PHQ-9, and YBOCS scales were applied. To estimate the RNFL, macula, and choroidal thickness changes before and after rTMS treatment, spectral domain optical coherence tomography (SD-OCT) and enhanced depth imaging OCT (EDI-OCT) were used. The response to TMS therapy and its effects on the retina were calculated using further statistical analysis.

Result: In this present study, it was demonstrated that TMS therapy did not lead to a significant change in RNLF, macula, or choroid thickness. Following TMS therapy, a change of over 50% in the HAM-17 and PHQ9 scales was considered a response to the treatment, and it was observed that the response of patients to the treatment was significant ($p<0.001$). The retinal variables of patients responding to r-TMS therapy were evaluated in comparison to those who did not respond, and no significant difference was observed ($p > 0.5$).

Conclusion: It was demonstrated that r-TMS treatment had no significant effect on RNLF, macula, or choroid thickness. It is considered that, for patients with high myopia and being followed for retinal detachment diagnosis, there is no need for an additional retinal examination beyond the pre-TMS treatment assessments.

No conflict of interest

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ACUTE DIAZEPAM CHALLENGE NORMALISES HIPPOCAMPAL CEREBRAL BLOOD FLOW IN INDIVIDUALS AT CLINICAL HIGH-RISK FOR PSYCHOSIS

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Background: Hippocampal and subfield-specific hyperactivity (i.e., increased resting cerebral blood flow/volume [rCBF/rCBV]) observed in individuals at clinical high-risk for psychosis (CHR-P) may be a novel pharmacological target. Preclinical studies in a neurodeveopmental disruption model have demonstrated GABAergic pharmacological agents such as benzodiazepines can downregulate hippocampal hyperactivity and prevent the emergence of psychosis-like phenotypes. This suggests GABAergic treatments may be a potential therapeutic option for psychosis prevention in CHR-P individuals. However, mechanistic evidence of the effects of a GABAergic drug on hippocampal hyperactivity in this clinical population is first required.

Aims: To determine whether acute dose of diazepam can reduce and normalise hippocampal and subfield rCBF in CHR-P individuals.

Methods: We conducted a within-subject, double-blind, placebo-controlled, randomised, cross-over design study in 24 CHR-P individuals (mean [±SD] age: 24.1 [±4.8] years, 15F). Participants underwent two MRI sessions, three weeks apart; once under a single dose of diazepam (5 mg) and once under placebo (50 mg ascorbic acid). rCBF was measured using a pseudocontinuous arterial spin labelling sequence and a previously collected dataset of 21 healthy controls (HC) was used for comparison. Subject-specific hippocampus and subfield masks were generated using the MAGeT Brain toolbox. Using the minc-toolkit-v2/1.9.18, these masks were registered and resampled to the individual's respective rCBF map, and the mean rCBF value was extracted per hemisphere in native space from the following regions: whole hippocampus, CA1, subiculum, CA4/dentate gyrus, and total brain grey matter. Individual Mixed ANCOVAs (covarying for global rCBF, age, and sex) and linear mixed-effects models (participant ID as random effect) investigated the effect of group (CHR-P placebo vs. HC and CHR-P diazepam vs. HC) and drug (CHR-P placebo vs. diazepam), respectively, on hippocampal/subfield rCBF per ROI. These models were repeated voxel-wise in study-specific template space to investigate whole-brain effects. Significance was set at $pFDR<0.05$. Pearson's correlations assessed whether baseline clinical characteristics could predict diazepam-induced changes in hippocampal rCBF.

Results: CHR-P individuals under placebo showed significantly increased rCBF compared to HC in the hippocampus ($F(1,41)=24.7$, $p_{FDR}<0.001$), and this was significantly reduced by diazepam ($t(69)=-5.1$, $p_{FDR}<0.001$) to the extent that it no longer differed from HC ($F(1,41)=0.4$, $p_{FDR}=0.204$). This effect of hyperactivity and normalisation under diazepam was seen across all subfields studied and in several psychosis-relevant cortical and subcortical regions connected to the hippocampus, including medial/dorsolateral prefrontal cortex, nucleus accumbens, and amygdala. Smallest reductions in diazepam-induced bilateral hippocampal rCBF change were observed in CHR-P individuals with highest attenuated psychotic symptom severity ($r= 0.494$, $p=0.014$) and poorest social functioning ($r=-0.416$, $p=0.043$) at baseline, which appeared to be driven by the left CA4/DG (positive symptom severity: $r=0.528$, $p=0.008$; social functioning: $r=-0.503$, $p=0.012$).

Conclusions: Acute diazepam challenge effectively reduced increased rCBF in the hippocampus and subfields of CHR-P individuals, providing proof-of-concept of the efficacy of GABA-enhancing drugs to modulate hippocampal hyperactivity in this clinical group. Our results that CHR-P individuals who were clinically most unwell showed the smallest changes in rCBF suggest the development of more hippocampal-selective GABAergic pharmacological agents (e.g., those targeting a5-$GABA_A$ receptors) as a promising strategy for regulating hippocampal hyperactivity and preventing psychosis development.

No conflict of interest

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EFFECTS OF CHRONIC OXYTOCIN ADMINISTRATION ON THE ENDOGENOUS OXYTOCIN SYSTEM IN CHILDREN WITH AUTISM

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Background: In recent years, single dose administration of oxytocin nasal spray has been increasingly explored as a potential therapeutic approach for autism given its beneficial effects on both social communication and repetitive and restrictive Behaviours and interests (RRBI's). Research into chronic administration, on the other hand, shows a more complex pattern of results with some studies yielding positive outcomes, while others demonstrated no behavioural benefit from receiving oxytocin, compared to placebo. An important, yet unknown, underlying explanation for these inter-individual differences might relate to differences in oxytocin's biological effects and in particular how chronic administration regimes impact endogenous oxytocinergic function. This knowledge is important, since biological changes might underlie oxytocin-induced behavioural-clinical outcomes [1] and therefore allow delineating possible biological mechanisms of inter-individual variation in clinical treatment responses.

Methods: We conducted a double-blind, randomized, placebo-controlled trial investigating the effects of multiple-dose oxytocin administration (4 weeks, daily 2 x 12 IU) in children with autism. 79 children with autism (8 to 12 years old, 16 females) were included. During this trial salivary sampling, for assessing hormonal levels of oxytocin and DNA methylation of the oxytocin-receptor gene (OXTR DNAm), was performed at baseline (pre-treatment, T0), immediately (24 hours) after the four-week nasal spray administration period (T1) and at a follow-up session, four weeks after the last nasal spray administration (T2). To assess oxytocin-induced effects, OXTR DNAm and hormonal levels were analysed using mixed-effects analyses of variances and Bonferroni-corrected post-hoc tests. Next, Spearman correlation analyses were performed to examine whether variations in increases in salivary oxytocin levels, were associated to variations in OXTR DNAm or variations in clinical-behavioural assessments within the oxytocin group.

Results: Results revealed a significant nasal spray x assessment session interaction effect ($F(1,74) = 15.71$; $p < .001$; $\eta p^2 = .18$), indicating that children receiving the oxytocin nasal spray, compared to placebo, displayed significantly higher salivary oxytocin levels at T1, but no longer at the T2. Regarding epigenetics, oxytocin-induced reductions in OXTR DNAm were observed both at T1 and T2, reflecting a facilitation of oxytocin receptor expression in the oxytocin, compared to the placebo group ($F(1,70) = 7.76$; $p = .007$; $\eta p^2 = 0.10$). Notably, heightened oxytocin levels post-treatment were significantly associated with reduced OXTR DNAm ($\rho = -.39$; $p = .018$) and improved feelings of secure attachment ($\rho = .35$; $p = .030$).

Conclusion: Four weeks of chronic oxytocin administration stimulated the oxytocinergic system in children with autism, as evidenced by increased salivary oxytocin levels and reduced OXTR DNAm. Furthermore, elevated oxytocin levels post-treatment were associated with a better clinical presentation, indicating an important mechanistic link between oxytocin's chronic biological and clinical-behavioural effects. This important knowledge may lead to a personalized therapeutic approach for children with autism, depending on their naturally occurring oxytocin.

References

[1] K. J. Parker et al., "Intranasal oxytocin treatment for social deficits and