

Supplementary table 2. Literature review of cognitive impairment in MOGAD

Reference	Country	Sample size	Control group	Tests used	Domains attributed	Definition of impairment	Result	Correlations, associations and substrates	Absent correlations, associations and substrates	Criticisms
Deiva <i>et al.</i> , 2020	France	76 (paediatric)	N/A	N/A	N/A	"Academic accommodations made, grades repeated, children left school early or children needed to attend special education schools"	26% children had "academic difficulties" after median 4.5 years	Significantly higher risk of academic difficulties if onset age ≤ 10 years, lesions in deep grey matter and ADEM at presentation	No association with annualised relapse rate, sex or use of IST	Paediatric cases only; no formal cognitive assessment tools used; retrospective; no control group; no premorbid assessments; definition of cognitive impairment vague and subjective; does not account for academic accommodations due to visual/physical impairments or missed schooling due to illness; depends on self/parental-report; only onset MRI scans considered (may miss delayed lesion development); no onset MRI brain available for 26/76;

Supplementary table 2. Literature review of cognitive impairment in MOGAD

										univariable regression not suitable when independent variables are correlated (cannot determine independence); no exploration of effect of later attacks on cognition
Eyre <i>et al.</i> , 2024	UK	22 (paediatric)	38 pw paediatric MS + each pwMS or MOGAD matched with up to 10 controls according to school, calendar year, sex, race and social deprivation index	Teacher-based assessments of key stages 1 & 3, SAT scores, GCSE grades, A-level grades	N/A	N/A	Median key stage 1 writing and mathematics grades significantly lower in MOGAD group vs controls. 4 patients tested pre-onset not statistically different, 7 patients post-onset significantly lower vs controls. Median SAT scores lower in pre-onset MS and whole MOGAD group vs controls. Children with MOGAD (n = 3) performed	N/A	N/A	Small samples; subgroup analyses of MOGAD patients unreliable due to sample size; analyses at higher stages progressively more underpowered; paediatric only; patients recruited from London Paediatric Neurology centres (potential for bias towards recurrent/severely affected children); age at onset older, social deprivation and Black race more common in MS

Supplementary table 2. Literature review of cognitive impairment in MOGAD

							significantly worse than controls at English & mathematics at key stage 3. Children with MS (n = 7) not statistically different from controls. At combined GCSE/A-level, pwMOGAD and pwMS not on DMT scored lower than controls. No significant difference between pwMS on effective DMT and controls.			group; only pre-onset MS cases were included in key stage 1 analyses (incomparable with MOGAD group with 7/11 post-onset; no adjustment for depression, pain, fatigue or absenteeism
Fabri <i>et al.</i> , 2022	Canada & Pennsylvania	12 (paediatric)	68 paediatric onset MS, 108 HCs	Penn Computerized Neurocognitive Battery (Letter N- Back, Penn Conditional Exclusion)	Executive (flexibility and abstraction, attention and working memory), episodic memory (face, object, word	N/A	MOGAD group mean score lower than HCs on all but 1 test, only significant for Verbal Reasoning and Time Constrained Response Time, leading to significantly lower scores in complex	N/A	N/A	Small sample; paediatric onset only; only included relapsing disease (potential for biased results); groups not matched for EDSS, socioeconomic status, age at onset & duration and not included in regression models;

Supplementary table 2. Literature review of cognitive impairment in MOGAD

				n Test, Go-No-Go, Face Memory, Spatial Memory, Working Memory, Verbal Reasoning, Matrix Reasoning, JLOT, Age Differentiation, Emotion Recognition, Emotion Differentiation, Time-Constrained Response Time, Memory Response Time,	memory), complex cognition (language, non-verbal, spatial reasoning) and social cognition (emotional recognition and emotional and age differentiation), response times		cognition and response time domains. No difference on overall score. MS group significantly lower mean scores than HCs on multiple tests covering all domains. Mean scores of pwMOGAD significantly higher than pwMS on Letter N-Back test (executive function domain) and overall score			fatigue scores, emotional distress & depression scores, education & EDSS not included in regression models; no adjustment for multiple comparisons; beta values and significance in regressions not reportedly significantly lower domain scores in MOGAD reflect statistically lower results on only 1 subtest
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Supplementary table 2. Literature review of cognitive impairment in MOGAD

				Open Window Response Time)						
Griffiths-King <i>et al.</i> , 2024	UK	10 (paediatric)	11 pADS, 10 HCs	WISC, WIAT	Verbal comprehension, visuospatial function, fluid reasoning (resolve mental problems without language), processing speed, working memory, full scale IQ (WISC); total reading, basic reading (real and non-real words), total reading comprehension & oral	≥1 SDs below scaled normative mean on ≥2 tests; number of subtest scaled scores "concerning" (70-85, i.e., 1-2 SDs below scaled norm) or impaired (<70, i.e., ≥2 SDs below scaled norm)	No statistically significant differences on any test. Means in 3 groups within normal ranges on all tests. Non-significant trend towards higher scores in HCs vs pwMOGAD and in pADS. 1 child with MOGAD and 1 with MS ≥ 2 SDs below norm on verbal comprehension index. 1 child with MOGAD impaired on each of working memory and processing speed indices. A higher proportion of pADS scored 1-2 SDs below scaled norm vs pwMOGAD except	Of 2 pwMOGAD-CI with scores > 2 SDs below norm in any test, 1 had MDEM, 1 had encephalitis	Across groups, age, sex, disease duration, age at onset, relapsing vs monophasic not significantly different between patients with scores >1 SDs below norm in ≥2 tests. Across groups, no correlation with age at onset or duration. No significant difference in scores for ADEM-onset vs other phenotype	Small sample; paediatric cases only; unclear if pADS group systematically tested for MOG antibody; other pADS not specified; HCs not tested with WIAT; no statistical comparison of proportions of children with "concerning" WISC index scores or WIAT scores in each group; up to 18.2% HCs scored 1-2 SDs below scaled norms on each index; unclear clinical significance of a score 1-2 SDs below norm; only examined associations between scores and demographic/ clinical factors in

Supplementary table 2. Literature review of cognitive impairment in MOGAD

					fluency, mathematics (WIAT)		processing speed (40% pwMOGAD vs 20% pADS) (statistical significance unknown). Higher proportions of pADS scored ≥ 1 SD below scaled norms on each of the WIAT tests except mathematics (statistical significance unknown). Significantly more pADS scored ≥ 1 SD below scaled mean on >1 test vs pwMOGAD			combined cohort; arbitrary decision to study discriminators of scores >1 SDs below norm in ≥ 2 tests; no consideration of depression, fatigue, EDSS
Hacohen <i>et al.</i> , 2018	Multinational	102 (paediatric)	N/A	N/A	N/A	Not reported	Brain involvement significantly more likely in children <9 years & mean age at onset of ADEM and MDEM lower than ON or ON plus TM	40% of children with ADEM/MDEM had cognitive impairment after median 6.3 years compared with 6.5% of children with ON or ON plus TM. 27.7% patients with abnormal	N/A	Paediatric relapsing cases only; no definition of cognitive impairment; no uniform cognitive tests; no control group; no premorbid cognitive assessments; cognitive outcomes not compared

Supplementary table 2. Literature review of cognitive impairment in MOGAD

								MRI brain had cognitive problems, compared with 5.4% patients with normal MRI brain		across/ correlated with relevant covariates
Kogel et al., 2024	Germany	32	32 HCs	Alertness subtest of Testbatterie zur Aufmerksamkeitsprüfung, phonematic category change subtest of Regensburger Wortflüssigkeitstest, visual reproduction test of WMS-R, subtest	Attention, mental flexibility/ executive function, visual memory, visual processing, verbal working/ short term memory, verbal learning and memory	Demographically adjusted scores <7th percentile ≥2 tests	21.9% met criteria for CI. Most commonly affected domains were mental flexibility and alertness. White matter and deep grey matter volumes reduced compared with HCs. No difference in cortical volumes	Significant effect of previous ADEM/ ADEM-like attacks and attack number on risk of CI. pwMOGAD-CI lower white matter, grey matter, cortical and deep grey volumes vs HCs, only significant for total & deep grey matter volumes. pwMOGAD-CI had significantly lower total & deep grey matter volumes vs MOGAD-CP. Multiple discrete grey matter structures implicated	No effect of previous cortical encephalitis, sex or age. Median depression & fatigue scores not different between patients with CI vs CP.	Many tests not validated in inflammatory CNS disease; many tests not validated internationally; no test of processing speed; did not account for age at onset (interaction with ADEM/ ADEM-like phenotypes); no adjustment for multiple comparisons in MRI data; method for "demographically adjusting" scores not discussed; depression and fatigue excluded from logistic regression; education not considered

Supplementary table 2. Literature review of cognitive impairment in MOGAD

				7 of the Leistungsprüfungssystem, digit span from WMS-R; Verbaler Lern- und Merkfähigkeitstest recall 5 and 7						
Maniscalco <i>et al.</i> , 2025	Italy	19	19 pwMS	Rao BRB-N (SRT, 10/36 SPART, PASAT, SDMT, COWAT) & Stroop Colour Word Test	Verbal learning & memory, visuospatial learning & memory, complex attention and processing speed (PASAT & SDMT), verbal fluency, executive function	Score ≥ 1.5 SDs below normative value	Mean scores lower in MS group on every test except Stroop test but only significant for SPART. At least 1 MOGAD patient impaired on each test except Stroop Colour Word Test. Most commonly affected tests in MOGAD group were delayed verbal recall & delayed visuospatial recall	SDMT correlated negatively with depression score and positively with quality-of-life score. Stroop test time correlated negatively with quality-of-life score	N/A	Small samples; comparisons with normative means from 2006 not reliable; unclear whether demographic or clinical variables entered into correlations; did not adjust/ perform multivariable regression with correlated psychosocial covariates; total number of patients impaired not

Supplementary table 2. Literature review of cognitive impairment in MOGAD

										assessed; unclear if correlations were performed for pwMS <i>and</i> MOGAD or MOGAD alone
Mittelman <i>et al.</i> , 2024	France	51 (48 with follow-up data) (paediatric)	N/A	10 assessed with WISC	Verbal comprehension, visual-spatial function, working memory	Educational interventions included any of "special education; repeating the school year; academic accommodation ; a learning support assistant; and part-time schooling". Academic accommodations included "requirement for particular equipment (e.g. computer), additional time, or any personalized assistance". WISC scores 70-79 borderline,	39.5% pwMOGAD required educational interventions at last follow-up. Of 6 children with global WISC scores, 1 was borderline, 2 low average, 3 average. Domains affected were heterogeneous. 9/10 patients who underwent formal assessment were diagnosed with one or more of attention disorder, dyspraxia, executive function disorder, specific learning disorder. Of 27 ADEM patients with follow-up, 55.6% required education	78.9% pwMOGAD-CI had ADEM at onset vs 41.3% pwMOGAD-CP	No significant differences in age at onset, early normalisation or improvement of MRI scans	Retrospective; paediatric only; dependence on patient medical records for educational outcomes (lack sensitivity and specificity); "academic accommodations" may include need for assistance with visual or motor disability; do not account for absenteeism; parental education & socioeconomic factors may influence access to accommodation/ recognition of academic problems; only 10 patients underwent formal testing and 9 had raised

Supplementary table 2. Literature review of cognitive impairment in MOGAD

						80 - 89 low average	interventions (3 pre-existing; 5 ADEM onset pre-school). Of 17 patients with ON, 23.5% required educational interventions (1 pre-existing). None of 3 patients with TM or the 1 patient with other brain manifestations with follow up required educational intervention.			concerns about academic progress (biased results); only patients with ADEM underwent formal cognitive testing; attention disorder interfered with formal testing in some patients; increasing proportion requiring assistance over time may reflect usual delay to recognise cognitive impairment rather than deficits triggered by disease (need control group); follow-up time longer in patients with CI (risk overestimating CI if well children lost to follow up; risk underestimating if CI emerges after delay); no accounting for depression, fatigue,
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Supplementary table 2. Literature review of cognitive impairment in MOGAD

										EDSS or relapse phenotypes
Passoke <i>et al.</i> , 2024	Germany	113	N/A	PASAT-3, SDMT, Multiple Sclerosis Inventory Cognition (MuSIC) scores	Auditory processing speed, visual processing speed and immediate and delayed auditory recall, semantic fluency, visual processing speed & inhibition (MuSIC)	Score <5th percentile of normative distribution on ≥ 2 tests	11% met criteria for CI. MuSIC congruent speed test (visual processing speed) most commonly affected. Only mean semantic fluency and visual processing speed (congruent speed subtest of MuSIC) significantly lower than normative values. PASAT and inhibition (congruent-incongruent speed) lower but not significant. Immediate recall list B significantly higher than normative values and SDMT approached statistical superiority	SDMT correlated negatively with age; SDMT, immediate and delayed recall higher in group with high school education compared with secondary school education. Age, education and presence of cerebral lesions survived multivariable regression of SDMT. Cerebral lesions survived multiple regression of semantic fluency	No significant correlation between any test and visual FSS, motor FSS, fatigue score or depression score. No covariate survived multivariable regression of PASAT, immediate recall list A or B, delayed recall list A, congruent speed (visual processing speed) or congruent-incongruent speed (inhibition).	Median disease duration short; large proportion on IST including rituximab (not generalisable to UK); <50% completed PASAT, just over half completed MuSIC; approx. half sample completed depression & fatigue scores; incongruent results on two tests of visual processing speed
Risi <i>et al.</i> , 2025	Italy	8	32 pwMS, 22 HCs	Rao BRB-N (SRT,	Verbal memory, visuospatial	≥ 1.5 SDs below HC mean in ≥ 2 tests	12 mo after onset 50% pwMOGAD met criteria for CI,	Of 8 MOGAD patients, only the 4 with ADEM/	N/A	Small samples; "non-relapsing" defined as no

Supplementary table 2. Literature review of cognitive impairment in MOGAD

				10/36 SPART, PASAT, SDMT, COWAT) & Stroop Colour Word Test	memory, working memory, processing speed, verbal fluency, executive function & inhibitory control		3 with ADEM and 1 with cortical encephalitis. 2 patients with ON and 2 with TM were CP. 6/8 pwMOGAD scored below adjusted normal mean in ≥5 tests. Mean age-, sex- and education-adjusted scores of pwMOGAD lower on all tests vs HCs, only significant for SRT-LTS and PASAT. Mean scores of pwMS significantly lower on SRT-LTS, SRT-CLTR & PASAT.	cortical encephalitis had CI		relapse after first attack but median follow up only 30 months; potential learning effect; did not compare outcomes of tests in MOGAD with MS; no adjustment/ correlation with depression, fatigue and EDSS scores; no comparison of demographic/ clinical features of pwMOGAD-CI vs pwMOGAD-CP
Tan <i>et al.</i> , 2021	US	7 (paediatric)	N/A	Multiple tests varying according to patient.	Not defined	≥1 SD below age normative mean	1/7 impaired Delis-Kaplan Executive Functioning System, 1/7 impaired digit span (working memory), 2/7 mildly impaired SDMT or symbol	N/A	Of 2 patients presenting with ADEM aged 3 & 7, 1 had mild deficit on TMT-A. 1 patient with ON & TM with multiple brain lesions aged 13 had deficits in	Small sample; paediatric cases only; retrospective; short follow-up (long-term effects not studied); 3 patients met MacDonald criteria for MS, had CSF-OCBs and relapsing

Supplementary table 2. Literature review of cognitive impairment in MOGAD

							search (visual processing speed), 2/7 impaired TMT-A (visual attention & processing speed), 2/7 impaired TMT-B (executive function), 2 impaired CVLT-II learning (verbal learning); 4/7 impaired on tests of visuomotor integration. 1 child with MS presentation, history of dyslexia & recent seizures had multidomain deficits. Most patient mild impairments in 1 or 2 domains		tests of visuomotor integration & CVLT-II learning. A 12-year-old with isolated ON had mild deficit on digit span. 3 with MS had various deficits on TMT-A and -B, Delis-Kaplan Executive Functioning System, SDMT, CVLT-II learning and various tests of visuospatial integration. Suggests brain lesions not determinants of CI or modulated by interaction with age	course (likely not MOGAD); testing protocols varied; underpowered to examine effects of variables on outcomes (descriptive only); premorbid learning disability in 1 patient
Zhuo <i>et al.</i> , 2021	China	17	20 AQP4+ NMOSD, 28 HCs	MoCA, SDMT, CVLT-II	Not defined	N/A	Median MoCA, SDMT & CVLT-II scores of pwMOGAD significantly lower than HCs but same as pwNMOSD. 47%	MoCA & SDMT scores correlated with grey matter volume right superior temporal gyrus. CVLT-II score	No correlations between cognitive scores and FA or MD	Small samples; not all participants completed each cognitive test; report corrected significance for some MRI features and uncorrected for

Supplementary table 2. Literature review of cognitive impairment in MOGAD

							<p>MOGAD group had brain lesions, lesion volume higher in MOGAD vs NMOSD. Grey matter volumes in several cortical areas, thalami & hippocampi reduced vs HCs. FA in optic radiation reduced and MD in corona radiata increased vs HCs. DC lower in right cerebellum and higher in superior temporal gyrus vs HCs.</p>	<p>correlated with left hippocampal volume BUT most correlations lost after adjusting for covariates</p>		<p>others; examined correlations between demographic, clinical & cognitive variables with MRI measures but not with cognitive scores; after adjustment partial correlations lost statistical significance but only shown in supplemental data; EDSS and cognitive scores related to hippocampal atrophy but interaction not assessed; incomplete correction for multiple comparison of voxel-based measures</p>
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