

changes caused by axonal and myelin loss in demyelinating lesions, such as occur in multiple sclerosis, there is a need for an in vivo technique that measures macromolecular loss; MT imaging, which is based on the specific interaction between macromolecular and free water protons, has shown promise in this regard. Pronounced reductions in MTR have been found in lysolecithin induced demyelination,² chronic experimental allergic encephalomyelitis lesions (in which there is demyelination), and progressive multifocal leucoencephalopathy (a condition in which demyelination predominates with a relative lack of inflammation or axonal loss). On the other hand, in acute experimental allergic encephalomyelitis in which there is inflammation and oedema without demyelination, only mild reductions in MTR are seen.³ In optic neuritis, reduction of MTR within the optic nerve lesion correlates with the latency of the visual evoked potential,⁴ suggesting that a graded relation may exist between MTR reduction and the extent of demyelination. This present patient provides additional evidence in favour of myelin itself being a major contributor to the MT effect.

A wide range of values of MTR is seen in multiple sclerosis lesions, and a correlation exists between lesion MTR and disability.⁵ It is uncertain whether MTR measurement will be able to separate demyelination alone from demyelination which occurs as a consequence of axonal loss. The second may be more important for irreversible disability in multiple sclerosis. Further experimental studies are needed to elucidate the quantitative MTR changes that occur in these two processes. Nevertheless, MTR measurement seems a robust, quantitative, and clinically relevant indicator of myelin integrity and may have an important role in monitoring the natural history of multiple sclerosis and its modification by treatment.

The NMR Research Unit is supported by a generous grant from the Multiple Sclerosis Society of Great Britain and Northern Ireland.

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Raised plasma polyamine concentrations in patients with severe head injury

Polyamines have been shown to be raised in response to neurological trauma in experimental models.^{1,2} There are no reports that a similar process occurs in humans, prompting us to investigate whether plasma polyamines are raised in patients with head injury. Large increases in polyamines occur in the cerebral cortex after neurological trauma,² and, if reflected by increased plasma concentrations occurring as a result of disruption to the blood brain barrier, this could be a useful diagnostic and prognostic tool.

Seventeen patients with head injury were studied. The patients varied in the circumstance of injury, the time the sample was taken after the initial injury, and the CT findings, which showed extradural and subdural haematomas and cerebral contusions. One patient sustained an associated cardiac injury and four sustained associated musculoskeletal injuries; the other patients had no obvious organ damage apart from brain injury.

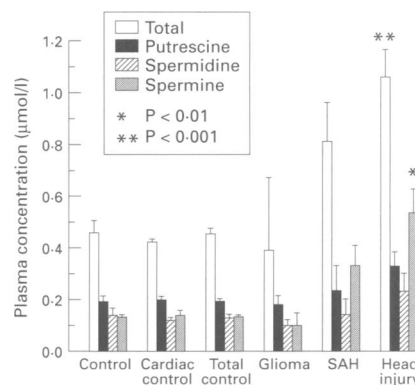
Blood samples were also taken from eight patients who had intracranial pathology unrelated to trauma (five with subarachnoid haemorrhage and three with malignant primary brain tumours). Control samples were taken from seven patients who underwent coronary artery bypass grafts (non-head injury traumatic controls) and seven normal subjects.

Dabsylation of polyamines was carried out as previously described³ on plasma samples after protein precipitation with diaminoazobenzene sulphonyl chloride. The derivatives were separated by high performance liquid chromatography (HPLC) using a reverse phase C18 column and gradient elution with sodium acetate and acetonitrile. The total plasma polyamine concentration (spermine, spermidine, and putrescine) in $\mu\text{mol/l}$ was quantified for each patient. Recovery of polyamines from standard mixtures (after dabsylation and HPLC) was >95% and >90% for standards (putrescine, spermine, and spermidine) added after trichloroacetic acid extraction and subjected to normal analytical procedures. The HPLC allowed separation of dabsyl derivatives of polyamines, which were identified using polyamine standards. The retention times were reproducible, showing variation between runs of <0.1 minutes.

A non-parametric analysis of the data was undertaken by Kruskal-Wallis test.

The figure shows the results of the mean plasma concentrations of polyamines in each group. There was a significant ($P < 0.001$) increase in total polyamine in the head injury group ($n = 17$ mean = $1.04 \mu\text{mol/l}$); spermine was also significantly increased. None of the other subgroups were significantly raised above the normal and cardiac control groups, however, the polyamine concentrations tended to be increased in the subarachnoid haemorrhage group.

The total polyamine concentrations in the head injury group ranged from 0.34 – $1.86 \mu\text{mol/l}$. It was difficult to correlate an increase in the plasma polyamine concentration with the degree of severity in a small group of patients with such diverse mechanisms of head injury, and differences in the time after head injury that the sample was taken. The lowest concentrations were, however, found in patients after evacuation of an extradural haematoma and the highest con-



Plasma polyamines were extracted, fractionated, and quantified by HPLC. Values are means (SEM). Significant differences are v control group.

centrations were found in those patients with the most severe trauma. A time dependent increase in polyamines was noted, a significant correlation being shown by regression analysis between both the total polyamines ($P < 0.017$) and putrescine ($P < 0.0001$) and the time after injury (up to 48 hours).

Both plasma and erythrocyte concentrations of each polyamine were assayed separately. The major pool of polyamines in blood is present in erythrocytes, which account for 80–90% of polyamine content in whole blood. No pronounced differences were detected in the erythrocyte samples between control and trauma groups. This may be because polyamines are synthesised within erythrocytes and therefore this pool would reflect largely locally synthesised polyamines whereas plasma polyamines would reflect concentrations of polyamines arising from an exogenous source more accurately. Erythrocytes do possess the ability to take up polyamines by a transporter but this may not affect internal concentrations of polyamines sufficiently to significantly alter concentration in erythrocytes in most trauma patients.

In animal experiments, the intracellular polyamines, especially putrescine, are raised in neurotrauma but extracellular concentrations are low after cerebral ischaemia.⁴ From our own experience the effects of insults to the CNS on the induction of ornithine decarboxylase are enormous with severalfold increases in putrescine occurring. We therefore reasoned that if leakage due to trauma occurred we would be able to detect changes in plasma polyamines. The fact that significant effects are only detected for spermine, spermidine, and total polyamines indicates that extraneuronal transformations have occurred, both spermine and spermidine being derived from putrescine.

In conclusion, polyamines are increased in serious neurological trauma and the increase is detected in the peripheral blood in human subjects. A more detailed study will be necessary to elucidate the pattern of the "polyamine response" in the different head injury groups with a view to understanding the role of polyamines in intracranial trauma.

The work was supported by the special trustees of Charing Cross and Westminster Hospital and Medical School.

We acknowledge A Sofat, M Sharr, J Wickenden, NV Wilson, and SJ Booth.

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Hatred of the hemiparetic limbs (misoplegia) in a 10 year old child

Injury to the right parietal region in adults may cause disorders of visuospatial ability in drawing and construction, neglect of the left side of space, denial of left hemiparesis (anosognosia), and sometimes an active hatred of the paralysed limb (misoplegia), occasionally associated with a personification of a limb (calling it "the nuisance"), or attempting to injure the paralysed left limbs.¹⁻³ Although misoplegia is reputed to be fairly common,³ it seems not to have been reported in adults since the classic work of Critchley.²

These neuropsychological signs have been far less often reported in children. There have been reports of left neglect and extinction in children,^{4,5} together with reports of a general tendency in children with head injury to deny their deficit. However, there seem to be no previous reports of anosognosia proper, or misoplegia, in children in relation to the classic pattern of right parietal neuropsychological deficits.

A 10 year old right handed boy, with no previous neurological history of note, had an episode of acute loss of consciousness (Glasgow Coma Scale score 6) after a spontaneous intracerebral haemorrhage. Brain CT showed a lesion in the deep white matter and basal ganglia of the right temporoparietal region (figure).

He had a dense left hemiparesis with reduced sensation, hemianopia, and a tendency to ignore things on the left side (for example, failing to dress his left limbs). His mother reported that he seemed to have regressed emotionally (for example, he had episodes of swearing, tantrums, and impulsive behaviour). He had become more self centred, often feeling that he had been "left out". His physiotherapist and occupational therapist reported that it was impossible to please him, as he found their treatment "wrong" or "faulty". This was dramatically different from his premorbid state, where he was described as a normal and emotionally stable child. Corroborating accounts of his change in behaviour were reported by his school teachers, although they noted no decline in his general intellectual abilities,

and he returned to his old class at school.

His mother reported that everything was "a laugh", and that you could not hold a serious conversation with him (although his serious side "came back" when he was "in trouble"). His physiotherapist reported that he avoided conversations about his hemiparesis, "as if it wasn't there", and instead talked excessively about other things. In an early physiotherapy session he insisted that he could run, but soon tripped and fell as a result of his hemiparesis. He had been a member of a football team and maintained that he would be able to return to the team, but he was clearly unable to play and was not selected. He then asserted that the team was inferior, and promised to find a better team. Both his physiotherapist and occupational therapist reported that it was difficult to gain his cooperation in therapy because of his denial of deficit. However, apart from anosognosia, he showed no other delusional beliefs.

In sharp contrast with this denial of deficit, his family, physiotherapist, and occupational therapist also reported that he held some unusual attitudes towards his left side. He was angry about his left limbs, often "hated" them, blamed them, and wanted to get rid of them. In the acute period in hospital he once actually threw himself out of his bed, on to his left side, in an attempt to injure his left arm and leg. He would often bend the fingers of his left hand backwards, attempting to break them. Both his mother and his physiotherapist reported him as saying that he "would rather destroy it, if he couldn't use it". They also reported that he expressed a desire that his left side might be replaced, with that of his mother.

He was assessed by us three months after the cerebrovascular accident, at which stage the left hemianopia and hemiparesis were still present, although the paresis had improved slightly so that he could now walk (with typical circumduction in gait). His left arm had recovered proximal movement, but he still had very poor control over his hand and finger movements. During our assessment his speech was entirely normal, as was his recent memory and recognition of well known faces. However, he performed poorly on drawing and constructional tasks (the block design subtest of the WISC-III, scaled score 5), showing some features of constructional dyspraxia, as well as occasionally



Brain CT of patient.

omitting components on the left. He showed further features of hemispatial neglect—missing some words on the left in reading, bisecting lines well to the right of true centre (mean line length 9.7cm, mean bisection position 59.7% from the left) and omitting items on the left in a figure cancellation task (Bell test, 11 of 16 targets identified in the left hemispace, 17 of 17 in the right).

At this stage he was anosognosic for his hemiparesis and neglect, but was aware that his drawing and constructional abilities seemed poor. Although he agreed that his left arm was "not the same" as before the injury, he denied that it caused him any disability. Asked directly to judge whether he might be able to use his arm to open a door, he said that this would not be a problem. When challenged to do this, he found it impossible, and solved the problem by using his right (good) hand to wrap the fingers of the left hand around the handle, and then pulled the door open using his body.

As regards the misoplegia, he said that he hated his arm and leg because he couldn't use them, and that he wanted to break them. He believed that, if the bones were broken, "the muscles might grow back together again", and he would be miraculously healed. Concerning his wish to have the left side replaced with that of his mother he confirmed that he had, quite naturally, asked her to do this.

This patient therefore showed the classic pattern of neuropsychological deficits seen after right parietal lesion in adults: misoplegia, anosognosia, left hemispatial neglect, and constructional apraxia.¹⁻³ The case seems to be the first in which misoplegia has been reported in a child. It has been suggested that signs of denial of deficit are common in all children after brain injury, but it is of clinical relevance to be able to differentiate between different forms of denial of illness. A pattern of neuropsychological deficit known to be associated with anosognosia, involving signs such as left neglect, visuospatial errors, and constructional apraxia, would be a suitable marker in making a distinction between anosognosia as part of a right parietal syndrome, and denial of deficit for other reasons (for example, as part of a frontal syndrome, or as a purely psychogenic defence mechanism).

The nature of the misoplegia in this case seems to be largely the same as that found in adults,¹⁻³ in that it involved a hatred for the left limbs, and a desire to injure them. In one respect, however, his attitude was different from that of misoplegic adults, in that he expressed a desire for the limbs to be "replaced", and it is surprising that his mother was chosen as the source of the exchanged body parts.

Another interesting feature of the case is the finding that anosognosia and misoplegia coexisted in one patient. This is surprising given that they reflect polar opposites in attitude to the disabled limbs. However, we noted during our assessment that the anosognosia and misoplegia were never present *simultaneously*. Rather he often switched between hating the left limb and denying his hemiparesis.

We thank Emily Le Marie and Jannette Bell for their reports on the patient, and Professor Christine Temple for her assistance with the literature on neglect in children.

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