

Correlation among in vivo 1H-MRS metabolic profiles, genetic and clinical data in schizophrenic patients

B. Celda^{1,2}, B. Martínez-Granados¹, M. Martínez-Bisbal², O. Brotons³, E. J. Aguilar³, L. Martí-Bonmatí⁴, R. de Frutos⁵, O. Rivero⁵, and J. Sanjuán⁶

¹Physical Chemistry, University of Valencia, Burjassot, Valencia, Spain, ²Physical Chemistry-UVEG, CIBER-BBN, Burjassot, Valencia, Spain, ³Clinic Hospital Valencia, Psychiatry Unit, Valencia, Valencia, Spain, ⁴Radiology Unit, Dr. Peset Hospital, Valencia, Valencia, Spain, ⁵Genetics, University of Valencia, Burjassot, Valencia, Spain, ⁶Department of Psychiatry, University of Valencia-CIBERSAM, Valencia, Valencia, Spain

Introduction

Schizophrenia is a severe mental disorder affecting nearly 1% of the population. The nature and ethiology of this dysfunction remain unknown. Researches suggest that schizophrenia impacts on several brain regions. Auditory hallucinations (AH) are one of the core symptoms in Schizophrenia. A recent model suggests an alteration in language and emotional processing in which the thalamus is largely involved. In vivo metabolic alterations in thalamus have been previously reported for schizophrenia patients [1]. These thalamus metabolic modifications were larger in schizophrenic patients with AH. Likewise, it has been shown that AH can be related to genetically prone subjects (genes involved in language-FOXP2 gene- and gene 5-HTT gene) [2,3]

Purpose

The aim of this communication is to explore the relation between Magnetic Resonance Spectroscopy (MRS) metabolic abnormalities of thalamus with some particular hallucinations features through specific clinical scale and with two genes involved in AH: FOXP2 and 5-HTT.

Material and Methods

MRS studies (MRI 1.5 T unit) were performed in 43 schizophrenic patients and 29 control subjects for the genetic/metabolic correlation study and in a subgroup of 20 patients with schizophrenia suffering AH for the correlation with clinical data. 1H-MRS imaging was used to acquire 2 transverse slices where representative voxels of each thalamus were chosen, Figure 1. The areas of metabolites were integrated with the jMRUI program. The 20 patients were clinically assessed with Psychotic Symptom Rating Scale (PSYRATS) which measures several dimensions of AH on a five-point scale (frequency, duration, location, loudness, beliefs about the origin of the voices, amount of negative content, degree of negative content, amount of distress, intensity of distress, disruption to life and controllability of voices). Genomic DNA data was extracted from peripheral blood of patients with schizophrenia and controls according to the standard procedures [3].

Results

Regression analysis performed to evaluate the relation between each of the metabolic ratios (NAA/Cr, NAA/Co, Co/Cr) of each thalamus (right and left) and total PSYRATS score are shown in Table 1.

Significant correlations were found in the following PSYRATS items: **a**) *Intensity of distress*: negative correlation to NAA/Co ratio was found in right ($p=0.01$, $R=-0.564$, $b=-1.443$) and left thalamus ($p=0.03$, $R=-0.623$, $b=-1.516$); positive correlation to Co/Cr was found in left thalamus ($p=0.009$, $R=0.569$, $b=4.014$); **b**) *Amount of distress*: Co/Cr ratio positively correlated to “amount of distress” item in left thalamus ($p=0.031$, $R=0.484$, $B=3.665$); **c**) *AH duration*: this item correlated positively to Co/Cr item in both thalamus, right ($p=0.05$, $R=0.607$, $b=2.923$) and left ($p=0.048$, $R=0.447$, $b=3.086$); **d**) *AH loudness*: the results showed a negative correlation to NAA/Cr ratio in left thalamus ($p=0.042$, $R=-0.459$, $b=-0.767$); **e**) *Degree of negative content of the A*: this item correlated positively to Co/Cr in left thalamus ($p=0.046$, $R=0.452$, $b=2.64$).

Total PSYRATS score correlation: a negative and bilateral correlation to NAA/Co and positively to Co/Cr in left thalamus, Table 1.

The rest of the PSYRATS items (frequency of AH, location, beliefs about the origin of the voices, amount of negative content, disruption to life and controllability of voices) didn't show significant correlations to any of the metabolite ratios.

NAA/Cr value was lower in schizophrenic patients with *SS* polymorphism in the serotonin transporter gene (5-HTT) than for those with *SL* one, whereas NAA/Cr was higher for the patients with *LL* polymorphism. Statistical significant differences were found for NAA/Cr when grouped patients and controls with *SS+SL* polymorphisms respect to those with *LL*. Non statistical results between metabolic profiles and language-FOXP2 gene were obtained.

Discussion/Conclusion

Metabolic ratios alterations correlate with two features of hallucinations: a) those with an emotional content (intensity and amount of distress) and b) those related to language (duration, intensity and negative content of the voices). Likewise, an interesting correlation between metabolic results in thalamus and 5-HTT polymorphism with some items of PSYRATS subscale and with total score of PSYRATS has been found [3]. These results may support thalamus implication in the pathogenesis of AH.

References

[1] Martínez-Granados et al. Schizophr Res 2008; 104: 13-22; [2] Sanjuán et al. British J Psychiatry 2006; 188: 190 ; [3] Sanjuán et al. Int J Neuropsychopharmacol 2006; 9: 131-3.

Acknowledgements

Ministerio de Educación y Ciencia del Gobierno de España (SAF2007-6547) and European project: eTUMOUR (contract no. FP6-2002-LIFESCIHEALTH 503094).

Table1.- Correlation total PSYRATS score-metabolite ratios (Rho Spearmann)

PSYRATS	NAA/Co		NAA/Cr		Co/Cr	
	Right thalamus	Left thalamus	Right thalamus	Left thalamus	Right thalamus	Left thalamus
Rho	-0.567	-0.569	-0.235	-315	0.349	0.560
p	p=0.009	p=0.009	p=0.319	p=176	p=0.131	p=0.10

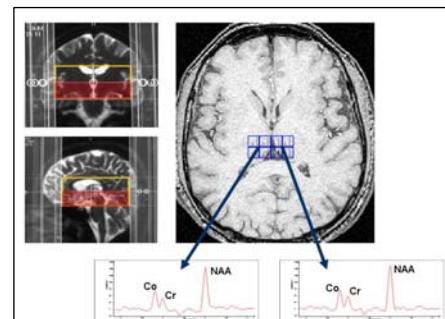


Figure 1.- Example of MRSI location and spectra results. Left: coronal and sagittal slices with the slab saturation bands. Right: transversal MRI slice with the 4 spectrum used for the average of left and right thalamus metabolic studies.