EFFECTS OF CAFETERIA DIET AND VOLUNTARY RUNNING ON BRAIN STRUCTURE AND METABOLISM IN MICE

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Introduction:

Obesity is one of the major health burdens of modern societies associated with a great variety of health-threatening sequela such as diabetes, cardiovascular diseases, cancer and even psychiatric disorders. Excessive calorie intake, as a consequence of changes in appetite and satiety control, as well as limited energy expenditure is mediated by distinct brain networks. We conducted a magnetic resonance (MR) spectroscopy study investigating metabolic changes in mice receiving high lipid and carbohydrate containing diet (cafeteria diet) vs. control mice receiving standard chow in the right hippocampus and prefrontal cortex area in conjunction with voxel based morphometry (VBM) analyses.

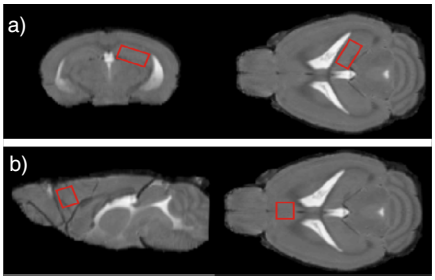

Fig. 1: a) Localization of the hippocampal voxel and b) of the voxel in the prefrontal cortex

Method:

In our experiments, we subjected 6 week old male mice to a high-caloric and highly palatable cafeteria-diet. Cafeteria-mouse models are established animal models [1] for metabolic syndrome in humans. **Cafeteria-mice** (**CAF**) were provided with 14 human snack foods varied every two days in addition to ad libitum standard chow. Control mice received only **standard chow** (**SC**). The CAF diet foods were provided in excess and included cookies, cereals, cheese, processed meats, and crackers. Before and after consumption, CAF and SC diets were weighted and corrected for drying. In addition, half of the mice received **running wheels** (**RUN**) or **blocked running wheels** (**SED**). Thus 4 experimental groups were studied CAF-RUN, CAF-SED, SC-RUN and SC-SED. The daily distance of voluntary running was continuously monitored. After 8-9 weeks of running and diet consumption mice were analysed by MR spectroscopy and VBM at a 9.4T animal scanner equipped with a cryogenic mouse brain coil (Bruker, Ettlingen, Germany). Fig. 1 a/b shows the location of the two spectroscopy voxel. Sequence details: water-suppressed PRESS, TE/TR/NEX 10ms/4s/256, voxel size (Hipp): 2.2 x 1.2 x 1.2mm³; voxel size (PFC): 1.6 x 1.2 x 1.3mm³. A typical spectrum of the hippocampus voxel can be seen in Fig. 2. Absolute quantification was performed by LCModel using an unsuppressed water spectrum (PRESS, TE/NEX 10ms/1) of the respective voxel for waterscaling. For VBM a 3D T2-weighted image data set (RARE sequence with a spatial resolution of 78 x 78 x 156µm³; acq. time: 23min2s) was acquired. Group specific prior knowledge tissue maps were created according to [2]. Overall 44 mice were examined. Spectroscopic results with a Cramer-Rao Lower Bound of >20% were excluded. VBM gray matter (GM) tissue maps were analysed with SPM8 using a full flexible second level model with the effects running (RUN) and cafeteria diet (CAF).

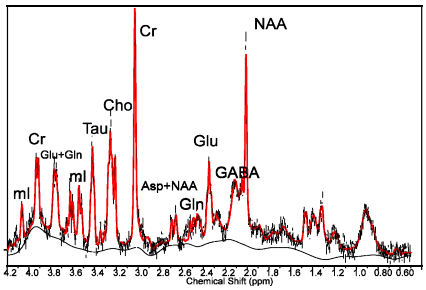

Fig. 2: Typical spectrum of the hippocampus

Results:

The groups did not differ in age (97 ± 5 d). CAF had a highly significant influence ($p < 0.001$) on weight which also showed an interaction RUN*CAF ($p = 0.037$). Running compensated the increase in weight in the CAF-RUN group. In the RUN group CAF mice had a higher average running distance (SC-RUN 7.1 ± 1.4 km/d; CAF-RUN 8.7 ± 1.8 km/d). A 2x2 factor GLM analyses yielded increased NAA+NAAG and Glu+Gln in the hippocampal voxel with the effect RUN without significant changes in the PFC. CAF results in significant decreased NAA+NAAG and Glu+Gln in the hippocampus. The latter effect is also visible in the PFC (see Tab. 1). The mean values and results of the respective group analyses (t-test) for the hippocampus MRS data are shown in Fig. 3. Note that there is no significant change between the CAF-RUN and CAF-SED group. Voxel based morphometry showed a GM increase mainly in the hippocampal area only with the effect RUN (N = 23 vs. 20) (Fig. 4a), while effect CAF (N =21 vs. 22) had no influence on brain structure (Fig. 4b). Please note that these are first results of an ongoing evaluation.

Significance of 2x2 factor GLM (Diff contrast)		
RUN	NAA+NAAG	Glu+Gln
Region Hipp	**0.024**	**0.025**
Region PFC	0.587	0.433
CAF		
Region Hipp	**<0.001**	**0.017**
Region PFC	0.43	**0.038**

Tab. 1: 2x2 GLM analyses results of MRS data.

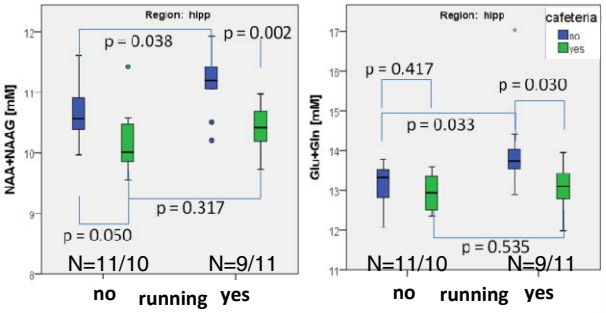

Fig. 3: Mean values of metabolites "NAA+NAAG" and "Glu+Gln" of the four different groups. Additionally p values and group sizes N are shown.

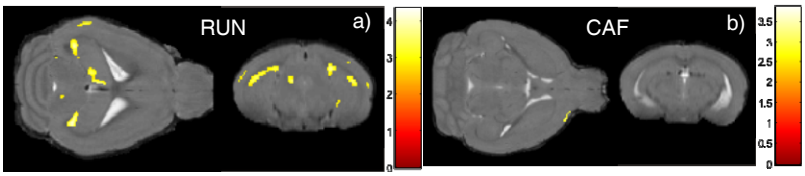

Fig. 4: a) GM increase with the effect RUN in the hippocampal area. b) Effect CAF has no influence on brain structure. (All p<0.005; uncor.)

Discussion:

We could confirm previous studies e.g. [2-5] which showed that physical exercise has an impact on the brain structure in the hippocampal area. Furthermore, we found that exercise and cafeteria diet have opposite effects. While exercising mice show increased metabolite concentrations (NAA+NAAG and Glu+Gln) and increased volume within the hippocampus, cafeteria diet counteracts the metabolic "running" effect without impact on the brain structure.

References:

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