Physical exercise impacts brain structure: A longitudinal VBM and TBSS study in overweight and obese subjects

Karsten Mueller[1], Harald E Möller[1], Alfred Anwander[1], Franziska Busse[1], Annette Horstmann[1,2], Matthias Raschpichler[2], Jöran Lepsien[1], Matthias L Schroeter[1,3], Matthias Blüher[2,4], Arno Villringer[1,3], and Burkhard Pleger[1,3]

[1]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Sachsen, Germany, [2]Integrated Research and Treatment Center (IFB) AdiposityDiseases, Leipzig, Sachsen, Germany, [3]Clinic for Cognitive Neurology, Leipzig, Sachsen, Germany, [4]Department for Internal Medicine, University Hospital Leipzig, Leipzig, Sachsen, Germany

Target audience: Researchers interested in structural brain plasticity and obesity; researchers interested in VBM.

Purpose: A growing number of magnetic resonance imaging studies show a relationship between human brain structure and body weight. Investigations in lean, overweight, and obese subjects using voxel-based morphometry (VBM) [1,2,3] and tract-based spatial statistics (TBSS) yield correlations between body weight and brain structure [4,5]. However, an open question remains whether these structural brain changes are persistent or reversible, for instance, after changes in body weight due to intensive physical exercise. To address this question, we compared parameters of grey and white matter structure in overweight to obese subjects before and after a 3-month physical exercise program in relation to the parallel loss in body weight.

Methods: Sixteen young overweight and obese volunteers (9 female, age 27.2±6.7 y, BMI 33.6±5.9 kg/m^2) participated in two structural MR scanning sessions before and after a fitness course with intensive physical training twice a week over a period of 3 months. The exercise program was accompanied by an average weight loss of 2.27 kg. In both scanning sessions, T1-weighted images were acquired on a whole-body 3T TIM Trio scanner (Siemens, Erlangen, Germany) with a 12-channel head coil using the MP-RAGE sequence. Images were processed using SPM8 and the VBM8 toolbox. Grey matter density (GMD) differences between both sessions were assessed using a paired *t*-test with a voxel threshold of $p<0.001$. To correct for multiple comparisons, significant clusters were reported with family-wise error (FWE) correction, $p<0.05$. The relationship between the individual decrease in BMI and GMD was computed using a flexible factorial design.

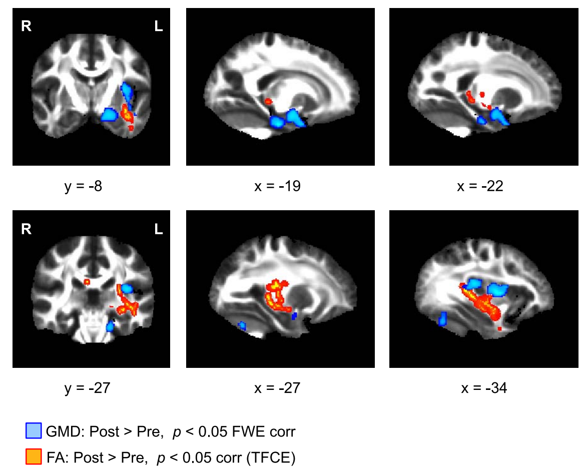

Fig. 1. Significant increase of GMD (blue) and FA (red) comparing images of two scanning sessions before and after a 3-months physical exercise program.

In addition to T1-weighted imaging, whole-brain diffusion-weighted (DW) imaging was performed (72 axial slices; 1.7mm nominal isotropic resolution; 60 gradient directions, b = 1000 s/mm², GRAPPA accel. fact. 2, NEX = 3). DW images were corrected for subject motion and registered to the T1 anatomy using rigid-body transformation computed with FLIRT. For each voxel, a diffusion tensor was fitted to the data, and the fractional anisotropy (FA) was computed. Non-linear registration was performed for inter-subject alignment with FNIRT. Using the deformed FA images, a mean image was created and thinned to create a mean skeleton, which represents the centres of all tracts common to the group. For TBSS [6], each subject's aligned FA was projected to the mean skeleton (Smith 2006). In order to detect a difference between both FA images within all subjects, randomization tests were performed with 30,000 permutations [7]. In addition to the FA, parallel and perpendicular diffusion was studied by investigating axial and radial diffusivity. Significant changes were detected using threshold-free cluster enhancement (TFCE) and correction for multiple comparisons in order to give an inference at the $p<0.05$ (corrected) level [8].

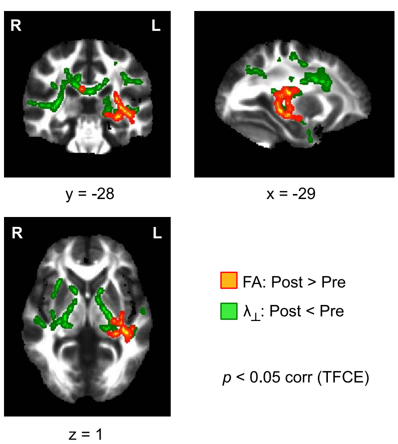

Fig. 2. Significant increase of FA (red) and decrease of radial diffusivity (green) between both scanning sessions.

Results: A comparison of the T1-weighted MRI scans before and after the 3-month exercise program yielded a significant increase of GMD in the left hippocampus, insula, and cerebellum (Fig. 1, blue). These grey matter changes were accompanied by an FA increase in white matter in the vicinity of the left hippocampus and insula (Fig. 1 and Fig. 2, red). In addition to the FA increase, a reduction of radial diffusivity was found in the same brain areas but also in further regions including the entire corpus callosum (Fig. 2, green). We did not find any significant change of axial diffusivity. In addition to the statistical pre-post-comparison, a parametric analysis was performed using a flexible-factorial design, which revealed a significant negative correlation between GMD and BMI in the left cerebellum (Fig. 3, red). This correlation was localized within the same cerebellar region as identified with the pre-post-comparison (Fig. 3, blue).

Discussion: Since previous studies found a reduced GMD in the hippocampus and cerebellum in relation to an increasing BMI [1,2,3], our findings suggest that physical exercise together with the parallel loss in body weight can reverse body weight-related grey matter changes in these brain regions. Comparing TBSS results before and after the workout program we also identified exercise-dependent changes in white matter structure in the vicinity of the altered grey matter regions as well as in further brain regions and along the corpus callosum. Previous TBSS experiments revealed a BMI-related increase of callosal radial diffusivity, specifically in women [4]. Here we found a decrease in radial diffusivity with physical exercise in a number of white matter locations including the entire corpus callosum suggesting the reversal of body-weight-dependent structural changes.

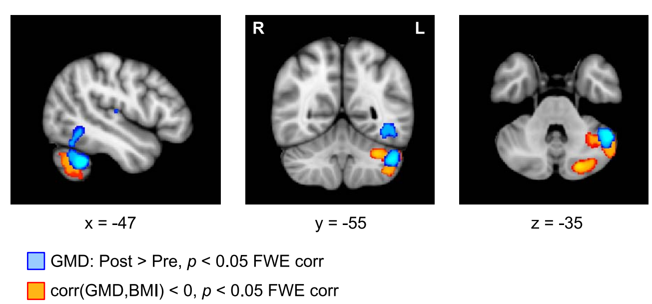

Fig. 3. Increase GMD between both sessions (blue, see Fig. 1) and significant negative correlation between GMD and BMI reduction (yellow).

Conclusion: Although only a part of the observed exercise-dependent changes in brain structure directly related to the parallel loss in body weight, our findings suggest that physical exercise can reverse some of the changes in human brain structure related to an elevated body weight.

References: **[1]** Taki Y et al. *Obesity* 2008:16:119-24. **[2]** Walther K et al. *Human Brain Mapping* 2010:31:1052-64. **[3]** Raschpichler M et al. *BMJ Open* 2012: in press. **[4]** Mueller K et al. *PLoS ONE* 2011:6:e18544. **[5]** Stanek KM et al. *Obesity* 2012:19:500-4. **[6]** Smith S et al. *NeuroImage* 2006:31:1487-505. **[7]** Nichols TE and Holmes AP. *Human Brain Mapping* 2002:15:1-25. **[8]** Smith S et al. *NeuroImage* 2009:44:83-98.