2k brief Neurology
https://wiki.oroboros.at/index.php/O2k-Publications:_Nervous_system
High-resolution respirometry: Fatty acid liver disease and brain

Partial MCT1 invalidation protects against diet-induced non-alcoholic fatty liver disease and the associated brain dysfunction

Anna Hadjihambi [1], Christos Konstantinou [2], Jan Klohs [3], Katia Monsorno [4], Adrien Le Guennec [5], Chris Donnelly [6], Jane Cox [7], Anjali Kusumbe [8], Patrick S Hosford [9], Ugo Soffientini [10], Salvatore Lecca [11], Manuel Mameli [12], Rajiv Jalan [13], Rosa Chiara Paolicelli [14], Luc Pellerin [15]

Monocarboxylate transporter-1 haploinsufficient (MCT1$^{+/-}$) mice on a high fat diet with high fructose/glucose do not experience non-alcoholic fatty liver disease-associated anxiety and depression-related behavior compared to controls (MCT1$^{+/+}$)

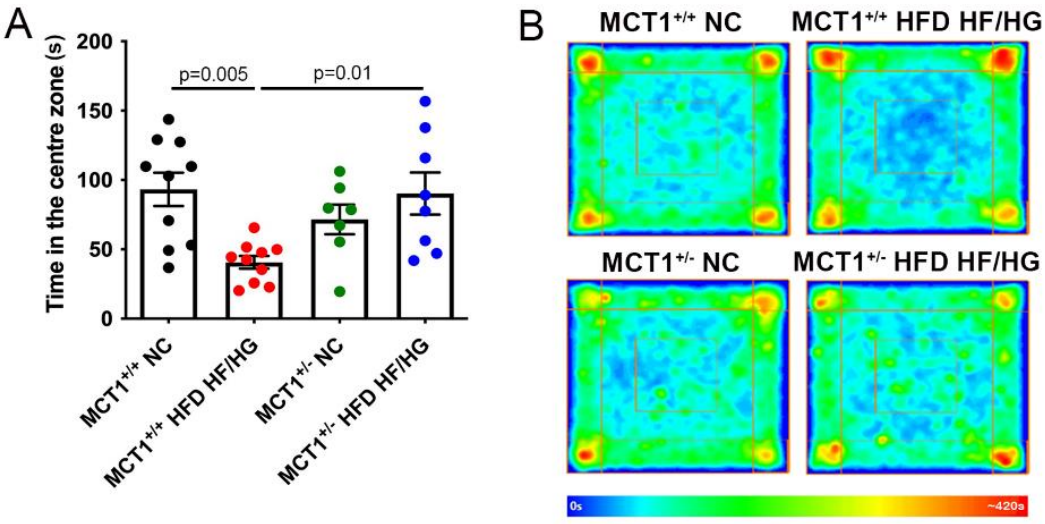

Figure 1. Assessment of anxiety and depression related behavior in MCT1$^{+/+}$ and MCT1$^{+/-}$ mice fed with normal chow (NC) or high fat diet with high fructose/glucose (HFDHF/HG). (A) Measurement of mean time spent by MCT1$^{+/+}$ and MCT1$^{+/-}$ mice fed with NC or HFDHF/HG exploring the center zone of the arena, assessed by the open field (OF) test. **(B)** Representative heat maps indicating the time spent by MCT1$^{+/+}$ and MCT1$^{+/-}$ mice fed with NC or HFDHF/HG exploring each zone during the OF test.

O2k-brief communicated by E Leo and L Tindle-Solomon
Oroboros Instruments

Obese MCT1$^{+/+}$ animals with NAFLD present higher mitochondrial respiratory capacities but not improved metabolic outcome, while obese MCT1$^{+/-}$ animals remain unaffected

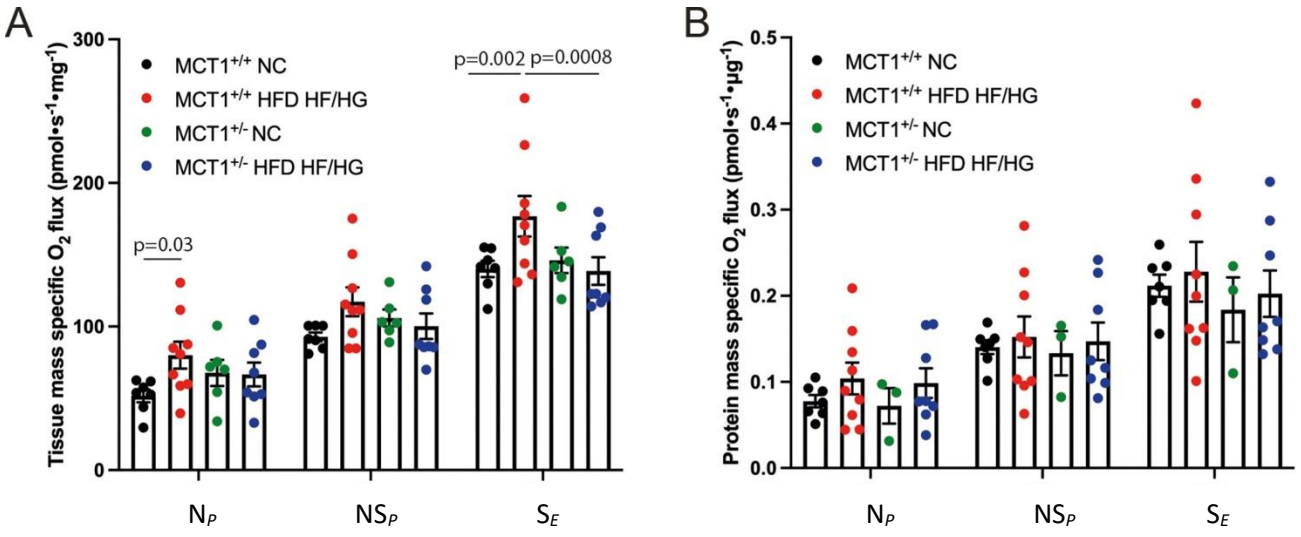

Figure 2. Determination of cortical mitochondrial respiratory capacities by high-resolution respirometry in MCT1$^{+/+}$ and MCT1$^{+/-}$ mice fed with NC or HFDHF/HG. (A) Tissue mass and **(B)** protein mass specific oxygen fluxes in somatosensory cortical tissue samples from MCT1$^{+/+}$ and MCT1$^{+/-}$ mice fed with NC or HFDHF/HG: OXPHOS-capacity (N_P and NS_P) and ET-capacity (NS_E). S, succinate-pathway; N, NADH-pathway.

Non-alcoholic fatty liver disease (NAFLD) induced brain inflammation and decreased brain tissue oxygenation in mice. Such effects translated into increased anxiety and depression, symptoms classically correlated with obesity in humans. Brain mitochondria from NAFLD mice had higher respiratory capacity per tissue mass, and the unchanged OXPHOS complex subunits content suggested this was due to functional changes.

Monocarboxylate transporter-1 (MCT1) seems to play a role in development of NAFLD and correlated brain inflammation since haploinsufficient MCT1 mice presented fat accumulation but neither NADLF nor cerebral alterations.

Reference: Hadjihambi A, Konstantinou C, Klohs J, Monsorno K, Le Guennec A, Donnelly C, Cox J, Kusumbe A, Hosford PS, Soffientini U, Lecca S, Mameli M, Jalan R, Paolicelli RC, Pellerin L (2022) Partial MCT1 invalidation protects against diet-induced non-alcoholic fatty liver disease and the associated brain dysfunction. https://doi.org/10.1016/j.jhep.2022.08.008

Text slightly modified based on the recommendations of the COST Action MitoEAGLE CA15203. doi:10.26124/bec:2020-0001.v1

O2k-brief communicated by E Leo and L Tindle-Solomon
Oroboros Instruments