Analysis of the Paraventricular Nucleus of the Hypothalamus After Exposure to Decabromodiphenyl Ether in Mice

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Background

The paraventricular nucleus of the hypothalamus (PVN) is an important autonomic control center in the brain. It regulates stress, metabolism, growth, reproduction, immune responses, and gastrointestinal, and cardiovascular processes. The PVN can be altered due to exposure to common chemicals such as decabromodiphenyl ether (decaBDE).

DecaBDE belongs to the group of flame-retardant chemicals known as polybrominated diphenyl ethers (PBDE). After exposure, decaBDE negatively impacts brain development and can cause neurobehavioral deficits. In children, hyperactivity, loss in fine motor skills, and other motor deficits are directly correlated with decaBDE exposure during gestation.

DecaBDE has been shown to reduce thyroid hormone levels, therefore disrupting brain homeostasis. Thyroid hormones are crucial for brain, muscle, bone development, growth hormone, and as well as regulating axonal myelination. The cognitive and motor behavior of adult mice has been found to be impaired, with lowered thyroid hormone levels being the most probable cause due to postnatal exposure to decaBDE. The current study aims to show that decaBDE will negatively affect the development of the PVN.

Results

We learned that sex differences were present since females (M = 0.23, SEM = 0.9) had larger PVNs compared to males (M = 0.6, SEM = 0.01) (Figure 2). The size of the PVN was found to be smaller in the control group (M = 0.9, SEM = 0.03) compared to the group of mice exposed (M = 0.25, SEM = 0.12) to the decaBDE (Figure 3). When data for mice of the same sex was compared, the female exposed group (M = 0.45, SEM = 0.28) had larger PVNs than the females in the control group (M = 0.54, SEM = 0.04). When males were compared, there was no significant difference found in the size of the PVN for both the control group (M = 0.13, SEM = 0.03) and the exposed group (M = 0.11, SEM = 0.05) (Figure 4).

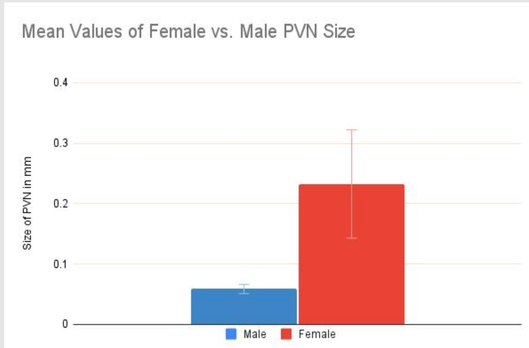

Figure 2: Comparison of the PVN between male and female mice.

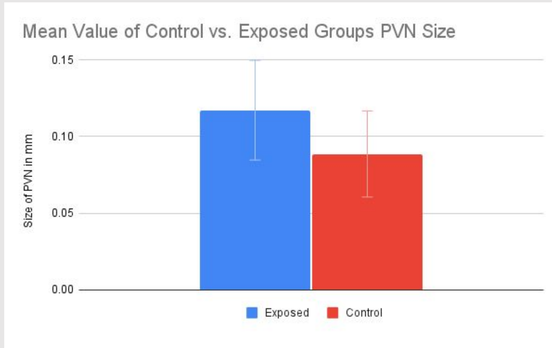

Figure 3: Comparison of the PVN between the control and exposed mice.

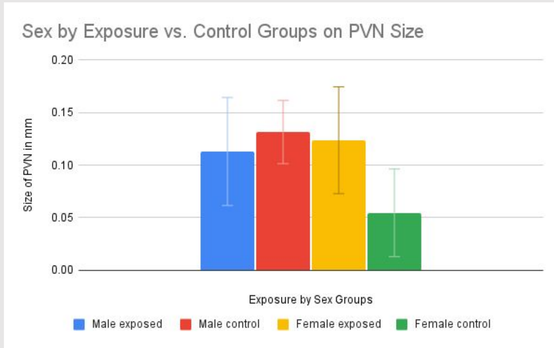

Figure 4: Comparison of the PVN between sex with the exposed and controlled groups.

Methods

From a sample of 14 mice, composed of 7 males and 7 females. 5 mice were in the exposure group and given decaBDE orally to see the effect it had on the brain, while 9 mice were in a control group.

DecaBDE was administered to the exposure group from 1-21 days of age. On day 22, brains were removed, flash-frozen, and sectioned on a cryostat. Sections were mounted on slides, and stained with cresyl violet which highlighted the PVN. The slides were then analyzed with the computer program, ImageJ, a software package designed to capture and measure images under high magnification. Lastly, the area of the PVN on both the left and right hemispheres was measured.

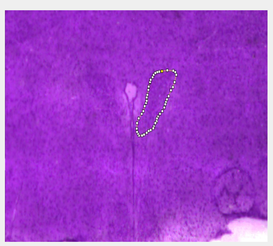

Figure 1: Outlined image of the PVN using ImageJ.

Discussion

The study aimed to highlight the effects of decaBDE on the size of the PVN. This region plays an important role in thyroid hormone activity, which is crucial for development. It was originally hypothesized that exposure to decaBDE would result in a smaller PVN size and thus negatively affect development. However, smaller PVN sizes were not reflected in the data because results show that when exposed to decaBDE, the PVN had no statistical size difference when compared to the control group. There is a lot of variation between the male and female samples, with the PVN size for females being smaller than males for the control group, but larger than males for the exposed group. There could have been differences in PVN sizes between the sexes that were overlooked. Even though it is known that decaBDE affects thyroid hormone production and regulation, there may need to be a longer exposure period for effects to be reflected in PVN size. Only looking at the PVN does not show the full effect of decaBDE exposure in the thyroid hormones, developmental impairments, and neurobehavioral deficits. In a previous study, it was shown that hormone levels in mice that were exposed to decaBDE were significantly different compared to the control group. This indicates that even though their PVN seemed to have no differences, there are still changes happening in the brain due to the decaBDE.

Limitations of this study are due to the slides being not properly sectioned and/or stained, which made the PVN difficult to view, thus, limiting the sample size. Within the sample, there were more control mice than mice exposed to decaBDE. Another limitation of the experiment was the inability to test thyroid hormone levels to see if there were differences between the control and exposed group. With the sample size being so small, there is not enough to draw a statistical conclusion from the data.

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Future Directions

If the project were to be replicated, a larger sample size is needed to test for statistical significance. Since this study was motivated by the adverse health effects caused by decaBDE exposure, there should be mice with different dosage levels to see what kind of damage is caused at which degree of exposure. Research could also be done to see if the damage done to the PVN is reversible. The results also noted sex differences in the PVN sizes between the mice, further research could be done to figure out why that is the case.

References

Alkemade A. (2015). Thyroid hormone and the developing hypothalamus. Frontiers in neuroanatomy, 9, 15. https://doi.org/10.3389/fnana.2015.00015

Edwards, C. M., Small, D., Bell, T., David-Drori, J., Hansen, C., Morris-Schaffer, K., Canale, C., Ng, J., & Markowski, V. P. (2020). Early postnatal decabromodiphenyl ether exposure reduces thyroid hormone and astrocyte density in the juvenile mouse dentate gyrus. Physiology & behavior, 216, 112798. https://doi.org/10.1016/j.physbeh.2020.112798

Ferguson, A. V., Latchford, K. J., & Samson, W. K. (2008). The paraventricular nucleus of the hypothalamus - a potential target for integrative treatment of autonomic dysfunction. Expert opinion on therapeutic targets, 12(6), 717–727. https://doi.org/10.1517/14728222.12.6.717

Markowski, V. P., Miller-Rhodes, P., Cheung, R., Goeke, C., Pecoraro, V., Cohen, G., & Small, D. J. (2017). Motor deficits, impaired response inhibition, and blunted response to methylphenidate following neonatal exposure to decabromodiphenyl ether. *Neurotoxicology and Teratology*, *63*, 51-59. https://doi.org/10.1016/j.ntt.2017.07.003

Rice, D. C., Thompson, W. D., Reeve, E. A., Onos, K. D., Assadollahzadeh, M., & Markowski, V. P. (2009). Behavioral changes in aging but not young mice after neonatal exposure to the polybrominated flame retardant decaBDE. Environmental health perspectives, 117(12), 1903–1911. https://doi.org/10.1289/ehp.11814

Rice, D. C., Reeve, E. A., Herlihy, A., Zoeller, R. T., Thompson, W. D., & Markowski, V. P. (2007). Developmental delays and locomotor activity in the C57BL6/J mouse following neonatal exposure to the fully-brominated PBDE, decabromodiphenyl ether. Neurotoxicology and teratology, 29(4), 511–520. https://doi.org/10.1016/j.ntt.2007.03.061