DIET PREVENTS SOCIAL STRESS-INDUCED MALADAPTIVE NEUROBEHAVIORAL AND GUT MICROBIOTA CHANGES IN A HISTAMINE-DEPENDENT MANNER

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BACKGROUND & AIM OF THE STUDY

Psychosocial stress is a substantial risk factor in the occurrence of mood and anxiety disorders[1].

A healthy diet, rich in polyphenols, vitamins, and omega-3 polyunsaturated fatty acids (Omega3-PUFAs), exerts favourable effects on cognitive performance and stress reactivity[2]. Altered Polyunsaturated fatty acids (PUFAs) metabolism has been reported to be involved in different neurological disorders via sustained neuroinflammatory processes[3]

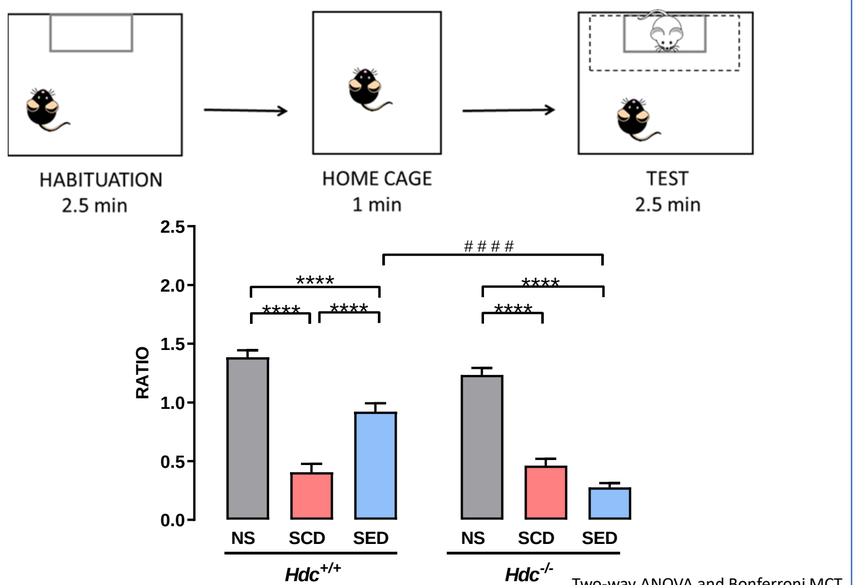
As the brain histaminergic system is crucial in controlling arousal and cognition and is profoundly affected by stress[4], here **WE INVESTIGATED ITS INVOLVEMENT IN THE EFFECTS PRODUCED BY CHRONIC STRESS AND DIETARY SUPPLEMENTATION WITH ω-3 PUFA/VITAMIN-A IN MICE**.

MATERIALS AND METHODS

C57Bl/6 histidine depleted animals (*Hdc*$^{-/-}$) mice and *Hdc*$^{+/+}$ littermates fed with control (SCD) or enriched diet (SED) after weaning were subjected to 10-days chronic social defeat stress (CSDS). Non-stressed HDC$^{-/-}$ and HDC$^{+/+}$ mice fed with control diet served as controls (NS). At the end of the stress protocol, we tested mice social aversion in the Social Interaction Test (SIT) and cognitive performance in the Novel object recognition (NOR) and Novel Object Location (NOL) tests. Then, we collected faecal pellets for microbiota analysis and hippocampus (hip) for Long-Term Potentiation and fatty acid analysis.

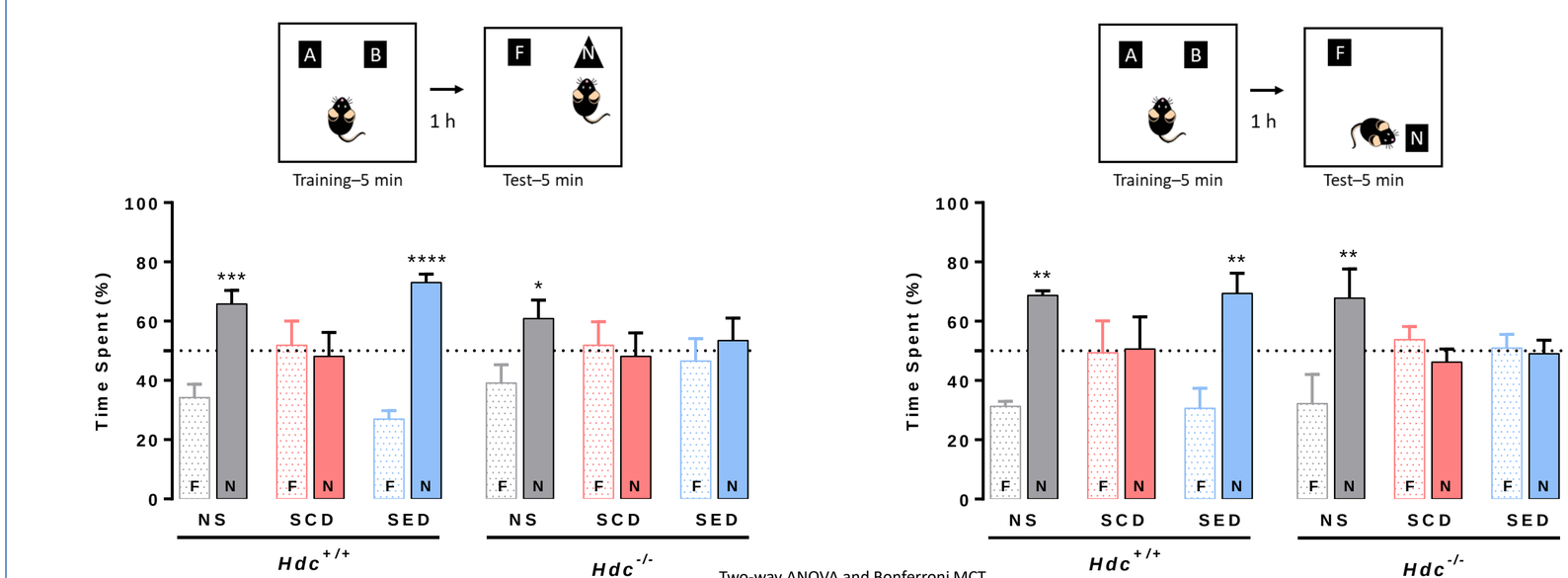
RESULTS

Diet reduces social avoidance induced by CSDS in HDC$^{+/+}$ mice



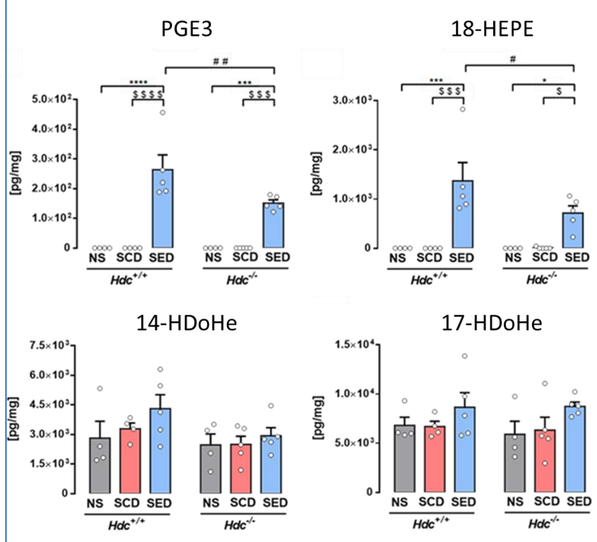
Two-way ANOVA and Bonferroni MCT
**** p<0,0001; n=27-34

Diet ameliorates the memory impairment induced by CSDS in HDC$^{+/+}$ mice but not in HDC $^{-/-}$



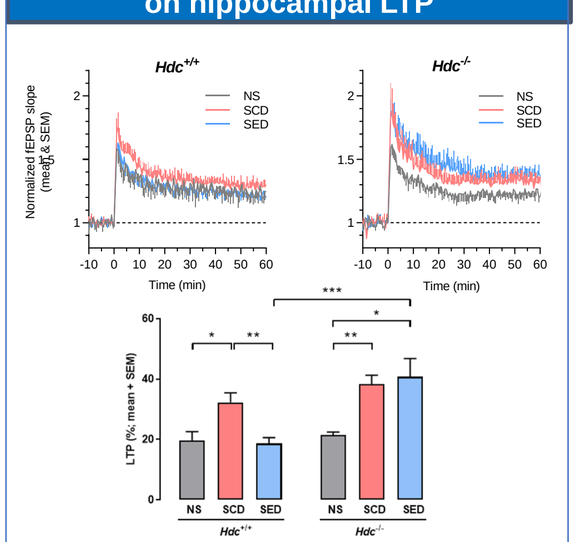
Two-way ANOVA and Bonferroni MCT
**** p<0,0001; ***p<0,001; ** p<0,01; *p<0,05 n=5-9

Diet increases EPA metabolite



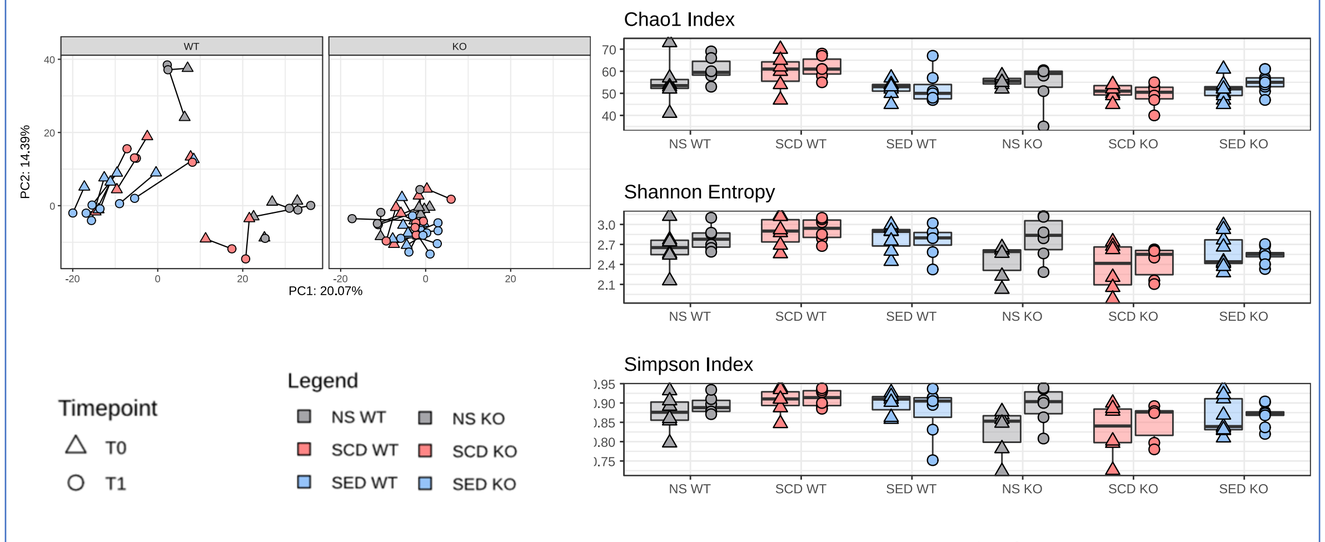
Two-way ANOVA and Bonferroni MCT
**** p<0,0001; ***p<0,001; ** p<0,01; *p<0,05 n=4-5

Diet prevents CSDS-induced alteration on hippocampal LTP



Two-way ANOVA and Bonferroni MCT
***p<0,001; ** p<0,01; *p<0,05 n=4-5

Absence of histamine affects the microbiota composition in stress and diet



Two-way ANOVA and Bonferroni MCT
n=5-6

CONCLUSION

CSDS induced social avoidance, poor recognition memory, affected long-term potentiation in hippocampal CA1 region, caused changes in microbiota profile, brain fatty acid and oxylipins composition of both *Hdc*$^{-/-}$ and *Hdc*$^{+/+}$ mice. Dietary enrichment counteracted stress-induced deficits only in *Hdc*$^{+/+}$ mice; histamine deficiency prevented almost all these diet-related beneficial effects. Our results suggest that peripheral signals generated by the diet converge onto the central histaminergic system that provides the necessary central signalling to prevent CSDS-induced alterations. Our data also indicate that histidine decarboxylase has a role in modulating diet-microbiome interactions following stress with potential implications for the microbiota-gut-brain axis.

References

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Acknowledgments

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