HYPOTHESIS

Low plasma taurine and later neurodevelopment

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Dietary taurine intake may explain the benefits of both breast milk and preterm formula to neurodevelopment. Low plasma neonatal taurine was associated with lower scores on the Bayley mental development index at 18 months and the WISC-R arithmetic subtest at 7 years. Currently it is not mandatory to add taurine to infant formulas.

Preterm babies born in 1982–1985, randomly assigned to a standard formula designed for term babies, subsequently had lower developmental scores than those receiving a multinutrient enriched preterm formula. Yet, paradoxically, infants randomly assigned donated banked breast milk or the same preterm formula had similar scores, despite the lower macronutrient content of human milk.[1–3]

Consideration of the nutrient content of the feeds suggested that taurine was a candidate single nutrient to explain this paradox as term formula contained only a trace, whereas preterm formula and breast milk contained 5 μmol/100 ml (table 1). Furthermore, as taurine is neurotrophic and affects neurotransmission,[4] the possible explanation was biologically plausible. We therefore explored the hypothesis that taurine was an explanatory nutrient for the benefits of both breast milk and the higher nutrient formula to long term neurodevelopment.

PATIENTS AND METHODS

Neonatal plasma taurine concentrations,[5] Bayley Scales of Infant Development (corrected for gestational age) at 18 months of age, and the Wechsler Intelligence Scale for Children-revised (WISC-R) at 7 years were available in 157 children (mean (SD) birth weight, 1398 (277) g; gestation, 31 (2.4) weeks). The lowest (minimum) plasma taurine concentration during their hospital stay was obtained for each subject.

RESULTS

Minimum plasma taurine concentrations correlated with corrected Bayley mental development index ($r = 0.28$, $p < 0.001$) and WISC-R arithmetic subtest score ($r = 0.22$, $p = 0.006$) (fig 1).

These relations remained significant after adjustment for possible confounding factors: (*a*) clinical illness—birth weight, gestational age, weight for gestation, days inpatient, days ventilated; (*b*) possible undernutrition—plasma concentrations of other amino acids, total protein, urea; (*c*) amount of intravenous amino acids.

Minimum taurine was not related to the Bayley psychomotor development nor, after the confounding factors had been allowed for, to the other subtests of the WISC-R. Neither maximum nor mean taurine measurements were related to neurodevelopment.

The length of hospital stay also contributed to lower mental development scores, and gestational age to the WISC-R arithmetic scores. After these factors had been allowed for, the relations of minimum taurine to mental development and to the arithmetic subtest remained significant (partial correlations: $r = 0.19$, $p = 0.016$; $r = 0.18$, $p = 0.024$). There was no interaction between minimum taurine and hospital stay or gestation.

The positive association of neurodevelopment with own mother's milk, described previously, was no longer significant after taurine had been allowed for (partial correlations with mental development: $r = 0.03$, $p = 0.70$; with the arithmetic subtest: $r = 0.09$, $p = 0.24$).

DISCUSSION

The results support the hypothesis that low taurine status in the neonatal period of preterm babies adversely influences later neurodevelopment, and that the advantages of breast milk are partly due to taurine. Some caution is necessary. This was not a randomised trial. The strengths of the relations, although significant, were modest ($r = 0.28$, 0.22), but greater than those seen in this study between either Bayley mental development or the arithmetic subtest of WISC-R with birth weight ($r = 0.17$, 0.18) or gestational age ($r = 0.16$, 0.19).

These data support the view that taurine is a conditionally essential nutrient, as a dietary supply was required for optimum outcome. It is one more example of short term nutritional differences in the newborn having apparent long term effects.

The relations of taurine to mental rather than motor development, and to arithmetic but not other WISC-R subtests, indicate that transiently low neonatal taurine status (''hypotaurinaemia'') has selective neurodevelopmental effects. Transiently low blood concentrations of other metabolic factors have been shown by us and others to be associated with subsequent reduced developmental scores,

Table 1 Nutrient content of breast milk and preterm and term formulas

Energy or nutrients/100 ml	Breast milk*	Preterm formula†	Term formula†
Energy (kcal)	70	80	68
Protein (g)	1.3	2‡	1.5‡
Fat (g)	4.2	4.9§	3.8§
Carbohydrate (g)	7	7.0¶	7.0**
Taurine (μmol)	4.8	5.1	Trace

*Based on analysis of national sample of expressed milk in the United Kingdom.
†Manufacturer's information.
‡Casein to whey ratio 40:60.
§Same fat blend. Saturated to unsaturated ratio 40:60, long chain polyunsaturated fatty acids were not added at time of this trial.
¶Lactose 6 g, maltodextrin 1 g.
**Lactose.
Generally the preterm formula contained a greater concentration of vitamins and minerals except for iron: preterm formula, 40 μg per 100 ml; term formula, 650 μg per 100 ml (all infants received additional iron).

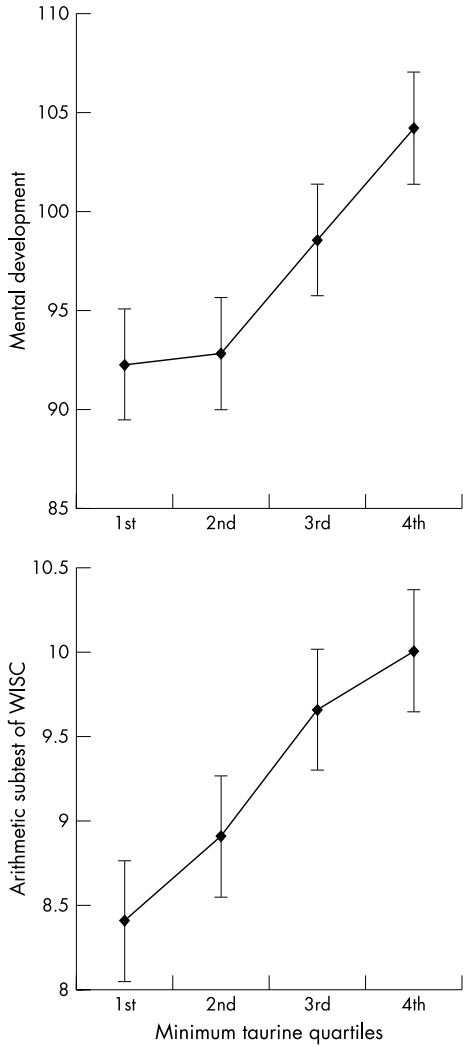

Figure 1 Bayley mental development index at 18 months, arithmetic subtest of WISC-R at 7 years, and minimum neonatal plasma taurine concentration (μmol/l). Taurine, 1st quartile, 20–43; 2nd quartile, 44–55; 3rd quartile, 56–67; 4th quartile, 68–180. Mental development index, mean (SE) 97 (2). Arithmetic score, mean (SE) 9 (0.3).

notably hypoglycaemia and low thyroid hormone status. The mechanisms for this selection are not known, but there are different concentrations of taurine in different parts of the brain. The selective effects of such early influences on brain function require further study. Other work from this centre has shown that calculation deficits are associated with decreased grey matter in the left parietal cortex, and it may be that taurine is implicated in development and function in this region of the brain.[6] Therefore more detailed cognitive testing and neuroimaging studies using magnetic resonance imaging are planned as the children get older.

Although further work is needed to test whether taurine is a conditionally essential nutrient for neurodevelopment in healthy term as well as preterm infants, it seems prudent to ensure adequate early taurine intake. Yet, currently, it is not mandatory to add taurine to infant formulas.

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Contributors: BAW was involved in formulating the hypothesis, analysis of results, and initial write up. RM organised and analysed the Bayley and WISC tests. EBI helped in the results analysis and advised on psychology interpretation. TJC gave statistical advice. AL set up the original nutritional intervention trials and the continuing investigation of the children involved. All authors have contributed to, read, and approved the manuscript. AL is guarantor.

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Conflict of interest: BAW has advised the UK Department of Health, European Union, WHO and food companies on various aspects of child nutrition including taurine. Fees for advice/opinions on nutritional child health have been received from WHO and food companies. AL has advised government departments, professional bodies, and industry in the field of nutrition.

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