Three decades of normal pressure hydrocephalus: are we wiser now?

In his excellent editorial on this subject, Vanneste refers to the place of CSF removal and pressure monitoring tests in the diagnosis of normal pressure hydrocephalus, and their possible predictive role for the success of shunt procedures. With regard to lumbar CSF infusion methods, he regards their invasiveness and the need for technical expertise, as making them unsuitable for widespread clinical use.

In the early days of recognition of the syndrome, and well before the advent of modern imaging techniques, we described a simple bedside CSF manometric procedure. This involved CSF pressure readings after withdrawal of fluid into a syringe and its reinsertion after the pressure returned to its previous level. The immediate resulting pressure rise lasted for only a few minutes in cases where normal pressure hydrocephalus was not present, but for a long period in those patients in whom the diagnosis of normal pressure hydrocephalus was considered acceptable. The assumption, in view of the physiopathological basis of normal pressure hydrocephalus prevalent at the time, was that the test reflected reduced fluid reabsorptive capacity responsible for the syndrome. It would seem now that according to Vanneste’s reference to modern views, the results would have been explained somehow in terms of obstructions, either subarachnoid or intraventricular. The essential predictive value for benefits resulting from shunt diversion was not followed up at that time.

Incidentally I think that we owe McHugh credit for the first report describing the clinical normal pressure hydrocephalus syndrome.

Post-traumatic syringomyelia

The excellent study of Squier and Lehtö reports that post-traumatic syringes based on clinical examination and spinal CT occur with an incidence of between 1 and 4.5%, based on MRI studies with an incidence of 12–22%. Their own pathological findings in 20 spinal cords examined between two days and 43 years after spinal injury yielded four cases (20%) with cysts extending at least two segments from the site of original trauma. The table summarises the positive results.

<table>
<thead>
<tr>
<th>Time after injury</th>
<th>Level of initial cord lesion</th>
<th>Extent of pathological syrinx</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>T5</td>
<td>T5-T8</td>
</tr>
<tr>
<td>12 weeks</td>
<td>C7</td>
<td>C4-C6</td>
</tr>
<tr>
<td>22 years</td>
<td>T12</td>
<td>T12-T8</td>
</tr>
<tr>
<td>34 years</td>
<td>L3</td>
<td>C8-L3</td>
</tr>
</tbody>
</table>

Before we accept the important inferences suggested by these data, we should examine the defining criteria. The authors do not provide clinical data to establish to what extent, if any, their four patients had clinical signs of a syrinx. A mixture of myelomalacia, fibrillary gliosis, and often cystic change is found at the level of injury in all cases after the first few months, and extends locally, rostrally, and/or caudally in relation to the severity and extent of the softening, infarction, and atrophic damage. Any persisting bone fragments or malignation may increase the size of the cord damage and cyst formation.

The criterion of a cystic cavity extending for at least two segments is, I suggest, arbitrary. For if we took the defining limit as more than three segments, the incidence would be in 20% (5%), a figure roughly that previously accepted for clinical post-traumatic syringomyelia. This single case survived 34 years from an injury at the time of 25. It may be that many patients with an extensive syrinx shown at MRI have no clinical signs, and we do not know how long it takes for the MR image of a syrinx to become symptomatic; indeed in some such injuries in middle aged and elderly people it is likely that the syrinx may never cause appreciable symptoms or deterioration of neurological function. The medicolegal implications are self-evident.

Verbal fluency in cortical and subcortical dementia

In a recent issue Rosser and Hodges have presented some potentially interesting data relating to measures of verbal fluency in patients with Alzheimer type dementia, Huntington’s disease, and progressive supranuclear palsy. Their main finding is a far from significant analysis. The effect being sought by Rosser and Hodges and which they claim to have found, is a differential pattern between the four measures across different measures of fluency between the different patient groups. To confirm what they were seeking in statistical terms, they have computed a correlation the test for four measures and type of dementia. In their investigation they have employed four separate groups (including a control group as well as the three patient groups already mentioned) with patients in each of these being tested on three separate fluency measures. This corresponds to what is commonly described as a split plot analysis of variance model having both within subject and between subject effects. Data obtained in accordance with this model and subjected to an appropriate analysis did enable the computation of a group x measures interaction. By contrast what Rosser and Hodges report for their statistical analyses are three one way analyses of variance carried out on each of the three measures with these followed by post hoc comparisons of particular pairs of groups. Apart from possibly being unsuitable in other ways, this form of analysis does not permit the computation of interaction terms. It is also possible for the effects described as emerging from these analyses to appear and yet to find that the more appropriate analysis fails to achieve the
Critically significant groups x measures interaction.

The effect that Rosser and Hodges claim may well be present in their data and, if so, would help to contribute to the understanding of the relation between allegedly cortical and subcortical dementias. Unfortunately the analyses actually reported do not properly permit the suggested conclusion to be drawn and it would therefore be useful to know if the relevant interaction really is significant.

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Hodges replies:
We are very grateful for Miller’s comments on our paper. We have now performed a split plot analysis of variance with both within subject and between subject effects, which confirmed the presence of a significant interaction (F (df 51.3) = 19.6, P < 0.001). This highly significant group conditions interaction confirms the differential effect of Alzheimer’s disease vs Huntington’s disease and progressive supranuclear palsy on category and letter based fluency tests, which we hope will convince Professor Miller.

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Jarisch-Herxheimer reaction in a patient with neurosyphilis: non-convulsive status epilepticus?

In their lesson of the month Zifko et al described a patient with neurosyphilis who developed fluctuating consciousness, disorientation, restlessness, and fever 10 hours after starting intravenous penicillin G. He had tachycardia and hyperhidrosis. An EEG showed generalised 3/6 rhythmic activity (periodic lateralised epileptiform discharges). These findings were attributed to a Jarisch-Herxheimer reaction. We suggest that non-convulsive status epilepticus is an alternative explanation. Altered consciousness and prolonged confusion are the central clinical findings of non-convulsive status, which may occur without preceding or accompanying generalised tonic clonic seizures, may resolve spontaneously, and may be associated with the autonomic symptoms of fever and tachycardia.1 Periodic lateralised epileptiform discharges are one of the EEG correlates of non-convulsive status.1 As stated by the authors, patients with neurosyphilis are susceptible to epileptic seizures, both due to the condition itself1 and due to a Jarisch-Herxheimer reaction. In addition, penicillin itself may precipitate seizures.2 In their patient, non-convulsive status may have been evoked by one of these mechanisms. It would be of value to know whether patients such as this respond to antiepileptic medication.

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Zifko et al reply:
We appreciated the interesting response of Dune and Heye to our article. Although we cannot completely exclude the possibility of non-convulsive status epilepticus in our patient, we have several arguments that make their theory unlikely.

Firstly, autonomic symptoms of fever and tachycardia in our patient occurred before onset of confusion and altered consciousness, and were not present during the period of disorientation and psychomotor restlessness, as mentioned in the text. Secondly, although periodic lateralised epileptiform discharges may be a sign of non-convulsive status, this abnormality is non-specific. Thirdly, during CT, psychomotor restlessness was treated with 70 mg intravenous diazepam, which did not affect the confusion. Non-convulsive status of complex partial type usually responds well to diazepam.

Risperidone in Parkinson’s disease

A recent, excellent review of the management of Parkinson’s disease called attention to the atypical neuroleptic drug clozapine (an antagonist of dopamine D₂ and serotonin 5HT₃ receptors) for amelioration of psychotic symptoms derived from dopaminergic treatments, when temporary withdrawal of antiparkinsonian drugs fails.1 Small doses of the atypical neuroleptic drug risperidone (0·25–1·25 mg/day) can also be used for ameliorating hallucinations induced by levodopa without worsening motor symptoms in Parkinson’s disease.2 Risperidone has a strong affinity for 5HT₂ receptors and only moderate affinity for D₂ receptors. For parkinsonian patients in whom the 1–2% risk of agranulocytosis with clozapine is unacceptable, risperidone is another option.

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CORRECTION


During production, the figure was incorrectly printed. The correct version is given here.