Name(s)
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Project Number
38486

Project Title
Effects on Learning/Memory of a Mutation in Da7: A Fruit Fly Homolog of the Alzheimer's Related Gene for the nAChR a7

Abstract

Objectives/Goals
The purpose of this project is to test the effects on learning/memory and locomotion of a mutation of the gene D-Alpha 7 (Da7) (specifically the P-Delta-EY6 allele - PDEY6), a Drosophila melanogaster (fruit fly) homolog of the Alzheimer's Disease (AD) related human gene that encodes the Nicotinic Acetylcholine Receptor Alpha 7 (nAChR a7). My hypothesis was that the mutants expressing the Da7 PDEY6, which impedes the production of the fruit fly equivalent of the nAChR a7, will show a significant decline in learning/memory retention and locomotion, similar to the Amyloid-Beta Arc-42 (AB-42) mutants (AD model), when compared to flies that express the corresponding wild type (WT) receptor.

Methods/Materials
Drosophila stocks and care: Da7 PDEY6 as test subject, AB-42 as positive control, WT flies as negative control, Instant Drosophila Media, Appropriate Vials/Caps, Dissecting Microscope. For Olfactory Shock Learning: T-maze (self-built), Training Chamber (self-built), Shock - 60 volts/3.75 seconds, Odors - 3-Octanol and 4-Methylcyclohexanol (MCH).

Results
1. Climbing Assay Success Rates: PDEY6 -- 61.2%, AB-42 -- 60.2%, WT -- 79.5%
2. Short Term Memory Success Rates: PDEY6 -- 49%, AB-42 -- 46%, WT -- 81%
3. Long Term Memory Success Rates: PDEY6 -- 41.5%, AB-42 -- 39%, WT -- 78%
4. P-value for AB-42, PDEY6 consistently ~90%
5. P-value for WT & AB-42/PDEY6 consistently less than 10^-6

Conclusions/Discussion
1. Hypothesis proven: PDEY6 (and AB-42) populations show ~40% decline in short/long term memory, ~23% deterioration in locomotion relative to the WT populations.
2. For both short and long term memory tests: The differences between the 3-week and 4-week flies not statistically significant; Additionally, no performance impact by odor
3. Additional "loss" of long term memory compared to short term for 15% of mutants, 5% of WT flies
4. Higher impact of lack of Da7 on memory/learning than climbing, which is expected
5. For AB-42 & PDEY6: Null hypothesis rejected - Strong relationship between mutants exists
6. For WT/AB-42 & WT/PDEY6: Null hypothesis accepted - Relationship between WT and mutants non-existent
7. These conclusions provide further motivation to study nAChR a7 and its potential for AD research.

Summary Statement
I proved that the lack of the Nicotinic Acetylcholine Receptor a7 equivalent in fruit flies drives an Alzheimer's Disease-like response, indicated by AD's primary symptoms: decline in memory retention and locomotive ability.

Help Received
I want to thank my mentor, Dr. Cuellar, for her support and input whenever I had inquiries regarding biological techniques and processes. I also want to thank Schmahl Science Workshops, which provided me with the necessary equipment and lab space for this project.