DOES PRENATAL NUTRITION AFFECT MENTAL PERFORMANCE IN CHILDHOOD?

Dr Claire Horton
Beta Technology Ltd
Doncaster

In scientific literature, there is growing evidence pointing to a link between diet and brain development and later mental performance. Not just the diet of the child, but that of the mother while pregnant. Of all our organs, the brain is one of the slowest to develop and is also one of the most complex structures we know. It begins to form 18 days after conception, develops rapidly during pregnancy and continues to develop into adolescence. This article outlines some of the work of the European Commission-funded NUTRIMENTHE project which is researching the effect of diet on the mental performance of children.

The NUTRIMENTHE project aims to provide a greater insight into the extent to which nutritional influences in early life, including prenatal life, programme a person's mental development. The research is being carried out by a multidisciplinary team of scientists from 20 research centres based mainly in Europe, coordinated by the University of Granada in Spain, and includes research into the influence of a mother's diet, pre- and postnatal intervention studies and nutritional intervention in children, on later mental performance. The nutrients of interest include long-chain omega-3 polyunsaturated fatty acids (PUFA), B-vitamins, folic acid, iron, zinc, iodine and protein (in breast and formula milk). There are large cohort studies involved in NUTRIMENTHE, based at study centres around Europe and through these, NUTRIMENTHE expects to generate much new information as to how diet affects mental performance.

MEASURING COGNITIVE FUNCTION

A major aim of NUTRIMENTHE is to measure cognitive function but, the term 'cognitive function' covers many domains of mental performance. IQ, which is usually chosen to measure cognitive function, does not fully capture the complexity of cognitive development, so NUTRIMENTHE has developed a battery of neuropsychological tests which cover the main domains of cognitive function (perception, motor, memory, attention, language, executive functions and emotion). The tests are currently being used by NUTRIMENTHE's partners to assess the mental performance of the children taking part in the studies.

NUTRIMENTHE's findings to date relate mainly to the influence of maternal diet on mental performance, but much more is due to emerge in the coming months relating mental performance to pre- and postnatal nutritional intervention in children.

MATERNAL FOLIC ACID STATUS

Folic acid, which should be taken by women wishing to become, or who already are pregnant, is known to reduce the incidence of neural tube defects, but are there any further effects after neural tube closure? This has been investigated by NUTRIMENTHE partners from The Erasmus Medical Centre in The Netherlands using the Generation R cohort from Rotterdam. They have found that failure to use folic acid supplements is associated with a higher risk of behavioural and emotional problems in toddlers aged 18 months. The problems may persist as children observed at age three, also show an increased risk of emotional problems. For instance, signs of being anxious or depressed, withdrawn behaviour and sleep problems are still present if their mother failed to take folic acid. The mechanism(s) of action can only be speculated at present (1,2).

MATERNAL THYROID HORMONE STATUS

It has been known since the 1970s that thyroid hormones play a crucial role in brain development and that a lack can result in mental retardation. In NUTRIMENTHE, research from the Generation R cohort has shown that children born to women showing severe hypothyroxinaemia, demonstrated a higher risk of developing expressive language delay, which includes the ability to form sentences, use grammar correctly and retell a story or event at 18 months and 30 months (3).

EATING FISH WHILE PREGNANT

In the UK, women are advised by the Department of Health to eat two portions of fish a week, including one of oily fish. Indeed, the ALSPAC study, a longitudinal cohort study from Bristol, has shown that children born to women who reported the highest fish intake while pregnant, demonstrated better outcomes in tests for verbal intelligence, motor skills and prosocial behaviour (giving, helping and sharing) when measured from six months to 48 months of age. Furthermore, fish eating was positively associated with verbal IQ in the children at age eight (4). In further research involving the ALSPAC cohort, NUTRIMENTHE researchers from the University of Bristol are looking into what constituent of fish might be mediating the effect. The long-chain omega-3 PUFA, docosahexaenoic acid (DHA) is a top candidate.

Omega-3 PUFAs receive much attention regarding their possible links to good health. Since humans cannot make these fatty acids de novo they must be obtained from the diet. The long-chain omega-3 PUFAs, DHA and eicosapentaenoic acid (EPA), are important structural components of cells, especially the cell membranes of the brain. Indeed, the EC recently supported health claims that intake during pregnancy of DHA 'contributes to the normal brain development of the foetus and breastfed infants' and 'to the normal development of the eye of the foetus and breastfed infants' (Commission Regulation No. 440/2011).

Oily fish is an excellent source of DHA and EPA and fish eating in pregnancy is associated with maternal plasma levels of DHA which is transferred to the foetus via the

Claire has over 25 years' experience in the bioscience sector. She graduated in 1985 with a Biology degree and embarked on a career in medical research, culminating in her gaining a PhD in 1996. She then entered the pharmaceutical industry and in 2003 joined Beta Technology where she currently represents Beta on the FP7-funded NUTRIMENTHE project.

placenta, but are maternal DHA levels related to outcomes in children? In a study of over 2,000 mother-child pairs from the ALSPAC cohort, after adjustment for a number of confounders, no associations were found between the level of maternal DHA and childhood IQ. Thus, DHA did not appear to be the 'missing link' and it may be that other nutrients in fish, such as iodine, vitamin D or selenium, may be mediating the effect. Or, it may be that the child's diet is more important. Or, it may be that IQ was not an optimal measure of mental performance (unpublished). Furthermore, NUTRIMENTHE researchers from The Medical University of Warsaw conducted a systematic review of randomised controlled trials (RCTs) that studied the effect on neurodevelopment and visual function of children born to women supplemented with long-chain omega-3 whilst pregnant or breastfeeding. The evidence from the RCTs included in the review demonstrated that there is not a clear and consistent benefit on either neurodevelopment or visual acuity from supplementation with long-chain omega-3 PUFA during pregnancy or breastfeeding. However, the review did highlight the marked heterogeneity of the included studies and the varied approaches to outcome assessment. Also, none of the studies involved children over the age of four and the sample size in some trials was small. This serves to highlight the necessity for well-designed RCTs and the need for more follow-up studies in school-age children and beyond (5).

THE INFLUENCE OF GENETICS

NUTRIMENTHE is investigating how our genetic make-up influences how we process certain nutrients. The project is investigating how polymorphisms in the fatty acid desaturase (FADS) gene cluster influence how PUFAs are processed during pregnancy. The FADS genes code for the enzymes delta-5 and delta-6 desaturase are involved in the synthesis of omega-3 and omega-6 fatty acids (6, 7). NUTRIMENTHE has published work showing that genetic variants of FADS genes are associated with levels of PUFA in the red blood cells of pregnant women (8) and in breast milk (9). Further work (10) has demonstrated that the composition of omega-3 and omega-6 PUFAs in cord blood is dependent on maternal and child genotypes, such that maternal genotypes are mainly associated with omega-6 precursors and that child genotypes are mainly associated with omega-6 products. The child's metabolism therefore seems important for its own neonatal supply of n-6 LC-PUFA. In contrast, DHA amounts were equally associated with child and maternal genotypes, suggesting that DHA levels are dependent on both maternal and child metabolism. DHA supplied by the mother may thus be very important to satisfy the high foetal demand of DHA during pregnancy.

THE FUTURE

The NUTRIMENTHE project is revealing that seemly subtle changes in biochemistry during pregnancy may have effects on later mental performance. The biological mechanisms will certainly be complex and clearly, much remains to be discovered, especially in terms of the role of long chain omega-3 PUFAs. Although it is accepted that long chain omega-3 PUFAs are required for brain development, the requirements for omega-3 remain to be established. This project has much more to achieve and many more results will emerge leading to further insight into how diet during prenatal and early life affects mental performance.

NUTRIMENTHE is funded until December 2013 and will hold its final conference on the 13th and 14th of September, 2013 in Granada, Spain in advance of the 20th International Congress of Nutrition.

The NUTRIMENTHE project acknowledges 5.9m€ funding from the European Community's 7th Framework Programme for Research and Development (FP7/2008-2013) under grant agreement nº 212652 (NUTRIMENTHE Project 'The Effect of Diet on the Mental Performance of Children').

NUTRIMENTHE website: www.nutrimenthe.eu

References

1 Roza et al (2010). Maternal folic acid supplement use in early pregnancy and child behavioural problems. The Generation R Study. British Journal of Nutrition 103(3): 445-52
2 Steenweg de Graaff et al (2012). Maternal folate status in early pregnancy and child emotional and behavioural problems: The Generation R Study. American Journal of Clinical Nutrition. June: 95(6):1413-21
3 Henrichs et al (2010). Maternal thyroid function during early pregnancy and cognitive functioning in early childhood: the Generation R study. Journal of Clinical Endocrinology and Metabolism. 95: 4227-4234
4 Hibbeln et al (2007). Maternal seafood consumption in pregnancy and neurodevelopment outcomes in childhood (ASLPAC study): an observational cohort study. Lancet 369: 578-85
5 Dziechciarz et al (2010). Effects of n-3 long-chain polyunsaturated fatty acids supplementation during pregnancy and/or lactation on neurodevelopment and visual function in children: a systematic review of randomised controlled trials. Journal of the American College of Nutrition. 29 (5): 443-454
6 Glaser et al (2011). Genetic variation in polyunsaturated fatty acid metabolism and its potential relevance for human development and health. Maternal and Child Nutrition 7(suppl 2), 27-40
7 Lattka et al (2010). Do FADS genotypes enhance our knowledge about fatty acid related phenotypes? Clinical Nutrition 29: 277-87
8 Koletzko et al (2011). Genetic variants of the fatty acids desaturase gene cluster predict amounts of red blood cell docosahexaenoic and other polyunsaturated fatty acids in pregnant women: findings from the Avon Longitudinal Study of Parents and Children. American Journal of Clinical Nutrition. 93: 211-9
9 Lattka et al (2011). Genetic variants in the FADS gene cluster are associated with arachidonic acid concentrations in human breast milk at 1.5 and 6 months postpartum and influence the course of milk dodecanoic, tetracoenoic and trans-9-octadecanoic acid concentrations over the course of lactation. American Journal of Clinical Nutrition 93: 382-91
10 Lattka et al (2012). Umbilical cord PUFA are determined by maternal and child fatty acid desaturase (FADS) genetic variants in the Avon Longitudinal Study of Parents and Children (ALSPAC). British Journal of Nutrition. Aug 9:1-15. [Epub ahead of print]