

Supplementary table 1. Literature review of cognitive impairment in NMOSD

Reference	Country	Sample size	% seropositive	Control group	Tests	Domains attributed	Definition of impairment	Result	Correlations, associations and substrates	Absent correlations, associations and substrates	Criticisms
Ashtari <i>et al.</i> , 2024	Iran	31	Not reported	29 pwMS, 20 HCs	MACFIMS (COWAT, JLO, CVLT-II, BVM-T-R, SDMT, PASAT), Delis-Kaplan Executive Function System	Verbal fluency, visuospatial perception, verbal learning & memory, visuospatial learning & memory, processing speed & working memory, processing speed & attention, executive function	N/A	Almost all mean scores lower in NMOSD group vs HCs but only significant for SDMT and COWAT. Mean BVM-T-R score lower in MS group than NMOSD group. Lesion load higher, thalamic, grey & white matter volumes lower in MS vs NMOSD	In NMOSD, SDMT and CVLT-II delayed recall correlated with lesion volume, CVLT-II learning correlated with grey matter volume	No score correlated with thalamic volume, white matter volume or total brain volume	Small samples; retrospective study; % seronegative not reported; exclusion of patients with high depression scores could bias results; group comparisons and correlations measured but no multivariable/interaction models used; assessed effects of MRI but not demographic & clinical covariates on cognitive scores
Blanc <i>et al.</i> , 2008	France	30	56.7	30 pwMS, 30 HCs	Rao BRB-N (French version; SRT, 10/36 SPART, PASAT-2 and -3, WLGT, SDMT), cross tapping test, go/no-go test, WAIS direct &	Verbal episodic memory, visuospatial episodic memory, processing speed & attention, verbal initiation, processing speed, task shifting & resistance to interference (executive	>2 SDs below HC mean in ≥ 1 test	56.7% pwNMOSD impaired vs 36.7% pwMS. pwNMOSD and pwMS significantly poorer than HCs in PASAT-2 and -3 (processing speed & attention), SDMT (processing speed), phonemic fluencies, direct and indirect digit span (audioverbal working memory).	SDMT correlated negatively with EDSS	No correlation between any test and depression or disease duration	Small samples; high proportion seronegative NMOSD; group comparisons and correlations measured but no multivariable/interaction models used; correlations but no adjustment of scores for relevant clinical and demographic variables; unclear what demographic, clinical, psychosocial and

Supplementary table 1. Literature review of cognitive impairment in NMOSD

					indirect digit span	function), inhibition (executive function), audioverbal working memory		NMOSD 30% impaired long-term memory, 26.7% impaired executive function, 20% impaired processing speed, 13.3%			radiological features were assessed; comparing means, ANOVA and Pearson's correlation assume parametric distribution and homoscedasticity of residuals
Blanc <i>et al.</i> , 2012	France	28	43.0	28 HCs	Rao BRB-N (French version; SRT, 10/36 SPART, PASAT-2 and -3, WLGT, SDMT), cross tapping test, go/ no-go test, WAIS direct & indirect digit span	Verbal episodic memory, visuospatial episodic memory, processing speed & attention, verbal initiation, processing speed, task shifting & resistance to interference (executive function), inhibition (executive function), audioverbal working memory	Impaired on test if score ≥ 2 SDs below HC mean; cognitively impaired if on $\geq 4/14$ tests	54% pwnMOSD cognitively impaired. Most common tests affected SDMT (46%), audioverbal learning (43%), PASAT-3 (39%), SRT free recall (39%), SRT delayed recall (32%) and backward digit span (32%). Every test impaired in at least 11%. Global and multifocal white matter volumes reduced compared with HCs.	Total brain volume and white matter volume lower in NMOSD-CI than NMOSD-CP. SRT learning & PASAT correlated with EDSS. Number of tests impaired correlated with total brain volume and trend towards correlation with white matter volume. Trend towards correlation between PASAT score and white matter volume. SRT, 10/36 SPART, SDMT, backward digit span, phonemic	No difference in grey matter volumes, age, education or EDSS between NMOSD-CI and NMOSD-CP. No correlation between any test and duration, treatment or serostatus	Small samples; high proportion of seronegative NMOSD, many with CSF restricted OCBs; exclusion of patients with high depression and EDSS scores may bias results; scores adjusted for age, sex and education but no other clinical or demographic variables; no statistical method provided for comparisons of cognitive scores between groups; Pearson correlations assume parametric distribution and homoscedasticity of residuals

Supplementary table 1. Literature review of cognitive impairment in NMOSD

									fluency and PASAT correlated with various focal white matter volumes		
Cacciaguerra <i>et al.</i> , 2022		28	100	101 HCs	Rao BRB-N (SRT, 10/36 SPART, PASAT, SDMT, COWAT) & Stroop Colour Word Test	Not defined	z scores ≤ -1.64 on ≥ 2 tests	46.4% pwNMOSD met criteria for CI. Mean verbal memory & attention domain scores lower in NMOSD vs HCs but only significant for attention. Attention most frequently impaired domain (60.7%). Mean normalised brain volume and total grey matter volumes lower in NMOSD vs HCs. Mean left hippocampal volume & various right and left subfields lower in NMOSD group.	Mean age of NMOSD-CI higher, educational levels of NMOSD-CI lower and mean EDSS of NMOSD-CI higher than NMOSD-CP. Left CA3 & CA4 subfield volumes lower in patients with CI than CP but did not survive false discovery rate correction. Verbal memory impairment associated with significantly lower volumes in multiple hippocampal subfields. Associations between volumes and	No difference in % female or disease duration in NMOSD-CI vs NMOSD-CP	HCs and pwNMOSD not matched for age or sex; only examined hippocampal volumes; unclear what demographic factors used to correct z scores (MRI measures adjusted for age and sex); EDSS, education and age correlate with scores but scores not adjusted for these variables; uncertain accuracy of subfield volume measurements

Supplementary table 1. Literature review of cognitive impairment in NMOSD

									other domains did not survive correction		
Camera <i>et al.</i> , 2021	UK	49	100	N/A	Multiple & varied between cases	N/A	<i>Either</i> documented learning disability requiring a minimum of a special educational needs coordinator or score <5th percentile of normative values on any formal assessment	After mean interval of 79 months, 25.8% met criteria for CI. All children with CI had ≥1 episode of cerebral syndrome. 14.3% children presenting with cerebral syndrome at onset had residual cognitive impairment. Most common deficits in processing speed, attention and executive function.	Cerebral syndrome and requirement for second line rescue therapy increased risk of CI	No effect of sex, race, age (<12 vs ≥12) or onset attack severity on risk of CI	Paediatric cases only; retrospective; broad definition of CI; no uniform assessments; did not account for premorbid abilities; no consideration of psychosocial covariates; no assessment of interactions between independent variables
Chavarro <i>et al.</i> , 2020	Germany	29	100	22	Rao BRB-N (SRT, 10/36 SPART, PASAT, SDMT, COWAT)	Verbal learning, verbal memory, visual learning, visual memory, attention & concentration (SDMT & PASAT), executive function	Global score ≥2 SDs below HC mean	All age, sex & education-adjusted scores lower in NMOSD vs HCs. Significantly lower global scores and attention & concentration scores. Only 1 patient (3.4%) CI. Learning & short-term memory,	In HCs, global score and short-term memory significantly <i>negatively</i> correlated with visual network functional connectivity. Trend towards <i>negative</i> correlation with attention &	N/A	Small samples; only examined visual network; trend towards lower education and higher age in NMOSD group; no correction for multiple comparisons; no analysis of effects of covariates on cognitive scores

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								long-term memory and executive function in normal ranges. Visual network functional connectivity higher in NMOSD group	concentration and executive function. In NMOSD, <i>positive</i> correlation between functional connectivity and executive function. 19% variance in cognitive score in HCs predicted by functional connectivity in visual network vs 2% in NMOSD		
Cho <i>et al.</i> , 2018	Korea	14	93.0	21 HCs	Digit span, TMT-A, PASAT-3, SDMT, spatial span forward and backward, Boston Naming Test, Rey Complex Figure Test, CVLT, COWAT, TMT-B	Attention, working memory & processing speed (digit span, TMT-A, PASAT & SDMT), visuospatial/ perceptual processing, language, visuospatial function, recognition & memory, verbal memory & recognition, semantic fluency,	N/A	Median scores of NMOSD group lower on almost all tests, significant for TMT-A, PASAT, SDMT, backward digit span, TMT-B & COWAT. Depression scores higher in pwNMOSD but not significant. Total network strength (white matter connectivity in whole brain) lower in NMOSD. Identified 2	After controlling for age, sex and education, depression score correlated with TMT-B and PASAT-2 score in NMOSD. Total network strength correlated with PASAT-3 in NMOSD. TMT-B, SDMT and PASAT-3 correlated with various local and regional measures of efficiency	No correlation between subtest scores and disease duration, ARR, EDSS, anxiety score or presence of brain lesions	Small samples; no adjustment of correlations between scores and connectivity measures for clinical/ demographic/ psychosocial variables; groups not matched for age; inaccuracies inherent in diffusion-tensor based tractography; disparate results on tests purporting to assess same domains

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						executive function		subnetworks with significantly lower connectivity in NMOSD group			
Chou <i>et al.</i> , 2019	UK	14	64.3	12 pwMS, 10 HCs	PASAT-3	Not defined	N/A	PASAT-3 scores significantly lower in NMOSD group than MS or HC groups. Lesion number and volume higher in MS group than NMOSD group. T1 relaxation time and MTR of NAWM were lower in pwNMOSD than HCs but not different from pwMS.	Lesional T1 relaxation time correlated negatively with PASAT-3 score in NMOSD group only	No correlation between NAWM T1 relaxation time or MTR and PASAT-3	Small sample; high proportion seronegative; single measure of cognition; pwNMOSD older than HCs and pwMS longer duration than pwNMOSD; did not assess correlations between demographic/clinical features and PASAT; comparison of mean score with ANOVA assumes normal distribution
Constantine scu <i>et al.</i> , 2015	UK	14	Not disclosed	43 pwMS, 14 pwCIS, 11 HCs	PASAT-3	Attention & memory	Not reported	PASAT-3 scores significantly lower in NMOSD group than any other group	N/A	PASAT-3 not correlated with EDSS, fatigue scores or disease duration	Abstract only; single measure of cognitive function; small samples; % seropositive not reported; matching of groups not reported; statistical methods not reported; unclear what covariates studied and/or adjusted for
Foolad <i>et al.</i> , 2019	Iran	12	66.7	12 HCs	SDMT	Processing speed	N/A	Mean SDMT score lower in NMOSD group vs HC group but not	SDMT score correlated negatively with EDSS (not significant),	N/A	Small samples; high proportion seronegative; low median EDSS (not representative); single

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								statistically significant	number of attacks and duration (significant)		test of cognition; unclear what variables were entered into correlation analyses with SDMT
Fujimori <i>et al.</i> , 2018	Japan	12	100	14 pwMS (test scores compared with normative values of 163 HCs from previous research)	WAIS-III, WMS-R	Verbal IQ, performance IQ, full scale IQ, verbal comprehension, perceptual organisation, working memory, processing speed (WAIS-III); verbal, visual & general memory, attention, delayed recall (WMS-R)	Scores ≥ 2 SDs below normative Japanese mean in 2 domains in combined WAIS-III and WMS-R	2 pwNMOSD had chronic non-specific, asymptomatic white matter lesions, 1 pwNMOSD had chronic, large lesion previously symptomatic. 5/14 pwMS diagnosed CI. 1/12 pwNMOSD diagnosed CI	Only pwNMOSD diagnosed with CI was the single patient with symptomatic brain lesion. 2 other patients scored ≥ 2 SDs below normative mean in 1 domain, 1 of whom had asymptomatic brain lesions	Patient with CI had longest time in education, EDSS < median, age at testing < median (suggests factors not associated)	Small samples; exclusion of patients with high EDSS scores may bias results; no comparison of demographic variables between NMOSD and HC groups; mean age of pwNMOSD greater than pwMS and HCs; binary outcome (no correlation between scores and predictors); several relevant demographic and clinical predictors not assessed; use of means and t tests assumes normal distribution of cognitive scores
Guo <i>et al.</i> , 2018	China	56	Not reported	63 HCs	MMSE, MoCA, CVLT-II, BVM-T-R, SDMT	Visuospatial & executive function, naming, attention, abstraction, memory, orientation (MoCA), verbal learning and recall;	N/A	Mean MMSE & MoCA scores lower in pwNMOSD vs HCs. NMOSD group means lower on all tests, only significantly for BVM-T total learning, SDMT, CVLT short- and	Before correcting for multiple comparisons, many correlations between test scores/ EDSS and CBF:ReHo ratios in regions with significant	N/A	% seropositive not reported; novel methods used require inference (e.g., ReHo only theoretical proxy of neuronal activity); using an alternative method to measure neuronal activity eliminated significant differences in neurovascular

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						visuospatial learning and memory; processing speed & working memory		long-delay cued recall and short delay free recall. Global CBF-ReHo correlation (neurovascular coupling) weaker in NMOSD. Regional CBF and CBF:ReHo higher or lower in multiple areas in NMOSD group vs HCs	differences between NMOSD group and HCs. In regions with lower CBF:ReHo in pwNMOSD, higher ratios associated with better performance on some tests. In regions with higher CBF:ReHo in pwNMOSD, higher ratios associated with worse performance on some tests. After correcting for multiple comparisons only superior parietal lobule CBF:ReHo ratio remained significantly correlated with MoCA		coupling between groups; unclear how lesioned tissue analysed; maximum 48 patients completed any cognitive test; no analysis of effects of demographic/ clinical covariates on test scores; no adjustment for covariates in correlations between test scores and imaging parameters; t-tests used to compare means of cognitive tests assumes normal distribution
Han <i>et al.</i> , 2020	China	41	Not reported	41 HCs	MMSE, MoCA	Not defined	scores ≥ 2 SDs below normative mean on both tests	NMOSD group mean scores significantly lower on MMSE and MoCA. NMOSD	Functional connectivity of parahippocampal gyrus (cerebellar hub	No significant correlation between MoCA score and	Aquaporin 4 serostatus only available for 20 patients; limited cognitive testing; studied correlations of

Supplementary table 1. Literature review of cognitive impairment in NMOSD

							(adjusted for educational level)	group showed increased resting state functional connectivity in regions of default mode network, thalamic network & dorsal attention network and decreased functional connectivity in visual network & cerebellar network	network) correlated negatively with MoCA score	disease duration	demographic & clinical variables & test scores with functional connectivity but not correlations between demographic & clinical variables and cognitive test scores; no consideration of psychosocial variables; analyses limited to preselected networks; identified functional networks are theoretical; no adjustment for grey matter or lesion volumes; possible confounding between effect of disease duration and connectivity in parahippocampal gyrus on MoCA; no attempt to look at correlations in HC group; results do not match those of Savoldi <i>et al.</i>
He <i>et al.</i> , 2011 (Brain & Cog)	China	21	Not reported	21 HCs	CVLT-II, backward digit span, CLOX, SDMT, PASAT-3	Verbal memory, numeric memory, executive function, processing speed, attention	N/A	NMOSD group mean scores significantly lower on CVLT-II short delay free and cued recall, backward digit span, SDMT and	Short delay free recall correlated positively with FA in genu of corpus callosum, negatively with MD in genu and	N/A	Small samples; % seropositive not reported; only including patients during relapses risks overestimating prevalence of CI, inflating fatigue and

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								PASAT but not long delay free and cued recall or CLOX. Mean FA higher and mean MD lower in body, genu and splenium of corpus callosum in NMOSD	splenium of corpus callosum; SDMT correlated positively with FA in 3 regions of the body of the corpus callosum and negatively with MD in same areas and anterior cingulate. PASAT-3 correlated positively with FA in splenium of corpus callosum and frontal cortex and negatively with MD in same areas.		depression scores; exclusion of patients with brain lesions may underestimate effects of disease on cognition; exclusion of patients on immunosuppression may exclude patients with more severe disease; exclusion of patients with high fatigue and depression scores may bias results; some results contrast with results of earlier study by same group; no examination of correlations between FA/MD and cognitive tests in HCs; controls used in DTI studies different to those used in cognitive testing; no examination of or adjustment of scores for relevant clinical and demographic variables; comparing means, ANOVA and Pearson correlations assume parametric distribution and homoscedasticity of residuals
He <i>et al.</i> , 2011 (Int J Neurosci)	China	22	Not reported	22 HCs, 22	CVLT-II, backward digit span,	Verbal memory, numeric memory,	N/A	Mean scores of pwNMOSD lower than means of	in NMOSD group, negative correlations	N/A	Small samples; % seropositive not reported; limited to

Supplementary table 1. Literature review of cognitive impairment in NMOSD

				people with depression	CLOX, SDMT, PASAT-3	executive function, processing speed, attention		HCs on every test, significantly for CVLT-short delay cued recall, long delay free and cued recall, digit span backward, SDMT and PASAT. Also significantly lower than means of group with depression on CVLT-short delay cued recall, digit span backward, SDMT and PASAT. Fatigue and depression measures significantly lower in pwNMOSD vs people with depression.	between PASAT and depression, fatigue and EDSS scores. SDMT correlated negatively with depression and fatigue scores. Digit span backward correlated negatively with fatigue, CLOX correlated negatively with depression.		patients with relapse in preceding 6 weeks; excluded patients with brain lesions; no attempts to correlate psychological scores with cognitive outcomes in depressed group or HCs; do not account for confounders, like pain; no exploration of interactions/ multivariable regression; ANOVA & Pearson's correlation assume a normal distribution of scores
Hümmert <i>et al.</i> , 2023	Germany	217 (maximum completing any cognitive test = 135)	80.0	Minimum 158 HCs	PASAT, SDMT, MuSIC (word list immediate and delayed recall, verbal fluency test, modified	Auditory processing speed, visual processing speed, immediate auditory recall, delayed auditory recall, semantic fluency & category switching, congruent visual	Z score \leq 5th percentile in ≥ 1 test	40% pwNMOSD impaired on ≥ 1 test; 19% impaired on ≥ 1 tests. pwNMOSD significantly lower z scores on SDMT, verbal fluency and congruent processing speed. pwNMOSD performed significantly <i>better</i>	SDMT correlated negatively with age, EDSS visual and motor scores and depression score. Immediate and delayed verbal recall correlated with age. Immediate verbal recall	No difference between seropositive and seronegative groups on any test. In multivariable regressions, other than age predicting SDMT, no demographic	Only a subgroup of patients completed each of the baseline tests; fewer had follow-up data; % patients impaired on any test decreased over follow-up (possible biased follow-up cohort or learning effect); HCs for SDMT & PASAT different from MuSIC; no demographic data from

Supplementary table 1. Literature review of cognitive impairment in NMOSD

					Stroop Test)	processing speed, & inhibition (Stroop Test)		than controls on immediate verbal recall test B. 12% pwNMOSD moderate-severe depression, 49% moderate-severe fatigue. No significant change in scores at 1- & 2-year follow up	correlated with education. In multivariable regression, age remained a significant predictor of SDMT (borderline effect of EDSS, $p = 0.06$)	(age, education) or clinical factors (serostatus, disease duration, EDSS, depression, fatigue) remained significant predictors of any test after Bonferroni correction	HCs; correlations not assessed for HCs; included patients >60 years old but normative values from people aged 18 - 60
Hyun <i>et al.</i> , 2017	Korea	67	90.0	42 pwMS, 44 HCs	Seoul Verbal Learning Test, Rey Complex Figure Test, COWAT, PASAT, SDMT, digit span & Stroop Colour Word Test	Verbal learning & memory, visuospatial function & visual memory, semantic verbal fluency, attention & processing speed, attention and visual search precision, working memory & attention, executive function	Score <5th centile of HC distribution in ≥ 3 domains	A third of patients with NMOSD met criteria for CI. After adjusting for age, sex and depression, thalamic volume reduced in NMOSD group compared with HCs. No difference in other deep grey matter structures. Multiple deep grey matter volumes smaller in MS vs NMOSD	Thalamic volumes lower in NMOSD-CI compared with NMOSD-CP or HCs. Thalamic volume correlated with global cognitive score in NMOSD. Thalamic volume correlated negatively with EDSS. Thalamic volumes significantly lower in presence of brain lesions	N/A	Appears to test same cohort as Kim <i>et al.</i> , 2016; maximum age for inclusion 50 years; not all patients with MRI results ($n = 91$) completed cognitive tests ($n = 67$); MS and NMOSD groups not matched on some variables; exploration of effects of clinical and demographic variables on thalamic volumes and correlation between thalamic volumes and cognitive score BUT no analysis of effects of relevant covariates on cognitive score; no

Supplementary table 1. Literature review of cognitive impairment in NMOSD

									(NMOSD thalamic volumes same as HC thalamic volumes in absence of lesions)		correlations/regression s for subtest scores
Kawahara <i>et al.</i> , 2014	Japan	10	Not reported	15 HCs	4 novel computerised touch-screen tests (beating devils, flipping cards, arranging pictures & finding mistakes), MMSE, Hasegawa Dementia Scale Revised, Frontal Assessment battery	Orientation, registration, attention & calculation, recall, naming, language comprehension, writing and construction (MMSE); orientation, immediate recall, verbal recall, visual recall, attention & calculation, working memory and verbal fluency (Hasegawa Dementia Scale-Revised); conceptualization, mental flexibility, motor sequences and inhibition (Frontal	N/A	No significant differences between pwNMOSD and HCs on MMSE, Hasegawa Dementia Scale or Frontal Assessment Battery. pwNMOSD slower at card flipping and picture sorting but did not reach statistical significance	Number of intracranial lesions negatively correlated with card flipping task. Apathy score correlated negatively with MMSE and Hasegawa Dementia Scale	EDSS and depression not correlated with any test result	Small samples; % seropositive not reported; large differences in scores on 2 touch screen tests did not reach statistical significance due to underpowering; domains associated with touch screen tests unclear; touch screen tests unvalidated; mean/median values of MMSE, Hasegawa Dementia Scale and Frontal Assessment Battery not provided and test subscores not explored; some correlations explored but no adjustment of scores for relevant clinical and demographic variables; no correction for multiple comparisons; t tests assume parametric distribution and homoscedasticity

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						Assessment Battery)					of residuals; no correction for multiple comparisons
Kim <i>et al.</i> , 2016 (Eur J Neurol)	Korea	67	Not reported	42 pwMS, 44 HCs	Seoul Verbal Learning Test, Rey Complex Figure Test, COWAT, PASAT, SDMT, digit span & Stroop Colour Word Test	Verbal learning & memory, visuospatial function & visual memory, semantic verbal fluency, attention & processing speed, attention and visual search precision, working memory & attention, executive function	Not defined	Mean scores of NMOSD group lower than HCs after adjusting for age, sex, depression and education on delayed Rey Complex Figure Test, PASAT, SDMT and backward digit span. Mean total brain volume smaller and cortex thinner in NMOSD group compared with HCs (but larger/ thicker than MS group). Mean scores of NMOSD group better than MS in immediate and delayed verbal & visuospatial recall and global cognitive score	N/A	After adjusting for age, sex, depression and education, no correlations between test score and any cortical thickness in NMOSD group	Maximum age for inclusion 50 years; not all patients with MRI results (n = 91) completed cognitive tests (n = 67); % seropositive not reported; no definition of impairment; MS and NMOSD groups not matched on some variables; performed univariable and multivariable regression and partial correlation for predictors of cortical thickness but not test scores; means to create z scores and ANCOVA assume normal distribution of test scores
Kim <i>et al.</i> , 2016 (MSJ)	Korea	82	87.0	58 pwMS, 45 HCs	Seoul Verbal Learning Test, Rey Complex Figure Test,	Verbal learning & memory, visual memory, phonemic verbal fluency, auditory attention &	Score <5th centile of HC distribution in ≥3 domains	After adjusting for age, education, sex and depression, 29% pwNMOSD had CI vs 50% pwMS.	Global cognitive score in NMOSD predicted by depression score and education	No association with age at testing, EDSS, fatigue score. No significant correlation	Cognitive test results contrast with earlier study by same group; only 67% pwNMOSD had brain MRI available; EDSS and disease

Supplementary table 1. Literature review of cognitive impairment in NMOSD

					COWAT, PASAT-3, SDMT, digit span & Stroop Colour Word Test	processing speed, visual attention & processing speed, working memory, executive function		35% impaired in ≥ 2 domains. Mean scores of NMOSD lower than HCs on SDMT and backward digit span only. Means cores MS group significantly lower than HCs in multiple domains. Mean scores MS group significantly lower than NMOSD group on visual and auditory immediate and delayed recall. Brain parenchymal fraction significantly lower in NMOSD vs HCs.		between global cognitive score and brain lesion volume, brain parenchymal fraction, grey or white matter fractions	duration higher in NMOSD group than MS group; comparison of means, ANCOVA & linear regression assume normal distribution of test scores
Kim <i>et al.</i> , 2017	Korea	73	89.0	44 HCs	Seoul Verbal Learning Test, Rey Complex Figure Test, COWAT, PASAT-3, SDMT, digit span & Stroop	Verbal learning & memory, visual memory, phonemic verbal fluency, auditory attention & processing speed, visual attention & processing speed, working memory,	Score <5th centile of HC distribution in ≥ 3 domains	32% pwNMOSD met criteria for CI. After adjusting for depression, age and education, mean scores in NMOSD group significantly lower on visual immediate and delayed recall, SDMT, backward	Mean education shorter and mean depression scores higher in NMOSD-CI vs NMOSD-CP and HCs. Mean volumes of total white matter, thalamus and caudate lower in	No differences in age, EDSS, serostatus or duration between NMOSD-CI and NMOSD-CP. No correlations between any test score and lesion volume	Median EDSS low (not representative); maximum age of participants 50 years; groups not matched for sex; only depression included as psychosocial variable; linear regression assumes homoscedasticity and

Supplementary table 1. Literature review of cognitive impairment in NMOSD

					Colour Word Test	executive function		digit span, PASAT, interference on Stroop test & global cognitive score. Mean scores on all tests lower in NMOSD- CI vs NMOSD-CP. pwNMOSD had lower grey matter volume, brain parenchymal fraction, cortical thickness, FA values & higher MD values. NMOSD-CI	NMOSD-CI vs NMOSD-CP. Mean white matter FA lower and MD higher in NMOSD-CI than NMOSD-CP. Mean white matter fraction, thalamic & caudate volumes and mean FA lower in NMOSD-CI vs NMOSD-CP. MD, axial and radial diffusivity higher in NMOSD-CI vs NMOSD-CP. Global cognitive score predicted by education, depression, EDSS, FA, MD, brain parenchymal fraction, white matter fractions, volumes of thalamus, caudate & nucleus accumbens. Multiple subtest score correlated with age, EDSS,	or cortical thickness	normal distribution of residuals
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Supplementary table 1. Literature review of cognitive impairment in NMOSD

									FA, various deep grey matter volumes		
Kong <i>et al.</i> , 2022	China	66	100	22 HCs	CVLT-II, BVM-T-R, SDMT, PASAT, Digit Span, CLOX, WCST	Verbal memory, visual memory, attention and processing speed (SDMT, PASAT & digit span) executive function (CLOX & WCST)	Score ≥ 1 SD below HC mean in any test	67.6% impaired on ≥ 1 test. 4 profile model gave best fit preserved cognition, mild attentional, moderate multidomain, severe multidomain. 10.6% met criteria for severe multidomain impairment	Significant differences in age at onset, age at testing, educational level, EDSS, 12-item MS Walking Scale and 25 ft Timed Walk between groups. Cognitive group significantly explained by age at onset, age at testing, 9 hole peg test, MS Walking Scale & 25ft Timed Walk. Age at testing, 25ft Timed Walk & EDSS survived multivariable regression. A smaller proportion of patients with preserved cognition (53%) or mild attentional deficit (60%) had brain lesions	No significant differences between cognitive groups in disease duration, depression, fatigue, attack number, 9-hole peg test, % with brain lesions	Exclusion of smokers and patients with visual impairment may bias results

Supplementary table 1. Literature review of cognitive impairment in NMOSD

									compared with mild multidomain (86%) or severe multidomain (80%) but did not reach statistical significance		
Liu <i>et al.</i> , 2015	China	54	70.4	27 HCs	CVLT, BVMT-R, SDMT, JLO, COWAT and WCST	Verbal memory, visuospatial memory, processing speed, visual processing, language & executive function	Score ≥ 1.5 SDs below HC mean in ≥ 2 domains	CI in 48.2% pwNMOSD. CVLT-II, BVMT-R, SDMT, COWAT & global average cognitive score significantly lower in NMOSD group.	Age at testing higher, education shorter and hippocampal volumes lower in NMOSD-CI compared with NMOSD-CP. Deep grey matter volumes smaller in CI compared with HCs. Global cognitive scores correlated negatively with age, positively with education and volumes of deep grey matter structures. Best multivariable model included education and hippocampal volume.	No difference in total white matter FA and MD between HCs, NMOSD-CI and NMOSD-CP. No correlation between global cognitive score and lesion volume, cortical thickness or white matter diffusion measures.	Small samples; high proportion seronegative NMOSD; no adjustment for depression, fatigue etc; use of means assumes normal distribution of test scores

Supplementary table 1. Literature review of cognitive impairment in NMOSD

Liu <i>et al.</i> , 2018	China	35	67.5	36 HCs	PASAT, MMSE	Not defined	N/A	MMSE, PASAT-2 and PASAT-3 scores significantly lower in NMOSD group vs HCs. Widespread grey matter atrophy including thalami & cortical regions in NMOSD group. Diffuse regional decreases in FA and increases in MD. ALFF and wFCS reduced in visual cortex, ALFF reduced in sensorimotor cortex and wFCS reduced in cingulate and cerebellum	PASAT-2 correlated with left thalamic volume, FA in brainstem, MD in right thalamus; PASAT-3 correlated with volumes right parahippocampus and superior temporal gyrus	N/A	High proportion seronegative; unclear why correlations with PASAT-2 scores differ from those with PASAT-3 scores; limited cognitive testing; correlate clinical & demographic features with MRI measures but not with cognitive outcomes; correlations between MRI measures and cognitive scores not adjusted for relevant covariates; psychosocial variables (e.g., depression) not accounted for; excluding patients with clinical brain involvement may bias results
Lopes <i>et al.</i> , 2025	Portugal	19	42.1	27 pwMS, 18 HCs	MoCA, BICAMS (CVLT-II, BVMT-R, SDMT), Verbal Fluency Test	Executive function, visuospatial abilities, short-term memory, language, attention, concentration, working memory, temporal & spatial orientation	Score <5th percentile of distribution on ≥1 test	Mean scores of NMOSD group lower on all subtests compared with MS and HCs but only significant for MoCA, SDMT and phonemic fluency	Depression score associated with presence of CI and correlated with SDMT and BVMT-R, EDSS correlated with CVLT-II and SDMT. Depression score, disease duration and	Education, anxiety and age did not predict CI	Small samples; high proportion seronegative; retrospective; 21% seronegative NMOSD had MOG antibodies; exclusion of patients with higher EDSS scores could bias results; disease duration and depression scores not matched; no detailed

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						(MoCA), verbal learning & memory, visuospatial learning & memory, processing speed, semantic & phonemic fluency			EDSS predicted CI in multivariable regression.		statistical methods described; multivariable regression performed for combined NMOSD and MS groups
Masuda <i>et al.</i> , 2017	Japan	16	94.0	20 pwMS	WAIS-III (vocabulary, similarities & information; arithmetic, digit span & letter-number sequencing; picture completion, block design & matrix reasoning; SDMT & digit search) WMS-R (general memory index, visual	Not defined	N/A	All mean WAIS-III and WMS-R subtest scores lower in pwMS vs NMOSD but only processing speed, general memory, verbal memory and delayed recall statistically significant. Total & fractional lesion volumes larger in MS vs NMOSD (not significant). Only superior temporal gyrus significantly smaller in MS	Visual cancellation and SDMT correlated with volume of superior temporal gyrus in NMOSD. Fractional lesion volume correlated negatively with visual cancellation, SDMT and TMT performance in NMOSD. Patterns of correlations differed between MS and NMOSD	No correlation between processing speed, verbal memory, general memory & delayed recall and superior temporal gyrus volume in NMOSD	Small samples; NMOSD & MS groups not matched for age or sex; 81.3% NMOSD group not on IST (not generalisable); no HC group (normative values of tests used); no assessment of effect of brain volumes not different between groups; tests purporting to examine the same domains had different outcomes; no assessment of effects of clinical/ demographic variables and interactions with MRI outcomes on cognitive outcomes

Supplementary table 1. Literature review of cognitive impairment in NMOSD

					memory index, verbal memory index, delayed recall index), TMT, Clinical Assessment for Attention (visual cancellation, auditory detection)						
Moore <i>et al.</i> , 2016	UK	42	71.4	42 pwMS, 42 HCs	CVLT-II, WAIS digit span, SDMT, fluency subsets of Delis-Kaplan Executive Functioning System	Verbal learning & recall, attention & working memory, processing speed, executive function	>2 SDs below publisher-determined age-adjusted mean	CI in ≥1 test in 67% NMOSD group and 50% MS group. No difference in incidence of CI between NMOSD and MS. Effect of diagnosis on CVLT-II learning, SDMT, Delis-Kaplan tests, digit span and memory, executive and global composite scores	EDSS and depression scores correlated negatively with "cognitive performance" (possibly global cognitive score) in NMOSD	Duration and anxiety not correlated to "cognition" (possibly global cognitive score) in NMOSD. "Cognitive score" (possibly global cognitive score) not different in seropositive vs seronegative or presence vs	High proportion seronegative NMOSD; NMOSD and HC groups not matched for sex; MS and NMOSD groups not matched for duration; unclear if correlations are tested for individual tests or global scores; post hoc group comparisons not presented- unclear whether differences between NMOSD group and HC group significant; correlations and comparisons but no multivariable models; correlations

Supplementary table 1. Literature review of cognitive impairment in NMOSD

										absence of brain lesions or treated vs untreated	assessed but scores not adjusted for covariates; comparison of means and MANOVA assume parametric distribution and homoscedasticity of residuals
Paolilo <i>et al.</i> , 2020	Multinational	67	100	N/A	N/A	N/A	"Significant school support, grade repetition, or needing of special education schools."	72.1% had abnormal brain MRI at onset. After median follow-up 4 years, 25.4% met criteria for CI	Younger age at onset predicted CI. Abnormal brain MRI at onset in 85% children with CI and 69% children with CP but did not reach statistical significance	No effect of ethnicity, phenotype at onset, abnormal MRI at onset, time to treatment, relapse number	Paediatric cases only; study designed to investigate effects of IST on outcomes; no formalised cognitive assessments; definition of CI vague, not sensitive or specific; psychosocial covariates and EDSS not included in regression for cognitive outcome; only onset MRI considered in regression; do not account for premorbid function
Saji <i>et al.</i> , 2013	Japan	14	100	17 pwMS, 37 HCs	Rao BRN-N (SRT, 10/36 SPART, PASAT, SDMT and COWAT)	Verbal immediate and delayed recall, spatial immediate and delayed recall, attention, processing speed, verbal fluency	<5th percentile of HC results on ≥ 3 tests	CI in 57% pwNMOSD and 47% pwMS. Tests most commonly impaired in NMOSD were PASAT-3 (64%), PASAT-2 (57%), SDMT (54%), SRT-LTS (50%) & CLTR (50%). NMOSD	Age correlated negatively with SDMT, PASAT, 10/36 SPART & 10/36 SPART-delayed. EDSS correlated negatively with 10/36 SPART. Pain correlated	No correlation between any test and duration, education, steroid dose, depression score, apathy score, grey matter or	Small samples; mean/median scores not provided

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								group scores significantly lower on PASAT, SDMT, SRT-LTS, SRT-CLTR and SRT-delayed. Impairment persisted after adjusting for age and pain	negatively with SRT-LTS.	white matter volumes.	
Salama <i>et al.</i> , 2020	Egypt	20	50.0	N/A	MoCA & BICAMS (CVLT-II, BVMT-R, SDMT)	Attention & concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation (MoCA), processing speed, immediate verbal recall, immediate visual recall	>2 SDs below HC mean in ≥ 2 domains	75% pwNMOSD met criteria for CI. 75% impaired SDMT, 70% impaired CVLT, 55% impaired BVMT. Mean total BICAMS score and subtest scores significantly lower in NMOSD group vs HCs. MoCA score also lower ($p = 0.054$).	All scores correlated positively with education, BVMT and MoCA scores correlated negatively with onset age. MoCA correlated negatively with EDSS. MoCA, global score and BVMT significantly lower in seropositive NMOSD.	N/A	Small samples; high proportion seronegative; unclear if translated BICAMS and MoCA appropriate for culture; HCs recruited from hospital staff (possibly inflating HC scores); unclear what variables were examined in correlations; values of most predictor variables not published; did not test long-term memory; included results 2 patients unable to complete tests (underestimate true mean score); unclear if MoCA results included in assessment of impairment; statistical methods not published; compared

Supplementary table 1. Literature review of cognitive impairment in NMOSD

											means (assume normal distribution of scores)
Savoldi <i>et al.</i> , 2020	Italy	25	100	30 HCs	Rao BRB-N (SRT, 10/36 SPART, PASAT, SDMT), Stroop Colour Word Test	Verbal memory, visual memory, attention & processing speed (PASAT & SDMT), executive function	Not defined	56% impaired attention and/or processing speed, 24% impaired executive function, 20% impaired memory. 68% pwNMOSD had brain lesions, no differences in age- and sex-adjusted total brain volume or white matter volume. Reduced total grey matter volume in NMOSD group, including thalami and several cortical regions. Resting state functional connectivity significantly higher in default mode network, right working memory network, executive control network & salience network in NMOSD. Functional connectivity lower	Attention/processing speed, memory & global cognitive scores correlated negatively with grey matter volumes in NMOSD. Resting state functional connectivity in default mode, right working memory & executive control networks correlated positively with attention/processing speed score. Functional connectivity in default mode network correlated positively with executive score. Functional connectivity in left working memory network correlated	No significant correlation between any cognitive domain score and lesion load or regional grey matter volumes	Exclusion of participants with depression or fatigue may bias results; identified functional networks are theoretical; no definition of CI; no attempt to look at correlations in HC group; covariates in multivariable regression not disclosed; results differ from those of Han <i>et al.</i>

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								in left working memory network in NMOSD	negatively with global cognitive score		
Vanotti <i>et al.</i> , 2013	Argentina	14	Not reported	14 pwMS, 14 HCs	SRT, 7/24 Spatial Recall Test, PASAT-2, PASAT-3, SDMT, COWAT	Verbal learning, verbal recall, visuospatial memory, calculation & attention, processing speed, verbal fluency	<5th percentile of HC scores on ≥2 of SRT, 7/24 Spatial Recall Test, COWAT or PASAT	pwNMOSD significantly lower mean PASAT-2 score than HCs. No other mean significantly lower. Most commonly impaired tests in NMOSD were SDMT (64.3%), COWAT (48.9%) and SRT (35.7%). No significant test differences between pwNMOSD and pwMS.	Claim presence of brain lesions in NMOSD associated with lower SRT-LTS score. Depression scores correlated negatively with PASAT. Age correlated negatively and education correlated positively with COWAT, SRT- delayed recall and PASAT	No test correlated with EDSS	Small samples; % seropositive not reported; results of SDMT not considered in diagnosis of CI; compared group mean test scores to identify impairment at group level but compared with local normative values to assess percentage impaired on each test; only 6 patients had brain lesions, insufficient to determine whether brain lesions affect scores; correlations but no adjustment of scores for relevant clinical and demographic variables; ANOVA and Pearson correlations assume parametric distribution and homoscedasticity of residuals
Vlahovic <i>et al.</i> , 2024	USA	219	79.0	N/A	MoCA	visuospatial/exe cutive (5/30), naming (3/30), attention (6/30), language (3/30), abstraction	Score <26	34% met criteria for CI on initial MoCA. Language and MoCA most affected	MoCA score correlated negatively with pain & EDSS scores. Trend towards	No effect of annualised relapse rate, duration sex, presence of supratentorial	High proportion seronegative; retrospective; single measure of cognition; fluctuations in scores on serial testing

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						(2/30), delayed recall (5/30), and orientation			negative correlation with age. Higher education levels were associated with higher MoCA scores. Black race and rituximab exposure were associated with lower MoCA scores. EDSS score, education and race survived multivariable regression with borderline effects of pain and age.	brain lesions, serostatus. No statistically significant decline in score over time	suggest measure is unstable construct; attrition on serial testing (potential for bias); potential learning effect of repeat testing; "trends" included patients with only 2 assessments; no adjustment for depression or anxiety; no HCs to compare performance patterns on serial testing; maximum Pearson correlation 0.28 (weak); discrete coding of serial MoCA scores (increase or decrease of 1 point classed as upward or downward trajectory with ceiling effect at score 30; use of t-tests, ANOVA and linear regression assumes homoscedasticity & normal distribution of residuals
Wang <i>et al.</i> , 2015	China	50	64.0	50 HCs	CVLT-II, PASAT, SDMT, WCST, COWAT	Verbal learning & memory, auditory processing speed & working memory, visual processing speed & working	N/A	Mean scores in NMOSD group significantly lower on CVLT-II short delay cued recall, long delay free recall, long delay cued recall, SDMT	CVLT-II immediate recall correlated positively with volume of medial prefrontal cortex; short	N/A	High proportion of seronegative patients; methods of comparing scores between groups unclear; sensitivity and specificity of COWAT in ideographic language unclear; demographic

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						memory, phonemic fluency, executive function		and COWAT. Grey matter volumes reduced (medial prefrontal cortex, right thalamus, left inferior temporal gyrus)	delay and long delay free recall correlated with volume of right thalamus		and clinical variables correlated with grey matter volumes but not test scores; no adjustment of test scores for relevant variables; use of means assumes normal distribution of data
Yabalak <i>et al.</i> , 2022	Turkey	22	81.8	N/A	Addenbrooke's Cognitive Evaluation-Revised, Rao BRB-N (SRT, 10/36 SPART, SDMT, PASAT, COWAT)	Not defined	<5th percentile on ≥ 2 tests vs normative means	45.5% met criteria for CI. PASAT, SRT short term, SRT-LT and COWAT correlated negatively with depression.	PASAT, SRT-ST and SRT-LT correlated positively with education. SRT short term correlated negatively with age. depression scores significantly higher in patients with CI. pwNMOSD-CI significantly older, shorter education, higher mean EDSS. Borderline effect of serostatus (100% NMOSD-CI were AQP4+ vs 66% NMOSD-CP). Borderline effect of MRI lesions (60%	No difference in disease duration or attack number in NMOSD-CI vs NMOSD-CP. No correlation between any score and duration or attack number	Small sample; no control group; low baseline education; unclear applicability of tests to Turkish population; unclear if normative means adjusted for age/education/sex; results of Addenbrooke's Cognitive Evaluation not disclosed; limiting to patients without severe disability may bias results; no adjustment for multiple comparisons; group comparisons show associations only, no correlations/ coefficients/ effect sizes

Supplementary table 1. Literature review of cognitive impairment in NMOSD

									NMOSD-CI had brain lesions vs 25% NMOSD-CP). SRT-long term, SRT-short term & PASAT correlated negatively with depression score and positively with education. SRT-short term correlated negatively with age. COWAT correlated negatively with depression score		
Yang <i>et al.</i> , 2022	China	28	48.3	28 HCs	MMSE, MoCA, Auditory Verbal Learning Test, TMT-A, TMT-B, SDMT, Stroop Colour Word Test, COWAT	Verbal learning and memory, attention, processing speed, executive function (TMT-B, Stroop test), verbal fluency	N/A	NMOSD group scores significantly lower on MMSE, MoCA, Auditory Verbal Learning Test, SDMT, TMT-A, TMT-B and composites of processing speed, attention & total cognition. Grey and white matter volumes in medial prefrontal cortex and thalamus not	In patients, GABA levels in medial prefrontal cortex correlated with overall cognitive score and verbal memory	No correlation between any test score and glutamate in medial prefrontal cortex or thalamus or GABA in the thalamus	Small sample; high proportion seronegative; excluding patients with significant depression or anxiety may bias results; analyses restricted to left thalamus and medial prefrontal cortex; other metabolites detected in GABA range; differences in mean MMSE and MoCA scores small ($p < 0.05$); no adjustment for

Supplementary table 1. Literature review of cognitive impairment in NMOSD

								significantly different in NMOSD group and HCs. GABA levels in medial prefrontal cortex reduced in NMOSD vs HCs. No significant differences in glutamate. No significant differences in thalamic GABA or glutamate.			anxiety and depression scores, despite group differences; test scores not adjusted for other demographic and clinical variables; correlations between relevant covariates and test scores not assessed (only partial correlations between test scores and neurotransmitter levels); unclear if adjusted for false discovery rates/ multiple comparisons
Zhang <i>et al.</i> , 2015	China	36	69.4	30 HCs	MoCA, MMSE, PASAT, SDMT, CVLT-II, BVMT-R, JLO, COWAT, WCST	visuospatial processing, naming, verbal memory, attention, language, abstraction, orientation (MoCA), Orientation, registration, attention & calculation, recall, naming, language comprehension, writing and construction (MMSE),	>2 SDs below HC mean in ≥2 domains	36.1% pwNMOSD were impaired. Mean MMSE and MoCA scores lower in pwNMOSD than HCs. Mean PASAT, SDMT, CVLT (short and long delay free recall, long delay cued recall, total learning), BVMT-R, semantic fluency. Most commonly impaired domains processing speed (SDMT or PASAT, 38.9%) memory	NMOSD-CI group older at onset, older at testing, shorter education than NMOSD-CP group. Only education survived multivariable regression	No differences in EDSS, % seropositive, relapse frequency, presence of brain lesions, grey matter volume or white matter volume in NMOSD-CI and NMOSD-CP groups.	High proportion of seronegative patients; exclusion of patients with high depression and EDSS scores may bias results; 31.6% not on IST so not comparable with UK population; 14% were not imaged; uncertain sensitivity and specificity of COWAT in ideographic language; no adjustment for psychosocial variables (depression, fatigue etc); comparisons of means, t tests & linear regression assume a

Supplementary table 1. Literature review of cognitive impairment in NMOSD

						auditory processing speed, working memory & attention, visual processing speed & working memory, verbal memory, visuospatial memory, visual processing, fluency, executive function		(CVT-II or BVMT-R, 36.1%), semantic fluency (25.0%)			normal distribution and homoscedasticity of residuals
Zhao <i>et al.</i> , 2024	China	39	100	41 HCs	MoCA, Auditory Verbal Learning Test, SDMT; Stroop Colour-Word Test, TMT-A & TMT-B	"General cognitive function", verbal memory, processing speed, attention, executive function		Mean results of MoCA and TMT-A significantly poorer in pwNMOSD. Other cognitive scores similar between groups. In pwNMOSD, GABA concentrations were lower in anterior and posterior cingulate. Glutamate and glutathione levels higher in anterior cingulate.	In NMOSD group, negative correlation between glutathione levels in posterior cingulate and TMT-A after adjusting for age, sex and education. Anxiety correlated negatively with GABA levels in the posterior cingulate	No association between any other test and metabolite levels in anterior or posterior cingulate or occipital cortex	No adjustment/ correlation of cognitive test scores with depression, anxiety, fatigue, EDSS etc; correlate test scores with metabolite levels but not other demographic/ clinical factors; potential contaminants of metabolite peaks by other molecules; claim significant differences in metabolite levels but significance is lost when metabolite: creatine ratio is used; <i>a priori</i> focus on occipital cortex and anterior and posterior cingulate;

Supplementary table 1. Literature review of cognitive impairment in NMOSD

											partial correlations performed in NMOSD group but not controls; no adjustment for multiple comparisons; t-tests and Pearson correlations assume normal distributions of test scores
Zheng <i>et al.</i> , 2022	China	Maximum 103	62.6	Maximum 65 pwMS, maximum 57 HCs	CVLT-2, BVMT-R, PASAT-3	Not defined	N/A	Mean CVLT-II, BVMT-R & PASAT-3 lower in NMOSD group vs HCs. Mean lesion volume higher in pwMS vs pwNMOSD. Hippocampal volume and FA significantly lower and MD significantly higher in MS vs NMOSD Volume and FA significantly higher and MD significantly lower in NMOSD group vs HCs. In NMOSD, lesion volume and disease duration correlated with hippocampal FA.	In NMOSD CVLT-II correlated positively with left hippocampal volume, BVMT-R correlated positively with bilateral ALFF but none survived false discovery rate correction. In MS, PASAT scores correlated with volume, FA, MD of the hippocampus after correction.	N/A	High proportion seronegative; serostatus not available for all patients; retrospective; MS and NMOSD groups not matched for age, onset age, sex, disease duration or EDSS; only subset of patients recruited completed each test; included patients in relapse phase; only examined hippocampal MRI parameters; correlation analyses between demographic & clinical covariates and MRI measures but not cognitive scores; effects of centre, age and sex included in regression models for MRI characteristics but not cognitive scores;

Supplementary table 1. Literature review of cognitive impairment in NMOSD

											psychosocial variables not assessed
Zhuo <i>et al.</i> , 2021	China	20	100	17 pwMO GAD, 28 HCs	MoCA, SDMT, CVLT-II	Not defined	N/A	Median MoCA, SDMT & CVLT-II scores of pwNMOSD significantly lower than HCs but same as pwMOGAD. 55% pwNMOSD had brain lesions. Grey matter volumes in several cortical areas, thalami reduced vs HCs. FA in optic radiation reduced and MD in corona radiata increased vs HCs. FA lower and MD higher in optic radiation and splenium vs MOGAD. DC lower in occipital gyrus and higher in right cerebellum vs HCs	MoCA score correlated positively with volume of left rectus gyrus and negatively with FA in right medial lemniscus. SDMT correlated positively with volume right superior temporal gyrus, DC left middle occipital gyrus	N/A	Small samples; not all participants completed each cognitive test; report corrected significance for some MRI features and uncorrected for others; examined correlations between demographic, clinical & cognitive variables with MRI measures but not with cognitive scores; incomplete correction for multiple comparison of voxel-based measures