

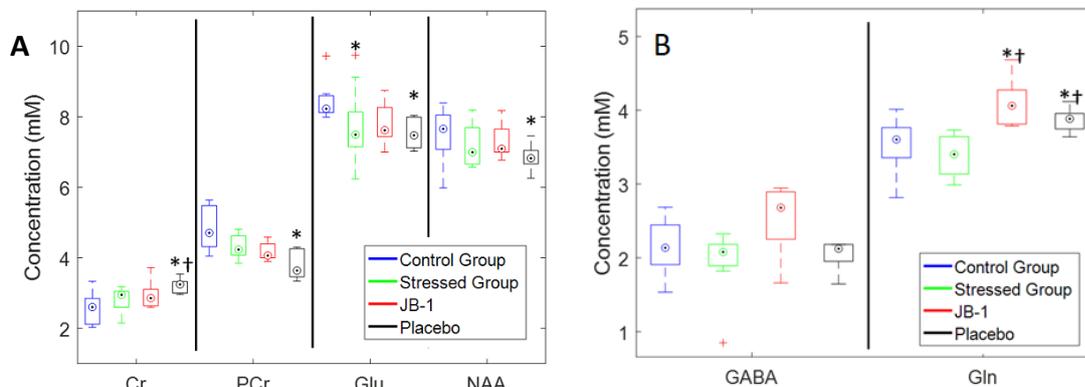
# In vivo <sup>1</sup>H MRS study at 7T for the assessment of metabolic changes in the rat model of chronic unpredictable mild stress with *Lactobacillus rhamnosus* (JB-1) treatment

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**Introduction** The purpose of this study was to investigate neuro-metabolic alteration in hippocampus and its regulation by a probiotic LR-JB1™ dietary supplement in a rat model of depressive-like disorder induced by chronic unpredictable mild stress (CUMS), using <sup>1</sup>H MRS at 7T.

**Methods** The studied populations consisted of Wistar rats (250g), which was split into control group (CG, N=10), and stressed group (SG, N=10). The MRS study of stressed group was repeated after 28 days of treatment with *Lactobacillus Rhamnosus* bacteria strain (JB-1): JB-1 group (N=5) or placebo diet: PB group (N=5). Single-voxel <sup>1</sup>H MRS experiments were performed on a 7T MRI scanner (70/16 Pharma Scan, Bruker Biospin, GmbH, Germany). VOI size was 22  $\mu$ L (2 x 2 x 5.5 mm<sup>3</sup>) located in the hippocampus, spectra acquired using the PRESS sequence (TE/TR=16 ms/2.5s), with bandwidth = 3 kHz, 4096 data points and 1024 number of averages. MR spectra were processed using LC Model software.



**Figure 1A** Concentrations of Cr were higher while PCr, Glu and NAA were lower in SG than in CG.

**Figure 2B** Concentrations of GABA and glutamine (Gln) were highest in the JB-1 treated group.

\* indicates a statistically significant difference relative to the CG

† indicates a statistically significant difference relative to the SG

**Results** The results from all groups revealed increased Cr and decreased PCr, Glu, and NAA concentrations after CUMS compared to CG, and then continued the trend when treated with placebo, but either slowed or reversed the trend when treated with JB-1 (Figure 1). GABA levels increased in the JB-1 treated group relative to all other groups a trend which approached significance relative to SG ( $p=0.06$ ) (Figure 2). Following treatment, concentrations of Gln were elevated in both JB-1 and PB, a change which may be related to the time point rather than either diet or treatment (Figure 2).

**Discussion** The JB-1 dietary supplement resulted in a trend towards increased GABA ( $p=0.06$ ) and a significant increase in Gln ( $p=0.003$ ), relative to their concentration in the stressed group immediately prior to treatment, by ~30 and ~20% respectively. This is consistent with our previous findings in BALB/c mice where we have observed increases in GABA by ~25% and in Glx (Glu + Gln) by 10% following JB-1 supplementation.

**Conclusion** In summary, we found significant differential changes in the levels of two important biomarkers of brain function: GABA and glutamine, after treatment with a specific *Lactobacillus* strain, JB-1, in depressive-like disorder. GABA is the chief inhibitory neurotransmitter in the brain and is likely synthesized there since it does not normally cross the blood-brain barrier [1]. Glutamate is an important precursor of GABA and a decrease in its content in the anterior cingulate cortex (ACC) and prefrontal cortex has been shown to be associated with major depressive disorder (MDD) [2]

## References

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