Abstract Book

Background: Recent advancements in understanding the microbiota-gut-brain axis (MGB) have posited microbial modulation as a novel intervention strategy in autism. However, prior trials of probiotics were not informed by the complex interactions between the MBG axis and clinical phenotypes, leading to a lack of targeted treatment outcomes. Our upstream research revealed the correlations between depleted gut microbial production of GABA and elevated sensory hyperresponsiveness and anxiety symptoms in autism. A novel synbiotic formula, SCM06, with a combination of prebiotics and probiotic species that upregulate GABA production and immune function, was developed as a specific treatment of anxiety and sensory symptoms in young autistic children.
Objectives: This study aimed to assess the safety, tolerability, and preliminary efficacy of the SCM06 formula in alleviating anxiety and sensory hyperresponsiveness symptoms in young autistic children.
Methods: Young autistic children with significant anxiety and sensory hyperresponsiveness symptoms were recruited in this open-label pilot study from a Child and Adolescent Psychiatric Center affiliated with a University Teaching Hospital in Hong Kong (ClinicalTrials.gov ID: NCT06126185). Participants consumed one sachet of the SCM06 formula daily for 12 weeks. Anxiety, sensory hyper-responsiveness, core autistic symptoms, attention deficit and hyperactivity disorder (ADHD) and externalizing behavioural symptoms, and presence of functional gastrointestinal disorders (FGID) were evaluated at Weeks 0, 6, and 12 using the following parent-rated questionnaires: Anxiety Scale for Children-Autism Spectrum Disorder scale (ASC-ASD), the Sensory Experience Questionnaire (SEQ), Social Responsiveness Scale 2nd edition, Child Behavioural Checklist and Rome IV Diagnostic Questionnaires for Pediatric FGID.
Results: A group of thirty prepubertal ASD children with normal IQ, aged 4 to 11 (22 males and 4 females) were recruited and completed the study. SCM06 was safe and tolerable, with only 3.33% and 6.67% of participants reporting self-limiting loose stool and reduced appetite. Significant improvements from Week 0 to Week 12 were observed in both anxiety ($F = 7.47$, $df = 2,58$, $p = 0.001$, $\eta_p^2 = 0.205$) and sensory hyperresponsiveness ($F = 3.87$, $df = 2,58$, $p = 0.026$, $\eta_p^2 = 0.118$) (Figure 1). The prevalence of functional abdominal pain disorders decreased from 26.7% at Week 0 to 10.0% at Week 12 ($\chi^2 = 5.00$, $df = 1$, $p = 0.025$). Other symptoms such as ADHD and core ASD features, which were not associated with depleted gut microbial GABA production, did not change significantly. This suggested a specific effect of SCM06 on the two targeted symptom domains.
Conclusions: The concurrent relief of gastrointestinal, sensory, and anxiety symptoms corroborated with our upstream observational studies, alluding to the specific therapeutic action of SCM06 on the MBG axis. Nevertheless, an adequately powered RCT is needed to evaluate SCM06's efficacy properly.

423.206 Predictors of Placebo Response in the Study of Oxytocin in Autism to Improve Reciprocal Social Behaviors (SOARS-B)

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Background: Although randomized clinical trials (RCTs) have sought to identify treatments for social communication difficulties and repetitive behaviors in autism, none has yet shown consistent superiority over placebo. In part this may be because the substantial placebo response reported in many autism RCTs impedes the ability to detect meaningful treatment effects. Meta-analyses have identified trial-level factors that predict an increased placebo response rate in autism, including longer trial duration and larger sample size, but only two studies of individual-level factors have been conducted to date. These studies found that lower baseline symptom severity and enrollment at a commercial rather than academic study site may make a particular autistic individual more likely to respond to placebo. However, little is known about what other factors might be influential in predicting individual-level placebo response.
Objectives: We sought to identify individual-level predictors of placebo response in data from SOARS-B, a 24-week RCT of intranasal oxytocin for social impairment in autistic youth. In our primary analysis, we examined predictors of change in Aberrant Behavioral Checklist-modified Social Withdrawal (ABC-mSW) score, a caregiver-rated index of social impairment, at 24 weeks in SOARS-B participants taking placebo. In secondary analyses, we examined predictors of ABC-mSW change at 12 weeks and predictors of Clinical Global Impression – Improvement (CGI-I), a clinician-rated index of clinical improvement or its lack relative to baseline, at 24 and 12 weeks. For comparison, we also examined predictors of ABC-mSW change and CGI-I at 24 and 12 weeks among SOARS-B participants taking oxytocin.
Methods: For each analysis, we first used lasso regression to identify potentially influential predictors from among a large group that included demographic factors, rating scale data, study site, and prescribed medications. We then estimated an unpenalized linear regression model for the outcome of interest that included only those variables retained by the optimal lasso. We considered any variables with statistically significant coefficients to be influential predictors.
Results: We found that a higher baseline ABC-mSW score was the only influential predictor of ABC-mSW change in the placebo group at 24 and at 12 weeks. Regarding CGI-I, we found no influential predictors at 24 weeks, but at 12 weeks found that age, IQ and study site were influential. In our comparative analysis, we found that ABC-mSW was also an influential predictor of ABC-mSW change at 24 and 12 weeks in the oxytocin group. Predictors of CGI-I, however, were inconsistent with those in the placebo group, suggesting that random variability explained the observed effects.
Conclusions: In this analysis of SOARS-B data, higher baseline severity on an index of social impairment (the ABC-mSW) predicted greater placebo response. This contrasts with a prior analysis of data from a trial of citalopram for repetitive behaviors in autism, in which lower baseline severity of a composite measure that included core autism features and mood symptoms predicted greater placebo response. This may indicate that different factors contribute to placebo response in different symptom domains. Further analyses of individual-level RCT data are necessary to better understand predictors of placebo response in autism.