

Commentary: Fatty Acids, Breastfeeding and Autism Spectrum Disorder

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Abstract

Fatty acid deficiencies are linked to Autism Spectrum Disorder. This commentary discusses the protective role of breastfeeding and the urgency of research into the human infant's intake of colostrum to prevent fatty acid deficiency.

Keywords: *Autism; Breastfeeding; Fatty Acids; Colostrum*

Introduction

Autistic Spectrum Disorder (ASD) has been growing in prevalence over the last decade and new estimates suggest that rates in Australia could now be as high as 1 in 160 children (Williams, MacDermott, Ridley, Glasson, & Wray, 2008). Whilst there is no general agreement as to the reason/s for the increase, with the number of children diagnosed with ASD growing, research into the disorder gathers even more urgency and the burden on families, health, education and welfare services ever greater.

Research has shown fatty acid deficiencies to be over-represented in Attention Deficit Hyperactivity Disorder (ADHD), Schizophrenia, Depression, Pervasive Developmental Disorder, Developmental Coordination Disorder, Epilepsy and, more recently, ASD (Bell et al., 2004; Freeman et al., 2006; Richardson, 2004; Vancassel et al., 2001). Often found in the ASD population are the physical signs of fatty acid deficiency including excessive thirst, frequent urination, keratosis pilaris on the upper arms or upper thighs, dandruff, and atopic tendencies (Bell et al., 2004), as are lower plasma levels of fatty acids and elevated cytosolic PLA2 enzymes compared with matched controls (Bell et al., 2004; Richardson, 2004). Some researchers, based on clinical reports and correlational studies, have gone so far as to propose a causal role for a disorder of fatty acid metabolism in ASD (Clark-Taylor & Clark-Taylor, 2004; Richardson & Ross, 2000).

If we are to accept that fatty acid deficiency (or a fatty acid metabolism impairment) may be relevant in ASD (whether as a causal agent, risk factor or

epiphenomenal biological presence), then it is critically important to ensure that an infant has adequate supplies of fatty acids in utero and post-natally. The long chain polyunsaturated omega-3 and omega-6 fatty acids are so essential for the developing foetus that circulating levels double in maternal plasma (Crawford, 2000). An increase in omega-3 rich seafood in the maternal diet during pregnancy has been found to be correlated with optimum outcomes for prosocial behaviour, fine motor, communication and social development scores in children aged from 6 months to 3.5 years of age (Hibbeln et al., 2007). Omega-3 and omega-6 fatty acids also account for the majority of fats found in breast milk (Gibson & Kneebone, 1981). Given this fact, it seems reasonable to expect that breastfeeding would serve to protect the child from neurodevelopmental conditions such as ASD. Indeed, this is what studies have found (Schultz et al., 2006; Tanoue & Oda, 1989).

Schultz et al. (2006) surveyed 861 parents of children with ASD and 123 parents of children without ASD, and found that the children with ASD were significantly less likely to have been breastfed. The absence of breastfeeding significantly increased the odds of a later ASD diagnosis (OR 2.48, 95% CI 1.42, 4.35). The apparent link between ASD and breastfeeding was first cogently addressed by Tanoue and Oda (1989), who found that a significant number of infants subsequently diagnosed with an ASD had been weaned within one week of the commencement of breastfeeding with the duration of breastfeeding proposed as a protective factor. Similarly, the odds of being diagnosed with ASD also reduced with the duration of breastfeeding in the Schultz et al study, but not significantly. One major limitation of both of these studies is that colostrum intake was not accounted for.

In humans, and all mammals, lactation has three distinct stages: colostrum, transitional milk and mature milk, and at each stage the composition of the milk differs (Davis et al., 2007). Colostral milk contains immunoglobulins such as IgA, which play an important role in gut mucosal immunity (Vassilev & Veleva, 1996), and a higher level of protein than mature milk

(Davis et al., 2007). Colostrum also contains twice the long chain polyunsaturated fatty acids of mature milk and this is consistent in all lactating women in all parts of the world (Fidler & Koletzko, 2000). Hence colostrum can supply the breastfed neonate with significant amounts of preformed fatty acids during the first few days after birth even though the total milk intake is less than a mature milk feed (Fidler & Koletzko, 2000).

The World Health Organization (WHO) definition of exclusive breastfeeding is that the infant only receives breast milk without any additional food or drink, not even water, on demand day and night for the first six months of life (WHO, 2009). The remainder of the WHO guidelines lead to a critical issue for researchers in this field: that is, the recommendation that initiation of breastfeeding takes place *within the first hour of life* (italics added). Adherence to the WHO recommendation ensures that infants are able to access and utilise the preformed and highly digestible omega-6 and omega-3 fatty acids found in colostrum immediately after birth. As the timing of the establishment of breast feeding varies due to a number of circumstances, especially in premature babies, it is critical to determine whether infant fatty acid status and/or metabolism can be compromised by a lack of colostrum in the early stages after birth. An indication of the seriousness with which this issue should be taken is provided by numerous animal studies that have demonstrated fatty acid metabolism impairments and fatty acid deficiencies to be linked to low colostrum intake. For example, the best protection for newborn piglets, calves and horses is immediate colostrum feeding followed by an extended period of suckling over many weeks (Baxter, Baxter, & MacCormack, 1983; Gerrard, 1974). One study of neonatal calves found that delaying their colostrum intake by just 24 hours impaired their fatty acid, carotene, retinol and alpha-tocopherol status (Blum, Hadorn, Sallmann, & Schuep, 1997). Concentrations of fatty acids and fat-soluble vitamins in colostrum decrease as the time since parturition increases, and the infant calves' absorptive capacity is decreased due to gut closure. In animals, there is clear evidence of a critical timeframe (24 hours post-birth) where colostrum must be accessed to ensure optimal fatty acid metabolism (Blum et al., 1997).

In stark contrast to the well accepted norms of animal management, the importance of colostrum ingestion in human infants is largely overlooked. If a human infant does not receive the fatty acid rich colostrum in a timely fashion, does this interrupt the establishment of a functional fatty acid metabolism as it seems to for animals? It would strike us as unusual if it didn't but, at this point, there is no way of answering the question definitively. One human study (Vukavic, 1984) found that if the initiation of breastfeeding is postponed, spontaneous gut closure may not take place within the first 30 hours leaving the infant exposed to potential

environmental contaminants (Blum et al., 1997). As colostrum is known to be implicated in the process of gut closure (Blum et al., 1997; Vukavic, 1984), infants who do not receive colostrum may have their health compromised by a delay in gut closure and a reduction in essential fatty acids.

This issue may be particularly important for premature infants who are invariably fatty acid depleted at birth due to the bulk of Docosahexaenoic Acid (DHA) accretion into the brain and central nervous system (CNS) occurring via the placenta in the last trimester of pregnancy (Makrides et al., 2009). Makrides et al. found that premature infant girls supplemented with a high level of DHA performed better at 18 months of age on the Mental Development Index of the Bayley Scales of Infant Development than non-supplemented peers. No such effect was found for males, however. Unfortunately, no information is given in regard to infant colostrum intake. Of interest is the finding that females, in comparison to males, metabolise fatty acids at a rate of 4 to 1 (Burdge, 2004) seemingly due to the fact that testosterone can inhibit fatty acid synthesis (Marra & de Alaniz, 1989) and that both prematurity and male gender are independent risk factors for ASD (Kolevzon, Gross, & Reichenberg, 2007).

Pragmatic and/or medical issues prevent breastfeeding to WHO guidelines in all cases. Therefore, a critical research question relates to whether the current practice of not attempting to substitute for colostrum and moving directly to a mature milk replacement (formula) is the most effective approach to take for infants unable to be breastfed. Until 2002, if fatty acids were found in formula they were in the form of Linoleic Acid (LA) the omega-6 precursor to Arachidonic Acid (AA) and alpha Linolenic Acid (ALA) the omega-3 precursor to DHA (Alessandri et al., 2004). This led Alessandri et al. to make the observation that as infants have a limited capacity to synthesise DHA from ALA (which reduces with gestational age), artificially fed human infants are the only mammals that do not receive 20 and 22 carbon polyunsaturated fatty acids during their first months of life (Alessandri et al., 2004). Since 2002, DHA and AA have been included in selected infant formulas, although unsupplemented formulas are still widely available.

Infants fed unsupplemented formula have been shown to have lower DHA in their CNS, plasma and red blood cells, and autopsy studies have shown that these infants show depletion of their adipose tissue DHA stores by six months of age, whilst breastfed infants have maintained their DHA levels (Sarkadi-Nagy et al., 2004). Simply adding fatty acids to formula is a complex process, however, as dietary fatty acids synthesise via metabolic competition and a dietary source of one can deplete the synthesis of another (Sarkadi-Nagy et al., 2004). In a study of term and

preterm baboon neonates designed to measure the effects of supplementing formula with DHA and AA, supplemented formula was shown to partially restore the biosynthesis of DHA/AA to lower breastfed levels but the commonly available formula DHA concentrations were found to be inadequate to ensure a complete match of breastfed levels (Sarkadi-Nagy et al., 2004). The use of infant formula without DHA or AA supplementation versus exclusive breastfeeding was also significantly associated with an increase in ASD in the Schultz et al. (2006) study (OR 4.41, 95% CI 1.27, 15.7). Despite the limitations of the study (non-random sample and self-reported infant feeding practices) there appears to be mounting evidence that fatty acids serve a protective function in regard to the development of a number of neurodevelopmental disorders (Crawford, 2000; Richardson, 2004).

Clinical trials of fatty acids as a treatment in ASD are in their infancy and clear protocols regarding form of fatty acid, dose and agreement on adequate placebos in research trials require further clarification (Richardson, 2004). Furthermore, research in this field in the future would be greatly improved by ensuring thorough documentation of fatty acid intake beyond superficial examinations of intake in supplemental form. Specifically, researchers must examine colostrum and mature milk intake separately, and also consider the source of any fatty acid supplementation and the relative ratios of the major fatty acid types (particularly of omega-3 to omega-6). With a more thorough understanding of fatty acid metabolism and its role in development, new and effective preventative and treatment measures are possible, not only with relevance to ASD, but other developmental conditions such as learning disorders and ADHD.

Acknowledgments

The authors acknowledge the Friends of SABRI.

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exploring the relationship between autism and early infant feeding and nutrition.

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