Reviewer's report

Title: Elevated Nerve Growth Factor and Neurotrophin-3 Levels in Cerebrospinal Fluid of Children with Hydrocephalus

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Reviewer: Dr J Gilmore

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after revision, which I do not need to see

1. Are the conclusions drawn adequately supported by the data shown: if not, what are the shortcomings and could they be overcome?
   Yes

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?
   Details of sample collection and ELISA assay need to be presented.

3. Does the manuscript adhere to the relevant standards for reporting and data deposition: if not, in what ways?
   Yes

4. Is the writing acceptable? (nb. Since we do not charge for access to published research, we cannot undertake the costs of editing poorly written manuscript. If you tell us that the writing is not acceptable for publication, we will ask the authors to find someone, or an editing service, to help them rewrite it. If you tell us that the manuscript
is too poorly written for it to be peer reviewed, we will ask them to rewrite it now.)

Yes

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Please note that both your comments and answers to the questions below will be forwarded to the authors, and published on the site if the article is accepted.

Comments

Please number your comments and indicate which are major and which are minor. In addition to making your own comments, please answer the questions below.

This is an interesting article that seeks to document levels of neurotrophic factors in the CSF of children with hydrocephalus. It is hypothesized that elevated NGF and NT-3 levels represent adaptive response of the brain to increased intracranial pressure.

The sample and sampling procedure should be better characterized so that the results can be generalized. The clinical situation for the CSF sample is mentioned in the discussion but should be delineated in the methods? tap, LP, shunt placement, shunt revision. Were the CSF samples centrifuged? Were there associated medical problems in the children with hydrocephalus that might have an impact on NGF and NT-3 levels? Were children with positive CSF cultures being treated with antibiotics? Were there other children with sterile CSF being treated with antibiotics?

Details of the ELISA assay should be presented. Were the samples run in duplicate or triplicate? What was the intra-assay and inter-assay variability? Were samples diluted or run neat? What was the level of detection for the assays?

Controls samples were all obtained by LP. Could differences in neurotrophin levels between children with hydrocephalus (samples from ventricles) and controls (samples from lumbar space) be due to the presence of a concentration gradient along the brain/spinal cord?

Bacterial infection many not be associated with NGF or NT-3 differences in children with hydrocephalus, as hydrocephalus many have increased levels independently of bacterial infection. We previously found high levels of NT-3 in the CSF of children with hydrocephalus undergoing shunt placement and in children with active CNS infection (Gilmore JH et al., Neurotrophin-3 levels in the cerebrospinal fluid of patients with schizophrenia or medical illness. Psychiatry Research 1997; 73: 109-113).

In results section the authors state that there was ?no obvious relationship? between NGF and NT-3 or with ICP. Was this tested statistically?
Typo: Reference 9 should read ?NT-3? 

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Competing interests:

None declared.