Integrity of the fornix-hippocampus circuit and relationship with peripheral oxidative stress markers in early phase psychosis

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INTRODUCTION

- Hippocampal atrophy is well described in chronic schizophrenia and is closely associated with loss of integrity in the fornix. Whether this relationship is already present in the earlier stages of the disease is unknown.
- Further, in an animal model of schizophrenia with glutathione deficit (GCLM-KO mouse), the fornix ***(See poster 619 by A. Corcoba)*** and hippocampus are very vulnerable to oxidative stress.
- The purposes of the current study were: i) confirm the presence of white matter alterations in the fornix in the beginning of the disease, ii) assess hippocampus integrity with volumetry and diffusion MRI, iii) study the correlation between fornix metrics and hippocampus metrics, iv) study the relationship between loss of integrity in the fornix-hippocampus circuit and peripheral oxidative stress markers

METHOD

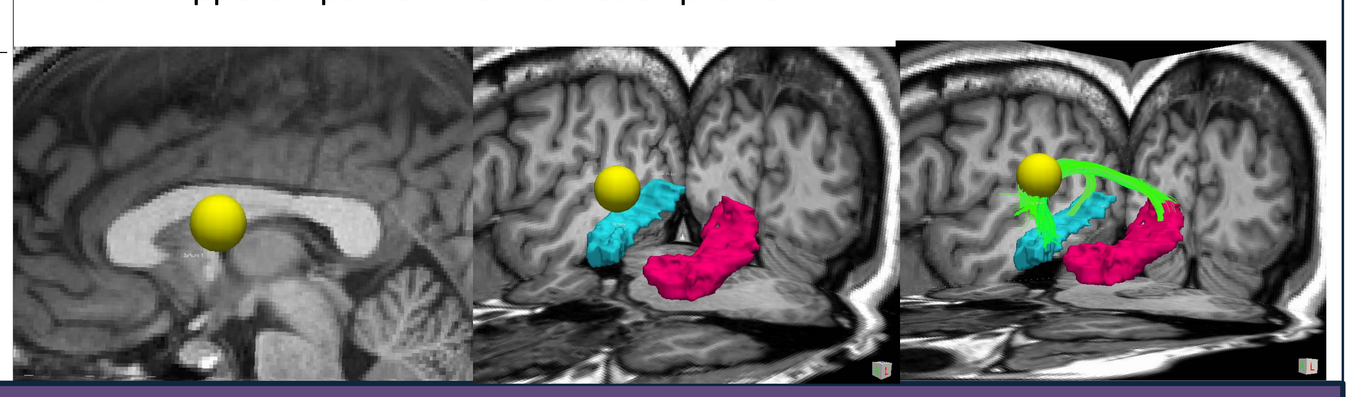
Sample description

- Patients in the early phase of psychosis, having met psychosis threshold (CAARMS criteria) (27) were recruited from the TIPP Program (Treatment and Early Intervention in Psychosis Program, University Hospital, Lausanne, Switzerland)

	Early psychosis patients N=38 Mean +/- SD	Control subjects N=38 Mean +/- SD	T-test* or chi-square**
Age, years	25.1 ±5.8	25.1± 5.7	p=0.997*
Gender, M/F	23/15	27/11	p=0.333**
Handedness R/L/A	32/4/2	31/6/1	p=0.688**
Duration of illness, days	760.7 ± 648.3 (112-2615)	--	--
Medication dose, mg	339.1 ± 217.7	--	--

Imaging method

- Diffusion Spectrum Imaging (DSI) and T1 weighted high resolution MRI were used to assess fornix and hippocampus in 38 EP patients as well as 38 gender and age-matched controls.
- Generalized Fractional Anisotropy (gFA), Apparent Diffusion Coefficient (ADC) and structure volume were used to measure fornix and hippocampal integrity.
- Pearson correlation was used to assess the relationship of gFA in the fornix and hippocampal volume with redox profile.

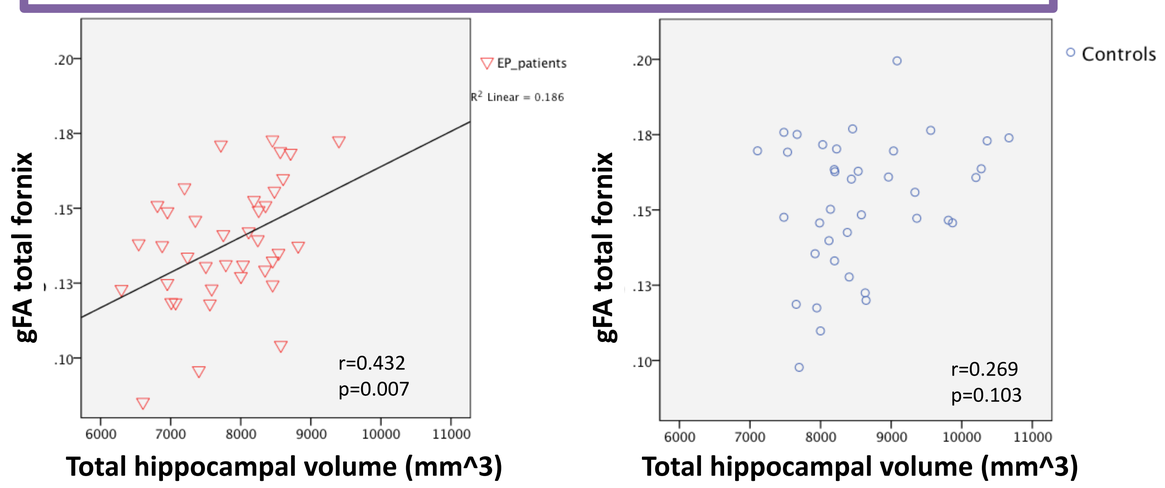


RESULTS

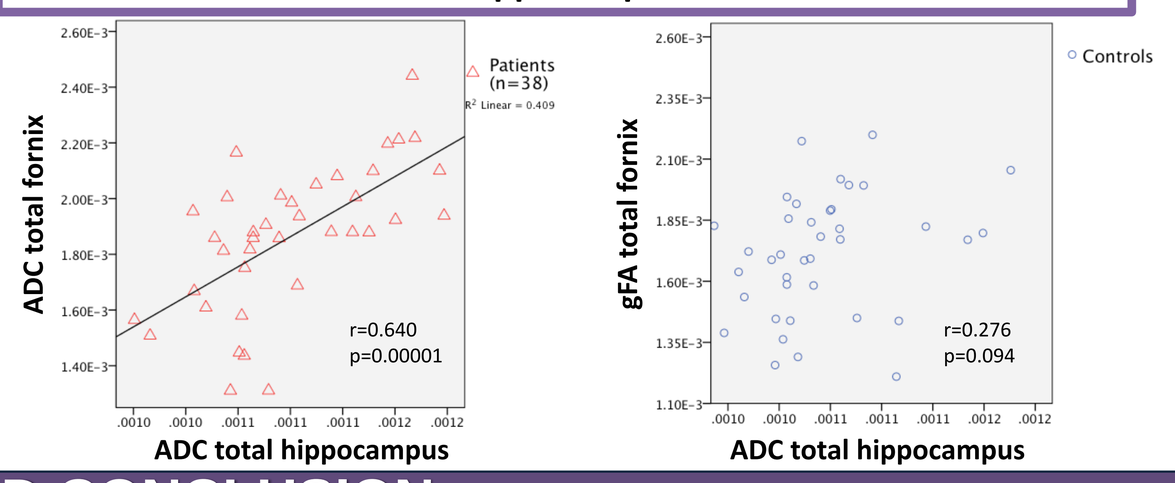
Differences between patients and controls

left + right	Mean controls (n=38)	SD	Mean patients (n=38)	SD	p value
Hippocampus volume (mm^3)	8583.0	901.0	7810.4	750.2	0.000**
corrected hippocampus volume (mm^3)	8583.0	642.1	8135.2	661.3	0.004**
ADC hippocampus	0.001	0.000066	0.001	0.000077	0.001**
gFA hippocampus	0.080	0.0052	0.077	0.0072	0.065
volume fornix (mm^3)	3.54	0.58	3.11	0.84	0.012**
gFA fornix	0.152	0.022	0.138	0.020	0.005**
ADC fornix	0.0017	0.00025	0.00190	0.00026	0.012**

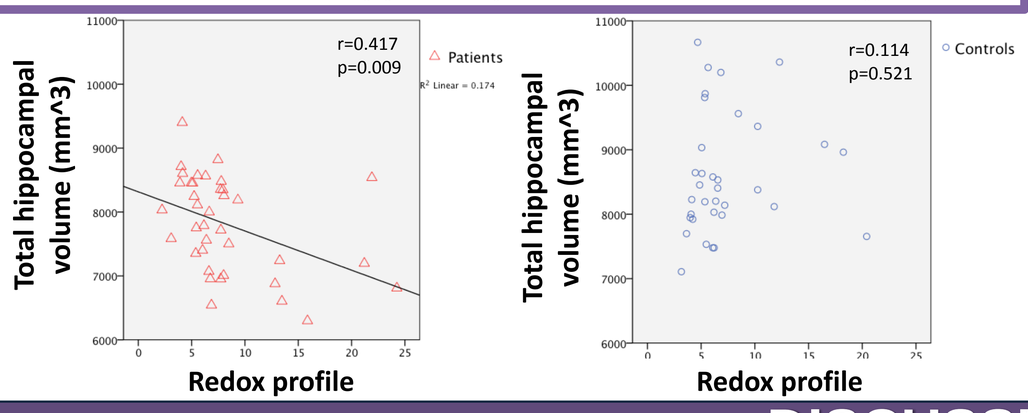
Correlation between hippocampus volume and fornix gFA



Correlation between hippocampus ADC and fornix ADC



Correlation of total hippocampal volume with redox profile



DISCUSSION AND CONCLUSION

- Abnormalities in the fornix and hippocampus are already present in the early stages of psychosis and are closely related to each other.
- In EP but not in controls, lower hippocampal volume (but not fornix integrity) was associated with redox profile dysregulation, which adds to the existing literature implicating redox dysregulation in schizophrenia and may pave the way for the search for clinical useful peripheral biomarkers.

ACKNOWLEDGMENT

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