

Letters to the editor

'The acidosis paradox: asphyxial brain injury without coincident acidemia'

SIR—Hermansen raises important clinical issues in his annotation: 'The acidosis paradox: asphyxial brain injury without coincident acidemia',¹ which provides data supporting the relative protective effect of mild to moderate lactic acidemia to the brain. By contrast, non-acidaemic babies with 1-minute Apgar score of less than 3 fared poorly.

The suggestions that asphyxiated babies with acidemia (possibly arising from a lag-time between tissue acidosis and the advent of acidemia) might benefit from cerebral vasodilatation of acidemia, ability to utilize lactate as a nutrient, the Bohr effect, or suppression of excitatory amino acids are clearly appealing explanations for more severe brain injury in those without acidemia.

Apart from lactic acid tissue sequestration, an alternative explanation for the lack of severe lactic acidosis presumably includes concomitant hypoglycaemia. This seems relevant as an inability to raise lactate levels in the face of hypoglycaemia would expose the brain to injury from lack of appropriate fuel substrate, as hepatic ketogenesis is known to be limited in the newborn, and fails to rise in the fasted newborn and in the hypoglycaemic newborn.² Particularly relevant is the reporting of inappropriate hyperinsulinism in postasphyxial newborns, which was associated with poor neurodevelopmental outcome.³ In an Indian study of 2224 babies screened for hypoglycaemia the risk factors for this condition included: birth asphyxia (24.2%), diabetic mothers (23.8%), respiratory distress (13.9%) and septicemia (11.6%).⁴ This poses the question: 'How many of the babies in the various studies quoted also exhibited hypoglycaemia?'.

Low birthweight is one of the most significant predictors of asphyxia. Asphyxia occurred in 68% of babies of less than 1000g birthweight and decreased to 1.2% in babies of 3 to 4kg birthweight.⁵ But gestational maturity also determines outcome since the impact of asphyxia on neonatal mortality is most pronounced in more mature babies: the mortality increasing only 3-fold in babies of less than 34 weeks' gestation but over 27-fold for babies of greater than 38 weeks' gestation.⁵ This indicates different selective vulnerability to asphyxia in babies of differing birthweight and gestational age.

On a technical note, it would have been useful to know how many children, in absolute terms, fell into the high-risk categories for cohorts in Table I. In the Dennis et al. study,⁶ although 9 out of 10 children with a 1-minute Apgar of less than 3 and pH > 7.18 had neurodevelopmental problems, the authors state that 'The highest proportion of unimpaired children was found among those who were most severely acidotic at birth (pH ≤ 7.04; 2 standard deviations below the mean), but this finding was not statistically significant.' Table II in Hermansen (2003) leaves the reader uncertain concerning the 'floating' numbers between columns 'pH 7–7.2%', and 'pH > 7.2%'.

These deliberations and the multiplicity of publications in this field should caution against reliance on single variables as predictors of outcome.

DOI: 10.1017/S0012162204210702

Jean-Pierre Lin

Department of Paediatric Neurology

Guy's and St Thomas' NHS Trust, London

E-mail: jean-pierre.lin@gstt.stbames.nhs.uk

References

1. Hermansen MC. (2003) The acidosis paradox: asphyxial brain injury without coincident acidemia. *Dev Med Child Neurol* 45: 353–356.
2. Volpe JJ. (1995) Hypoglycaemia and brain injury. In: *Neurology of the Newborn*. 3rd edn. Philadelphia: WB Saunders Company. p 472.
3. Davis DJ, Creery WD, Radziuk J. (1999) Inappropriately high plasma insulin levels in suspected perinatal asphyxia. *Acta Paediatr* 88: 76–81.
4. Singhal PK, Singh M, Paul VK, Deorari AK, Ghorpade MG, Malhotra A. (1992) Neonatal hypoglycemia – clinical profile and glucose requirements. *Indian Pediatr* 29: 167–171.
5. Mir NA, Faquih AM, Legnain M. (1989) Perinatal risk factors in birth asphyxia: relationship of obstetric and neonatal complications to neonatal mortality in 16,365 consecutive live births. *Asia Oceania J Obstet Gynaecol* 15: 351–357.
6. Dennis J, Johnson A, Mutch L, Yudkin P, Johnson P. (1989) Acid-base status at birth and neurodevelopmental outcome at four and one-half years. *Am J Obstet Gynecol* 161: 213–220.

'Hermansen replies'

SIR—I appreciate the critical evaluation that Dr Lin has given to 'the acidosis paradox.' Dr Lin apparently accepts the concept that some asphyxiated newborns do not become acidemic, and furthermore these infants are at higher risk of adverse outcomes than those asphyxiated newborns that develop a mild or moderate acidemia.

Our annotation, in 'Developmental Medicine & Child Neurology', proposed various possible mechanisms for this 'beneficial acidemia', and Dr Lin suggests two other reasonable explanations: firstly, that some asphyxiated babies may have a concomitant hypoglycaemia, where the combination of asphyxia and hypoglycaemia may present a very high risk situation regardless of the level of acidemia; and secondly, that other factors such as gestational age and maturity may influence an infant's susceptibility to damages from asphyxia, again regardless of the level of acidemia.

Finally, Dr Lin asks for a clarification of Table II. Three referenced studies combined all infants with a pH > 7, and it was not possible to determine how many had mild/moderate acidemia (pH 7–7.2) and how many had no acidemia (pH > 7.2). The infants between the two columns in Table II represent the combination of all these infants with a pH > 7.

DOI: 10.1017/S0012162204220709

Marcus C Hermansen MD

Department of Pediatrics

Dartmouth Medical School

Hanover, NH, USA

E-mail: marcus.bermansen@snbmc.org

'Attention deficits and subclinical epileptiform discharges: are EEG diagnostics in ADHD optional or essential?'

SIR—We read with interest two recent papers in 'Developmental Medicine & Child Neurology'^{1,2} regarding the association of childhood epilepsy and attention-deficit-hyperactivity disorder (ADHD). Both studies were focused on neuropsychiatric disorders in children with epilepsy. Based on a recent study on

ADHD and associated subclinical electroencephalogram (EEG) discharges,³ we would like to present arguments on an association between epilepsy and ADHD from a child psychiatrist's perspective.

We examined Rolandic spikes in 483 children with ADHD without epilepsy, and found a significantly higher frequency of spikes than expected (5.6% and 2.4% respectively; $p < 0.001$); we based our expected value for frequency on epidemiological studies.³ None of the patients had a bioelectrical status epilepticus during slow-wave sleep. Our data replicated previous reports on the same incidence of focal epileptiform discharges in children with ADHD without epilepsy.⁴ In our study, children with ADHD with Rolandic spikes were significantly younger at admission than those with ADHD only. This suggests that Rolandic spikes, or the underlying mechanisms of epileptogenesis, will either decrease the vulnerability threshold or advance the onset of ADHD. Since the temporal sequence of the manifestation of subclinical epileptiform activity in relation to ADHD cannot be assessed in retrospect, then we must remain speculative as to whether our data present an example of the successive comorbidity outlined by Noeker and Haverkamp.² Future studies will have to determine whether antiepileptic treatment instead of, or adjunctive to, stimulants is justified for this ADHD subgroup.

Our study, in contrast to the findings of Dunn et al.,¹ showed that children with ADHD plus Rolandic spikes tend to exhibit more hyperactive-impulsive symptoms than those with ADHD only. As in most psychiatric samples,⁵ these symptoms were evident in a larger proportion of those diagnosed with ADHD combined type than ADHD inattentive type. In addition, preliminary results of an ongoing neuropsychological study suggest that children with ADHD with Rolandic spikes show a higher frequency of impulsive behaviour compared to children with ADHD without spikes. This is indicated by a significantly larger amount of commission errors in a cued continuous performance task.⁶ These findings add to the data provided by Noeker and Haverkamp,² who reported selective and sustained attention deficits in their patients with epilepsy.

In conclusion, these results give rise to two points: firstly, whether there is a relationship between ADHD symptoms and the presence of the epileptiform discharges; and secondly, the importance of performing EEGs in the diagnostic assessment of ADHD.

The EEG remains controversial, as part of the routine assessment of ADHD. The American Academy of Child and Adolescent Psychiatry practice parameters for the assessment and treatment of children with ADHD,⁷ advise an EEG only in the presence of clinical suggestions of either seizure disorders or of focal neurological signs, or degenerative conditions in children and adolescents with psychiatric disorders. However, there is an increasing awareness that a considerable proportion not only of children with Rolandic epilepsy but even of nonepileptic children with subclinical Rolandic discharges have associated neuropsychiatric deficits resembling features typically observed in ADHD.^{3,8} The similarity between Rolandic epilepsy and ADHD is demonstrated by the following shared diagnostic features: deficits of executive functions; inhibition of control; being easily distracted; showing impulsive behaviour; and externalizing behavioural symptoms.^{9,10} Moreover, both begin in early childhood and occur more frequently in boys. Like Rolandic epilepsy, some cases of ADHD seem to be limited by puberty. Another similarity is the

cerebral immaturity suggested by EEG.

As some children with ADHD, without seizures, degenerative conditions, or focal neurologic signs show abnormalities such as Rolandic spikes in a routine EEGs, the inclusion of EEG in ADHD diagnostics seems essential to the identification of this subgroup. The EEG is the indicator of the need for specific testing, further evaluation and, perhaps, adequate therapy.

The waiver of routine EEG could result in the oversight of subclinical epileptic discharges in a considerable number of children with ADHD. We suggest that the update of practice parameters for the assessment and treatment of children with ADHD until puberty should include EEG, regardless of the lack of a prior history of overt seizures or other obvious neurological conditions.

DOI: 10.1017/S0012162204230705

Katja Becker MD^a

Judith K Sinzig MD^b

Martin Holtmann MD^c

^aDepartment of Child and Adolescent Psychiatry and Psychotherapy, Central Institute of Mental Health, Mannheim

^bDepartment of Child and Adolescent Psychiatry and Psychotherapy, University of Cologne

^cDepartment of Child and Adolescent Psychiatry and Psychotherapy, JWGoethe-University, Frankfurt/Main

Correspondence to:

^aDr Katja Becker

Department of Child and Adolescent Psychiatry and Psychotherapy

Central Institute of Mental Health

Mannheim, Germany

E-mail: kbecker@zi-mannheim.de

References

1. Dunn DW, Austin JK, Harezlak J, Ambrosius WT. (2003) ADHD and epilepsy in childhood. *Dev Med Child Neurol* 45: 50–54.
2. Noeker M, Haverkamp F. (2003) Neuropsychological deficiencies as a mediator between CNS dysfunction and inattentive behaviour in childhood epilepsy. *Dev Med Child Neurol* 45: 717–718.
3. Holtmann M, Becker K, Kentner-Figura B, Schmidt MH. (2003) Increased frequency of rolandic spikes in ADHD children. *Epilepsia* 44: 1241–1244.
4. Hemmer SA, Pasternak JF, Zecker SG, Trommer BL. (2001) Stimulant therapy and seizure risk in children with ADHD. *Pediatr Neurol* 24: 99–102.
5. Szatmari P, Offord DR, Boyle MH. (1989) Ontario Child Health Study: prevalence of attention deficit disorder with hyperactivity. *J Child Psychol Psychiatry* 30: 219–230.
6. Halperin JM. (1991) The clinical assessment of attention. *Int J Neurosci* 58: 171–182.
7. AACAP. (1997) Practice parameters for the assessment and treatment of children, adolescents and adults with ADHD. *J Am Acad Child Adolesc Psychiatry* 36: 85S–121S.
8. Deonna T, Zesiger P, Davidoff V, Maeder M, Mayor C, Roulet E. (2000) Benign partial epilepsy of childhood: a longitudinal neuropsychological and EEG study of cognitive function. *Dev Med Child Neurol* 42: 595–603.
9. Weglage J, Demsky A, Pietsch M, Kurlmann G. (1997) Neuropsychological, intellectual, and behavioral findings in patients with centrottemporal spikes with and without seizures. *Dev Med Child Neurol* 39: 646–651.
10. Baglietto MG, Battaglia FM, Nobili L, Tortorelli S, De Negri E, Caleva MG, Veneselli E, De Negri M. (2001) Neuropsychological disorders related to interictal epileptic discharges during sleep in benign epilepsy of childhood with centrottemporal or Rolandic spikes. *Dev Med Child Neurol* 43: 407–412.