

Isolation - How it Affects Fear Responses and Anxiety



Written by Ananya Sampathkumar

Abstract

Isolation is a common state for many people to feel. Despite this, isolation can have detrimental effects on people's emotions and brain. In particular, isolation affects the amygdala, specifically when it comes to anxiety and fear responses. Researchers have recently become further interested in the effects of isolation on the brain, especially following the COVID-19 quarantine. Understanding social isolation and its effects on the brain is crucial to learning more about the sociability of human beings, as well as how social anxiety can be caused or affected by interactions with others.

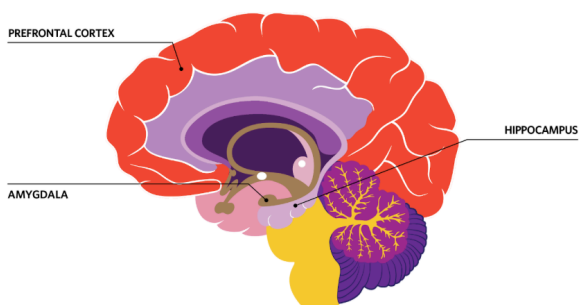
Introduction

Loneliness is commonly referred to as the feeling of social isolation. While this can be a familiar feeling for many people, loneliness is not ingrained into human nature (Finley, Schaefer, 2022). Humans are inherently social creatures: communication is so crucial for people that the usage of isolation as a torture tactic leads to drastic responses such as psychological disintegration or even death (Umberson, Montez, 2011). Like many other animals, complex social behavior and interactions are essential to proper health and survival (Young, 2008). Since socialization is consequential for proper health and development, the lack thereof can lead to several issues. Isolation is associated with higher rates of dementia and cardiovascular disease and an increased risk of mortality (Finley, Schaefer, 2022). When it comes to neurological symptoms, extended isolation can cause issues such as cognitive decline and lack of social understanding (Offord, 2020). These effects can be seen in the amygdala and the processes that it controls.

Figure 1. In the brain, the amygdala affects emotions, specifically fear and anger, which are heavily influenced by a lack of social interaction. Our current understanding of the amygdala suggests that increased levels of anxiety and further fear responses are mediated by the amygdala. (iStock.com, JamboJam)

How Social Isolation Changes the Amygdala:

Social isolation can cause the brain to undergo neural plasticity, or the changing and adaptation of the brain. Several circuit changes in the amygdala are associated with the effects of social isolation. To properly study this, Harry Harlow performed many well-known experiments with rhesus monkeys in 1944 (Offman, 2020). Harlow separated baby monkeys from their mothers and raised them in clinical settings. It was noticed that these monkeys showed strange behavior such as circling their cage mindlessly and self-mutilating (APS, 2018). Specifically, Harlow demonstrated that baby monkeys born and raised in social isolation were naturally more aggressive and struggled with maintaining social interactions with other monkeys in 1944. These experiments started many conversations regarding how social isolation can affect interactions between different lobes of the brain. One longitudinal study by the Bucharest Early Intervention Project followed 136 adopted children (mean age of 55.56 months) who were exposed to social isolation in institutions such as orphanages as young



children. This study utilized magnetic resonance imaging (MRI) in order to study the brain's structure and neural connections. In children raised in institutions, the connectivity between the PFC and amygdala was immature in comparison to a traditional upbringing; this link is crucial in regulating emotions and influencing fear learning. This could lead to a possible lack of rational decision-making, as if the amygdala is unable to communicate with the prefrontal cortex, then learning aversive stimuli would be strained. Interestingly, children who grew up socially isolated were found to have increased activity between the PFC and hippocampus regions associated with aversive learning through the same study. Although these findings seem to be contradictory, each brain connection is responsible for regulating and expressing specific emotions, reactions, or other important mechanisms; no one connection is responsible for the entirety of one large-scale interaction. The relationship between the PFC and the hippocampus being increased could be causing increased memory storage. By remembering more, the brain is able to make more educated decisions about more things, and this overthinking is often associated with higher levels of anxiety. The majority of other neural pathways affected by the increased social isolation in children who grew up in institutions are between the PFC, amygdala, hippocampus and striatum, all of which are associated with fear, anxiety, and rewards (Xiong, et al. 2023).

brain has been heavily associated with an increase of depression and anxiety, which can all be tied back to the social isolation's effects on the blood barrier of the amygdala (Wu, et al. 2022). Researchers at Peking University Health Science Center utilized male and female mice in a study to test childhood isolation's effects on the brain. Three-week-old mice were either caged alone or with four to six other mice for eight weeks. The results showed that female mice were incredibly affected by this isolation. Interestingly, there were minimal changes observed in male mice in comparison. When the female mice caged in isolation were examined, their brains showed signs of inflammation. Chronic stress can affect the blood barrier of the amygdala, and oftentimes, can lead to inflammation of the brain, and is likely a result of the social isolation that these mice underwent over the eight-week period (Wu, et al. 2022).

“...each brain connection is responsible for regulating and expressing specific emotions, reactions, or other important mechanisms...”

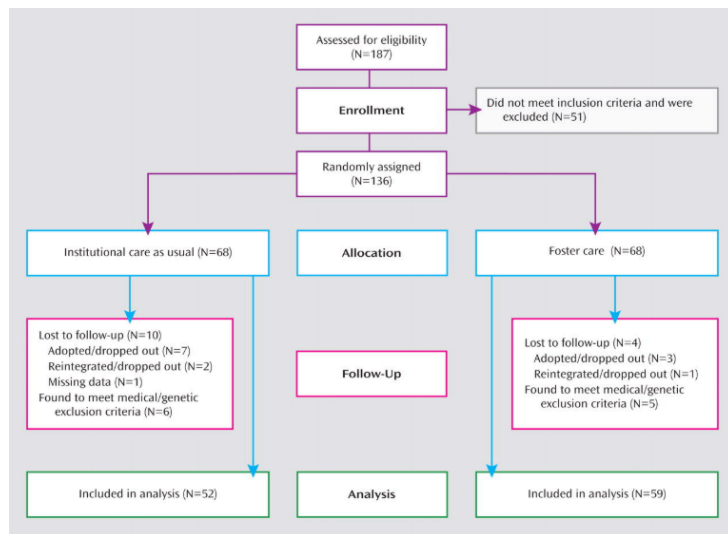


Figure 2. (Zeanah et al., 2009)

Moreover, the size of the brain can be affected by these changes as well. Researchers have found that the size of your amygdala is inversely proportional to the size of your social circle; generally, smaller amygdalas are associated with fewer angry emotions and increased socialization (Offman, 2020). These changes are fascinating and important to consider when it comes to the importance of social interaction in the brain. Finally, chronic stress caused by solitude during childhood has been shown to alter the blood-brain barrier of the amygdala. Inflammation in the

Long and Short-Term Effects of Social Isolation:

There are many long-term and short-term effects seen by individuals who have experienced social isolation of any kind. One of the major symptoms seen as a result of social isolation is the increase of chronic stress or anxiety. These disorders can be debilitating, and cause many issues and difficulties for many people who struggle with them. Furthermore, social isolation may lead to an increase in the likelihood of developing Alzheimer's. In 2018, researchers at the Tsinghua-Peking Center for Life Sciences studied how mice's ability to recognize one another was affected by social isolation. This was assessed by recording how long the mice spend interacted with one another. The mice were kept in isolation for either one day or seven days, and then given either 150 minutes or 15 minutes to explore a new environment with new mice. Interestingly, when mice were returned to their original enclosures afterward, they were able to interact with and recognize their colony mates again. This effect was also seen when researchers inhibited the Rac1 protein. Rac1 is a small signaling protein that is commonly linked to Alzheimer's and other memory loss issues (Offord, 2020). The inhibition of this protein means that signals are not being expressed as well as necessary for proper function, and specifically can affect the cell cycle and cellular plasticity. This can lead to many detrimental effects

such as memory loss (Tangella, et al. 2020). The expression of this protein during social isolation may contribute to the lack of recognition shown by the isolated mice, and seems to point towards a possible association between Alzheimer's and social isolation (Offord, 2020). These physical changes can cause many differing effects on the behavior of the individual experiencing social isolation such as heightened anxiety and depression. Still, there is still a large possibility that many of these effects are reversible. When it comes to the COVID-19 pandemic, there were many changes witnessed in the amygdala, such as a shrinkage in size. Fortunately, researchers have noted that after the social isolation period of the pandemic passed, the changes in the amygdala have returned to regular size and function, showing the plasticity of the brain (Xiong, et al. 2023).

A Case Study - Covid's Effects on the Brain

In late 2019, the world witnessed the most recent pandemic caused by SARS-CoV-2. This infectious disease spread throughout the world, forcing everyone into isolation in order to protect themselves and their loved ones from getting sick. As a result, the COVID pandemic stands as a great case study for the effects of social isolation on people for a long period of time. For many teenagers, this social isolation caused many mental health issues and neural changes. Adolescence is a major time for brain development, and the social isolation forced onto teenagers all over the world led to notable changes in their brain. A study performed on 16-year-olds reported that teenage brains had substantial physical changes from before and after the pandemic (Corrigan, et al. 2024). Following the pandemic, teenagers had lower average brain cortical thickness and larger bilateral hippocampal and amygdala volumes. These changes seem to indicate that the brains of these teenagers are maturing at a faster rate than they were prior to the pandemic. This can lead to issues such as early cognitive decline. This trend can be seen in children as well. Interestingly, this trend is more prominent in females than males. In order to track these changes, researchers utilized was 1.4 years, meaning that post pandemic male's brains were 1.4 years older than they should have been. The difference between female brains prior to and after the pandemic is more drastic. The average difference in ages between pre-pandemic female 16-year-old brains and post pandemic 16-year-old brains is about 4.2 years. This means that female brains have aged at a much faster rate than male brains during the pandemic (Corrigan, et al. 2024). While researchers are unsure as to exactly why male and female brains have aged, aging in the brain is often associated with increased rates of anxiety and depression. The faster your brain ages, the more likely anxiety and depression are to be risk factors for you (Han, et al. 2021).

Conclusion

Social isolation is the state of having very little social interaction or contact with other people. Human society is

built upon complex interactions with one another due to our social nature, and a lack of social interaction can lead to many issues. Whether those issues are neurological such as increased anxiety or more physical such as increased likelihood to develop cardiovascular disease, social isolation can be detrimental to the health of people. This is seen specifically in the amygdala, where we see increased levels of anxiety and fear response as a result of the neural circuits and structure being adapted by prolonged isolation. These long term and short term effects can be extremely difficult to adapt to, and this is clearly shown in experiments discussing the COVID-19 pandemic. Now that the peak of the pandemic was about three years ago, researchers have finally begun to start understanding the mental health effects of the quarantine on differing groups. We have finally started getting results about the neural implications of the pandemic, but there is still a lot of room to learn and understand more about the effects of social isolation on the brain and the lives of the people around us.

References

1. APS. (2018, June 20). *Harlow's classic studies revealed the importance of maternal contact*. Association for Psychological Science - APS. <https://www.psychologicalscience.org/publications/observe/obsonline/harlows-classic-studies-revealed-the-importance-of-maternal-contact.html#:~:text=Infant%20rhesus%20monkeys%20were%20taken,and%20engaging%20in%20self%2Dmutilation>
2. Catherine Offered. (2020, July 13). *How social isolation affects the brain*. Department of Psychiatry and Behavioral Neuroscience | The University of Chicago. <https://psychiatry.uchicago.edu/news/how-social-isolation-affects-brain>
3. Corrigan, N. M., Rokem, A., & Kuhl, P. K. (2024, September). *Covid-19 lockdown effects on adolescent brain structure*. ... PNAS. <https://www.pnas.org/doi/full/10.1073/pnas.2403200121>
4. Finley, A. J., & Schaefer, S. M. (2022). *Affective neuroscience of loneliness: Potential mechanisms underlying the association between perceived social isolation, health, and well-being*. *Journal of psychiatry and brain science*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9910279/>
5. Han, L. K. M., Schnack, H. G., Brouwer, R. M., Veltman, D. J., van der Wee, N. J. A., van Tol, M.-J., Aghajani, M., & Penninx, B. W. J. H. (2021, July 21). *Contributing factors to advanced brain aging in depression and anxiety disorders*. *Translational psychiatry*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8295382/>
6. Tangella, L., Clark, M. E., & Gray, E. S. (2020, September 18). *Resistance mechanisms to targeted therapy in BRAF-mutant melanoma - A mini review*. *Biochimica et Biophysica Acta (BBA) - General Subjects*. <https://www.sciencedirect.com/science/article/pii/S0304416520302488>

7. Umberson, D., & Montez, J. K. (2010). Social Relationships and Health: A flashpoint for health policy. *Journal of health and social behavior*.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3150158/>
8. Wu, X., Ding, Z., Fan, T., Wang, K., Li, S., Zhao, J., & Zhu, W. (2022, August 16). Childhood social isolation causes anxiety-like behaviors via the damage of blood-brain barrier in amygdala in female mice. *Frontiers in cell and developmental biology*.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9424755/>
9. Xiong, Y., Hong, H., Liu, C., & Zhang, Y. Q. (2023, January). Social isolation and the brain: Effects and mechanisms. *Molecular psychiatry*.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9702717/>
10. Young, S. N. (2008, September). The neurobiology of human social behaviour: An important but neglected topic. *Journal of psychiatry & neuroscience: JPN*.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2527715/>
11. Zeanah, C. H., Egger, H. L., Smyke, A. T., Nelson, C. A., Fox, N. A., Marshall, P. J., & Guthrie, D. (1970, July 1). Institutional rearing and psychiatric disorders in Romanian preschool children. *American Journal of Psychiatry*.
<https://psychiatryonline.org/doi/10.1176/appi.ajp.2009.08091438>



About the Author

Ananya Sampathkumar is a sophomore, majoring in Neuroscience with minors in Chemistry and Public Health. Outside of Brain Matters, Ananya is an assistant editor-in-chief for Double Helix Digest, a member of Starcourse, a volunteer at Carle Hospital, and works at the Office of Undergraduate Admissions as a tour guide and student ambassador. In her free time, Ananya likes to read books, make jewelry, watch movies, and hang out with her friends.

