SYNBIOTIC IMPROVES GUT MICROBIOME DIVERSITY AND GASTROINTESTINAL SYMPTOMS IN PRECLINICAL STUDY OF AUTISM SPECTRUM DISORDER

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Objectives
Autism spectrum disorder (ASD) is an umbrella term for autism, Asperger's syndrome and pervasive developmental disorder not otherwise specified. Current research suggests a link between ASD and the gut microbiota as many autistic children have dysbiotic gut microflora and gastrointestinal problems. The aim of this study was to evaluate whether use of synbiotic could re-establish gut homeostasis.

Methods
Female BALB/c mice (Velaz, Prague, Czech Republic) underwent antibiotic treatment (5 days) and subsequent convalescence (10 days) to obtain a pseudo germ-free status. Animals were divided into three groups: control group (CON, n=29), group with ASD (ASD, n=15) and synbiotic treated ASD group (SYN, n=15). ASD was induced by oral administration (3 days) of faecal microbiota transplantation from ASD children followed by a convalescence period (5 days). Subsequently, SYN group was treated by oral administration of synbiotic (*Lactobacillus plantarum* CCM 7512, *Lactobacillus reuteri* CCM 8617 in MRS broth with flax seeds) for 5 days. Scores of rectal bleeding were assessed during the entire experiment. DNA isolated from faecal samples was analysed by a commercial NGS provider (Novogene Europe, UK).

Results
ASD induction caused a significant decrease in abundance of *Lachnospiraceae* ($p<0,01$) which has been previously associated with the neurotypical (NT) phenotype. On the other hand, ASD group had a higher abundance of *Bacteroidaceae* ($p<0,01$), *Tannerellaceae* ($p<0,001$), *Fusobacteriaceae* ($p<0,01$), *Enterobacteriaceae* ($p<0,01$) and *Sutterellaceae* ($p<0,001$) compared to CON group. These bacterial families are associated with dysbiosis in ASD children. ASD group had a significantly higher score of rectal bleeding than CON group ($p<0,001$) suggesting an acute inflammation and tissue damage. After the treatment, the severity of gastrointestinal symptoms decreased, which was proven by the decrease of the rectal bleeding score ($p<0,01$). After the synbiotic supplementation the overall microbiome diversity significantly increased (simpson $p<0,05$; chao1 $p<0,05$). Moreover, abundances of

Tannerellaceae ($p<0,05$), *Fusobacteriaceae* ($p<0,01$) and *Enterobacteriaceae* ($p<0,01$) decreased to the level detected in the CON group.

Conclusion

Synbiotic proved to be a potential treatment option for gastrointestinal problems of children with ASD as it restored microbiome diversity and improved rectal bleeding score.

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