Short report

Elevated cerebrospinal fluid vasopressin in motor neuron disease

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SUMMARY CSF vasopressin levels were significantly elevated in eight patients with motor neuron disease (2.5 ± 0.4 pmol/l) compared with controls (0.7 ± 0.1 pmol/l). CSF oxytocin and plasma vasopressin concentrations were similar in the two groups. This finding may be a primary part of the disease process or an epiphenomenon related to increased autonomic and descending pathway activity secondary to abnormal function and/or loss of anterior horn cells.

There is increasing evidence that the pathological processes in motor neuron disease are not limited exclusively to motor pathways and cells.^{1,2} Patients with motor neuron disease have reduced concentrations of thyrotropin-releasing hormone in their cerebrospinal fluid (CSF)³ and in the ventral horns of the spinal cord.⁴ Two other hypothalamic peptides, vasopressin and oxytocin, have been demonstrated in human CSF and spinal cord by radioimmunoassay⁵ and immunohistochemistry.⁶ The origins and functions of these hormones in extra-hypothalamic regions of the CNS and the CSF are unknown. The classical stimuli to peripheral hormone release do not markedly affect CSF concentrations and neither peptide crosses the blood-brain barrier.⁷ It has been suggested that vasopressin and oxytocin may play a role in motor function.⁸ Both are found in the interneuronal networks close to the anterior horn cells.^{6,8,9}

We have investigated vasopressin and oxytocin in the CSF in patients with motor neuron disease.

Methods

Eight successive ambulant patients (aged 52–71 yr, mean 61.0; three males:five females) with motor neuron disease were investigated (table). Lumbar puncture was performed

as part of the routine clinical investigation; none had had previous lumbar puncture. The controls were 12 patients (aged 40–75 yr, mean 62.6; five males:seven females) undergoing lumbar puncture as part of the investigation of lumbar disc prolapse (3), peripheral neuropathy (2), possible multiple sclerosis (2), isolated cranial nerve palsy (2), acute leukaemia without CNS involvement (1), headache (1) and retinal embolism (1).

After 30 min recumbency, venous blood was drawn and then lumbar puncture performed in the lateral decubitus position. CSF pressure was estimated by direct manometry. CSF was obtained for microscopy and biochemistry and then a small aliquot (< 1 ml) taken for peptide assay. Blood was taken on ice, centrifuged at 4°C, the plasma separated and stored at –20°C prior to peptide assay. CSF was stored at –20°C. Plasma was extracted through octadecasilyl silica cartridges (Sep-pak, Waters, Mass.) prior to peptide assay; extraction yield >90%. CSF was estimated directly in sensitive and specific radioimmunoassays.¹⁰ Intra-assay coefficient of variation (CV) was <5% for vasopressin and oxytocin, interassay CV was 15% for vasopressin and 10% for oxytocin. The detection limit was 0.2 pmol/l for plasma and CSF vasopressin and 1.3 pmol/l for CSF oxytocin.

Peptide data were not normally distributed and were compared by the Mann-Whitney test. Values are means $\pm$ SE.

Results

CSF vasopressin was significantly higher in the motor neuron disease patients (2.5 ± 0.4 pmol/l) than the controls (0.7 ± 0.1 pmol/l), $p < 0.01$ (fig). CSF oxytocin was similar in both motor neuron disease patients (12.4 ± 1.6 pmol/l) and controls (10.6 ± 2.1 pmol/l). Plasma vasopressin was also similar in motor

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Table Clinical data of motor neuron disease patients

Sex	Age (yr)	MND type	Duration of illness	Time to severe incapacity	Major disability	CSF* protein g/l
F	55	B	27	21	Anarthria	—
M	71	ALS	7	5	Tetraparesis	0.67
M	64	B	17	—	Dysarthria	0.59
F	64	B	34	17	Anarthria	0.47
F	52	B	19	—	Dysarthria	0.40
F	68	B	26	24	Dysarthria	0.24
F	55	ALS	10	—	Dysarthria	0.69
M	59	ALS	36	12	Weak hands	0.52

*All patients had <3 cells/mm³. Times in months.
B, bulbar; ALS, amyotrophic lateral sclerosis.

neuron disease patients (2.1 ± 0.3 pmol/l) and in the controls (1.6 ± 0.3 pmol/l). CSF protein was identical in the two groups as was the intracranial pressure (15.0 ± 1.3 cm. CSF in motor neuron disease patients, 14.1 ± 1.3 in controls). There was no apparent relationship between CSF peptide concentration and motor neuron disease type, duration of illness or time to severe incapacity.

Discussion

We present evidence that CSF vasopressin is elevated

in motor neuron disease. This is not part of a generalised release of neurohypophyseal peptides into CSF in this disease as CSF oxytocin levels are similar to control values. Neither do the CSF vasopressin concentrations reflect changes in plasma levels of this hormone.

CSF vasopressin has been reported to be elevated in conditions associated with raised intracranial pressure.¹¹ This did not appear to be a factor in this study.

Vasopressin has been found in fibres in laminae II, V and VI of the spinal cord and oxytocin in laminae I, III, IV and IX.^{6,8} Laminae V and VI are closely related to the interneuronal network situated dorsally to lamina IX, which contains anterior horn cells. Thus the elevated CSF vasopressin levels may reflect increased activity of these neurons, either as a compensatory mechanism secondary to the primary pathology or as part of the underlying disease process. Alternatively, there may be loss of peptide secondary to non-specific damage to cells neighbouring the motor neurons, although the selective rise of vasopressin, but not of oxytocin which is more widely distributed, does not support this explanation.

Although patients with motor neuron disease do not usually describe symptoms of autonomic dysfunction, there is evidence of an impaired response to head-up tilt and increased sensitivity to infused noradrenalin, thought to involve central mechanisms.¹² The evidence of autonomic dysfunction has been supported by recent pathological findings.¹ There is increasing evidence for a role for vasopressin in the central control of autonomic function.^{13,14} The elevated CSF vasopressin levels in motor neuron disease may be associated with these changes.

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Fig CSF vasopressin (AVP) concentrations in patients with motor neuron disease and controls. Mann-Whitney test.

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