FACTSHEET

EVIDENCE FOR THE USE OF PROBIOTICS IN AUTISM

Autism is a developmental disease characterized by a spectrum of symptoms ranging from decreased verbal skills and social withdrawal, to repetitive behaviour and violent outbursts[1]. There is some evidence of a genetic predisposition to autism, but it is clear that other factors, such as environmental influences, play an important role in this disease[2].

GASTROINTESTINAL DISTURBANCE

Children with autistic spectrum disorders (ASDs) tend to suffer from severe dietary and/or gastrointestinal (GI) problems (including abdominal pain, constipation, diarrhoea and bloating)[3,4]. In children with ASD, the presence of GI dysfunction is often associated with increased irritability, tantrums, aggressive behaviour, and sleep disturbances. Typically, parents claim that GI problems and behavioural symptoms manifest concurrently[3]. In 2011 Adams *et al*[5] found that GI symptoms were strongly correlated with the severity of autism. He concluded that it is possible that autism symptoms are exacerbated by or even partially due to the underlying GI problems.

Dietary intolerances have been seen in children with ASD, particularly the abnormal digestion of grain and dairy proteins, gluten and casein[6,7,8]. Restricted diets, such as gluten-free and/or casein-free (GF/CF) diets, have been associated with reduced GI symptoms and improved behaviour[6].

GUT MICROFLORA

Many experts believe that these GI symptoms may be due to a disruption of the indigenous gut flora promoting the overgrowth of potentially pathogenic (toxin-producing) micro-organisms[3]. Activation of the mucosal immune response, damage to the gut lining and the presence of abnormal gut microbiota are repeatedly observed in these children[4].

A study by Parracho *et al*[3] in 2005 compared the faecal flora of patients with ASDs with their healthy siblings and unrelated healthy children. The faecal flora of the ASD patients contained a higher incidence of a pathogenic toxin-producing bacterium (*Clostridium histolyticum*), with their siblings also showing some levels of this pathogen. It had been thought therefore, that clostridia in the gut might be involved in autism because they are virulent organisms and spore-formers. Spores are known to resist antibacterial agents so that when antibiotics were discontinued the spores would germinate and by toxin production or by another mechanism could lead to autism[9]. However, a study in 2010 by Finegold *et al*[10] showed that *Desulfovibrio* and *Bacteroides vulgatus*, potentially pathogenic bacteria that are also resistant to antimicrobials, were more common in severely autistic subjects than in controls. These pathogenic bacteria species were also similarly found in the siblings of autistic children, again suggesting a possible connection to the family environment[10] or health of the mother's gut microbiota at birth.

Modulating gut bacteria with short-term antibiotic treatment has been shown to lead to temporary improvement in behavioural symptoms in some individuals with ASD[4]. However, it is unlikely that the cause of the intestinal disturbance in autistic children is due solely to one pathogen but rather a disturbance of the individual's entire gut ecology and a reduction in the protective microflora. A number of studies have shown ASD children to have lower levels of beneficial protective bacterial species such as

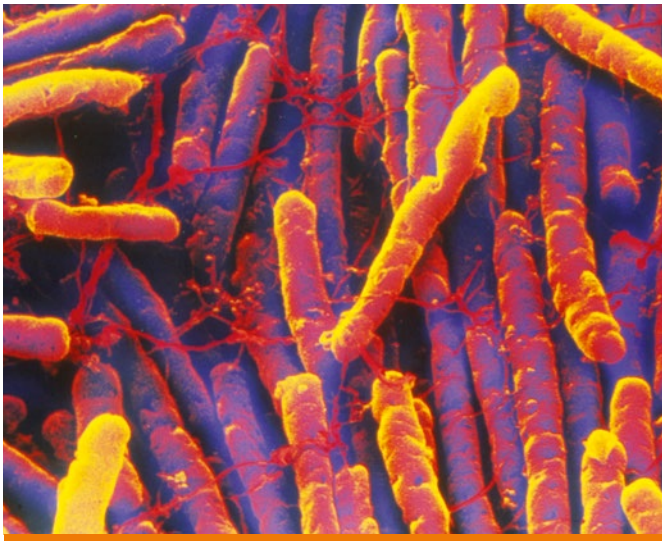

Figure 1: *Clostridium difficile*

Bifdobacterium compared to controls[2,5]. It is of concern to some that a significant percentage of individuals with autism have a history of extensive antibiotic use[11]. Oral antibiotics are now well known to significantly disrupt protective intestinal microbiota, creating a favourable environment for colonization by opportunistic pathogens[11,12,13] such as *Clostridium difficile* and *Desulfovibrio*[14].

Researchers do not yet know exactly how gut bacteria might influence behaviour, but one hypothesis is that a leaky gut may allow substances such as these bacterial toxins to pass into the bloodstream that could subsequently harm brain development and function[17].

PROBIOTICS

Probiotics are believed to influence microbiota composition, intestinal barrier function, mucosal immune responses, digestion and detoxification. The administration of probiotic bacteria to address changes in the microbiota, have been considered to ameliorate GI and ASD behavioural symptoms[4]. In 2009 it was estimated that alongside behavioural therapies over half of children with autism were using complementary therapies including the use of probiotics[16], often chosen because they are perceived as addressing the cause of symptoms opposed to just the symptoms themselves[17].

A study in 2013 incited an altered gut bacteria and inconsequence autism like symptoms in mice by infecting the mothers with a virus like molecule during pregnancy. By treating the rodents with a probiotic, the researchers were able to attenuate some, but not all, of their behavioural symptoms[17]. A later survey in 2013 by West *et al*[18] gave 33 autistic children a multi-strain probiotic for 6 months. Caregivers reported a significant decrease in severity of ASD symptoms (ATEC score) and significant improvements in diarrhoea and constipation severity, as well as improvements in stool frequency. Another study by Kałużna-Czaplińska and Błaszczyk in 2012[19] of ASD children receiving probiotics found changes in urine levels of metabolites associated with *Candida* species, suggesting an alteration of the gut microflora. This is certainly an area where we can expect to see much more research over the coming years.

Bio-Kult is a unique multi-strain probiotic with 14 different strains of beneficial bacteria. *In vitro*[20] work has demonstrated the antibacterial activity of the Bio-Kult multi-strain mix on three common GI pathogens *Clostridium difficile*, *Escheria coli* and *Salmonella typhimurium*.

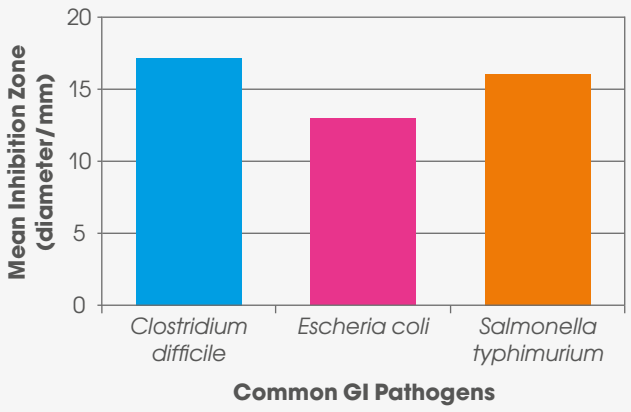

Figure 2: Antimicrobial Activity of Bio-Kult[20]

As each different probiotic strain has a slightly different beneficial effect within the body a multi-strain is believed to have more positive benefits overall and therefore be able to help a more diverse range of GI disorders.

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