Gastrointestinal Support in Neurological and Behavioural Conditions

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There has been considerable interest and research in recent years regarding the brain-gut connection, namely the significant effect each of these seemingly separate systems (nervous and digestive) can have on each other. The connection between the brain and the gut is evidenced by gastrointestinal disorders such as Irritable bowel syndrome (IBS) and Inflammatory bowel disease (IBD) that are seen to be associated with depression and anxiety. [1], [2] Gastrointestinal pathology has also been seen in conjunction with disorders such as Attention Deficit Disorder and autism.[3]

Neurological factors may also impact on the gastrointestinal system. Recent data suggest that stress induced alterations in gastrointestinal inflammation may be mediated through changes in hypothalamic-pituitary-adrenal (HPA) axis function and alterations in bacterial-mucosal interactions, and via mucosal mast cells and mediators such as corticotrophin releasing factor (CRF).[4]

Intestinal Pathology and Neurological Conditions

GI Inflammation

A study examining the brain effects of chronic gastrointestinal inflammation in a rat model of acquired IBD showed that chronic IBD activated periventricular gray, hypothalamic/visceral thalamic stress axes and cortical domains, and septal/preoptic/amygdala; brain areas abnormal in autism.[5]

Another study demonstrated intestinal mucosal pathology, characterised by ileo-colonic lymphoid nodular hyperplasia (LNH) associated with mucosal inflammation to be a characteristic pathological finding in children with Austistic Spectrum Disorder (ASD). 90% of ASD children compared with 30% of control children were found to exhibit LNH in the ileum, with 59% of ASD patients and only 23% of controls showing LNH in the colon.[6] Food allergies or sensitivities leading to immune activation and gastrointestinal inflammation are also a suspected cause of aggravation of behavioural symptoms in ASD.

Nutritional Support

- **Glutamine** is the most abundant amino acid in the bloodstream. Although the human body can produce this amino acid, during times of stress, requirements increase and it may be considered conditionally essential. Glutamine is the main metabolic fuel for enterocytes of the small intestine, lymphocytes, neutrophils and macrophages (i.e. intestinal immune cells and mucosal cells).
- **Quercetin** is a bioflavonoid that has an anti-inflammatory action. It has been shown to down-regulate a number of inflammatory mediators including lipoxygenase and cyclo-oxygenase pathways, NF-kappa B, TNF-alpha and also histamine release from mast cells. Gastrointestinal mast cells are involved in pathological effects of food hypersensitivity and allergy, a situation often seen in conditions like autism.
- **N-acetyl glucosamine** is a naturally occurring substance required for synthesis of proteoglycans and glycosaminoglycans, and is a component of blood vessels, cartilage, ligaments and also the mucous secretions of the digestive, respiratory and urinary tracts.[7] Recent evidence suggests N-acetyl glucosamine to have immunosuppressive effects, down-regulating T helper cells, highlighting its potential benefit for autoimmune and inflammatory conditions.

Impaired intestinal mucosal barrier

Leaky gut (or increased intestinal permeability) has long been hypothesised to be a contributing factor in autism. This hypothesis suggests that partially digested products of foods are able to enter the blood through the leaky mucosa and induce antigenic responses and also directly interfere with the central nervous system.[8] The gastrointestinal mucosa consists of epithelial cells, which are held together through junction complexes. The tight junction, sometimes referred to as the Zonula occludens, represents a major barrier within the paracellular pathway between the intestinal epithelial cells. Data demonstrate that barrier properties of tight junctions can by

modulated in response to physiological, pharmacological and pathophysiological stimuli. There are a number of factors that may affect tight junctions including food components (e.g. gluten, casein). Infectious organisms such as E. coli and C. difficile have the ability to disrupt the tight junctions of epithelial cells through their virulence factors.

Breakdown of the glycosaminoglycans may also be a consequence of inflammation at the mucosal surfaces of the intestine. Glycosaminoglycans are present in the extracellular matrix in most regions of the body and are thought to play a specific role in the mucosal barrier function of the intestinal wall.

Nutritional Support

- **Glutamine** may also prove beneficial for the integrity of the mucosal lining of the gastrointestinal tract. Supplementation of glutamine in highly stressed individuals has been shown to improve intestinal barrier function.[8] When levels of glutamine drop, the intestinal epithelial cells and lymphocytes may suffer reduction in function, which in turn may compromise the integrity of the epithelium and impaired barrier function.
- **N-acetyl glucosamine** may be directly incorporated into glycosaminoglycans and utilised for tissue repair. In vitro studies suggest n-acetyl glucosamine is preferentially taken up over glucosamine in inflammatory bowel biopsies.[9]
- **Fructooligosaccharides (FOS)** are a type of soluble fibre that escape digestion in the upper intestine and reach the colon where they are totally fermented to short chain fatty acids. FOS are noted for their bifidogenic power and higher production of the short chain fatty acid butyrate, which is essential to the colonocyte.[10] Butyrate may be able to enhance restoration of mucosal barrier function. Animal studies also show that butyrate may stimulate mucus release in the colon.[11]

Dysbiosis

Dysbiosis (bacterial overgrowth) of the gastrointestinal system may also contribute to psychological and neurological symptoms. Dysbiosis is associated with autism and attention deficit disorders. It has also been stated that imbalances of the symbiotic bacteria, presence of nematode or protozoan parasites, yeast (Candida) overgrowth caused by antibiotic overuse—once corrected can manifest as multi-system improvement, including sometimes marked clearing of the mental/behavioural symptoms.[12]

Nutritional Support

- **Antimicrobial herbs** may provide initial defence and therapy against dysbiosis, by inhibiting detrimental bacteria, fungi, worms and parasites.
- **Probiotics** are also extremely effective for re-balancing the intestinal ecology by providing beneficial strains of bacteria, which enhance both immune as well as digestive function.
- **Fructooligosaccharides** and other prebiotics may also promote a healthier environment through the growth of beneficial bacteria. Specifically fructooligosaccharides promote the growth of bifidobacteria. Bifidobacteria inhibit a large number of detrimental organisms and promote the production of short chain fatty acids including lactic and butyric acid. Studies have also demonstrated an anti-inflammatory effect of FOS supplementation.

The few examples mentioned above highlight the importance of addressing the integrity and function of the GI system in many different disorders for a holistic and integrative approach to treatment. Support of gastrointestinal function, including nutrients to decrease inflammation, enhance repair and support structural integrity of the gastrointestinal mucosa may contribute significantly to a reduction of behavioural symptoms.

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