayed Recall Trial; CVLT – TL, California Verbal Learning Test – II Total Learning Trials; EDSS, Expanded Disability Status Scale; EG, Egypt; FSS, Fatigue Severity Scale; HDRS, Hamilton Depression Rating Scale; HSCL, Hopkins Symptom Check List; LB, Lebanon; JA, journal article; MFIS, Modified Fatigue Impact Scale; MMSE, Mini Mental Status Examination; MOCA, Montreal Cognitive Assessment; N, no; NR, not reported; PA, poster abstract; PASAT, Paced Auditory Serial Addition Test; PHQ – 9, Patient Health Questionnaire – 9; PP, primary progressive; QE, quasi-experimental RR, relapsing remitting; SA, Saudi Arabia; SDMT, Symbol Digit Modalities Test; SP, secondary progressive; SY, Syria; TL, translated; TN, Tunisia; WAIS – DS, Digit Span subtest of the Wechsler Adult Intelligence Scale – Revised; WCST, Wisconsin Card Sorting Test; Y, yes

three studies reported adjusting for relevant covariates (e.g., age, sex, education).

Risk of Bias

Risk of bias within each study is presented in Table 2. Sample selection method was not reported for five studies, three of which were poster abstracts. Thus, risk of sample selection bias based on items from the QUADAS-2 could not be determined for those studies. For the remaining eight studies, three exhibited high risk of bias due to case control designs, and five exhibited low risk of bias with consecutive recruitment and enrollment procedures. Based on items from the NIH QAT, all studies included study objectives, stated target populations, and defined outcomes, however, studies varied with regard to study inclusion criteria and sample size justification. The three poster abstracts did not report on inclusion criteria, and only two studies provided sample size justifications (El Ayoubi et al., 2016; El-Ghoneimy et al., 2009). Overall, study quality was good for two studies, fair-to-good for eight, and unclear or fair for three. At the review level, risk of bias based on the ROBIS was low overall, and low within each dimension evaluated (i.e., study eligibility criteria, selection of studies, data collection, and synthesis; see Supplement 4).

Objective Cognitive Measures

Studies included a wide range of cognitive assessment measures, including global cognitive screeners, individual tests for specific cognitive domains, and multi-domain assessment batteries (see Table 1). The MOCA was included in four studies and was the most common global cognitive screener, followed by the MMSE ($n = 2$). The SDMT was the most common individual test ($n = 7$), followed by the Brief Visuospatial Memory Test – Revised (BVM-T-R; $n = 5$), Paced Auditory Serial Addition Test (PASAT; $n = 5$), California Verbal Learning Test – II (CVLT-II; $n = 3$), Controlled Oral Word Association Test (COWAT; $n = 3$), Digit Span subtest from the Wechsler Adult Intelligence Scale – Revised (WAIS-DS; $n = 2$), Wisconsin Card Sorting Test (WCST; $n = 2$), and Stroop test ($n = 1$).

The BICAMS battery, which consists of the BVM-T-R, CVLT-II, and SDMT, was included in three studies and was the only cognitive battery administered in its entirety. Overall, tests from the BICAMS were the most common measures included in the reviewed studies, which is consistent with established recommendations for assessing processing speed and learning efficiency in individuals with MS (Langdon et al., 2012). Although five of the MACFIMS battery subtests (i.e., BVM-T-R, CVLT-II, SDMT, COWAT, and PASAT) were included in several studies, no studies administered the remaining two MACFIMS subtests (i.e., Delis-Kaplan

Table 2 Risk of bias within studies

Author	Year	Country	Type	QUADAS-2				NIH QAT				
				Sample Selection Method	Inappropriate Exclusions	Sample Bias Risk	Stated Objective	Specified Population	Specified Criteria	Justified Sample Size	Outcomes Defined	Quality Rating
Alosaimi et al.	2017	SA	JA	CON	N	Low	Y	Y	Y	N	Y	Fair/Good
Ben Aljia et al.	2016	TN	PA	NR	NR	Unclear	Y	Y	Y	N	Y	Unclear/Fair
Darwish et al.	2017	LB	PA	NR	NR	Unclear	Y	Y	Y	N	Y	Unclear/Fair
El Ayoubi et al.	2016	LB	JA	CON	N	Low	Y	Y	Y	Y	Y	Good
El-Ghoneimy et al.	2009	EG	JA	NR	N	Unclear	Y	Y	Y	Y	Y	Good
El Ghoneimy et al.	2015	EG	JA	CC	N	High	Y	Y	Y	N	Y	Fair/Good
El-Kholy et al.	2012	EG	JA	CC	N	High	Y	Y	Y	N	Y	Fair/Good
Hamdy et al.	2013	EG	JA	CON	N	Low	Y	Y	Y	N	Y	Fair/Good
Kamel et al.	2004	EG	JA	CC	N	High	Y	Y	Y	N	Y	Fair/Good
Khalil et al.	2017	SA	JA	CON	N	Low	Y	Y	Y	N	Y	Fair/Good
Kishk et al.	2017	EG	PA	NR	NR	Unclear	Y	Y	Y	N	Y	Unclear/Fair
Yamout et al.	2010	LB	JA	NR	N	Unclear	Y	Y	Y	N	Y	Fair/Good
Yamout et al.	2013	LB/SY	JA	CON	N	Low	Y	Y	Y	N	Y	Fair/Good

Abbreviations: CC, case controlled sampling; CON, consecutive sampling; EG, Egypt; LB, Lebanon; JA, journal article; N, no; NIH QAT, National Institutes of Health Quality Assessment Tool; NR, not reported; PA, poster abstract; QUADAS-2, Quality Assessment of Diagnostic Accuracy Scale - 2; SA, Saudi Arabia; SY, Syria; TN, Tunisia; Y, yes

Executive Function System [DKEFS] Sorting Test and Judgment of Line Orientation Test [JLO]).

Translation and Adaptation

As per review inclusion criteria, all studies were conducted in countries where Arabic was the primary language. However, only six studies explicitly reported that the cognitive tests administered were translated into Arabic or adapted for use in the Arab population. Among those studies, the SDMT was the most commonly used individual test ($n = 4$), followed by the BVMT-R ($n = 3$), COWAT ($n = 3$), and CVLT-II ($n = 2$). Two studies used Arabic versions of the MOCA, however, as noted in one study (Alosaimi et al., 2017), use of this measure for individuals with MS is not ideal due to its lack of specificity for detecting processing speed deficits. The SDMT, in contrast, was cited as one of the most readily adaptable tests for Arabic-speaking MS patients due to its use of linguistically less demanding stimuli (El Ayoubi et al., 2016). Similarly, for assessment of executive function, the WCST was used in lieu of the DKEFS Sorting Test, which has not been adequately translated or normed for use in the Arab world.

Self-Report Measures

Seven of the 13 studies assessed fatigue or depressive symptoms in conjunction with cognitive function. Six studies assessed fatigue, using either the FSS ($n = 4$) or Modified Fatigue Impact Scale (MFIS; $n = 2$), both of which have been validated for use in other MS populations. Six studies assessed depressive symptomatology, using one of the following measures: Beck Depression Inventory – II (BDI-II; $n = 3$), PHQ-9 ($n = 1$), Hamilton Depression Rating Scale ($n = 1$), and Hopkins Symptom Checklist (HSCL). Translation of self-report measures to Arabic was only described in one study, which used the FSS and HDRS (Yamout et al., 2013). Although Arabic versions of the BDI-II and PHQ-9 are available and used in other Arab neurologic populations, none of the present studies described use of these translated or adapted measures.

Discussion

Epidemiological studies over the past decade have documented an increased prevalence of MS in the Arab world. Thus, a growing body of literature has aimed to characterize key aspects of MS in this population, including cognitive impairment. The present study systematically reviewed current use of cognitive assessment measures in observational and interventional studies of individuals with MS in the Arab world. A total of 13 studies were included.

In terms of availability and evidence for reliability, results supported the BICAMS as the optimal battery for assessing

cognitive function in Arabic-speaking individuals with MS. First, the BICAMS includes two subtests (SDMT and BVMT-R) stimuli for which are not linguistically demanding. Second, an Arabic version of the BICAMS was found to have good reliability (Kishk et al., 2017). Consistent with studies in other parts of the world, the BICAMS provides a brief assessment that is uniquely designed to assess the cognitive deficits most commonly observed in MS, namely, processing speed, learning efficiency, and working memory (Benedict et al., 2012). Additional individual cognitive measures, such as the PASAT and COWAT, are subtests of the MACFIMS and have also been investigated in this population. However, because no studies have examined the psychometric properties of the MACFIMS in its entirety, or in several of its subtests (e.g., PASAT, COWAT, JLO, and DKEFS Sorting Test), interpretation of performance on these measures remains an area requiring further investigation. Finally, studies in the present review were more likely than studies in North American or European populations to use the WCST as a measure of executive function. Results point to the need for additional translation, adaptation, and validation of common MS cognitive measures for use in Arabic-speaking populations.

Given the symptomatic overlap of fatigue and depressive symptoms with cognitive impairment in MS, the present study also reviewed use of self-report measures in the included studies, and whether studies adjusted for these variables in analyses. Assessment of fatigue or depressive symptoms was observed in approximately half of the studies reviewed and included Arabic versions of the Fatigue Severity Scale and Hamilton Depression Rating Scale. Arabic versions of the BDI-II, another common depressive symptom inventory, have been used in other Arab neurologic populations. Although the BDI-II was included in three of the present studies, information regarding its translation or adaptation was not reported. The relatively common use of the BDI-II was also somewhat unexpected given that in other parts of the world, research has recommended use of measures that rely less heavily on somatic depressive symptoms (e.g., psychomotor slowing). Measures such as the PHQ-9, which was included in only one of the present studies, or the BDI-Fast Screen, which was not included in any of the present studies, reduce the influence of somatic symptoms.

In terms of geographic and linguistic diversity, articles selected for the present review included: (1) MS patients predominately from Egypt and Lebanon, and (2) measures that had been translated or adapted to Modern Standard Arabic (Fous-ha). Although Egypt and Lebanon include some of the largest metropolitan areas of Arabic-speaking MS patients, results highlight that numerous countries remain underrepresented in this literature, including Iraq, Kuwait, Oman, and Algeria. Significant cultural variations exist between and within these countries based on urban versus rural regions and other sociopolitical factors that were not captured in the

present review. With regard to language, individuals in the Arab world also exhibit significant regional variations in the language and may use different pronunciations of certain letters, or even different vocabulary. While many assessments in the present review exhibit cross-cultural adaptability (e.g., SDMT), others may not generalize to all Arab cultures, even when the measure is translated to Arabic (e.g., COWAT). As a recent linguistic review noted, obstacles to the translation, adaptation, and use of assessments in the Arab world include the fact that some terms cannot be translated using a single term, and some concepts may not translate from a cultural perspective (Abou-Mrad et al., 2015).

Although measures like the BICAMS have been developed to assess cognitive impairment specific to MS in the Arab world, the measures and domains assessed were often initially selected based on the clinical presentations of MS populations within North America and Northern Europe. Additional research may be needed to ensure the BICAMS reflects the cognitive domains most affected by Arab MS patients. As noted by Fafous et al. (2017), several other cognitive assessment measures have been translated to Arabic and normed in other Arab neurologic populations (e.g., stroke, Parkinson's disease, traumatic brain injury). Examination of these other measures in Arabic-speaking MS patients may help to further identify tests that are optimally sensitive and specific for assessing cognitive impairments in this population.

Finally, it is important to note that there are a limited number of trained practitioners able to administer the recommended MS assessments to their patients. Estimates of the number of psychiatrists in the Arab world range from zero to five per 100,000 (compared to 16 per 100,000 in the U.S.), and there appear to be even fewer psychologists in the region (Melcon, Correale, & Melcon, 2014). For example, in the United Arab Emirates, often described as one of the most industrialized countries in the Arab world, a recent survey found that there are 0.3 psychiatrists and 0.51 psychologists per 100,000 (Al-Darmaki & Yaaqeib, 2015). Barriers to access range from lack of transportation and finance, to discrimination based on gender and religion, to health literacy (Kronfol, 2012). As such, it can be assumed that many individuals with MS in the Arab world do not have access to providers that use the assessments identified in this paper, even in countries where they may be available.

Limitations

We acknowledge several limitations regarding the results of the present review. First, despite current availability of the measures reviewed, this area of research is relatively new, with most included articles having been published in the past five years. Thus, implementation and use of recommended cognitive measures in clinical practice settings in the Arab world remains understudied. Future dissemination and implementation work is needed, as well as research to assess the

barriers clinicians may face in accessing these measures. We also acknowledge that availability does not necessarily equate to usage and perceived utility of these measures, as several of the measures are subject to copyright and require financial investment by the provider. It remains unclear whether researchers and clinicians are regularly seeking out Arabic translations or adapted versions of these measures.

In terms of methodological limitations, this study relied on Latin-character searches of English- and Arabic-language databases. However, the first author's fluency in Arabic minimized this possible limitation by allowing for searches in Arabic language. Nevertheless, it is possible that the search did not capture all available Arabic-language data. It is also possible that some assessment tools are either not available online, or are treated as proprietary by their authors or institutions and are not publicly listed.

Conclusion

This systematic review found wide variability in the availability and use of MS cognitive assessment tools across the Arab world. Although an Arabic version of the BICAMS represents the most recently translated and most commonly used cognitive battery, validation of the BICAMS is currently pending completion. BICAMS subtests, and those of the MACFIMS exist, but may lack broader application. Furthermore, despite the increasing prevalence of MS in the region, dissemination and implementation of these measures in MS clinics remains understudied.

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