Fly Lab, SRM Institute of Sciece and Technology

COMPREHENSIVE STUDY ON THE BISPHENOL-A INDUCED DROSOPHILA MODEL FOR AUTISM SPECTRUM DISORDERS WITH CO-TREATMENT BY CERIUM OXIDE NANOPARTICLES AND U0126 MAP-K INHIBITOR

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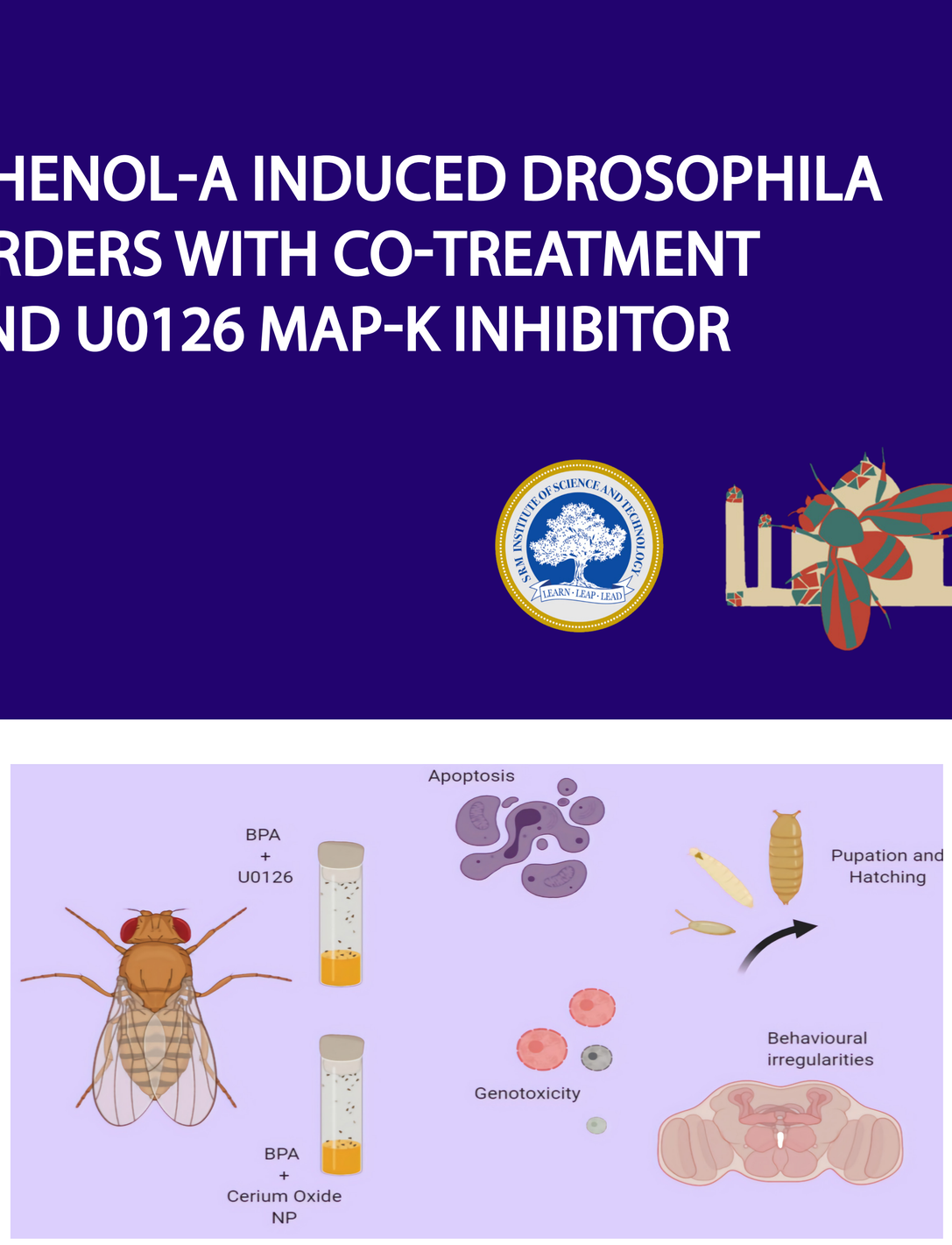
BISPHENOL-A IS OFTEN DESCRIBED AS THE XENOBIOTIC ETIOLOGY OF AUTISM SD.

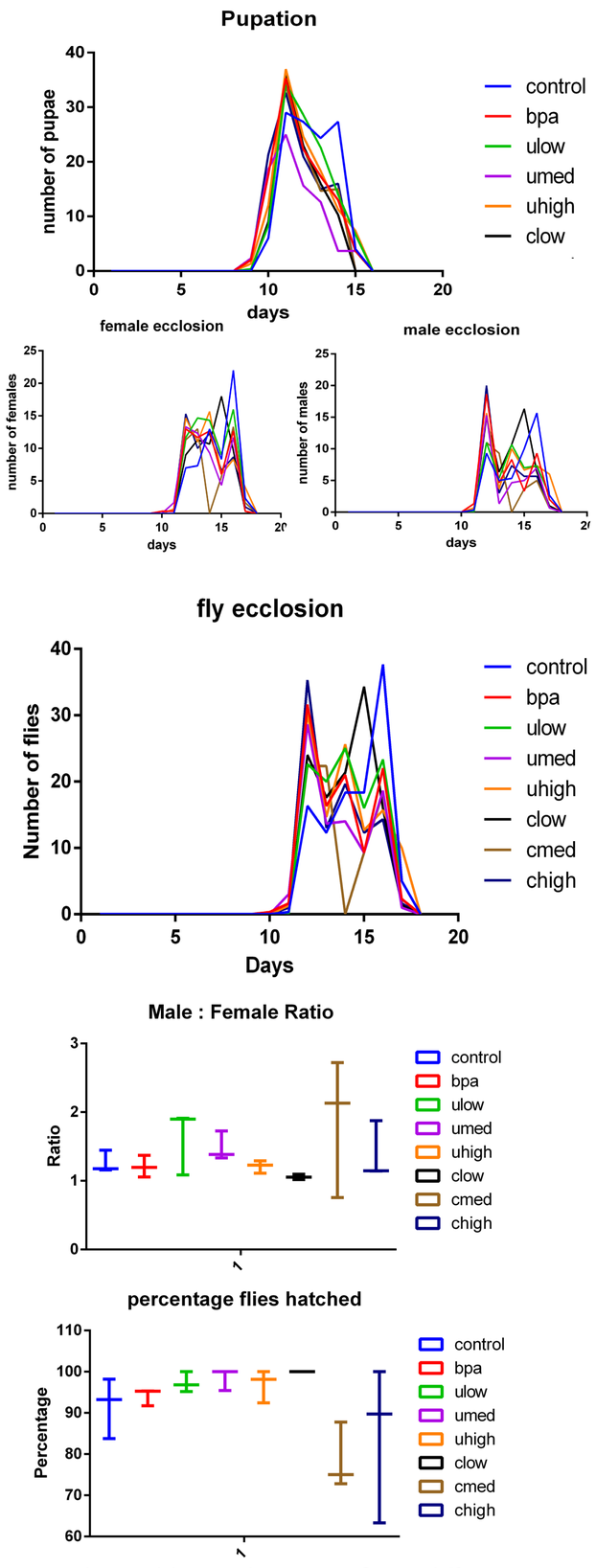
Recent evidence suggests that MAP-Kinase upregulation plays a critical role in most neurodevelopmental disorders under the autism spectrum. To determine whether BPA induced neurodevelopmental disorders are akin to the MAP-K autism model, flies were raised in co-treated food containing BPA and U0126, a potent MAPK inhibitor. Cerium Oxide Nanoparticles were used as a treatment for oxidative stress. The differences in the two might indicate towards the MAP-Kinase associated effects by BPA.



Basic overview of experimental design and aspects currently under focus.

PUPATION AND HATCHING

BPA is a known xenoestrogen and is expected to impact the number of pupae and the ratio of phenotypic sexes.



Despite observable trends, no significant difference was found. Advances and delays in peaks of male and female hatching was observed. Experiments done in triplicates, repeated thrice.

BISPHENOL-A AND ASD

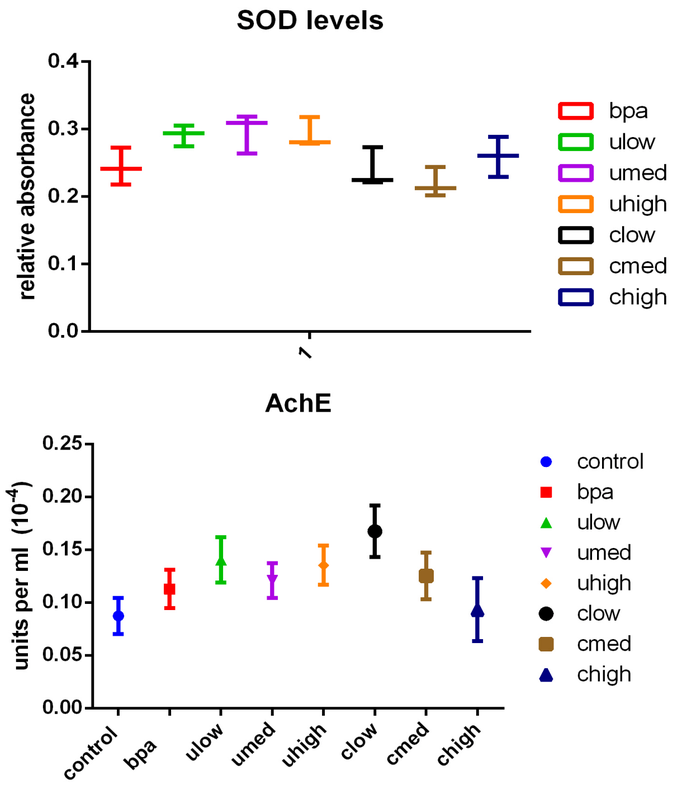
>World's largest produced chemical -constant exposure during development

> Autism Spectrum Disorders: an umbrella term for neurodevelopmental issues that lead to social, communication and decision making issues.

> BPA-model of ASD involves multiple toxic effects from xenoestrogen activity, irregularity in pupation and development, increased cellular ROS, Genotoxicity, Apoptosis to behavioural decision making

SOD & ACHE ACTIVITY

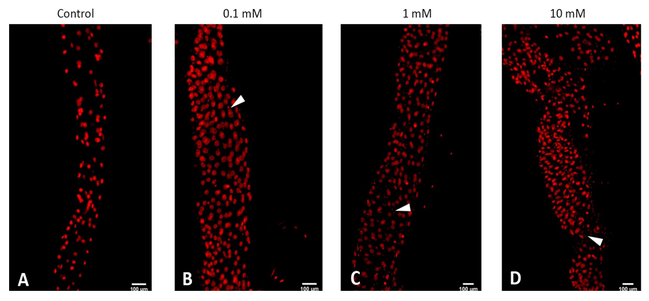
Superoxide dismutase levels and acetylcholine esterase levels serve as efficient markers for oxidative stress and neuromuscular junction health.

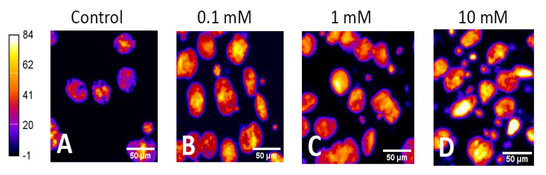


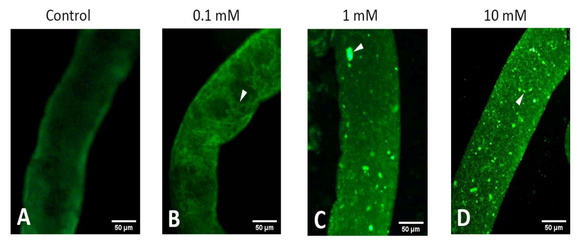
Trends in SOD suggest that U0126 worsens oxidative stress, perhaps as a response to it's xenoestrogen activity. AChE levels indicate good neuromuscular synapse health, and

GENOTOXICITY AND APOPTOSIS

The doses of BPA given to the flies is rather high to evoke neurodevelopmental deficits that can be significantly assayed. The amount taken up by individual flies cannot be accurately measured and therefore, toxicity is monitored instead. This is done by using actin-gal4>UAS-DsRed(nls) cross for visualisation of gut nuclei (worst affected) as well as staining by acridine orange for identifying apoptotic cells.







CONCLUSION

Bisphenol-A induces a multitude of effects on flies that show great variation within identical experimental sets. This makes it a significantly complex issue to solve. Despite ample repeats in these simple experiments we have not yet been able to perfectly identify the mechanisms. With future research in this direction, especially into a deeper understanding of fly social behaviour and mechanistic circuitry, one may identify how coumpounds such as Bisphenol-A may cause neurodevelopmental disorders in flies and humans. We hope that the data we have so far collected provides direction to future research.

Note: BPA unless mentioned is at a concentration of 0.5mM. U0126: ulow - 0.05 µM, umed - 0.125 µM and uhigh - 0.5 µM. CeriumOxide NP: clow - 0.2 mM, cmed - 0.5mM, chigh - 1 mM

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