Introduction

The NUTRIMENTHE project was set up in March 2008, to provide a greater insight into the extent to which pre- and post-natal nutrition ‘programmes’ mental performance in childhood. The project is partly funded by the European Commission (EC) and involves 20 organisations from across Europe and the USA. Of interest are the effects of a number of nutrients, including: B-vitamins, long-chain polyunsaturated fatty acids (LC-PUFAs), iodine, protein (in breast and formula milk), zinc and iron. The effects of these nutrients are being assessed in children from well-established cohorts (Generation R from Rotterdam, The Netherlands,1 ALSPAC from Bristol, UK2) and multicentre studies around Europe, including, NUHEAL3 (Spain, Germany and Hungary) and CHOP4 (Germany, Spain, Poland, Italy and Belgium). Mental performance is being assessed through the use of a battery of neuropsychological tests specially designed for these multicentre studies measuring different cognitive domains, such as perception, motor skills, memory, attention, language, executive functions, emotion and behaviour development.

Results from NUTRIMENTHE have added to the body of evidence showing that maternal, infant and childhood nutrition affects mental performance during early life, leading, potentially, to implications for public health practice, policy development and for our understanding of human biology, as well as impacting on food product development, economic progress and future wealth creation.

This article provides an insight into some of the work and results of NUTRIMENTHE.
Paediatrics | The NUTRIMENTHE Project

Taking folic acid supplements during pregnancy

In the UK, women are advised to take 400 µg/day of folic acid supplements if they are planning to become pregnant and to continue taking the supplements for the first trimester of their pregnancy. The supplements are taken to reduce the incidence of neural tube defects in the developing foetus but the longer term implications for mental performance are not known. NUTRIMENTHE researchers have looked at folic acid supplement use during pregnancy and child behaviour. Women from the Generation R cohort were asked about their use of folic acid supplements during pregnancy, whether they took them before conception, during pregnancy or not at all. Guidelines for use of folic acid supplements vary across Europe. In the Netherlands, supplements contain 400-500µg folic acid and should be taken until eight weeks after conception. Indeed, the EURRECA project, funded by the EC, was set up to address the variance in micronutrient recommendations that exist across Europe.

In the Generation R Study of Roza et al., child behaviour was assessed by parents using the Child Behaviour Checklist for Toddlers. This checklist includes an assessment of whether a child is emotionally reactive, anxious, depressed, has sleep problems (internalising behaviour), or attention problems and aggressive behaviour (externalising behaviour). After adjustment for confounding variables, the results suggested that low use of folic acid supplements results in a higher risk of the child having a behavioural problem. The problems may persist, as these children, observed again at age three, showed an increased risk of emotional problems if their mother failed to take folic acid while pregnant.

Eating fish during pregnancy

Work published by ALSPAC suggests that eating fish during pregnancy has a positive effect on children’s verbal intelligence, motor skills and prosocial behaviour (giving, helping and sharing) when measured from six months to 48 months of age. Furthermore, that eating fish during pregnancy is positively associated with verbal IQ at age eight.

Fish, especially oily fish such as salmon, herring and mackerel, is an excellent source of the LC-PUFA omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), which receive much attention regarding their possible links to good health. DHA is the most abundant omega-3 fatty acid in the mammalian brain, incorporated into cell membranes during the pre- and post-natal period of rapid neural growth. Indeed, the EC supported the health claim that intake of DHA during pregnancy ‘contributes to the normal brain development of the foetus’. The acceptable intake of DHA during pregnancy was defined as ‘200 mg of DHA in addition to the recommended daily intake for omega-3 fatty acids for adults, i.e. 250 mg DHA and EPA’. These levels could be obtained by eating up to two portions of oily fish per week. However, there are many other nutrients in fish that could be mediating the effects reported by ALSPAC.

Maternal iodine status and thyroid function

Iodine is an essential nutrient and is required for the synthesis of thyroid hormones, which in turn, are crucial for brain development. The foetus relies on a maternal supply of iodine throughout gestation and severe deficiency can result in mental retardation; thus, iodine sufficiency during pregnancy is crucial. The World Health Organisation (WHO) considers iodine deficiency to be the ‘single most important preventable cause of brain damage’ worldwide but the effect(s) of mild to moderate iodine deficiency and inadequate maternal thyroid function is less well known.

NUTRIMENTHE researchers are looking in more detail at the effect of maternal thyroid function and iodine status to determine the extent to which these might affect cognitive development in early childhood. Henrichs et al. have found that low levels of thyroid hormone in pregnant women from the Generation R cohort, puts their children at risk of expressive language delay at 18 and 30 months. Expressive language includes the ability to form sentences, use grammar correctly and to retell a story or event. A risk of non-verbal cognitive delay (block building, imitation, planning and organising) was also found. Low maternal intake of iodine has also been associated with impaired executive functioning in children aged four, and maternal hypothyroxinaemia has been associated with larger foetal and infant head size. Only longer term studies will show whether these children have an increased vulnerability for developing clinical disorders later in life.

Research from the ALSPAC cohort, part-funded by NUTRIMENTHE, has added significantly to the knowledge describing the effect of mild to moderate maternal iodine deficiency during pregnancy on cognitive outcomes in childhood. In this study, urinary iodine was measured in 1040 pregnant women during their first trimester. The majority of the group was found to be mildly to moderately iodine deficient according to the WHO population criteria for pregnancy. Verbal, performance and total IQ were measured in the child at age eight. At age nine, reading speed, accuracy and comprehension were assessed and a ‘Reading Score’ was obtained. After taking into account 21 confounding variables, children of women who had the lowest measures of urinary iodine, were more likely to have scores in the lowest quartile for verbal IQ, reading accuracy and reading comprehension. Two confounders included in this study were intake of omega-3 fatty acids from seafood and the use of fish oil supplements during pregnancy. The iodine association was independent of these, suggesting that iodine is a mediating nutrient for at least some of the effect on verbal IQ seen in previous ALSPAC work.

This study is the first to show that mild iodine deficiency in UK pregnant women is associated with impaired cognitive outcome in their children, when assessed at age eight and nine. A sample of adolescent girls in the UK shows that this population is also mildly iodine deficient; compared to WHO standards, resulting in the UK being placed among the top ten countries with low urinary iodine concentrations of school aged children. To help address this, authors of the study have published a fact sheet containing useful information about iodine and advice for women to consider if they are planning to become pregnant. Iodine deficiency is not confined to the UK, as other European countries are also mildly iodine deficient and, as such, iodine deficiency may be regarded as a European public health issue. Collaboration between partners of the NUTRIMENTHE consortium will address this further.

The effect of genetic variation on the processing of nutrients

Of particular interest to NUTRIMENTHE are the effects of polymorphisms in the fatty acid desaturase (FADS) gene cluster, that codes for the enzymes involved in the synthesis of omega-3 and omega-6 fatty acids, on how LC-PUFAs are synthesised. NUTRIMENTHE researchers have published work showing that common variants of FADS1 and FADS2 are associated with levels of LC-PUFAs, including DHA, in the red blood cells of pregnant women, independent of their diet, and also with LC-PUFA levels in breastmilk. Further work has established, for the first time, the influence of FADS genotypes on the composition of fatty acids in plasma from the umbilical cord, such that both maternal and child FADS genotypes contribute to the composition of omega-3 and omega-6 LC-PUFAs in cord blood. Taken together, the results suggest that FADS genotypes may modify the fatty acid supply to the child during development and that gene-nutrient interactions should be taken into account when considering the effect of diet on child mental performance.

Parental perceptions of the link between diet and mental performance

To provide effective messages for European consumers regarding the effect of diet on mental performance, it is useful to know what consumers currently know and understand. In NUTRIMENTHE, the views of parents, who have primary responsibility for providing their child’s diet and for establishing good eating habits, are of
The NUTRIMENTHE Project | Paediatrics


Acknowledgements: The NUTRIMENTHE project acknowledges 5.9m€ funding from the European Commission’s Seventh 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’).

Conclusions and future work

Through funding from the EC, the NUTRIMENTHE project has gathered together a consortium of European research groups with expertise in nutrition, paediatrics, neuropsychology, psychiatry and genetics. Through collaboration since 2008, this group of researchers has added to the evidence that maternal diet influences mental performance in childhood. The biological mechanisms have been shown to be complex and to involve genetic variation, as indicated by the work linking genetic variation in the FADS gene cluster to the processing of fatty acids. The role played by a child’s diet also needs to be considered and this question is being addressed through the inclusion of post-natal intervention studies in NUTRIMENTHE’s research plan. Mental performance is being assessed in children up to the age of eight years. However, brain development continues into adolescence, so longer term studies are required to follow mental performance through to teenage years. A relatively unexplored area of research also being considered by NUTRIMENTHE is the use of neuroimaging to study the link between environmental and genetic factors and brain development. Following on from the publication of a feasibility study, fMRI scans of the brain will be included in the Generation R study, in children now aged between eight and ten. In addition, the University of Granada has incorporated electroencephalography and fMRI scans into the NUHEAL study of children whose mothers had taken supplements of DHA and 5-methyltetrahydrofolate during pregnancy. Mothers had taken supplements of DHA and 5-methyltetrahydrofolate during pregnancy. The surveys are of particular importance to parents, as these habits could have long-term implications for health. The surveys of particular importance to parents, as these habits could have long-term implications for health. The surveys of particular importance to parents, as these habits could have long-term implications for health.

Biography & contact details

Clare Horton 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 Ph.D in 1997. She then entered the pharmaceutical industry and in 2003 joined Beta Technology as a consultant to Beta Technology. In 2005, she joined the company as a full-time employee and in 2007 was appointed as Director of Business Development. Clare Horton 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 Ph.D in 1997. She then entered the pharmaceutical industry and in 2003 joined Beta Technology as a consultant to Beta Technology. In 2005, she joined the company as a full-time employee and in 2007 was appointed as Director of Business Development.

Contact the author: claire.horton@betatechnology.co.uk

Website: www.nutrimenthe.eu

Find us on Facebook or follow us on Twitter @NUTRIMENTHEP?

The NUTRIMENTHE International Conference

13th and 14th September 2013, Granada Conference and Exhibition Centre, Granada, Spain. A showcase of the final results and key messages of the project www.barcelonagri.com.es/NUHEAL/NUHEAL2013/index.html

The NUTRIMENTHE Project

The NUTRIMENTHE project acknowledges 5.9m€ funding from the European Commission’s Seventh 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’).