A mouse model of Chronic Fatigue Syndrome validated by behavioural, metabolic and hormonal changes

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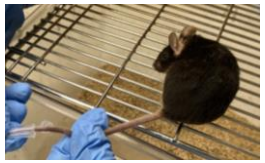
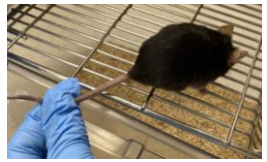
Chronic Fatigue Syndrome: Motivation

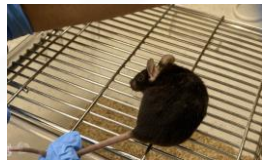
- *Ignored until recently, consequently poorly understood*
- *Information collected about the syndrome over the past two decades includes knowledge of significant physiological, e.g. hormonal changes*
- *Characterized by severe physical and mental fatigue that heavily effects quality of life and ability to work*
- *Occurs in a few percent of infections by viruses, some of which caused mass infections in the past (COVID 19, H1N1)*
- *Resulting from the previous two statements, related health insurance costs massively increased during and after the COVID pandemia which is likely to return*

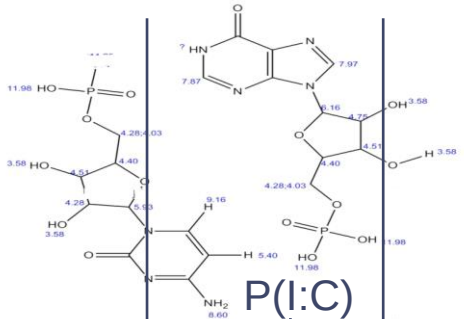
Chronic Fatigue Syndrome: Methodology

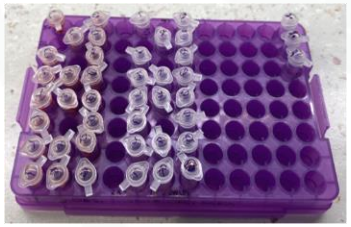
- *Injection with poly(inosinic acid) – poly(cytidylic acid) (P(I:C)) and following the mice for ten days after this is a good enough model for CFS as the viruses causing CFS in human are either double-stranded DNA viruses (EBV, Cytomegalovirus) or single-stranded RNA viruses (H1N1) and these two groups seem to be able to activate each other in humans.*
- *Furthermore, P(I:C) studies were already conducted on rats and on mice. [1]*
- *Anhedonia and tiredness that worsens after physical exercise and are typical of CFS can be measured in mice by sucrose preference test and time spent of running wheels, as mice run the wheel for fun. [2]*
- *Hormonal changes over the course of the long-term study can be followed by drawing blood from tail vein and analyzing the samples using HPLC*
- *Level of neurotransmitters can be measured in tissue samples collected post-terminally*

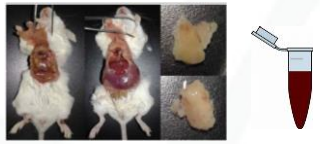
Experimental design





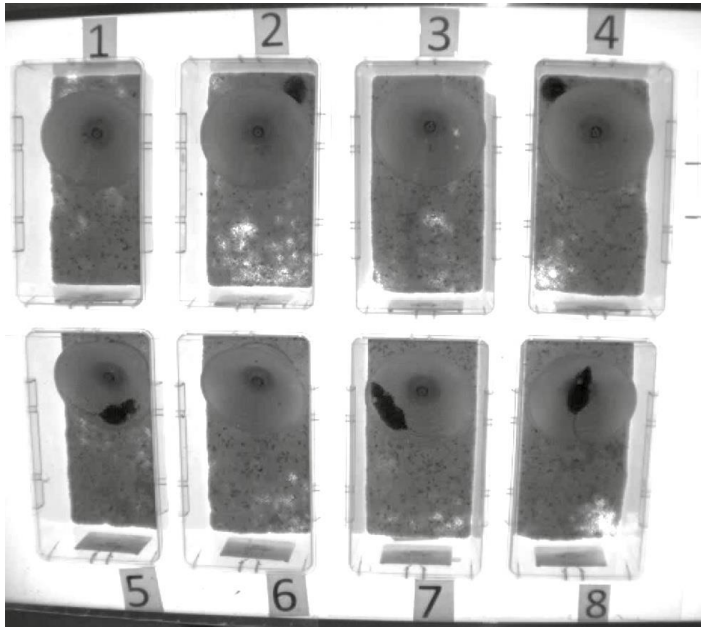




Blood collected by unrestrained tail snip 1 day before and 1, 4, 10 days after P(I:C) administration.

Termination 2 w. after P(I:C) adm. Blood, tissue collected.

Day 0 Day 1 Day 3 Day 9

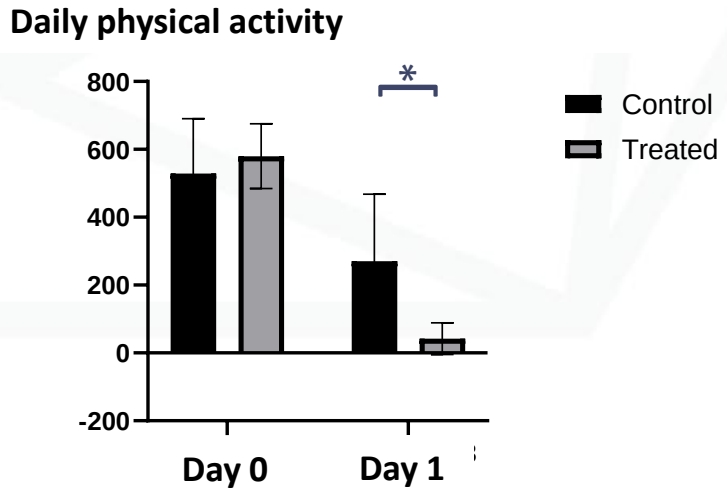


Daily behavioural tests: voluntary wheel running (following a 1-week period of training), sucrose preference test and body weight measurements following P(I:C) administration.

„Sample only” results

until we publish it all...

- *Physical activity shows a short-term (up to two days), metabolism a long-term (up to two weeks) decrease after P(I:C) treatment.*
- *In terms of sucrose consumption, we noticed no difference between different age groups, but in terms of the underlying metabolic changes (ATP plasma concentration, ADP/ATP ratio) and in terms of changes in the hormonal balance, the older animals are affected.*
- *In humans too, CFS is more frequent among the adult and middle-aged population. Notably, thyroid regulation as per the basic assessment of measuring fT4 in plasma, was intact.*



Based on these findings, we conclude that our model is suitable for studying the human disease on mice.

References:

1. Janowski et al. 2022.

2. Meijer and Robbers 2014.

Goals in the Data Repository Program

- *Testing the repository system by depositing the data collected for this project, the significant proportion of it being the videos recorded during the behavioral experiments*
- *Establishing good practices for data storage. e.g. providing the necessary metadata and introducing a schedule for maintenance*
- *Sharing the knowledge gained in practice and at the training sessions with the scientific community of the Institute of Experimental Medicine*
- *Collecting feedback on the usage of the repository system with the scientific community of the Institute of Experimental Medicine and forwarding it to the mentors of the Data Repository Program*

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