ADHD PLUS MINUS TREATMENT PLAN

-INTESTINAL DYSBIOSIS +PROBIOTICS

Dr. James Greenblatt, MD

The plan below is part of a guide for practitioners to add elements (+) or remove them (-) from the patient's environment or lifestyle as treatment for ADHD symptoms. Biochemical individuality will determine the most important elements for each patient.

INESTINAL MICROBIOME

The gastrointestinal (GI) tract communicates bi-directionally with the central nervous system. The microbiome plays a central role in gut-brain communication (Borre et. al., 2014; Mayer et. al., 2015). A disruption of the microbiome (termed dysbiosis) is associated with several physical and mental concerns, from obesity, pain, and autoimmunity, to depression, anxiety, bipolar disorder, autism spectrum disorder, schizophrenia, and ADHD (Cryan et. al., 2012; Butler et. al., 2019; Wang et. al., 2020).

The microbiome affects the brain via several mechanisms, including neurotransmitter modulation, inflammation, regulation of the hypothalamic-pitiutary-adrenal (HPA) axis, and via microbiome by-products of certain harmful or overgrown commensal GI flora (Clapp et. al., 2017; Bastiaanssen et. al., 2019).

Clostridia and HPHPA

The Clostridium genus of bacteria in the gut produces a substance called HPHPA (3-(3-hydroxyphenyl)-3-hydroxypropionic acid) that is neurotoxic and causes adverse psychiatric effects at chronically high levels (National Center for Biotechnology Information, 2005).

HPHPA crosses the blood brain barrier and inhibits dopamine beta-hydroxylase, the enzyme responsible for the conversion of dopamine to norepinephrine (Shaw, 2017). Resultant increases in dopamine can cause neuronal overstimulation and oxidative stress, while decreased norepinephrine can lead to inattention, low mood, anxiety, repetitive behaviours, and sleep problems (Kopečková et. al., 2006).

Elevated HPHPA has been associated with autism, childhood psychosis, and schizophrenia, as well as hyperactive behaviour. A 2010 case report documented extremely elevated levels of HPHPA in a patient during an acute psychotic episode. The HPHPA levels decreased significantly and the episode resolved with one week of oral antibiotic treatment (Shaw, 2010).

Candida Spp.

Similarly, an overgrowth of symbiotic fungus in the GI tract can also impact mental health through several mechanisms. Opportunistic overgrowth of the commensal yeast species *Candida* is associated with impaired memory in certain populations, autism spectrum disorder, schizophrenia, and ADHD (Crook, 1983; Burrus, 2012; Rucklidge, 2013; Severance et. al., 2017).

Probiotic Treatment of Dysbiosis

In 2020, a small placebo-controlled pilot study used lactobacillus probiotics as treatment for ADHD in children and adolescents. Self-reported health-related quality of life scores (PedsQL) improved significantly over baseline in the treatment group but not in the placebo group, whereas the ADHD Rating Scale Score improved significantly over baseline in both groups (Kumperscak et. al., 2020).

A trial comparing Ritalin with a multi-nutrient supplement containing lactobacillus probiotics for ADHD showed significantly improved impulse control and attention in both groups, with no significant difference between Ritalin and the multi-nutrient + probiotic supplement (Harding et. al., 2003)

Rucklidge (2013) documented a case study of a patient's ADHD and mood symptoms deteriorating when a Candida overgrowth was detected, followed by symptomatic improvement with successful treatment of the fungal overgrowth with an herbal antimicrobial and probiotics.

Probiotics may even be an effective preventive treatment for neurodevelopmental disorders. In one study, Infants who received lactobacillus probiotic supplementation for 6 months in early life were less likely to develop ADHD by the age of 13 (Pärtty et. al., (2015).

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TEST

Test for HPHPA levels and urinary markers of yeast overgrowth with a microbial organic acid test (MOAT) or standard organic acid test (OAT). Stool tests can also assess the profile of flora in the GI tract and identify overgrowths or infections of bacteria and yeast.

INDICATIONS

1. Treatment of HPHPA may be indicated if a patient exhibits signs of dopamine elevation, including:
- Agitation
- Hyperactivity
- Aggression
- Exacerbation of symptoms on a stimulant medications

2. Dysbiosis may be playing a role if the patient also complains of digestive symptoms, including bloating, abdominal pain, constipation, and/or diarrhea.

Safety

Probiotic supplementation may initially cause bloating or GI discomfort. Start with lower doses and increase to avoid this effect.

TREAT

If the patient has elevated HPHPA in organic acid testing (eg. >180mmol/mol creatinine) or elevated yeast markers, treat with high-dose probiotics: **200 billion CFUs per day, with food in divided doses, for 2-3 months.**

If symptoms abate after probiotic treatment, reduce to a maintenance dose of 10-20 billion CFUs per day. In the clinical experience of Dr. James Greenblatt, probiotic treatment is effective for 80% of indicated patients.

If symptoms do not improve with probiotic treatment (20% of indicated cases, usually adolescents with co-morbid psychiatric conditions), consider concurrent antibiotic-probiotic treatment with Flagyl or Vancomycin (clostridia-specific). The antibiotic is prescribed for 30 days, in 3x 10-day rotations (schedule below). Day "A" is probiotic + antibiotic (taken 12 hours apart), day "B" is the probiotic alone.

Day 1: A	Day 4: A	Day 7: A	Day 10: A
Day 2: B	Day 5: B	Day 8: B	Repeat 10 days 3x
Day 3: B	Day 6: B	Day 9: B	

Anti-Microbial Diet

Intestinal dysbiosis may also benefit from an anti-microbial/anti-candida diet during probiotic treatment. This diet limits simple carbohydrates and sugars, while increasing non-starchy vegetables and protein.

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