The role of genetic serotonin transporter deficiency in consequences of exposure to the Western diet: a study in mice

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1. Introduction

The “Western diet” (WD), a diet enriched with fat and cholesterol, is associated with obesity and development of metabolic syndrome and type 2 diabetes and increased incidence of affective disorders¹. Carriers of S allele of serotonin transporter (SERT), a genetic variant that reduces SERT expression, are more susceptible to emotionality-related disorders² and prone to obesity and diabetes³.

Aim: investigate the interaction of SERT deficit and WD consumption in aging with regard to their effects on behavioural, metabolic and molecular parameters using a mouse model.

2. Study design

3. Results

3.1 Increased depressive-like behaviour and altered cognitive functions in SERT-ko mice fed WD

3.2 Genetic absence of SERT exacerbates changes in blood metabolome induced by WD

3.3 Altered gene expression in hypothalamus of SERT-KO mice

4. Research highlights

1. Changes in metabolome, depressive-like behaviour and cognitive dysfunctions induced by Western diet are exacerbated in SERT-ko mice
2. Increased expression of serotonin and Insulin receptors and factor of mitochondrial biogenesis PPARGC1A in control SERT-ko mice may reflect compensatory CNS changes caused by serotonergic system dysregulation in these animals. Western diet inverses compensatory changes in serotonin and insulin receptors and PPARGC1A expression in SERT-ko mice
3. SERT-het mice show resilience to the effects of Western diet on behaviour in tube-test

STATISTICAL ANALYSIS
*- p<0.05 vs. control same genotype,
#- p<0.05 vs. WT same diet group,
&- p<0.05 vs. SERT-het same diet group, 2-way ANOVA
Data are shown as mean ± SEM

REFERENCES
1. de Wit et al., 2010, Psychiatry Res; Jacka et al., 2010, Am. J. Psychiatry Khosravi et al., 2015, Psychiatry Investig.
2. Lesch et al., 1996, Science; Caspi et al., 2003, Science
3. Sookoian et al., 2012, Obesity

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