The obesity epidemic: one more reason to be anxious

Consuming a high-fat Western diet during adolescence can alter the development of brain circuitry involved in fear. This can put an individual at a higher risk for anxiety-related disorders.

Forrest Fearington

Childhood obesity is a rising problem in the United States, affecting over 13.7 million adolescents in the U.S.[1] Adolescent obesity is known to have numerous adverse effects on mental health – especially anxiety and stress.[2,3,4] However, the reason for this correlation is not fully understood, making prevention and treatment difficult. In a paper recently published in *Brain, Behavior, and Immunity,* Vega-Torres and colleagues investigated whether a high-fat Western diet impairs the development of neural circuits associated with fear responses.[5] Using a rat model, they found that consuming a Western diet during adolescence does indeed alter the development of brain regions and brain circuitry involved in fear. The implications of this finding are significant because they can help neuroscientists better understand the mechanisms of obesity-facilitated anxiety, potentially leading to better, more informed methods of treatment.

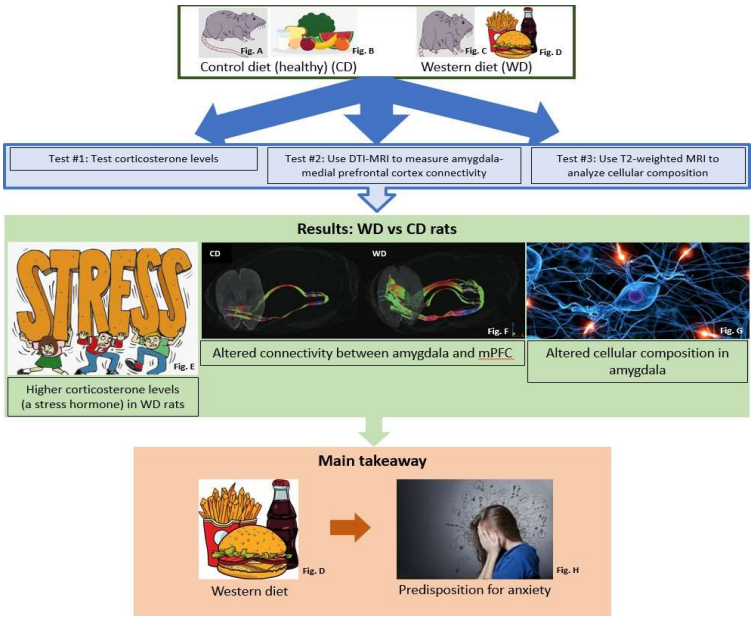
Numerous studies have suggested that obese children are at a higher risk for anxiety and impaired emotional processing.[2,3,4] However, these studies have failed to demonstrate whether social frowning on obesity is the main cause of anxiety or whether the obesogenic diet itself predisposes individuals to abnormal anxious responses.[5] From a physiological perspective, anxiety is generally associated with abnormal activity in the amygdala and medial prefrontal cortex.[6,7] These two brain structures undergo critical development stages during adolescence, and any interference during these stages can have detrimental long-term effects on one's emotional responses.[8] These pieces of evidence have led to the hypothesis that overconsumption of the high-fat Western diet during adolescence affects the development of brain cells and brain circuitry in the amygdala and medial prefrontal cortex, potentially predisposing obese individuals to anxiety-related disorders.[5] Using cutting-edge MRI imaging and chemical labeling techniques, Vega-Torres and colleagues set out to investigate this hypothesis using a rat model.

In the study, thirty-six 3-week-old rats were split into two equal groups and fed either a high-fat Western diet (41% fat) and allowed to become obese or a healthy control diet (13% fat) for 9 weeks. Rats then underwent a 2 day "stress program" to simulate exposure to traumatic events (e.g. electric shocks, loud noises). Post-mortem T2-MRI and DTI-MRI scans were obtained from the WD and CD groups, which provide information regarding cellular composition and connective pathways, respectively. Also, rat feces were collected at three points during the experiment and analyzed for corticosterone, which is a stress hormone similar to cortisol in humans.[9]

The WD rats had significantly higher corticosterone levels than their CD peers at all stages of the study. Corticosterone is closely involved in regulating stress responses, so the higher levels

found in WD rats indicate they were experiencing more stress compared to CD rats.[9,10]

The results of T2-MRI analysis showed more densely packed brain matter in WD rat amygdala. This suggests a different cellular composition between WD and CD rat amygdala, although histological analysis would be needed to confirm this. In addition, DTI-MRI analysis found that connectivity between the mPFC and amygdala (a pathway known as the uncinate fasciculus) differed greatly between WD and CD rats (Fig. F). WD rats showed more abundant connections to certain areas and less abundant connections to other areas in the amygdala and mPFC. This implies the neurocircuitry between WD and CD rats was significantly altered by diet alone.



Summary of methods and results. Rats from two groups were fed a healthy control diet (CD) and a high-fat Western diet (WD). Following 9 weeks of diet consumption and stress exposure, three tests were performed. Results showed higher stress hormone levels in WD rats, altered connectivity between the amygdala and medial prefrontal cortex (mPFC), and altered cellular composition in the amygdala in WD rats. This indicates that consuming a high-fat Western diet can predispose individuals to anxiety-related disorders.

The study clearly found that while keeping all other factors constant, consuming a high-fat Western diet alters brain connectivity, cellular composition, and hormone levels related to stress, likely predisposing these individuals to anxiety-related disorders.[5] The experiment could have been improved by investigating histological changes between WD and CD rat amygdala via staining and microscopic examination, which would have provided more insight on the cellular differences beyond a simple MRI. Interestingly, the article briefly mentioned another study by Paternain et al. that came to contrary conclusions – that is, a high-fat diet could actually reduce stress hormone levels.[10] However, Vega-Torres and colleagues merely discounted this as contrary evidence and never elaborated on possible explanations for the discrepancy, which weakens the reliability of their own findings. While it has its shortcomings, this study advances our understanding of the neural networks and structural changes that predispose obese adolescents to develop anxiety-related disorders, which may inform treatments of mental illness in the future.

References

1. Centers for Disease Control and Prevention. (2019, June 24). *Childhood obesity facts*. https://www.cdc.gov/obesity/data/childhood.html
2. Nigatu, Y. T., Reijneveld, S. A., Jonge, P., Rossum, E., & Bultmann, U. (2016) The combined effects of obesity, abdominal obesity and major depression/anxiety on health-related quality of life: the LifeLines cohort study. *PLoS ONE, 11*(2). https://doi.org/10.1371/journal.pone.0148871
3.Boitard, C., Parkes, S.L., Cavaroc, A., Tantot, F., Castanon, N., Layé, S., Tronel, S., Pacheco- Lopez, G., Coutureau, E., & Ferreira, G. (2016). Switching adolescent high-fat diet to adult control diet restores neurocognitive alterations. *Frontiers in Behavioral Neuroscience, 10*(225). https://doi.org/10.3389/fnbeh.2016.00225.
4. Kalarchian, M. A., & Marcus, M. D. (2012). Psychiatric comorbidity of childhood obesity. *International Review of Psychiatry.* 24(3), 241-246. https://doi.org/10.3109/09540261.2012.678818
5. Vega-Torres, J. D., Haddad, E., Lee, J. B., Kalyan-Masih, P., Maldonado George, W. I., López Pérez, L., Piñero Vázquez, D. M., Arroyo Torres, Y., Santiago Santana, J. M., Obenaus, A., & Figueroa, J.D. (2018). Exposure to an obesogenic diet during adolescence leads to abnormal maturation of neural and behavioral substrates underpinning fear and anxiety. *Brain, Behavior, and Immunity*, *70*, 96–117. https://ntserver1.wsulibs.wsu.edu:2137/10.1016/j.bbi.2018.01.011
6. Likhtik., E., Stujenske, J., Topiwala, M., Harris, A. Z., & Gordon, J. A. (2014). Prefrontal entrainment of amygdala activity signals safety in learned fear and innate anxiety. *Nature Neuroscience, 17*, 106- 113. https://doi.org/10.1038/nn.3582
7. Munshi, S., Loh, M. K., Ferrara, N., DeJoseph, M. R., Ritger, A., Padival, M., Record, M. J., Urban, J. H., & Rosenkranz, J. A. (2020). Repeated stress induces a pro-inflammatory state, increases amygdala neuronal and microglial activation, and causes anxiety in adult male rats. *Brain, Behavior & Immunity*, *84*, 180–199. https://ntserver1.wsulibs.wsu.edu:2137/10.1016/j.bbi.2019.11.023
8. Silvers, J.A., Insel, C., Powers, A., Franz, P., Helion, C., Martin, R., Weber, J., Mischel, W., Casey, B.J., & Ochsner, K.N. (2017). The transition from childhood to adolescence is marked by a general decrease in amygdala reactivity and an affect-specific ventral-to-dorsal shift in medial prefrontal recruitment. *Developmental Cognitive Neuroscience*, *25*, 128–137. https://doi.org/10.1016/j.dcn.2016.06.005.
9. Takei, Y., Ando, H., & Tsutsui, K. (Eds.). (2015). *Handbook of Hormones: Comparative Endocrinology for Basic and Clinical Research*. Elsevier Science & Technology.
10. Paternain, L., García-Diaz, D.F., Milagro, F.I., González-Muniesa, P., Martinez, J.A., & Campión, J.. (2011). Regulation by chronic-mild stress of glucocorticoids, monocyte chemoattractant protein-1 and adiposity in rats fed on a high-fat diet. *Physiology & Behavior, 103*(2), 173–180. https://doi.org/10.1016/j.physbeh.2011.01.017.
12. Figure A. Drawing of a rat. Adapted from Easy Drawing Guides. (no author), 2018, Retrieved from https://easydrawingguides.com/wp-content/uploads/2017/01/how-to-draw-a-rat_full-guide_EasyDrawingGuides.com_hdr-00070.pdf#page=1&zoom=auto,-150,798
13. Figure B. Healthy Food Cartoon. Adapted from pngkey. (no author), 2020, Retrieved from https://www.pngkey.com/detail/u2q8y3u2q8a9i1r5_healthy-food-png-image-with-transparent- background-healthy/
14. Figure C. Drawing of a rat. Adapted from Easy Drawing Guides. (no author), 2018, Retrieved from https://easydrawingguides.com/wp-content/uploads/2017/01/how-to-draw-a-rat_full-guide_EasyDrawingGuides.com_hdr-00070.pdf#page=1&zoom=auto,-150,798
15. Figure D. Cartoon image of junk food. Adapted from VetroStock. Lkeskinen, 2020, Retrieved from https://www.vectorstock.com/royalty-free-vector/cartoon-image-of-junk-food-cola-drink-vector- 14242372
16. Figure E. Stress cartoon. Retrieved from JING.FM. (no author), 2019, Retrieved from https://www.jing.fm/iclip/u2q8u2t4u2r5i1y3_stress-cartoon-stressed-clipart-png/
17. Figure F. DTI MRI brain scan. Adapted from "Exposure to an obesogenic diet during adolescence leads to abnormal maturation of neural and behavioral substrates underpinning fear and anxiety," by J.
18. D. Vega-Torres, E. Haddad, J. B. Lee, P. Kalyan-Masih, W. I. Maldonado George, L. López Pérez, D. M. Piñero Vázquez, Y. Arroyo Torres, J. M. Santiago Santana, A. Obenaus, & J. D. Figueroa, 2018, Brain, Behavior, and Immunity, 70, Retrieved from https://ntserver1.wsulibs.wsu.edu:2137/10.1016/j.bbi.2018.01.011
19. Figure G. Neuron image. Retrieved from Inc., by J. Stillman, 2015, Retrieved from https://www.inc.com/jessica-stillman/3-ways-to-grow-new-brain-cells.html
20. Figure H. Stressed woman image. Retrieved from Shutterstock. Billion Photos, 2020, Retrieved from https://www.shutterstock.com/image-photo/sad-young-man-worried-stressed-face-1297272154