Table e-1. Definition of patient groups.
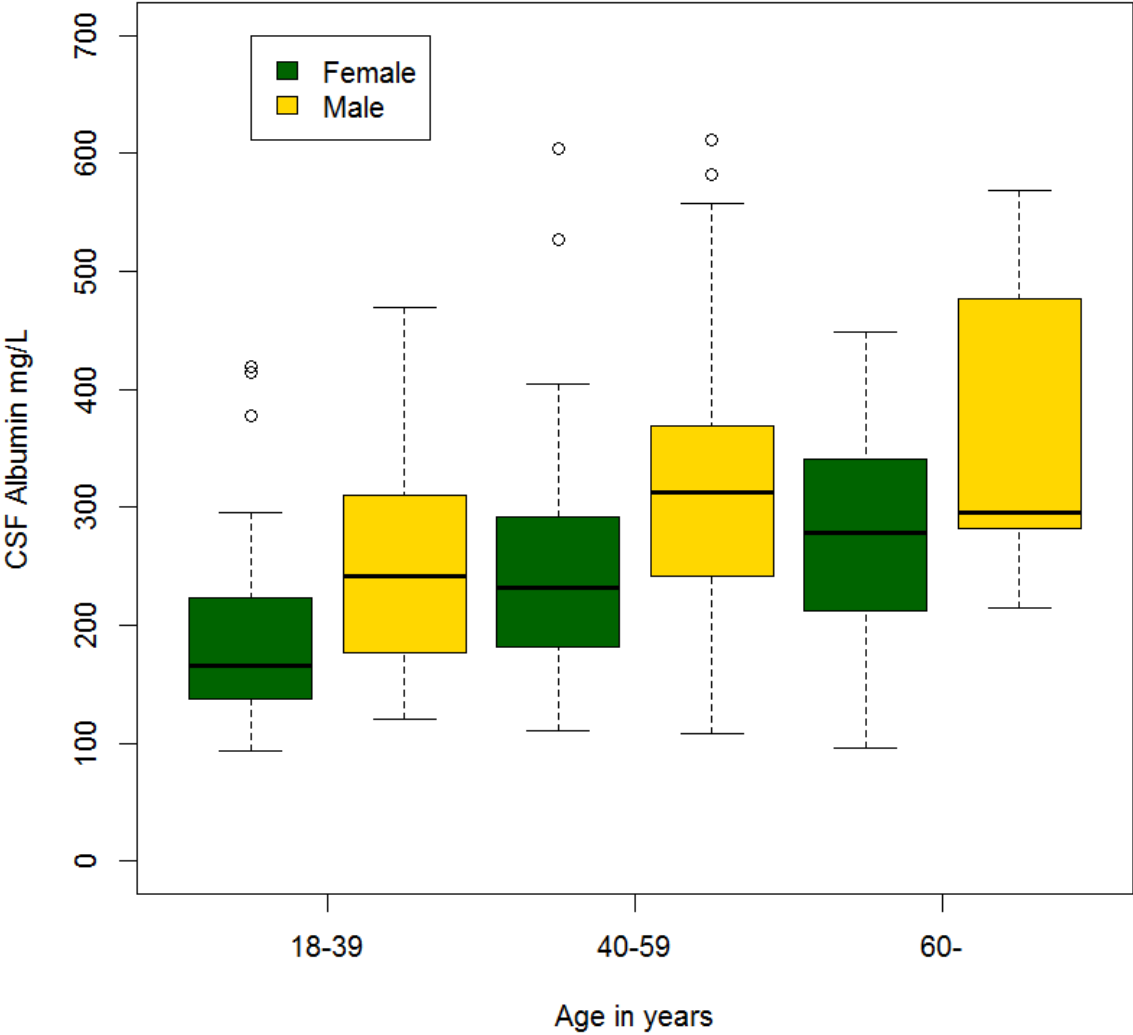
Patient group	Definition
HC	Volunteers without specific medical complaints (also not recurrent and disabling headache, back pain etc.) invited for research purposes only. Individuals with either current or previous neurological symptoms or signs when examined by a neurologist are excluded.
SC	This group comprised the diagnoses paresthesia (n=17), headache (=15), gait abnormality (n=6), sleep disturbance (n=5), fatigue (n=2), vertigo (n=2), alcohol withdrawal seizures (n=1), dysarthria (n=1), dysphasia (n=1), pneumonia with confusion (n=1), polymyalgia rheumatica with arm weakness (n=1), SLE with diffuse cognitive symptoms (n=1), SLE with headache (n=1), syncope (n=1) and visual disturbance (n=1), Thorough neurological examination and diagnostic tests were normal and did not reveal any neurological disease.
NINDC	This group comprised the diagnoses motor neuron disease (n=21), normal pressure hydrocephalus (n=11), stroke (n=8), narcolepsy (n=6), idiopathic intracranial hypertension (n=6), non-inflammatory polyneuropathy (n=6), psychosis (n=3), spinal stenosis (n=3), Parkinson's disease (n=3), cerebellar ataxia (n=2), peroneal nerve palsy (n=2), radiculopathy (n=2), sleep disorder (n=2), adrenomyeloneuropathy (n=1), alcohol induced encephalopathy (n=1), unspecified neuropsychiatric disorder (n=1), anoxic brain injury (n=1), atypical parkinsonism (n=1), primary CNS lymphoma (n=1), dystonia (n=1), myotonic dystrophy (n=1), epilepsy (n=1), essential tremor (n=1), Waldenström's macroglobulinemia with polyneuropathy (n=1), pineal germinoma (n=1), hereditary spastic paraparesis (n=1), pituitary adenoma (n=1), sudden idiopathic hearing loss (n=1), , KLL and neuropathy (n=1), meningeal carcinomatosis (n=1), migraine (n=1), motor neuron disease and monoclonal gammopathy of undetermined significance, MGUS (n=1), myopathy (n=1), Parkinson's disease and normal pressure hydrocephalus (n=1), periventricular leukomalacia (n=1), progressive supranuclear ophthalmoplegia (n=1), psoriatic arthritis and polyneuropathy (n=1), subarachnoid hemorrhage, SAH (n=1), secondary parkinsonism (n=1), idiopathic brachial neuritis (n=1), SLE with stroke (n=1), burnout (n=1) and Wernicke encephalopathy (n=1).
PINDC	This group comprised the diagnoses inflammatory polyneuropathy (n=4), myasthenia gravis (n=2), motor neuron disease and inflammatory polyneuropathy (n=1) Bell's palsy (n=2) and Guillain-Barré syndrome (n=1).
CINDC	This group comprised the diagnoses neurosarcoidosis (n=4), acute disseminated encephalomyelitis, ADEM (n=3), aseptic meningitis (n=3), autoimmune encephalitis (n=2), progressive multifocal leukoencephalopathy, PML (n=2), neuromyelitis optica, NMO (n=2), primary angiitis of the CNS (n=2), headache, HIV and Hepatitis C (n=1), bacterial meningitis (n=1), myelitis (n=1), neuropsychiatric SLE (n=1), anti-NMDA receptor encephalitis (n=1), tick borne encephalitis, TBE (n=1), viral encephalitis (n=1), chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids, CLIPPERS (n=1) and viral meningitis (n=1).
CIS/RIS	This group comprised the diagnoses CIS (n=17) and RIS (n=3).
MS	This group comprised the diagnoses RRMS (n=81), SPMS (n=17) and PPMS (n=7).

HC: healthy controls, SC: symptomatic controls, NINDC: non-inflammatory neurological disease controls, PINDC: peripheral inflammatory neurological disease controls, CINDC: central inflammatory neurological disease controls, CIS/RIS: clinically- or radiologically isolated syndrome, MS: multiple sclerosis.

Table e-2. KFLC metrics.

Metric	Formula	Unit
Q Alb	CSF Alb / P Alb x 1000	-
Q KFLC	CSF KFLC / P KFLC	-
KFLC Index	Q KFLC / Q Alb	-
KFLCLim[1]	KFLCLim = 0.9358 x Q Alb$^{0.6687}$	mg/L
KFLCLoc	(Q KFLC - KFLCLim) x P KFLC	mg/L
KFLC IF	(KFLCLoc / CSF KFLC)	-
Q Alb: Albumin quotient, Q KFLC: KFLC quotient, KFLCLim: the highest theoretical concentration of KFLC in CSF based on the individual albumin quotient, KFLCLoc: the theoretical intrathecal KFLC concentration based on KFLCLim, KFLC IF: the intrathecal fraction of KFLC.		

Figure e-1. CSF Alb (mg/L) in men and females in three age groups in the prospective cohort (n=335).

Box plots of CSF Alb for males and females in three different age groups.

References

1.   Presslauer SM, D.; Huebl, W.; Aboulenein-Djamshidian, F.; Krugluger, W.; Deisenhammer, F.; Senel, M.; Tumani, H.; Hegen, H. Validation of kappa free light chains as a diagnostic biomarker in multiple sclerosis and clinically isolated syndrome: A multicenter study. Multiple sclerosis 2016;22:502-510.