OR23-4: Low-Dose Gestational BPA Exposure Alters Circadian Rhythms in Mice

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Bisphenol A (BPA) is a well-characterized endocrine disruptor known to act via multiple steroid signaling pathways. Previously we have shown that the hypothalamus, a key regulator of neuroendocrine activity, is particularly susceptible to endocrine disruption by BPA, with low-dose gestational exposure resulting in accelerated neurogenesis and altered behavior, including hyperactivity, in both zebrafish and mice. The suprachiasmatic nucleus (SCN) of the hypothalamus is the regulator of the circadian clock, and we hypothesize a link between altered SCN function and the observed hyperactivity in BPA exposed animals. Here we present the effects of low-dose, environmentally relevant gestational BPA exposure on circadian rhythms in mice. We characterized mice exposed to BPA (50 µg/kg via diet) *in utero* by measuring their activity levels during a normal 12:12 light/dark (l/d) cycle, followed by entrainment to a 24h dark (d/d) period. We observed significant alterations in circadian rhythms as a result of gestational BPA exposure. BPA mice were significantly more active than control mice in l/d conditions, specifically in the late stages of the dark phase when control mice had usually completed their daily bouts of activity. BPA-exposed mice also exhibited less of an anticipatory onset of activity just prior to the start of the dark phase, and we observed a slight, female-specific increase in circadian period (tau). BPA-mediated disruptions of circadian rhythms were exaggerated under d/d conditions. BPA mice again showed significantly higher activity than control mice, and both male and female mice exhibited a significant decrease in tau. Finally, we observed that BPA-exposed mice appear to entrain more quickly to new conditions, both in the shift from l/d to d/d, and in response to short-term light exposure during the d/d testing. Overall, we conclude that low-dose gestational BPA exposure alters circadian rhythms under various conditions, the first such finding in a mammalian model *in vivo*, and that this may be a contributing factor to the observed hyperactivity in BPA-exposed mice.

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