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FoCus

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Topic: Obesity (Guided Poster Tour: Sunday, 29.5.16, 13:15-14:15, GP 130)

Hypothalamic inflammation in humans is not reversed by a profound weight loss and an improved insulin sensitivity due to bariatric surgery

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Introduction

Obesity is associated with hypothalamic inflammation (HI) in animal models. The mediobasal hypothalamus (MBH) is a brain region crucial for body weight control as it regulates appetite, which leads to changes in nutritional intake. While MRI studies in obese human subjects also found an increased density in the MBH, it remains unclear (1) if HI causes neuronal death and (2) if HI reverses during weight loss.

Patients and methods

n=50 obese subjects and n=50 age- and gender-matched controls where examined. MRI scans including spectroscopy were performed (s.Fig.1). Also, detailed nutritional questionnaires, serum lipidomics, 16s rDNA microbiome sequencing data as well as SNP genotyping data were obtained. n=10 obese subjects underwent bariatric surgery followed by a second MRI.

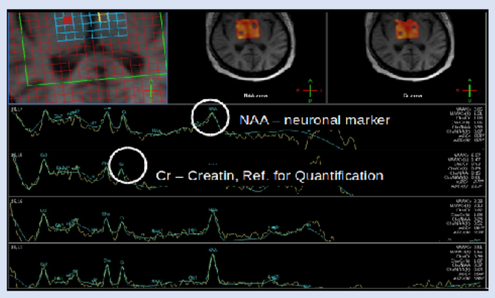

Fig.1: Spectroscopy illustration, method: ^{1}H NMR T_2 relaxation time
N-Acetylaspartat (NAA) and Creatin (Cr) measurements where used to calculate the NAA/Cr ratio, a marker for neuronal cell count.

Results

1) Obese subjects exhibit an increased density in the left, but not the right MBH compared to non-obese controls.

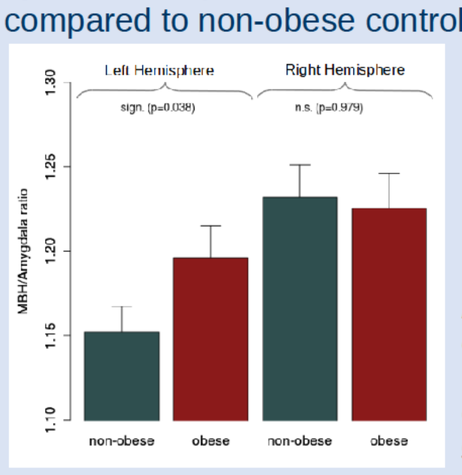

Fig.2: Comparison of MBH Density between non-obese and obese human subjects
The MBH/Amygdala ratio revealed significant differences (2-sided t-test) between the two obesity groups within the left hemisphere.

2) The number of neurons is not altered in the left MBH of obese human subjects despite increased MBH-Density, indicating that neurons might not be negatively affected by the inflammatory process.

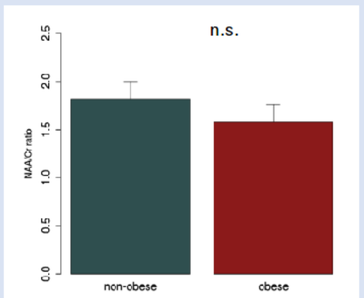

Fig.3: Comparison of neuronal cell count of non-obese vs. obese humans
The NAA/Cr ratio shows no significant differences (t-test) in cell numbers among the weight groups.

3) Weight loss due to bariatric surgery does not influence MBH-Density in obese humans.

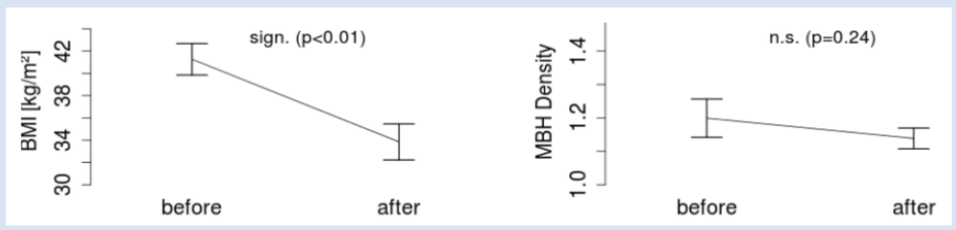

Fig.4: Before and after bariatric surgery
BMI and MBH-Density, measured as MBH/Amygdala ratio. Before- and after-comparison via t-test.

4) Increased density in the left MBH of obese humans is associated with systemic inflammation (A) but not with systemic glucose metabolism (B).

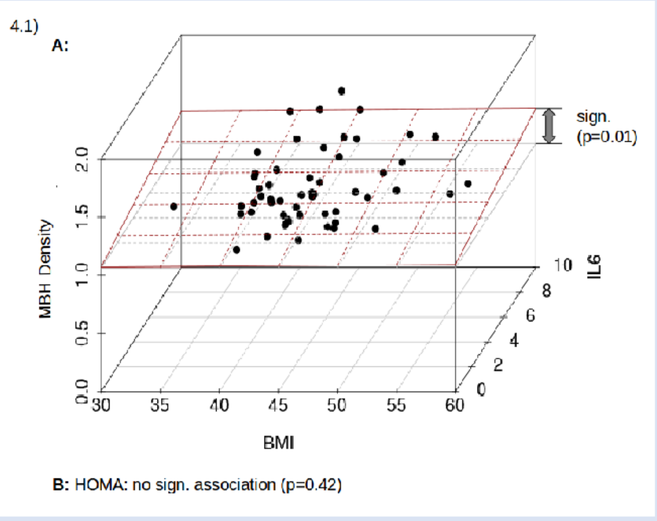

Fig.5: 3D-Scatterplot of MBH-Density, IL6 and BMI, within the obesity group
MBH-Density increase is significantly associated with increased IL6 serum levels rather than with BMI (linear model: MBH_density ~ BMI + IL6).

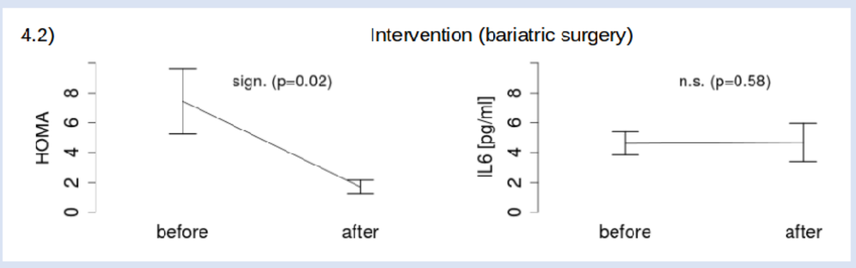

Fig.6: Before and after bariatric surgery
IL6 and HOMA (Homeostasis Model assessment – as a measure for insulin resistance). Before- and after-comparison via t-test.

5) GUT-BRAIN-AXIS: Alterations in the MBH-Density in obese humans are significantly associated with changes in the gut microbiome.

Phylum	Order	Genus	p-value	rho	BMI correlation (p-value)
Proteobacteria	Burkholderiales	Parasutterella	0.0073	-0.383	n.s. (0.878)
Bacteriodetes	Bacteriodales	Unclass. Marinilabiliaceae	0.0398	-0.299	n.s. (0.539)

Table 1: Univariate correlation tests of the core measurable gut microbiome (n=42) and MBH-Density (left). *The two bacterial genera are associated with MBH-Density but not with BMI. Correlation method: Spearman.*

6) A high-fat diet in obese humans induces a microbiome shift which is associated with the increase in the left MBH-Density.

Nutrient	p-value	rho
Fats	0.044	-0.30
Carbohydrates	n.s. (0.6)	-0.08
Proteins	n.s. (0.1)	-0.28

Table 2: Univariate correlation tests of nutrients and Parasutterella sp.
Data about nutritional intake where obtained by analysing food frequency questionnaires. Correlation method: Spearman.

Discussion

Obese human subjects exhibit an increased MRI-Density of the MBH suggesting HI. While HI and IL6 are not reversed by a significant weight loss due to bariatric surgery, the finding that the number of neurons is not altered in the MBH by HI might suggest that the function of the MBH in terms of appetite regulation might be reversible.

Disturbances in the gut-brain-axis induced by an unhealthy diet might in part explain the obesity associated hypothalamic pathology.

Wissen schafft Gesundheit

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