Nf1 Mutations Impair Memory-Related Plasticity in the *Drosophila melanogaster* Mushroom Body

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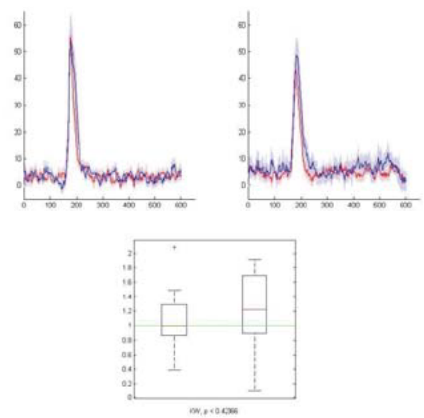
Introduction

- Neurofibromatosis Type 1 is a disease which displays an autosomal dominant pattern of inheritance. The rate of occurrence is 1 in 3,500 individuals, and it is known to cause cognitive deficits as well as other physiological symptoms.
- Activity of dopaminergic neurons is known to drive plasticity in neuronal networks that modulate learning. During olfactory classical conditioning, dopaminergic neurons are activated, which causes dopamine to be released across postsynaptic neurons.
- During olfactory classical conditioning, large subsets of dopaminergic neurons are activated, releasing dopamine across broad sets of postsynaptic neurons.

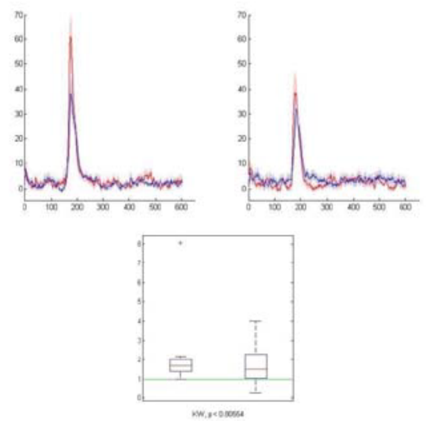
Method

- Gamma, Beta, and Lower stalk regions of the mushroom body in *Drosophila melanogaster* were studied through olfactory classical conditioning using an in vivo brain imaging technique.
- Control Group versus RNAi knockdown group were compared, both containing UAS-GCaMP6f/+; 238y-GAL4/+ for imaging
- Air and odor were administered in timed intervals to record odor-evoked Ca2+ transients in the mushroom body
- Flies were conditioned by elevating cAMP via administering 100 mM forskolin during the training period.
- This experiment was conducted to show which lobes of the mushroom body exhibited learning-related, cAMP-dependent plasticity, and to understand how this pattern of plasticity is altered in Nf1 mutants.

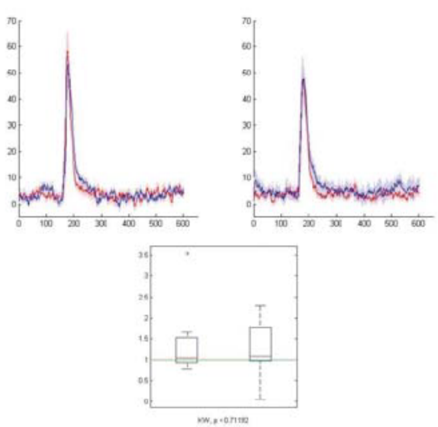
Beta Lobes Pre vs Post Conditioning

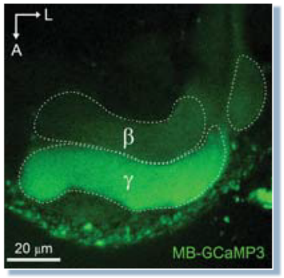


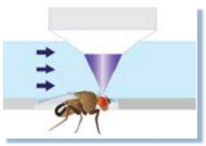
Gamma Lobes Pre vs Post Conditioning

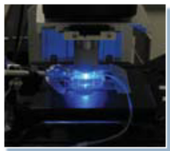


Lower Stalk Lobes Pre vs Post Conditioning









Results

- Knocking down *NF1* disrupts cAMP-dependent plasticity in the gamma lobes.
- It can be seen in the graphs that beta and lower stalk regions of the mushroom body do not present large changes of cAMP elevations pre versus post conditioning in both groups.

Discussion

- Dopaminergic neurons drive compartmentalized elevation of postsynaptic cAMP
- cAMP elevation drives postsynaptic plasticity in the mushroom bodies
- Pattern of learning-related plasticity is dependent on the postsynaptic neurons' sensitivity to cAMP signaling. This may represent a mechanism through which single-cycle conditioning allocates short-term memory to a specific subset of eligible neurons (gamma neurons).

References

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3. Boto, T., Louis, T., Jindachomthong, K., & Jalink, K. Tomchik, S., (2014, March 27). Dopaminergic Modulation of cAMP Drives Nonlinear Plasticity across the *Drosophila* Mushroom Body Lobes. *Current Biology*.

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