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Table 4.

Characteristics of the 15 studies included in the Stage 4 and 5: populations, methodology and findings

Study ID Country Design	**Sample Gender**	**Age (SD)**	**Education**	**Cognitive Domains** **Number of Tests**	**Cognitive Impairment (CI) %** **Cognitive Performance**	**Adjustments (A) Other Findings (OF) Limitations (L)**	**Modified Newcastle-Ottawa Quality Assessment Score (0-8)**
23. Brown et al (2002) USA Cross-sectional	RA: 121 83% F	56.07 (12.74)	Mean (SD) not provided 100% 8 years 66% ≤ college	• Attention/ Concentration • Memory • Judgment/ Problem solving Tests: 6	CI: Not specified	A: Controlled for age and depression. OF: Age, depression and pain associated with CI. Age independently of depression and pain. L: No control group	5.0
29. Abeare et al, (2010) USA Cross-sectional	RA: 157 89.2% F	54 (11.44)	13.5 (no SD) range 1-21	• Attention • Memory Tests: 2	CI: Not specified Pain related to poorer cognitive function (Judgment)	A: Age, education, RA duration, ESR, fatigue & mood. OF: Positive affect moderates pain's impact on CF. L: No control group; limited cognitive assessment.	3.0
30. Shin et al (2013) USA Cross-sectional	RA: 115 63.5% F	58.6 (10.8)	15.11 (2.26)	• Attention/ Concentration • Verbal function • Visual-spatial organization • Memory • Judgment/ Problem	CI: 31% on ≤4/16 tests Range: 8%-29% across tests CI based on 1 SD below the norm on 4/16	A: CF scores adjusted for age. CI lowest on semantic fluency (9%) and highest on visual special learning (29%). OF: 10 predictors explained 24%-34% of the variance in CI: key predictors: education, income, meds and CVD risk factors.	7.5

				solving Tests: 10 (16 sub-tests)	sub-tests.	L: No control group, pain, fatigue or sleep indicators.	
31. Meade et al (2013) Australia 24 hour test-retest	RA: 35 59% F	61.20 (12.72)	64% ≤12 years	• Memory • Judgment/ Problem solving Tests: 2	CI: 0%	A: Controlled for age (test scores) and MTX dose. Some age and pain association with cognitive function OF: High and low MTX groups did not differ across demographic, clinical and mood indicators. Low MTX group performed marginally better than the high MTX group. L: Small, convenient sample, limited CF assessment.	5.5
32. Bartolini et al (2002) Italy Cross-sectional	RA: 30 90% F	55.6 (11.1)	5.78 (2.5)	• Attention/ Concentration • Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 9	CI: 5% -71% (across 11 tests/sub-tests) Only 2/30 performed within normal range across all sub-tests Worst on Block Design (71%) and Rey Figure (50%)	A: Controlled for depression (excluded 17/47 based on BDI). OF: Cognitive performance related to disease indicators and age. MRI imaging: 35% to 85% had some abnormalities. L: No control group; lower education; no disease activity (quite high) control.	7.5
33. Appenzeller et al (2004)*	RA: 40 88% F Control: 40 95% F	37.2 (3.2) 35.9 (2.9)	RA: 7.2 (2.6) Control: 7.8 (1.3)	• Attention/ Concentration • Verbal function • Visual-spatial	CI: RA: 30% CI: Control: 7.5%	A: No correlation between CI and RA duration, corticosteroid, neurological abnormalities, disability, depression, anxiety.	6.0

Brazil Cross-sectional				organization • Memory • Judgment/ Problem solving Tests: Unclear	3/8 domains with ≥ 2 SD below the norm = moderate CI	OF: CI (Memory) linked to disease activity (6/12 with CI had cognitive problems & active RA). L: Lack of information of cognitive tests; no measure of pain or fatigue; small sample size.	
34. Hamed et al (2012)* Egypt Cross-sectional	RA: 55 100% F Control: 40	45.64 (10.91) Not provided	Not provided	• Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 2 (11 sub-tests)	CI: unclear 71% lower scores 11% with indication of NSI 9.35-13.2% brain abnormalities	A: Age, gender, SES, education matched. Age and illness duration controlled. OF: Found a link between biomarkers and CI; 7/55 RA had abnormal MRIs. These were not linked to disease activity or depression. L: Results based on correlations, no details on the score vs norms, only comparisons with Control.	6.0
35. Petersen et al (2014)* Brazil Cross-sectional	RA: 30 80% F Control: 15 75% F	50.60 (13.45) 49.37 (15.23)	6.83 (3.80) 8.37 (4.64)	• Memory Tests: 2	CI: Not specified	A: Controlled for age, mood and biomarker tests. RA performed poorer than Control. OF: RA and Control significantly different on biomarkers and predictors of CI. Case for 'inflammaging'. L: Not reported CI %.	6.0
36. Tomasević-Todorovic et al (2011)* Serbia Cross-sectional	RA: 60 88% F Control: 30 90% F	49.97 (7.56) 48.30 (6.42)	RA: 92% ≤ 12 years Control: 77% ≤ 12 years	• Memory Tests: 1	CI: Not specified	A: Control group matched on gender, age and education but not controlled for significant difference in mood. OF: RA performed significantly	4.5

						poorer on 4/5 cognitive sub-tasks compared to Control. Depression, anxiety and pain associated with CI in RA group. L: Not controlled for mood; not provided details on the CI results across five subscales.	
37. Akdogan et al (2013) Turkey Cross-sectional	RA: 28 FMS: 40 Control: 30 100% F	37.3 (6.0) 36.2 (7.3) 33.7 (8.0)	RA: 5-8 years: 27 (96.4%) 9-11 years: 1 (3.6%) FMS: 5-8 years: 34 (85%) 9-11 years: 6 (15%) Control: 5-8 years: 24 (80%) 9-11 years: 6 (20%)	• Attention Tests: 1	CI: Not specified Both RA and FMS had slower times but similar errors and corrections to Control	A: Age, education, risk factors (depression, anxiety, dizziness, sleep, fatigue). OF: Fatigue key predictor of CI. L: Small sample size; focus on FMS; only one domain/test.	4.0
38. Bilgici et al (2014) Turkey Cross-sectional	RA: 15 FMS: 16 Control: 15 100% F	38.1 (11.9) 36.8 (9.3) 35.3 (7.1)	RA: 7.3 (2.1) FMS: 8.4 (3.2) Control: 9.2 (5.6)	• Attention/ Concentration • Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 13	CI: Not specified	A: Matched for age. Both FMS and RA performed worse that control. RA performed better than FMS but only significantly so on Judgment. OF: In RA pain correlated with Attention only. Fatigue and sleep problems did not correlate with any CF measures. L: Not quite matched on age and	4.5

						education (not significant differences). Not provided details re depression rates; no RA vs Control comparison; focused on FMS.	
39. de Melo at al (2012)* Brazil Cross-sectional	FMS: 13 RA: 13 SLE: 11 97% F (1:37 M:F)	53.3 (3.85) 55.07 (8.33) 37.54 (5.90)	FMS: 2.07 (0.75) RA: 1.84 (0.68) SLE: 2.27 (0.78)	• Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 6	CI: Not specified	A: Not matched on age or education (SLE significantly younger). RA performed below norms on five sub-tests. OF: Each group performed below norms on some sub-tests. Significant age and education differences across sub-tests. L: Small sample not age or education matched, not separated for each group. Low education levels or a typographical error. Depression and clinical variables (pain, fatigue, disease activity) not measured.	4.5
40. Kozora et al (2001)* USA Cross-sectional	non-CNS-SLE: 15 RA: 15 Control: 15 100% F	39.7 (7.6) 38.7 (8.8) 37.7 (6.0)	13.5 (2.1) 13.2 (2.2) 13.5 (1.8)	• Attention/ Concentration • Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 12	CI: Not specified DHEA-S significantly lower in RA vs Control	A: Similar on age and education. Used t-scores for domains. Controlled depression for comparisons. OF: BDI and one biomarker explained 36% out of 46% variance in CI (learning) while the other biomarker marginally contributed to CI (attention) (36% together with meds and depression). L: Small sample, mild disease activity.	7.0

41. Yilmaz et al (2012)* Turkey Cross-sectional	Systemic Sclerosis: 31 96.7% F RA: 15 93.3% F Control: 20 95% F	Median (Range) 47(28-72) 46 (33-61) 47 (27-71)	Systemic Sclerosis: 8.8 (3.8) RA: 7.6 (6.6) Control: 10 (3.7)	• Attention/ Concentration • Verbal function • Visual-spatial organization • Memory • Judgment/ Problem solving Tests: 6	CI: Not specified	A: Groups matched on age, gender and education. Control performed better than both SS and RA on 5/6 tests. Suggest that Attention impairment leads to secondary memory problems. OF: RA performed better than SS. Education found to impact WCST test. L: Focus on SS, limited information on RA and small sample. No details re scores and norms.	7.0
42. Dick at al (2002)* Canada Cross-sectional	FMS: 20 90% F RA: 20 80% F MSD: 20 60% F Control: 20 35% F	48 (16.9) 62.9 (10.9) 52.3 (13.1) 60.0 (12.4)	12.5 (2.7) *Inpatient population **FMS not age matched	• Attention/ Concentration Tests: 1	CI: Not specified for each clinical group Clinical Groups: CI: 60% on 1/4 tests CI: 38% on more than 1/4 tests	A: Control only age matched to RA. FMS significantly younger; no education match. 60% of the clinic groups had one subtest score in the clinically impaired range; 38% had more than one out of four subscales. OF: None of the demographical or clinical variables were significantly correlated with TEA test. L: Not age, gender (Control mostly male) or meds matched. No specified CI % for each group – all pooled together.	4.0

* Included in effect size analyses (Table 5)