

**Supplemental Table 1: GFAP levels in the CSF of individuals with neurological conditions reflecting a wide range of etiologies are elevated**

CONDITION	CONTROLS			PATIENTS			S	REF
	n	mean ± SD ng/L	range	n	mean ± SD ng/L	range		
<i>Vascular</i>								
vasculitis	nr	[<750 younger] <sup>a</sup> [<1250 older] <sup>a</sup>	nr	32	10,791 ± 7646 (SEM)	nr	L	(1)
ischemic infarcts	18	7404 ± 2099 (SEM)	4138–11,518	25	16,005 ± 17,302 (SEM)	nr	L	(2)
infarcts	25	[~100–1300] <sup>a</sup>	nr	9	nr	~1000–100,000 <sub>b</sub>	L	(3)
ischemic infarcts - spinal cord	5	600 ± 300	300–1000	3	354,700 ± 459,000	2000–10 <sup>6</sup>	nr	(4)
ischemia – aortic aneurysm repair	nr	[375 ± 159 younger 95% < 700 671 ± 263 older 95% < 1200] <sup>a</sup>	nr	2	nr	190,000–330,000 <sup>b</sup>	L	(5)
subarachnoid hemorrhage	nr	95% < 9 (lumbar)	nr	5	18,950 ± 16,078	1550–40,630	V	(6)
<i>Trauma</i>								
traumatic brain injury	nr	95% < 9 (lumbar)	nr	11	16678 ± 15022	515–43,730	V	(6)
<i>Developmental</i>								
autism	10	67 ± 17 (SEM)	16–163	47	185 ± 20 (SEM)	~16–600	L	(7)
basal ganglia	10	[61 ± 17 (SEM)] <sup>a</sup>	nr	3	227 ± 34 (SEM)	nr	L	(8)
hydrocephalus	nr	700 ± 900 (lumbar)	nr	41 27 12	Gr 1: 19,000 ± 26,000 Gr 2: 20,000 ± 21,000 Gr 3: 2.2 x 10 <sup>6</sup> ± 3 x 10 <sup>6</sup>	nr	V	(9)
encephalopathies and white matter disorders	10	[67 ± 54] <sup>a</sup>	nr	nr	progr 223 ± 186 non-progr 128 ± 86	15–869 15–264	nr	(10)
metabolic - unspecified	nr	[< 10,000] <sup>a</sup>	nr	16	metabolic/storage	0–94,000	L	(11)
cerebral white matter	nr	[67 ± 17 (SEM)] <sup>a</sup>	nr	26	1188 ± 2508 (SEM)	nr	nr	(12)
neonatal asphyxia	8	538 median	458–1051	22	1428 median	427–49,706	L	(13)

premature birth	10	222 median	87–554	17 10	normal pre-term 106 (ns) abnormal pre-term 576	15–362 265–16,000	L	(14)
<b>Genetic</b>								
Alexander disease	nr	[<175] <sup>a</sup>	nr	3	na	4760–30,000	nr	(15)
<b>Infectious and Inflammatory</b>								
multiple sclerosis	5	142 ± 26	nr	13	RR 386 ± 169	nr	L	(16)
multiple sclerosis	25	250 ± 34	125–450	58 5 21 15	RR 300 (ns) <sup>b</sup> PR 300 (ns) <sup>b</sup> SP 375 <sup>b</sup> PP 400 <sup>b</sup>	125–600 <sup>b</sup> 125–700 <sup>b</sup> 130–625 <sup>b</sup> 130–900 <sup>b</sup>		(17)
meningitis/ encephalitis	25	nr	~100–1300	13	nr	~1000–30,000 <sup>b</sup>	L	(3)
Lyme neuroborreliosis	9	208 median	32–776	23	510 median <sup>b</sup>	nr	nr	(18)
systemic lupus erythematosus	99	_ 436 ± 152 (SEM) _ 387 ± 194	nr	31 54	NPSLE 1904 ± 975 (SEM) w/o CNS 534 ± 234	nr	L	(19)
neuromyelitis optica	5	600 ± 300	300–1000	10 3	7666 ± 15267 <sup>c</sup>  before Rx 17,827±26142 after Rx 1.8 ± 1.5	8000–80,000,000 <sup>b</sup>	nr	(4)
Guillain-Barrè	30	330 median	nr	12 9	AIDP 350 median (ns) axonal 550 median	nr	nr	(20)

<b>Degenerative</b>								
dementia	nr	[<10,000] <sup>a</sup>	nr	64 24 7 26	AD 10,800 multi-infarct 39,500 CJD 65,000 undefined 14,700	0–56,000 0–564,000 9000–175,000 0–53,000	L	(11)
dementia	25	nr	~100–1300	7/9	AD / vascular	~400–2000 <sup>b</sup>	L	(3)
dementia	39	569 ± 265	nr	8 5 29 20	pure AD 936 ± 431 (ns) frontal lobe 721 ± 208 (ns) AD-type 1081 ± 561 vascular 1270 ± 1142	nr	L	(21)
dementia	13 9 8	2960 ± 1040 young 2800 ± 1460 adult 3990 ± 1590 senescent	nr	27	AD 8960 ± 7800	nr	nr	(22)
dementia	nr	95% < 9	nr	68	1374 ± 11098	<5–91,540 <sup>d</sup>	L	(6)
<b>Miscellaneous</b>								
normal pressure hydrocephalus	18	4300 ± 700 (SEM)	2000–14,000	12	96,000 ± 23,000 <sup>e</sup> (SEM)	~5000–258,000	L	(23)
normal pressure hydrocephalus	40	637 ± 295	nr	65	1116 ± 1085	nr	L	(24)
normal pressure hydrocephalus	nr	95% < 9 (lumbar)	nr	12	1197 ± 1226	<5–2970	V	(6)
seizures	33	93 ± 88	<50–440	52	232 ± 440	<50–3100	nr	(25)
schizophrenia	17	1190 ± 920	nr	12	1210 ± 810 (ns)	nr	L	(26)

All values have been converted to ng/L to facilitate comparison. Unless otherwise noted, values are given as mean ± standard deviation (SD). Additional abbreviations used are “n” number of patients or controls, “SEM” standard error of the mean, “ns” not significant, “AD” Alzheimer’s disease, “CJD” Creutzfeldt-Jakob disease, “ADIP” acute demyelinating inflammatory neuropathy, “GBM” glioblastoma multiforme, “NPSLE” neuropsychiatric systemic lupus erythematosus, “RR” relapsing remitting, “PR” progressive remitting, “SP” secondary progressive, and “PP” primary progressive, “na” not applicable, “nr” not reported. “S” refers to lumbar (L) or ventricular (V) points of collection of CSF if specified by the authors – others are most likely lumbar.

<sup>a</sup> Values for controls surrounded brackets were derived from a prior study, literature, or manufacturer using the particular assay.

<sup>b</sup> Data was presented in graphical form, from which these are estimated values.

<sup>c</sup> Whether standard deviation or standard error of the mean was not specified.

<sup>d</sup> The outlier value at the high end was from a patient who had autopsy-proven CJD.

<sup>e</sup> Eight patients had ventricular samples collected as well, in each case giving values that were higher than those found in lumbar samples.

## Reference List

1. Nylén, K., et al. 2002. Cerebrospinal fluid neurofilament and glial fibrillary acidic protein in patients with cerebral vasculitis. *J. Neurosci. Res.* **67**:844–851.
2. Aurell, A., et al. 1991. Determination of S-100 and glial fibrillary acidic protein concentrations in cerebrospinal fluid after brain infarction. *Stroke* **22**:1254–1258.
3. Rosengren, L.E., Wikkelsø, C., and Hagberg, L. 1994. A sensitive ELISA for glial fibrillary acidic protein: Application in CSF of adults. *J. Neurosci. Methods* **51**:197–204.
4. Misu, T., et al. 2008. Marked increase of CSF GFAP in neuromyelitis optica - an astrocyte damage marker. *J. Neurol. Neurosurg. Psychiatry* In press.
5. Anderson, R.E., et al. 2003. Biochemical markers of cerebrospinal ischemia after repair of aneurysms of the descending and thoracoabdominal aorta. *J. Cardiothorac. Vasc. Anesth.* **17**:598–603.
6. Petzold, A., Keir, G., Green, A.J.E., Giovannoni, G., and Thompson, E.J. 2004. An ELISA for glial fibrillary acidic protein. *J. Immunol. Meth.* **287**:169–177.
7. Rosengren, L.E., et al. 1992. A sensitive ELISA for glial fibrillary acidic protein: Application in CSF of children. *J. Neurosci. Methods* **44**:113–119.
8. Ahlsén, G., et al. 1993. Glial fibrillary acidic protein in the cerebrospinal fluid of children with autism and other neuropsychiatric disorders. *Biol. Psychiatry* **33**:734–743.
9. Beems, T., et al. 2003. Serum- and CSF-concentrations of brain specific proteins in hydrocephalus. *Acta Neurochirurgica* **145**:37–43.
10. Ehlers, S., Kyllerman, M., and Rosengren, L. 1994. Analysis of glial fibrillary acidic protein in the cerebrospinal fluid of children investigated for encephalopathy. *Neuropediatrics* **25**:129–133.

11. Crols,R., Saerens,J., Noppe,M., and Lowenthal,A. 1986. Increased GFAP levels in CSF as a marker of organicity in patients with Alzheimer's disease and other types of irreversible chronic organic brain syndrome. *J. Neurol.* **233**:157–160.
12. Kristjánisdóttir,R., Uvebrant,P., and Rosengren,L. 2001. Glial fibrillary acidic protein and neurofilament in children with cerebral white matter abnormalities. *Neuropediatrics* **32**:307–312.
13. Blennow,M., Sävman,K., Ilves,P., Thoresen,M., and Rosengren,L. 2001. Brain-specific proteins in the cerebrospinal fluid of severely asphyxiated newborn infants. *Acta Paediatrica* **90**:1171–1175.
14. Blennow,M., et al. 1996. Glial fibrillary acidic protein is increased in the cerebrospinal fluid of preterm infants with abnormal neurological findings. *Acta Paediatr.* **85**:485–489.
15. Kyllerman,M., Rosengren,L., Wiklund,L.M., and Holmberg,E. 2005. Increased levels of GFAP in the cerebrospinal fluid in three subtypes of genetically confirmed Alexander disease. *Neuropediatrics* **36**:319–323.
16. Rosengren,L.E., Lycke,J., and Andersen,O. 1995. Glial fibrillary acidic protein in CSF of multiple sclerosis patients: Relation to neurological deficit. *J. Neurol. Sci.* **133**:61–65.
17. Norgren,N., e al. 2004. Neurofilament and glial fibrillary acidic protein in multiple sclerosis. *Neurology* **63**:1586–1590.
18. Dotevall,L., Hagberg,T., Karlsson,J.E., and Rosengren,L.E. 1999. Astroglial and neuronal proteins in cerebrospinal fluid as markers of CNS involvement in Lyme neuroborreliosis. *European Journal of Neurology* **6**:169–178.
19. Trysberg,E., Nylen,K., Rosengren,L.E., and Tarkowski,A. 2003. Neuronal and astrocytic damage in systemic lupus erythematosus patients with central nervous system involvement. *Arthritis & Rheumatism* **48**:2881–2887.
20. Notturmo,F., Caporale,C.M., De Laurentis,A., and Uncini,A. 2008. Glial fibrillary acidic protein: A marker of axonal Guillain-Barre syndrome and outcome. *Muscle Nerve* **38**:899–903.
21. Wallin,A., Blennow,K., and Rosengren,L.E. 1996. Glial fibrillary acidic protein in the cerebrospinal fluid of patients with dementia. *Dementia* **7**:267–272.

22. Fukuyama,R., Izumoto,T., and Fushiki,S. 2001. The cerebrospinal fluid level of glial fibrillary acidic protein is increased in cerebrospinal fluid from Alzheimer's disease patients and correlates with severity of dementia. *Eur. Neurol.* **46**:35–38.
23. Albrechtsen,M., Sørensen,P.S., Gjerris,F., and Bock,E. 1985. High cerebrospinal fluid concentration of glial fibrillary acidic protein (GFAP) in patients with normal pressure hydrocephalus. *J. Neurol. Sci.* **70**:269–274.
24. Tullberg,M., Rosengren,L., Blomsterwall,E., Karlsson,J.E., and Wikkelsø,C. 1998. CSF Neurofilament and glial fibrillary acidic protein in normal pressure hydrocephalus. *Neurology* **50**:1122–1127.
25. Gurnett,C.A., Landt,M., and Wong,M. 2003. Analysis of cerebrospinal fluid glial fibrillary acidic protein after seizures in children. *Epilepsia* **44**:1455–1458.
26. Steiner,J., et al. 2006. Increased cerebrospinal fluid and serum levels of S100B in first-onset schizophrenia are not related to a degenerative release of glial fibrillar acidic protein, myelin basic protein and neurone-specific enolase from glia or neurones. *J. Neurol. Neurosurg. Psychiatry* **77**:1284–1287.

**Supplemental Table 2: GFAP appears in the serum under certain circumstances**

CONDITION	CONTROLS			PATIENTS			REF
	n	mean $\pm$ SD ng/L	range	n	mean $\pm$ SD ng/L	range	
<i>Vascular</i>							
ischemic stroke	46	95% < 40	14–66 0	22	2000 $\pm$ 1500 (SEM) <sup>a</sup>		(1)
hemorrhagic stroke	52 3	<1.8 3.8–7.2	nr	42	112 $\pm$ 477	0–3096	(2)
subarachnoid hemorrhage	81	< 150	nr	116	1130 mean; 330 median	30–34,43 0	(3)
<i>Trauma</i>							
traumatic brain injury	70	97.5% < 33	2–49	25	100 $\pm$ 180 at admission	nr	(4)
traumatic brain injury	72	95% < 49	150–7 60	3	nr	5000–13, 000	(5)
traumatic brain injury - non-survivors		manufacturer data	30–30 0	39	~6000 median		(6)
traumatic brain injury	218	61 $\pm$ 44; 95 % < 150	nr	59	4520 $\pm$ 8690; 1170 median	140–49,5 80	(7)
<i>Developmental</i>							
hydrocephalus (not altered)	8	200 $\pm$ 200	nr	27 12	grade 1: 300 $\pm$ 300 (ns) grade 2: 500 $\pm$ 300 (ns)	nr	(8)
<i>Infectious and inflammatory</i>							
multiple sclerosis	30	410 median	nr	30	2810 median	nr	(9)
Guillain-Barré syndrome	30	410 median	nr	17 20	axonal : 740 median	nr	(9)

					ADIP: 580 median		
<i>Neoplastic</i>							
glioma	nr	< 150	nr	31	high grade: 239	30–1210	(10)
GBM	50 54	healthy: 0 non GBM: 0 median	0 0–24	50	GBM: 180 median	0–5600	(11)
<i>Miscellaneous</i>							
schizophrenia (not altered)	17	180 ± 150	nr	12	160 ± 150 (ns)	nr	(12)

All values have been converted to ng/L to facilitate comparison. Unless otherwise noted, values are given as mean ± standard deviation (SD). ADIP, acute demyelinating inflammatory neuropathy; GBM, glioblastoma multiforme; n, number of patients or controls; ns, not significant; SEM, standard error of the mean.

<sup>a</sup> Data was presented in graphical form, from which these are estimated values.

#### Reference List

1. Vissers, J.L.M., et al. 2006. Rapid immunoassay for the determination of glial fibrillary acidic protein (GFAP) in serum. *Clin. Chim. Acta* **366**:336–340.
2. Foerch, C., et al. 2006. Serum glial fibrillary acidic protein as a biomarker for intracerebral haemorrhage in patients with acute stroke. *J. Neurol. Neurosurg. Psychiatry* **77**:181–184.
3. Nylén, K., et al. 2007. Serum glial fibrillary acidic protein is related to focal brain injury and outcome after aneurysmal subarachnoid hemorrhage. *Stroke* **38**:1489–1494.
4. Missler, U., Wiesmann, M., Wittmann, G., Magerkurth, O., and Hagenström, H. 1999. Measurement of glial fibrillary acidic protein in human blood: analytical method and preliminary clinical results. *Clin. Chem.* **45**:138–141.



5. van Geel,W.J.A., et al. 2002. Measurement of glial fibrillary acidic protein in blood: an analytical method. *Clin. Chim. Acta* **326**:151–154.
6. Pelinka,L.E., et al. 2004. Glial fibrillary acidic protein in serum after traumatic brain injury and multiple trauma. *J. Trauma* **57**:1006–1012.
7. Nylén,K., et al. 2006. Increased serum-GFAP in patients with severe traumatic brain injury is related to outcome. *J. Neurol. Sci.* **240**:85–91.
8. Beems,T., et al. 2003. Serum- and CSF-concentrations of brain specific proteins in hydrocephalus. *Acta Neurochirurgica* **145**:37–43.
9. Notturmo,F., Caporale,C.M., De Laurentis,A., and Uncini,A. 2008. Glial fibrillary acidic protein: A marker of axonal Guillain-Barre syndrome and outcome. *Muscle Nerve* **38**:899–903.
10. Brommeland,T., Rosengren,L., Fridlund,S., Hennig,R., and Isaksen,V. 2007. Serum levels of glial fibrillary acidic protein correlate to tumour volume of high-grade gliomas. *Acta Neurol. Scand.* **116**:380–384.
11. Jung,C.S., et al. 2007. Serum GFAP is a diagnostic marker for glioblastoma multiforme. *Brain* **130**:3336–3341.
12. Steiner,J., et al. 2006. Increased cerebrospinal fluid and serum levels of S100B in first-onset schizophrenia are not related to a degenerative release of glial fibrillar acidic protein, myelin basic protein and neurone-specific enolase from glia or neurones. *J. Neurol. Neurosurg. Psychiatry* **77**:1284–1287.