and slight subjective hearing impairment on the left. Tracheostomy was performed on the third hospital day and IPPV was continued for two weeks. During subsequent weaning from the respirator his breathing was maintained while awake, but during sleep there were frequent episodes of central apnoea with arterial oxygen saturation frequently dropping to 85%.

Neurological improvement began two weeks after admission. At three months the major findings included continuing apnoeic episodes while asleep requiring nocturnal ventilation, complete left facial paralysis, markedly impaired swallowing, minor inco-ordination of the left arm and leg and mild unsteadiness of gait.

At the end of the fifth month there was development over five days of marked unsteadiness of gait, inco-ordination of the arms and increasing difficulty in swallowing. A CT brain scan and CSF examination were normal. Recovery to his previous state occurred over the next 6 weeks.

At the end of 8 months assisted respiration was no longer required during sleep and the tracheostomy had been closed. There were no significant changes during the next three years.

Somatosensory evoked potentials (SEPs) and brain stem auditory evoked potentials (BAEPs) were recorded during the acute illness and the recovery period using standard methods and normal values for this laboratory.⁹ On the second hospital day SEPs were normal but BAEPs following stimulation of the right ear showed slight prolongation of the Wave I-V interval. Nine days later SEPs remained normal but the BAEPs showed a further increase of the Wave I-V interval on the right and loss of all waves following Wave I on the left, despite stimulation at least 55 decibels above left ear hearing threshold. On hospital day 29, while the patient was recovering, the central somatosensory conduction time¹⁰ to the left hemisphere was relatively prolonged compared with that to the right. Subsequently the central conduction time to the right hemisphere became absolutely prolonged while that to the left remained unchanged. Although the BAEPs from the right ear returned to normal, those from the left beyond Wave I remained absent until recordings made at the time of deterioration in the 5th month, when they had returned but showed slight prolongation of the I-V interval. Thirty-two months after admission SEPs and BAEPs were normal.

This patient's presentation with a systemic prodromal illness followed by rapidly progressive multifocal signs in the brain

stem was similar to those previously reported in the literature. As in most of these cases, the organism was isolated from blood cultures but not from the CSF. The loss of automatic respiratory movements (Ondine's curse) has not been described in previous patients with listeria rhombencephalitis, although "respiratory failure" has occurred in two.^{2,7} This unusual but important complication might be expected in patchy disease of the lower brain stem from involvement of central respiratory control centres.

The evoked potential studies in this patient showed several unexpected features. The disappearance of all BAEPs beyond Wave I is consistent with a pontomedullary lesion; although this change with preservation of hearing may be seen in multiple sclerosis (unpublished observations) we have not observed it in any other neurological diseases. The later deterioration in the central somatosensory conduction time to the right hemisphere, occurring while the patient was recovering, suggested the development of a new subclinical brain stem lesion. Following this, another lesion in the brain stem-cerebellar connections occurred at five months causing inco-ordination and ataxia.

Little is known of the histopathology of listeria rhombencephalitis. Formation of multiple small abscesses with gram positive bacilli has been reported at necropsy^{1,6} and the evidence suggests that direct bacterial invasion occurs in the acute stage. There is an analogy in listeria infection of ruminants.¹ However, in this patient an additional mechanism must have been present with the appearance of clinical and subclinical lesions long after resolution of the infection. The pattern of disease raises the possibility of recurrent episodes of brain stem demyelination as a remote, post-infectious complication of *Listeria monocytogenes* infection of the central nervous system.

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Asymmetry of pathology in Alzheimer's disease

Sir: For much recent work on neurotransmitter abnormalities in Alzheimer's disease it has been the practice in many centres to fix one cerebral hemisphere for histological study and to freeze the other for neurochemical investigation. The assumption underlying this is that the disease process affects the brain symmetrically, allowing correlation to be made between histological changes on one side and chemical changes on the other. This assumption has been called into question in a recent study by Arendt *et al.*¹ These authors reported cell counts in the nucleus basalis and plaque counts in the cortex on both sides of the brain in cases of Alzheimer's disease. They found, in some cases, "marked differences in regional plaque counts between the two hemispheres". The differences in the mean counts for the hemispheres did not reach statistical significance, however. Nevertheless, we felt that the doubt cast on the current practice of dividing the brain sagittally called for review of other data in the literature and small additional study designed to address

Letters

the question of the symmetry of the pathology in Alzheimer's disease.

We examined material from the brains of five patients, four females and one male, aged 56–81 years (mean 70 years), with clinical and pathological features of Alzheimer's disease. These five cases spanned a fairly wide range of clinical (prospectively assessed) and pathological severity. Blocks were prepared from the superior and middle frontal gyri (areas 9 and 46), superior and middle temporal gyri (areas 38 and 21), and from parietal (area 7) and occipital (area 18) lobes from both cerebral hemispheres from each fixed brain. Sections of paraffin-embedded material were stained with the modified Palmgren technique² for neurofibrillary tangles, and frozen sections were stained using von Braunmühl's technique for argyrophilic plaques. Plaques and tangles were counted using a Weibel graticule at a magnification of $\times 80$ for plaque counts (field size 1.35 mm^2) and $\times 200$ for tangle counts (field size 0.25 mm^2), in 25 randomly selected fields from each of the frontal and temporal lobe sections, and in 15 fields from the sections of parietal and occipital lobes. The mean counts obtained from the left and right side of each brain were then compared (Student's *t* test). The

results are summarised in the table. It can be seen that in most areas there is a wide range of counts, greater for plaques than for tangles, and neither hemisphere consistently has a greater plaque or tangle count. However, there is a statistically significant difference between the two sides in plaque counts in the occipital lobe in two cases, and in all lobes in one case (the right side more affected in two lobes and the left in the other two). There is a greater agreement between mean tangle counts for each area than for plaque counts, although the range of counts is again wide. There is a significant difference between the two sides for tangle counts for the frontal lobe sections from one brain, and for the occipital lobe sections from another.

We have also counted the number of nucleolated pigmented neurons in both sides of the locus coeruleus from 10 prospectively assessed undemented subjects, mean age 79 years (range 55–102 years) and 13 patients with Alzheimer's disease, mean age 77 years (range 55–88 years). Cells were counted in a series of single $20 \mu\text{m}$ thick cresyl violet stained sections taken one-sixth, one-third, one-half, two-thirds and five-sixths of the way through the locus. For the undemented subjects the mean cell count on the left side

was 71 (SD 34.9) and on the right 68 (SD 33.9) and for the demented subjects the counts were 39 (SD 20.7) and 41 (SD 24.5) respectively. In neither group was the difference statistically significant. Spearman's rank correlation coefficient was also calculated in respect of the counts on both sides, and was 0.996 for the control subjects and 0.998 for the demented subjects.

The study in the literature which contains the most extensive information on the symmetry of Alzheimer's disease pathology is that of Jamada and Mehraein.³ Examination of the data in that study for plaques and tangles in frontal, parietal, temporal, occipital and cingulate cortex fails to show significant differences (Student's *t* test; Spearman's rank correlation coefficient). Similarly, Ball⁴ found no significant difference in tangle counts for the hippocampus on both sides in Alzheimer's disease, and Brun and Englund⁵ reported no semi-quantitative differences between the two sides of the brain in the regional patterns of neuron loss and pathological changes in Alzheimer's disease.

In our study and that of Arendt *et al.*,¹ among others, there is much more variation within one hemisphere in tangle and plaque counts between areas than there is for

Table Comparison of mean plaque and tangle counts (per field) on the two sides of the brain

Case No	Side	Frontal lobe				Parietal lobe				Temporal lobe				Occipital lobe			
		Plaques		Tangles		Plaques		Tangles		Plaques		Tangles		Plaques		Tangles	
		Mean	R	Mean	R	Mean	R	Mean	R	Mean	R	Mean	R	Mean	R	Mean	R
1 Female 84 yrs	L	0.8 (1.0)	0–3	9 (2.5)	5–14	4.4 (2.4)	1–9	0	—	9.3 (8.9)	1–34	4.9 (2.2)	0–10	12.7 (7.1)	3–29	0.7 (1.6)	0–5
	R	0.8 (1.2)	0–4	7.2 (1.9)	4–12	3.7 (1.9)	0–7	0	—	10.5 (7.7)	1–28	4.8 (3.1)	1–11	13.9 (10.2)	1–35	1.9 (3.1)	0–10
Significance*		ns		p < 0.01		ns		—		ns		ns		ns		ns	
2 Female 64 yrs	L	75 (29.8)	22–120	10.3 (2.8)	6–16	1.3 (1.6)	0–5	1.5 (1.5)	0–5	60 (21)	18–96	11.5 (3.9)	3–20	46 (19)	10–81	7.6 (3.1)	3–15
	R	72 (26.6)	35–122	9.6 (3.1)	5–20	1.8 (3.6)	0–14	2.1 (2.1)	0–6	56 (21)	23–91	12.2 (4.5)	4–19	50 (21)	23–95	6.3 (1.9)	4–11
Significance		ns		ns		ns		ns		ns		ns		ns		ns	
3 Female 56 yrs	L	47 (18)	19–92	8.4 (3.4)	4–17	29 (14)	10–56	2.9 (2.1)	0–6	47 (12)	22–66	9.1 (3.9)	4–17	78 (16)	58–110	11.1 (4.0)	6–20
	R	46 (14)	26–73	7.2 (4.0)	1–14	26 (12)	12–55	3.1 (2.2)	0–8	42 (11)	23–64	7.4 (4.8)	0–16	51 (20)	27–87	10.9 (3.8)	3–18
Significance		ns		ns		ns		ns		ns		ns		p < 0.01		ns	
4 Male 66 yrs	L	69 (19)	32–119	7.7 (2.5)	3–11	7.4 (3.0)	2–12	0.8 (1.3)	0–4	45 (25)	5–106	6.3 (2.6)	2–11	15 (8.7)	4–38	4.2 (3.8)	1–12
	R	59 (19)	23–93	8.0 (3.5)	1–16	7.7 (6.8)	2–22	0.7 (1.1)	0–3	35 (22)	4–71	5.1 (2.6)	1–12	23 (7.5)	14–38	8.9 (4.5)	6–19
Significance		ns		ns		ns		ns		ns		ns		p < 0.01		p < 0.01	
5 Female 81 yrs	L	68 (37)	19–180	7.8 (4.4)	0–16	21 (7.6)	11–33	0.3 (0.81)	0–3	20 (11)	5–48	10.1 (4.4)	3–21	25 (11)	11–45	0.4 (0.9)	0–3
	R	44 (24)	7–95	7.0 (3.7)	1–15	38 (8.7)	23–58	0.5 (1.1)	0–4	36 (12)	15–62	8.8 (4.9)	1–17	16 (9)	1–29	0.1 (0.3)	0–1
Significance		p < 0.01		ns		p < 0.01		ns		p < 0.01		ns		p < 0.01		ns	

*Student's *t* test; "ns" failure to reach significance of p < 0.05; standard deviations in parenthesis, R indicates range.

single area compared on the two sides. Although we found some statistically significant differences when comparing individual areas on both sides, particularly for plaque counts, these may, in such a small study, reflect the wide range of counts and the intrahemispheric variation rather than a true asymmetry in pathology. A larger study will be needed to resolve this question. Meanwhile, it would seem prudent, whenever possible, to perform correlative histology and biochemistry on material taken from the same side of the brain. Where this is impractical, the most satisfactory alternative would appear to be quantitation of tangles in one hemisphere for comparison with

neurochemical measurements on the other.

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Matters arising

Sir: Navarro and colleagues¹ report a patient with bilateral Parkinsonism secondary to a corpus callosal glioma. Their patient had signs of long-tract disease and other hemisphere dysfunction to point to the need for further investigation. We report the case of a 74 year old lady who developed bilateral Parkinsonism secondary to an intrinsic cerebral tumour without such clues. She had a long history of anxiety and depression and for 2 years had complained of vague headaches. During this time she also complained of dizziness for which prochlorperazine was prescribed. Within 4 days of starting this she suffered an unwitnessed episode of loss of consciousness which was attributed to the medication, which was promptly withdrawn. She had no more episodes of loss of consciousness. For 6 months she had noted slowness of movement, unsteadiness while walking and a resting tremor affecting both hands. Examination (by three examiners) showed bilateral impassive facies, a resting tremor (4-6 Hz) affecting both hands but worse on the right and cogwheel rigidity in all limbs but worse in the arms. There was no right arm swing during walking and she had difficulty turning around corners. There were no clear symptoms or signs of cortical dysfunction. No signs referable to the long tracts were found and there were no signs of raised intracranial pressure.

The 4 days of treatment with prochlorperazine (8 months previously) were not thought to be responsible for the Parkinsonism.

Fig CT Scan following injection of intravenous contrast medium shows an enhancing space occupying mass in the right hemisphere with contra-lateral hydrocephalus.