be associated with quality of life measures, is linked to gene and chromosomal regions, and there is evidence of familiarity (2–4). We have developed and have refined the MERS to better understand and assess cognitive and behavioral rigidity and inflexibility in ASD, and to help track changes with treatment. The MERS measures **1.** Degree of Behavioral Rigidity, **2.** Degree of Cognitive Rigidity, **3.** Interference associated with rigidity, and **4.** Distress associated with Rigidity. Since this domain of symptoms may have a unique neurobiological origin and differential treatment response, we recommended future ASD studies utilize this measure to stratify patients into more homogeneous groups and/or as an outcome measure to track changes in rigid behaviors.

Disclosure

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HYPERTHERMIA AND THE IMPROVEMENT OF ASD SYMPTOMS

Casara J Ferretti, MS, Bonnie P Taylor, PhD, Rachel Noone, MD, Emma Racine, Jonathan Kirsch, MD, Eric Hollander, MD

Montefiore Medical Center, Albert Einstein College of Medicine, Bronx NY, USA

Background: The observation that some ASD patients manifest clinical improvement in response to fever suggests that symptoms may be modulated by immune-inflammatory factors. The febrile hypothesis of ASD stems from this observation, and could be due to (1) the direct effect of temperature; (2) a resulting change in the immune inflammatory system function associated with the infection of fever; and/or (3) an increase in the functionality of a previously dysfunctional locus coeruleus-noradrenergic (LC-NA) system.
Methods: We completed a double blind crossover study of 15 children with ASD (5–17 years) using two treatment conditions, hyperthermia condition (102 °F) and control condition (98 °F) in a HydroWorx aquatic therapy pool. Five children with ASD without fever response acted as controls, completing only the hyperthermia condition, to ensure safety and feasibility. Safety measures and Social Responsiveness Scale (SRS) were collected. Ten patients with ASD and history of fever response were enrolled and received both treatment conditions. Vital signs, temperature monitoring and clinical observations were completed throughout their time in the pool. Parents completed the SRS and RBS-R. Pupillometry biomarker and buccal swabs for DNA and RNA extraction were collected pre and post pool entry.
Results: Five control subjects without a history of fever completed the hyperthermia condition at 102 °F, and demonstrated the safety and feasibility of the study. Ten subjects with ASD and a history of fever response were enrolled and completed the hyperthermia condition (102 °F) and control condition (98 °F) at the aquatic therapy pool. Improvement in social cognition and repetitive/restrictive behaviors were observed at the hyperthermia condition (102 °F) on parent (SRS, RBS-R) and rater (CGI-I) assessments. Pupillometry biomarker and gene expression can be correlated with clinical improvement. Side effects were minimal, and were the same as those observed in a hot tub/sauna (redness, nausea).
Discussion: We demonstrated improvement of socialization and repetitive and restricted behaviors at the hyperthermia condition (102 °F), and that we could reliably and safely increase children's temperatures into the fever range (mean max temperature of 101.7 °F). This temperature increase was observed to cause significant and convergent improvement on clinician ratings (CGI-I) and parent ratings (SRS, RBS-R), both of which were kept blinded to the temperature of the pool. Interestingly, each child's fever response history was correlated with the improvements observed at the elevated temperature. Those with a history of marked fever response had the most observable behavior changes. Behavior changes observed for each child were similar to those observed by parents during febrile episodes, including increased cooperation, communication and social reciprocity and decreased hyperactivity and inappropriate vocalizations. Although multiple rationales have been posited, this is the first study looking at the direct effect of temperature on ASD symptomatology. This study explores the direct effects of temperature on ASD symptoms and offers a window into understanding mechanisms involved in the improvement of ASD symptoms during febrile episodes. Future analyses will help to determine the genetic pathways involved in fever response, the role of the LC-NA system, and other immune-inflammatory pathways in mediating ASD symptoms.

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TRICHURIS SUIS OVA (TSO) AS AN IMMUNE-INFLAMMATORY TREATMENT FOR REPETITIVE BEHAVIORS IN ASD

Eric Hollander, MD, Casara J Ferretti, MS, Bonnie P Taylor, PhD, Rachel Noone, MD, Jonathan Kirsch, MD, Emma Racine

Montefiore Medical Center, Albert Einstein College of Medicine, Bronx NY, USA

Background: Inflammatory mechanisms have been implicated in Autism Spectrum Disorders (ASD) and immunomodulatory interventions, such as Trichuris Suis Ova (TSO), may be an experimental therapeutic option. ASD patients have dampened Th2 anti-inflammatory cytokine response, and increased Th1 proinflammatory cytokine response, and some improve in response to fever, suggesting a possible role of immune-inflammatory factors. Helminth worms, such as TSO, have been studied in autoimmune disorders in part from the hygiene hypothesis, which suggests that a rise in hygiene is associated with less protective microbes in humans and an increase in autoimmune inflammatory disorders and that stimulation of the immune system by microbes is protective against the development of inflammatory diseases.
Methods: A 28 week double-blinded, randomized crossover study of TSO vs. placebo in 10 adults, aged 17.5–35, with ASD was completed, with a 4 week washout period between each 12 week phase. Subjects had a personal/family history of allergies, baseline YBOCS score of ≥ 6 and an IQ ≥ 70. Eligible subjects received 2500 TSO ova every 2 weeks and completed subject, parent and clinician assessments, in addition to safety monitoring, clinical labs and stool sampling. Parent-rated measures included the Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS) and Repetitive Behavior Scale- Revised (RBS-R). Clinician rated measures included the Montefiore-Einstein Rigidity Scale (MERS) and the Yale-Brown Obsessive Compulsive Scale (YBOCS).
Results: This exploratory safety and efficacy study included young adults with high functioning ASD, normal intelligence and good verbal skills. Irritability scores on the ABC-I were low at baseline. Of interest, measures of rigidity, craving for sameness and restricted interests, distinct domains of repetitive behaviors, were noted to improve in patients on TSO vs placebo, with large effect sizes. These changes were observed on the MERS ($d=0.79$), RBS-R Sameness Subscale ($d=1.0$) and RBS-R Restricted Subscale ($d=0.82$). There were also improvements on the YBOCS Compulsion Subscale ($d=0.52$) and the ABC-Irritability Subscale ($d=0.78$). The side effect profile was low. Throughout the study only minimal gastrointestinal distress was observed in some patients.
Conclusion: This is the first placebo controlled trial of TSO in an ASD population. Our exploratory pilot study demonstrates the feasibility of completing a 28 week study of TSO in an ASD population, safety of TSO in this population, and potential efficacy for rigidity, insistence of sameness, and repetitive/restricted behaviors. TSO was tolerated well by subjects, with mild, limited side effects which resolved without medication or action taken to the study drug. Limitations of the trial included a small sample size, lack of irritability at baseline, and use of parent outcomes measures in this population that potentially impact our understanding of the results. Future studies are needed to replicate these preliminary findings in a younger population stratified for higher baseline irritability, and further exploration of target engagement with the immune system and relationship to clinical improvement in ASD.

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TOO MUCH DELIBERATION? CAUTIOUS DECISION-MAKING IN OCD

Paula Banca[a,b,c], Martin D. Vestergaard[d], Vladan Rankov[a], Simon Mitchell[a], Tatyana Lapa[a], Miguel Castelo-Branco[c], Valerie Voon[a]

[a]*Department of Psychiatry, University of Cambridge, Cambridge, UK.* [b]*PhD Programme in Experimental Biology and Biomedicine, Center for Neuroscience and Cell Biology, University of Coimbra, Portugal.* [c]*Institute for Biomedical Imaging and Life Sciences, University of Coimbra, Portugal.* [d]*Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK*

Introduction: Compulsive behaviours are typical symptoms of Obsessive-Compulsive Disorder (OCD) which may reflect difficulties to commit to ultimate decisions and may be conceptualized as a means to accumulate sufficient evidence prior to a decision. Here we investigate the process of evidence accumulation in OCD in perceptual