Effect of voluntary and forced exercise on FNDC5-Irisin pathway and muscle-to-brain crosstalk in a model of obesity

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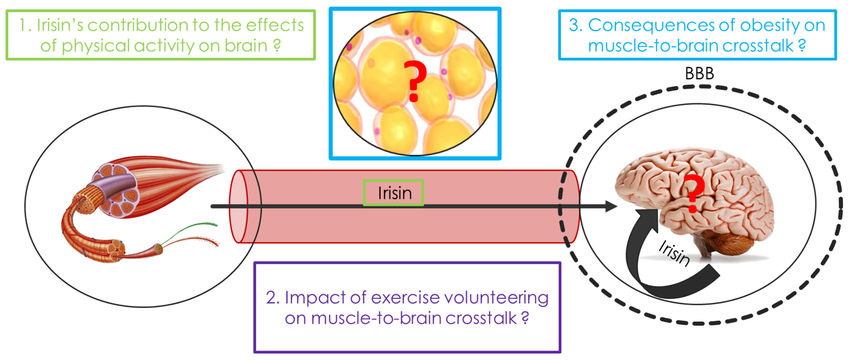
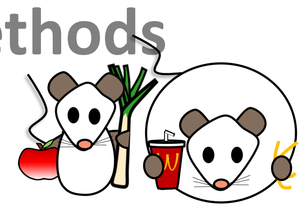
Aims

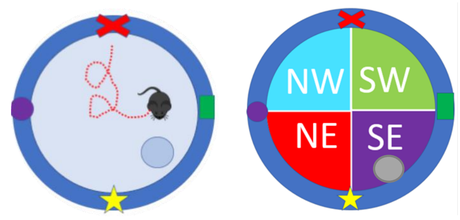


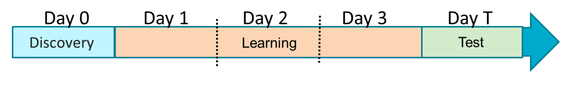
Exercise training (ET) has been shown to be beneficial in managing **obesity**-related disorders. ET was reported to have positive effects on the **brain**. Our project aims to define the role of **irisin** in this context. **Irisin** is an exercise-induced myokine also expressed in the hippocampus, an essential brain area for learning and memory.

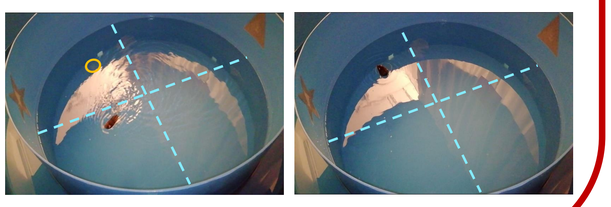
Methods



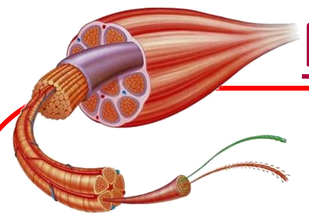
Morris Water Maze



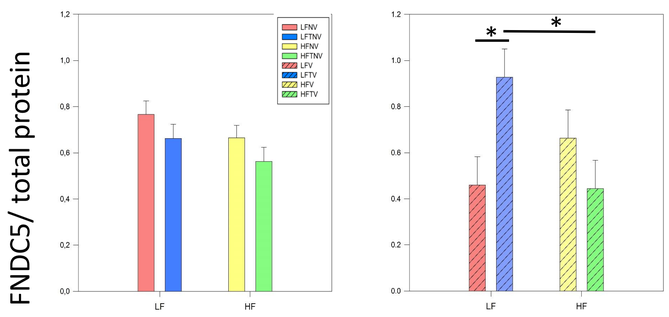




Muscle upon physical activity

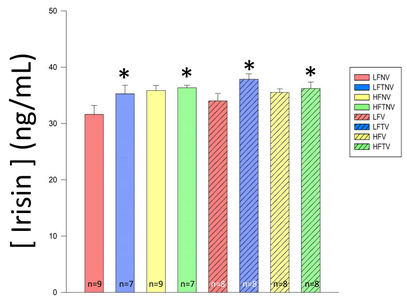


FNDC5 Level



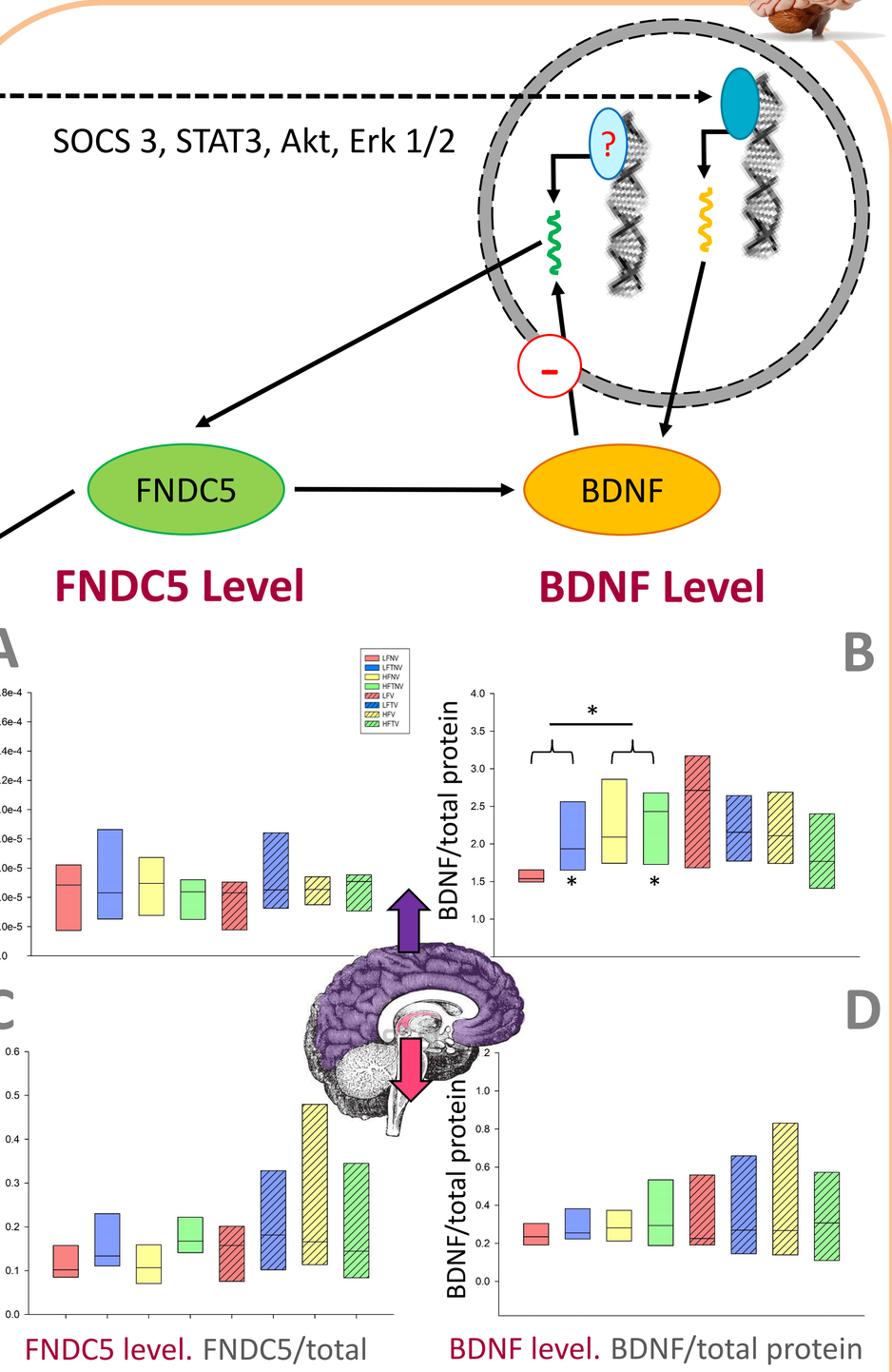
FNDC5 level. FNDC5/total protein ratio in *gastrocnemius* was determined by denaturant PAGE-SDS followed by a Western Blot. Ratio was obtained after densitometric analysis. Two Way ANOVA, * : $p < 0,05$

Irisin plasmatic level



Irisin plasmatic level. After 20 Weeks. Irisin concentration was measured by competitive ELISA. Three Way Anova, $p = 0,008$ T Vs UT

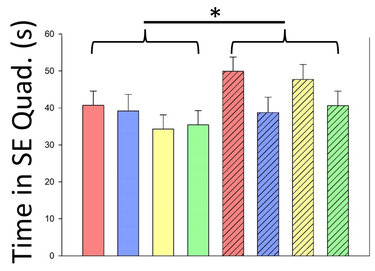
Brain upon physical activity



FNDC5 level. FNDC5/total protein was determined by denaturant PAGE-SDS followed by a Western Blot. Ratio was obtained after densitometric analysis.
Three Way ANOVA, NS

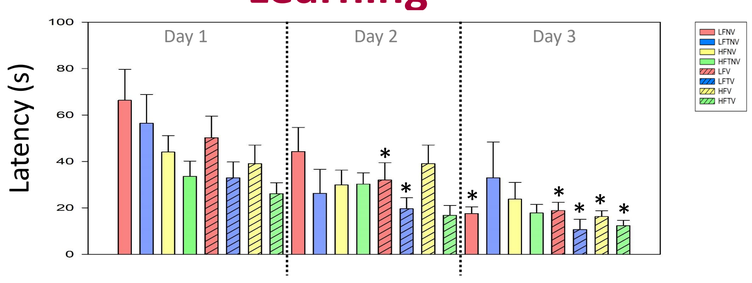
BDNF level. BDNF/total protein was determined by denaturant PAGE-SDS followed by a Western Blot. Ratio was obtained after densitometric analysis.
Three Way ANOVA,
B. * : $p < 0,05$ and $p < 0,05$ T Vs UT in NV
D. NS

Memory



Time in SE. During test day, time spent in the platform quad. was measured.
Three Way ANOVA,
* $p < 0,05$

Learning



Latency. During learning period, time taken by mouse to reach the platform was measured and is called latency. One Way ANOVA on Repeated Measures, * $p < 0,05$

Conclusion

Irisin plasmatic level is increased by ET, whatever ET modality or diet. However, FNDC5 modifications are dependant of training modalities, is tissue-specific and influenced by diet:

Voluntary ET is associated to an increased level of FNDC5 protein level in muscles of animals fed with a low-fat diet. This effect is impaired in HFD animals and is not observed in the brain cortex and hippocampus, whatever the diet. Enrichment in mice submitted to voluntary ET improves spatial learning and memory particularly in obese animals. However, the BDNF protein level is not modified by voluntary ET in the cortex and hippocampus whatever the diet.

Non-volontary ET does not modified FNDC5 protein level in muscular and brain tissues. Non-volontary ET does not modify, per se, the spacial learning and memory in mice and BDNF protein level is not modified in hippocampus. However, an increased BDNF protein level is observed in the brain cortex in trained animals and also, surprisingly, in HFD mice.

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