Magnetic resonance spectroscopy analysis in the right dorsolateral prefrontal cortex of patients at high-risk of developing schizophrenia

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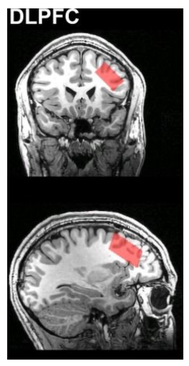
Introduction

- **Cognitive deficits can be observed before the first episode of psychosis** (FEP)[1], and in particular related to different memory domains[2].
- **Currently**: no significant metabolic alterations have been consistently reported in the dorsolateral prefrontal cortex (DLPFC) of individuals before and during FEP[3].
- **Why**: Mapping the effects of specific metabolites on cognition before and after transition to FEP may improve our understanding of how psychotic symptoms emerge.
- **Aim**: Compare effects of Glu, Gln, Glx, Ins, NAA, Cr, and GABA in the right dorsolateral prefrontal cortex (DLPFC) on different cognitive domains, for patients at risk of developing a first episode of psychosis (from familial high risk: HR-F, to clinical high risk: HR-NF, to FEP).

Methods

Data Acquisition



- CogState Test[4] : verbal memory, working memory, executive functioning, speed of processing, visual memory, visual attention and social cognition.
- Structural scan with Siemens 3T Magnetom (TE/TR=2.98 ms/2300 ms, TI=900 ms, α=9°, FOV = 256x240x176 mm3, 1.00 mm isotropic resolution).
- MRS scan with SPECIAL sequence of DLPFC[5] and water unsuppressed scan (TR/TE = 3000/8.5 ms, 2048 spectral points, 2000 Hz spectral width, 192 averages, shimming).

Metabolite Quantification

- MATLAB FID-A Toolkit[6] for spectral preprocessing (combination of receiver channels, motion corruption average removal, spectral registration, phase drift correction, left shifting. No apodization, filtering, baseline correction or residual water peak removal operations).
- LCModel 6.3[7] basis set fitting (spectral window of 0.4 and 4.2 ppm, eddy current correction, water scaling).
- Gannet 3.1[8] and SPM-12[9] for calculation of absolute concentration of neurotransmitters[10].

Statistical Analysis:

Vertex-wise linear model:

lm: (cognitive score) ~ (metabolite) * (group) + (age) + (sex)

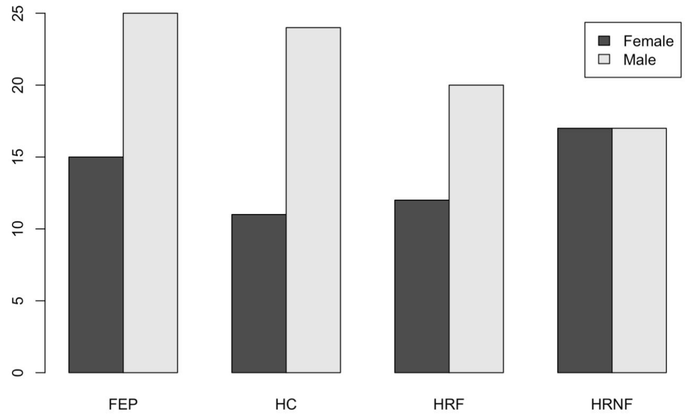
All 7 cognitive scores and 7 metabolites (mmol/kg) were z-scored and the standard deviation for the metabolite concentration was used as a weight in our model. All of t-values, p-values and Bonferroni corrections are reported.

Sample

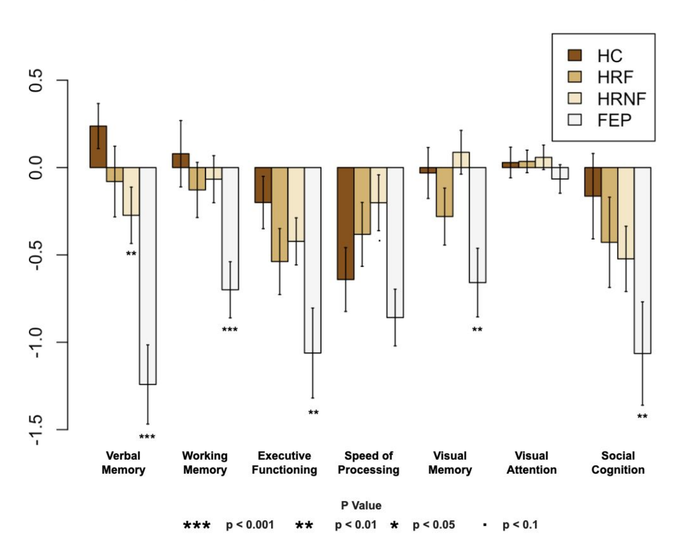
Source: Prevention and Early Intervention for Psychosis, Douglas Clinic.

Healthy Control (HC)	n = 35
High risk familial (HR-F)	n = 32
High risk non familial (HR-NF)	n = 34
First Episode of Psychosis (FEP)	n = 40

Age Range: 14-35 years old.
Sex Distribution:



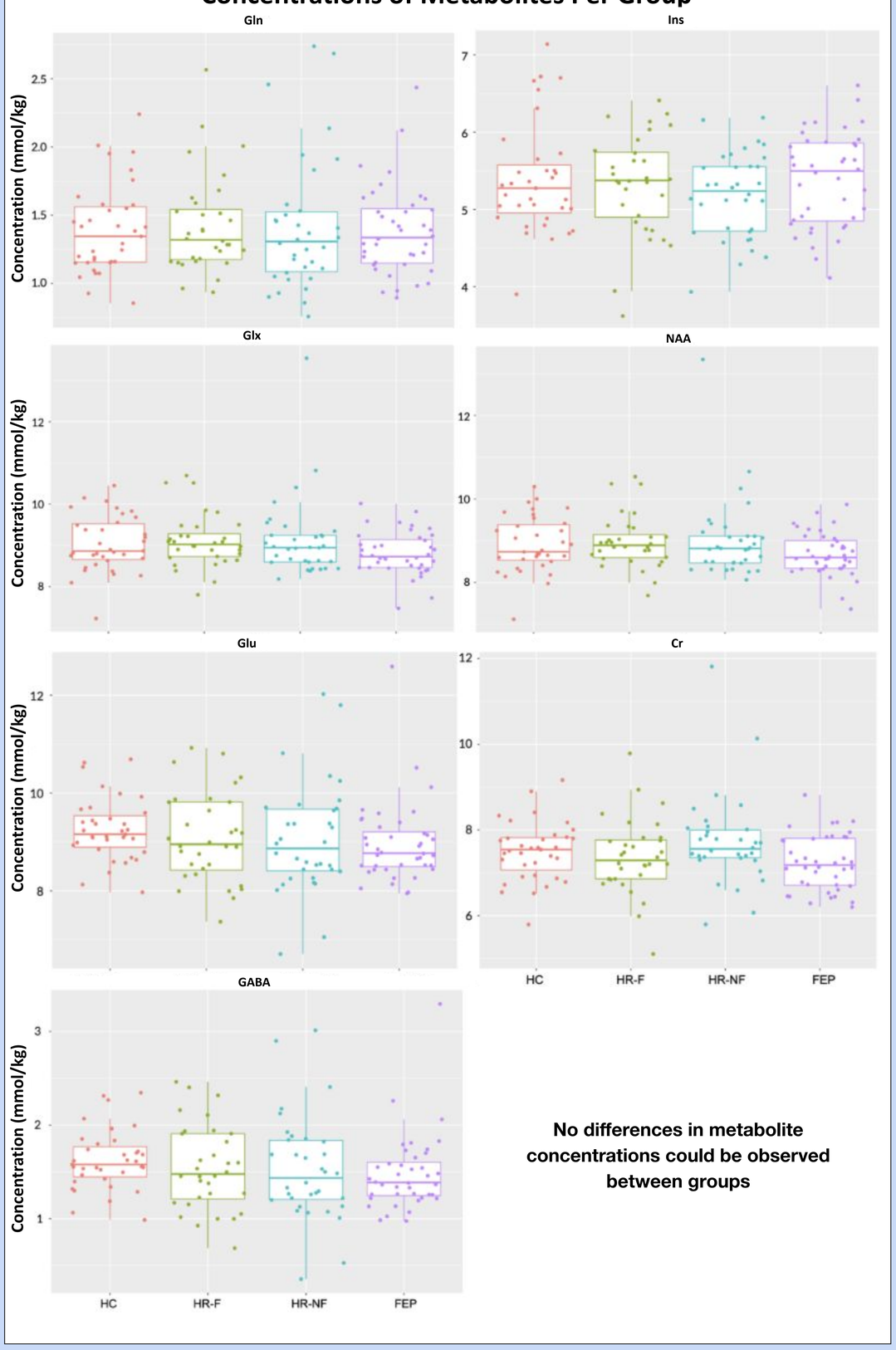
Average Cognitive Scores Per Group



There was a step-wise difference in cognitive deficits across groups:

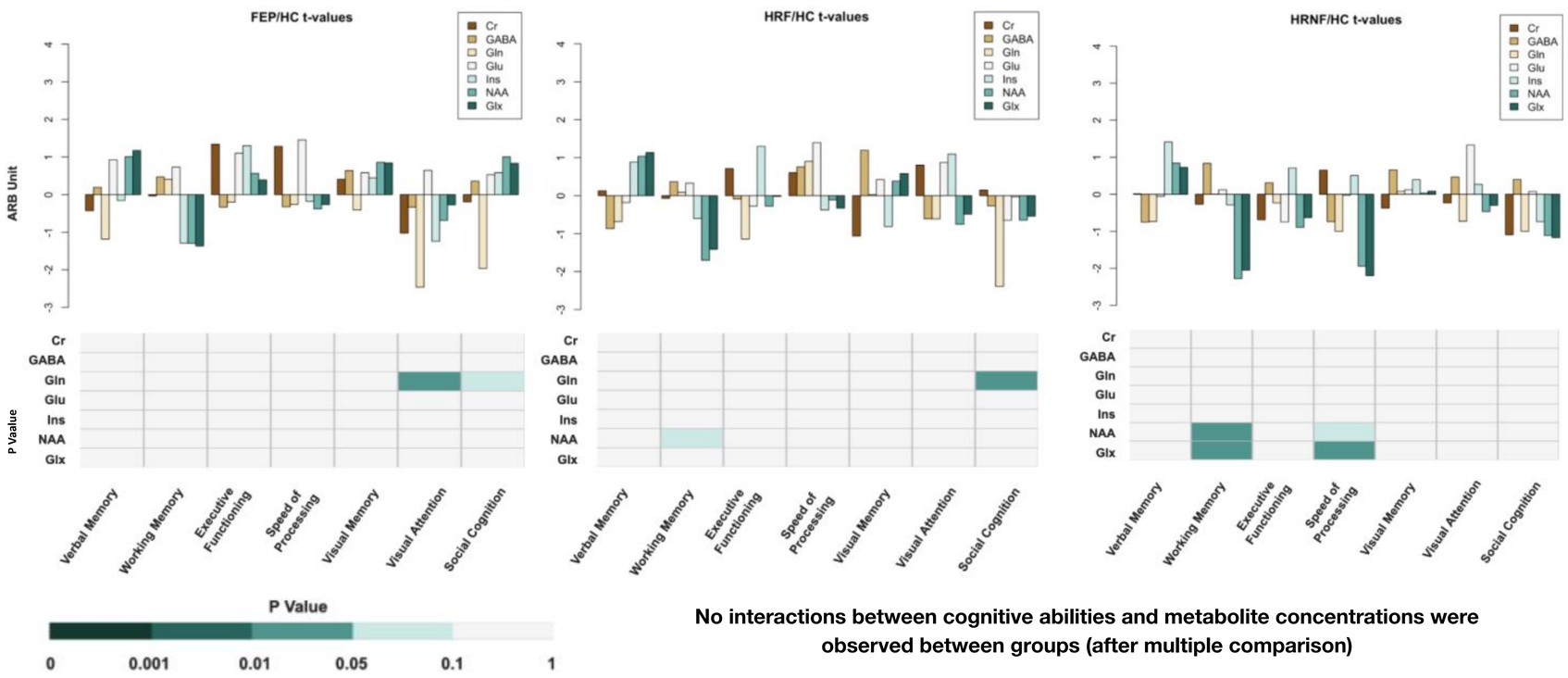
- Significant cognitive deficits for FEP,
- Significant deficits in verbal memory for HR-NF,
- No significant deficit for HR-NF,
- Note: Significant sex effects for verbal memory ($p < 0.001$).

Concentrations of Metabolites Per Group



No differences in metabolite concentrations could be observed between groups

Interactions between Cognitive Scores and Metabolites by Group Compared to Healthy Controls



No interactions between cognitive abilities and metabolite concentrations were observed between groups (after multiple comparison)

Summary

- Our results **do not indicate significant effects** of metabolites in the right DLPFC on the cognitive deficits observed across FEP and HR groups.
- **Other mechanisms and areas potentially responsible for negative symptomatology should be equally considered** in accounting for the neurobiological basis of psychosis.
- This study could be improved by: **being longitudinal**, **studying both the Left-DLPFC and Right-DLPFC in tandem.**

References

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