In vivo 9.4T 1H MRS for evaluation of brain metabolic changes in the Ts65Dn mouse model for Down syndrome

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Purpose:

Down Syndrom (DS) (human trisomy 21) is a chromosomal abnormality characterized by the presence of an additional copy of some genes on chrosome 21. This pathology is characterized by a set of behavioural, morphological and metabolic alterations. Ts65Dn model is the most widely studied mice model for DS. This mouse is trisomic for the chromosome 16 which is homologous to human chromosome 21. Some studies have been performed on Ts65Dn mice on the hippocampus and the cerebellum but never in vivo with MRS. The aim of this study was to quantify changes in brain metabolites for TS65Dn mice compared to disomic mice with 9.4T Magnetic Resonance Spectroscopy (MRS).

Material and methods:

20 mice were used in this study. They were divided into two groups: Ts65Dn and disomic (2n) mice. MR experiments were performed on a 9.4 T horizontal magnet (94/20 USR Bruker Biospec, Wissembourg, France) with a 35mm diameter birdcage coil. A PRESS sequence (TR=4s, TE=15ms) with water supression (VAPOR) and Outer Volume Supression (OVS) was used to record 1H spectra in a 2*2*2mm voxel in the hippocampus and in the cerebellum. 256 scan were performed for a total acquisition duration of 17 min. Several metabolites (NAA, choline, myo-inositol, glutamate, glutamine) were then quantified on the spectra with JMRUI3.0 (2001, www.mrui.uab.es/mrui/).

Results:

Quantification of metabolites for both cerebellum and hippocampus are presented tables 1 and 2:

		HIPPOCAMPUS		
	2n (n=10)	**Ts65Dn (n=10)**	**% change**	**p value**
Cr+PCr=Cx	**18865 (430)**	**20198 (510)**	**10%**	**NS**
NAA/Cx	**0.66 (0.02)**	**0.31 (0.03)**	**-54%**	**<0.01**
Gln+Glu/Cx	**0.38 (0.03)**	**0.29 (0.04)**	**-24%**	**<0.01**
Cho/Cx	**0.61 (0.04)**	**0.83 (0.03)**	**14%**	**<0.01**
Ins/Cx	**0.21 (0.03)**	**0.36 (0.02)**	**17%**	**<0.01**
Tau/Cx	**0.65 (0.02)**	**0.61 (0.04)**	**-6%**	**NS**
Lac/Cx	**0.34 (0.02)**	**0.35 (0.03)**	**11%**	**NS**

Table 1 : In vivo MRS results showing metabolites changes in 2n and Ts65Dn mice in the cerebellum. Values are expressed as mean (S.D). Mann-Whitney p values for comparison between 2n and Ts65Dn.

		CEREBELLUM		
	2n (n=10)	**Ts65Dn (n=10)**	**% change**	**p value**
Cr+PCr=Cx	**25280 (660)**	**24292 (570)**	**-4%-**	**NS**
NAA/Cx	**0.83 (0.11)**	**0.62 (0.02)**	**-25%**	**<0.01**
Gln+Glu/Cx	**0.45 (0.07)**	**0.20 (0.03)**	**-56%**	**<0.01**
Cho/Cx	**0.82 (0.05)**	**0.82 (0.04)**	**0%**	**NS**
Ins/Cx	**0.75 (0.2)**	**0.25 (0.01)**	**-67%**	**<0.01**
Tau/Cx	**0.39 (0.08)**	**0.35 (0.01)**	**-11%**	**NS**
Lac/Cx	**0.26 (0.02)**	**0.27 (0.04)**	**10%**	**NS**

Table 2 : In vivo MRS results showing metabolites changes in 2n and Ts65Dn mice in the hippocampus. Values are expressed as mean (S.D). Mann-Whitney p values for comparison between 2n and Ts65Dn.

In the Ts65Dn mice cerebellum, there are significant concentration decreases in myo-inositol (-67%), NAA (-25%) and glutamate + glutamine pool (Glx) (-56%).

In the Ts65Dn mice hippocampus, there are significant increases in myo-inositol (+17%) and choline (+14%) concentrations and decreases in NAA (-54%) and glutamate + glutamine pool(Glx) (-24%) concentrations.

Conclusion

Our 9.4T MRS study showed cerebral metabolism perturbations in hippocampus and cerebellum for Ts65Dn mice. In the cerebellum the decrease in myo-inositol and NAA may be related to a decrease in granular cells density. In the hippocampus the increase in myo-inositol may be related to the presence of SLC5A3 gene in three copies which codes for the Na+-myo inositol cotransporteur. The Decrease in NAA can be explained by a neurodegenerescence and loss of cholinergic neurons. The decrease in glutamate+glutamine pool may be related to neuronal loss or glial default.