

Effects of Ultrasound on Amyloid Beta 42 (Aβ42) Mediated Neurodegeneration

Sarah Byrne^{1,2}, Ankita Sarkar¹,
Amit Singh^{1,2,3,4}



- 1) Department of Biology, University of Dayton, 300 College Park Drive, Dayton, OH;
- 2) Premedical Program, University of Dayton;
- 3) Center for Tissue Regeneration and Engineering at Dayton (TREND), University of Dayton, 300 College Park Drive, Dayton, OH, 4) Center for Genomic Advocacy (TCGA), Indiana State University, Terre Haute, IN, USA.

Alzheimer's Disease

Causes:

1. Amyloid Plaques
2. Neurofibrillary Tangles
3. Neuronal loss
4. Oxidative stress due to ROS
5. Genetic basis of ApoE

Hypothesis: Can ultrasound wave regimen can dissociate Aβ42 plaques that cause neurodegeneration and rescue the phenotype

Ultrasound waves Regimen + Aβ42

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Determining Optimal Treatment Time

Wild Type larvae with treatment

Type	Amount of Water (ml)	Height (mm)	Time (seconds)	Number (Initial)	Survived (Final)	Percent
Wild Type	0	0	0	30	22	73.3%
Wild Type	2	10	10	30	10	33.3%
Wild Type	2	10	20	30	11	36.6%
Wild Type	2	10	30	30	8	26.7%

GMR-Aβ42 larvae with treatment

Type	Amount of Water (ml)	Height (mm)	Time (seconds)	Number (Initial)	Survived (Final)	Percent
GMR-Aβ42	2	10	0	30	16	53.3%
GMR-Aβ42	2	10	10	30	4	13.3%
GMR-Aβ42	2	10	20	30	1	3.3%

Imaginal Disc of GMR>Aβ42 Fly with Ultrasound Treatment Shows Rescue

Top Left: A: Wild Type larval imaging with Dig/Elav staining. Bottom Left: A': Wild Type Larval imaging with Dig/Elav Staining.

Top Right: B: GMR-Aβ42 Fly Adult image after 10 second ultrasound treatment in 2 ml of water. Bottom Right: B': GMR-Aβ42 Fly Larval imaging with Dig/Elav Staining.

Drosophila Life Cycle

Fertilization → Embryo (1 day) → First instar larva (1 day) → Second instar larva (1 day) → Third instar larva (1 day) → Pupa (2 1/2 - 3 days) → Adult (3 1/2 - 4 1/2 days in pupal stage).

Ultrasound Hypothesis and Testing

Theory:

- Energy disrupt plaques

Testing:

- Ultrasound wave regimen

Efficacy:

- Monitor survival rates
- Phenotype

Repeated Ultrasound Exposure Regimen Reduces Survival Rate of Flies in Comparison to Single Exposure

Type	Amount of Water (ml)	Height (mm)	Time (seconds)	Number (Initial)	Survived (Final)	Percent
Wild Type	2	0	0	30	22	73.3%
Wild Type	2	10	10	20	2	10%
Wild Type	2	10	20	20	0	0%
GMR-Aβ42	2	10	0	30	16	53.33%
GMR-Aβ42	2	10	10	30	1	3.33%
GMR-Aβ42	2	10	20	30	2	6.66%

Adult Eyes of GMR>Aβ42 Fly with Ultrasound Treatment Shows Rescue

Top Left: Wild Type no treatment. Top Middle: GMR-Aβ42 fly 10 seconds of treatment in pupal stage. Top Right: GMR-Aβ42 fly 20 seconds of treatment in pupal stage.

Bottom Left: GMR-Aβ42 fly no treatment. Bottom Middle: GMR-Aβ42 fly 10 seconds of treatment in larval stage. Bottom Right: GMR-Aβ42 fly 20 seconds of treatment in larval stage.

Misexpression of Aβ42 leads to progressive neuronal cell death

Larva → Pre-pupa → Pupa → Adult

Tare et al., 2011

Flies Subjected to the Treatment in Water had Higher Survival Rates Compared to Air

Type	Amount of Water (ml)	Height (mm)	Time (seconds)	Number (Initial)	Survived (Final)	Percent
Wild Type	0	10	30	20	0	0%
Wild Type	2	10	30	20	8	40%
Wild Type	0	10	16	20	8	40%
Wild Type	2	10	16	30	14	46%
GMR-Aβ42	0	10	10	30	4	13%
GMR-Aβ42	2	10	10	30	6	20%

Treating Pupal Flies Shows Higher Survival Rates than Treating Larval Flies

Type	Amount of Water (ml)	Height (mm)	Time (seconds)	Number (Initial)	Survived (Final)	Percent
Wild Type	2	10	10	30 (Pupal)	15	50%
Wild Type	2	10	20	30 (Pupal)	11	36.6%
Wild Type	2	10	30	30 (Larval)	13	43%
Wild Type	2	10	30 (Larval)	30	11	36.6%
GMR-Aβ42	2	10	10 (Pupal)	30	10	33.33%
GMR-Aβ42	2	10	20 (Pupal)	30	8	26.66%
GMR-Aβ42	2	10	30 (Larval)	30	6	20%
GMR-Aβ42	2	10	30 (Larval)	30	4	13%

Future Directions

Most effective treatment:

- Water
- Single Treatment
- 10-20 Seconds
- Pupal Stage

Pupal Retina Images of Optimum regimen