Understanding evolutionary hypotheses for depression and anxiety

Summary by : Vedika Handa
Date : August 2021
Professor : Ronald Mumme

About the Student : Vedika Handa is a student at the Indian High school, Dubai. This paper was prepared by Vedika as a part of her course work for LS190 - Introduction to College Level Research course at Allegheny College during summer 2021.

Summary:

Depression and anxiety are illnesses of modernity and valuable adaptations of the past. Reviewing the evolutionary theories allows us to understand the adaptive advantages of the symptoms of depression and anxiety and how it benefits survival and evolutionary fitness.

Thus, an evolutionary perspective proposes that psychiatry should consider disorders and disabilities in new ways. Natural selection has shaped the complexity of the human brain, including normal functioning and the possibility for dysfunctions, during evolutionary time. Reviewing the adaptive advantages of these disorders does not imply that they are necessary and useful in our modern environments. Depression still is one of the leading causes of deaths; 700,000 people die annually and it is estimated to affect 3.8% of the population worldwide (World Health Organization 2021). Finding a cure for these disorders may not be a prime focus for the future but minimizing negative interactions with our modern environment could be one of the future avenues of research. In conclusion, understanding the evolutionary origins of mental disorders is essential for a thorough understanding of the problem and its possible solutions.

Abstract

Natural selection is powerful at optimizing complex adaptations and is continually weeding out genetic variations that reduce average reproductive success. Nonetheless, human populations appear to be awash with unfavourable genes, with high heritability and prevalence rates of serious mental disorders, including anxiety and depression. Reviewing evolutionary theories can help guide future research in psychiatric genetics by providing a framework for understanding why genetic variants that increase the risk of mental disorder have persisted despite natural selection. Persistence of these genetic variants is most likely to be due to adaptive advantages that were more valuable in ancestral environments than our modern one. However, the prevalence of anxiety and depression has been rising significantly year by year, probably because of modern novel social environments that are very different from those of our ancestors.

Introduction

Natural selection is a process that repeatedly favors alleles that improve reproductive output and increase evolutionary fitness. It facilitates the passing of traits that enhance reproductive success,

and allows neutral traits with no phenotypic effect to persist in populations. To our misfortune and fortune, traits that make our life more convenient and longer may actually reduce evolutionary fitness, and traits that harm us can be favored by natural selection if they increase fitness. One would assume that depression and anxiety are disorders that directly harm us and would eventually be eliminated, but natural selection says otherwise. Despite contrary perception, mental disorders like depression and anxiety do persist. The question this paper resolves to address is why natural selection seems unable to eliminate genetic variants that predispose us to harmful, heritable mental disorders. Understanding the evolutionary hypotheses behind depression and anxiety would provide a better understanding of the origins and persistence of these disorders. Perhaps, a few hidden adaptive advantages lie underneath the mechanisms of these disorders which natural selection did not overlook.

Why do mental disorders persist?

The evolution of depression and anxiety can be considered through various environmental and social factors but estimates imply that heritable risk is significant (Kwong et al. 2019). This suggests that there are considerable hereditary components underlying mental illness vulnerability (Guffanti et al. 2016). Heritable risk would have been responsive to natural selection pressures throughout time, removing alleles associated with disorder from the population.These findings have caused some to question the so-called psychiatric disorder paradox: why do these problems still exist if they are regarded maladaptive and have a heritable risk? Explanations are described in the table below, modified from Durisko (2016):

Evolutionary Explanation	**Description**
Mutation-selection balance	Mutations that cause disorders arise quicker than selection can eliminate them from the population.
Ancestral neutrality	Alleles that are neither beneficial nor detrimental to the ability of an organism to survive and reproduce cause disorders due to interaction with the modern environment.
Antagonistic pleiotropy	Allele that provides fitness in one trait but causes disorder in another
Alternating selection	Alleles that increase risk of disorder in one sex of a species persists if it improves fitness in the other sex.
Environmental mismatch	The trait improved ancestral fitness but interacts negatively with some aspects of the modern environment.

Heterozygote advantage	Heterozygote combination has a fitness advantage over the corresponding homozygotes.
Stabilizing selection on continuous traits	Extreme phenotypes result in disorder so selection is done for moderate phenotypes with small numbers of risk alleles.
Functioning adaptations	Adaptations that are culturally not favored.

Role of genetics on depression and anxiety

It's established that almost every human disease is influenced by genetic variants, which confer vulnerability or resistance. Similarly, the risk of mental disease runs in families. One study analysed 177 probands with major depressive disorder and their same-sex twins. The probandwise concordance in monozygotic (n = 68) and dizygotic (n = 109) twins was 46% in monozygotic (n = 68) and 20% in dizygotic (n = 109) twins, which is a statistically significant difference (McGuffin et al. 1996). This means that there is a significant heritable component to the risk of severe depression disorder, and there is no evidence of a shared family environment effect.

It's vital to keep in mind that monozygotic twins don't always display the same disorders (Hyman 2000). If identical twins with the same genes do not have the same illness, there is strong evidence that environmental factors play a role. In this approach, both genes and environmental factors influence developing depression and anxiety.

Anxiety

The adaptive functions for the various symptoms of anxiety are as given below (Bateson et al. 2011):

Symptoms	**Adaptive function**
Sensitivity towards sounds	Faster detection of threats
Insomnia	Constant alertness
Increased heart rate	Pumps blood faster and improves escape tendencies
Overthinking	Analyzes the situation and the possible ways to escape or face the situation

The evolutionary explanations behind the persistence of anxiety include:

1. *Environmental mismatch*

In ancestral environments, when facing an imminent threat, such as a dangerous animal or natural disasters, being anxious allowed hunter-gatherers to activate fight-flight responses, be more aware of their surroundings and boost their escaping tendencies. It also gave rise to cautiousness and threat aversion which aids in preventing and avoiding future dangerous situations. Thus, anxiety allowed early humans to survive longer and subsequently reproduce. However, in modern environments anxiety is usually a false alarm triggered by non-dangerous threats which include social settings like public speeches and competitions.

2. *Stabilizing selection on continuous traits*

A small number of risk alleles and a moderate degree of a particular trait are beneficial, but extremes lead to disorder. Anxiety and depression are all instances of traits with maladaptive extremes but favorable intermediate phenotypes (Durisko 2016). Stabilizing selection selects for these intermediate phenotypes and propagates the risk alleles. However, occurrence of extremes cannot be completely eliminated and it unavoidably produces these rare extremes of individuals with too much anxiety or too little anxiety.

Depression

The adaptive functions associated with different symptoms of depression are as follows (Kinney and Tanaka 2009):

Symptoms	**Adaptive function**
Inactivity and tiredness	Encourages the affected person to rest so that the energy saved permits one to better allocate resources to the immune system.
Reducing want for social interaction	Leads to reduced chances of virus transmission
Loss of appetite	Minimizes parasite exposure through eating.
Fixated overthinking	Causes breakdown of problems into smaller components where each component becomes easier to solve compared to the initial issue. (Andrews and Thompson 2009)

The possible evolutionary explanations for depression include:

1. *Functional adaptation*
   The symptoms of depression which include lethargy, reduced desire for social interactions, food aversion and sadness are evolved adaptations that protect the body from infection and illness.
2. *Psychic pain hypothesis*
   According to this theory, the cognitive reaction that causes modern-day depression evolved as a tool for humans to determine whether they are pursuing an impossible goal and, if so, to urge them to leave it. It alerts the organism to the fact that it is being harmed, encouraging it to flee the source of the harm and to learn how to avoid similar situations in the future.
3. *Rank theory*
   The rank theory proposes that if a person is involved in a long battle for dominance in a social group and is losing, depression will force the person to give up and accept the submissive role. As a result, the individual is shielded from unwarranted injury. Depression contributes to the maintenance of social hierarchy in this way. This theory is a subset of a more general theory derived from the psychic pain hypothesis.
4. *Ancestral neutrality*
   For an allele to be truly neutral over the evolutionary long term, the allele must have fitness effects extremely close to neutrality within each generation. The very fact that neutral alleles have no fitness effects makes them unlikely to affect phenotypic development. By contrast, mental disorder susceptibility alleles do affect the phenotype in modern environments, and it is likely that they would have done so in ancestral environments as well. Thus, ancestral neutrality is one of the theories that is probably not applicable for explaining depression's evolutionary roots.
5. *Heterozygote advantage*
   A common example for heterozygote advantage is sickle cell anemia with 'AA' being the common allele susceptible to malaria and 'aa' being the less common allele diagnosed with sickle cell anemia. The heterozygous 'Aa' is the most ideal combination causing the individual to be immune from malaria and not have sickle cell anemia. If this combination is so useful, it would have been fixed eventually but this cannot happen because chances for producing 'aa' and 'AA' offspring still remain 0.25 each after mating.Heterozygote advantage appears to be rare in nature. Theoretically, a species would not be able to survive extensive deleterious polymorphisms without becoming extinct. Uneven crossover events that put both A and a on the same chromosomal arm, allowing them to be passed on together without disruption, or mutations that minimize the fitness costs of either homozygote would be greatly favored by selection (Keller and Miller 2006). Thus, heterozygote advantage is unlikely to be a general explanation for why genetic variants that contribute to depression persist.
6. *Analytical rumination hypothesis*

> According to this theory, depression is an adaptation that causes a person to focus their attention on a complex problem in order to evaluate and solve it (Andrews and Thompson, 2009).

Rates and trends of depression and anxiety

Another question that comes to light is whether the prevalence rates of depression and anxiety have increased over the years. One may presume that accumulation of material wealth and a higher, more comfortable standard of living would reduce the occurrence of mental disorders but available epidemiologic evidence suggests that over the last century, especially in recent decades, prevalence has climbed, with younger cohorts showing an earlier age of onset and greater lifetime risk. One can only speculate on the increase or decrease of rates of depression and anxiety since most surveys conducted are subject to recall bias. However, consideration of only longitudinal studies that prevent researchers from interfering with subjects and that take place over longer periods of time allows researchers to minimise this bias. One longitudinal survey studied the prevalence of major depressive disorders (MDD) in a Danish population which showed an increase from 2.0% to 4.9% during 2000–06. The data were collected through the means of answering postal questionnaires comprising variables on physical and mental health, demographic and socioeconomic factors, occupational environment, social relations, health behaviours, and depression (Andersen et al. 2011). Another study used face-to-face interviews, the same diagnostic criteria, and consistent assessment instruments in randomly drawn samples of the U.S. population conducted 10 years apart to find an increase from 3.3% to 7.1% between 1991–92 and 2001–02 (Compton et al. 2006).

Why do young people have a higher risk of depression than their parents and grandparents, despite a rising level of living?There are various socio-genetic factors that influence the risk of developing these disorders. First, an increased accessibility to drugs and other substances could contribute to the phenomenon because drug and alcohol abuse are often found in conjunction with depression (Regier et al. 1990). Other lines of evidence imply that aspects of modernization which include poor diet, physical inactivity, dysfunction caused by inadequate sunlight exposure (Penckofer 2010) and sleep are associated with the rise of depression and anxiety. A toxic social environment characterized by increasing competition, inequality, and social isolation may also contribute to the rise (Gilbert et al. 2009). Lastly, decrease in stigmatization of having depression and anxiety has led to higher chances of reporting of one's mental health issues (Bethune 2019).

The two-hit hypothesis explores the interaction of genes and aspects of modern environments (Nabeshima and Kim 2013). The initial "hit" happens during the embryonic or perinatal period, when early stressors can cause epigenetic modifications of genes and developmental problems. This generates a favourable environment for the onset of psychiatric disorders. ABCB1, HDAC6, 5-HTT LPR, DISC1, neuritin, dysbindin, neuregulin-1, catechol-O-methyl-transferase

(COMT), and proline dehydrogenase (PRODH) are among the genes that could produce this first 'hit' . The second "hit" is the environmental factors that include mental stress, social nonconformity, social injustices, competition, bullying, loss of a close relative, or addictive drug abuse. Having a genetic predisposition to depression and anxiety does not guarantee the development of the condition but it weakens resistance to environmental stresses. Without the ability to recover, a mental disorder develops (Nabeshima and Kim 2013).
Thus, these modern environmental issues combined with genetic predispositions contribute to the rise in depression and anxiety.

Conclusion

Depression and anxiety are illnesses of modernity and valuable adaptations of the past. Reviewing the evolutionary theories allows us to understand the adaptive advantages of the symptoms of depression and anxiety and how it benefits survival and evolutionary fitness. Thus, an evolutionary perspective proposes that psychiatry should consider disorders and disabilities in new ways. Natural selection has shaped the complexity of the human brain, including normal functioning and the possibility for dysfunctions, during evolutionary time. Reviewing the adaptive advantages of these disorders does not imply that they are necessary and useful in our modern environments. Depression still is one of the leading causes of deaths; 700,000 people die annually and it is estimated to affect 3.8% of the population worldwide (World Health Organization 2021). Finding a cure for these disorders may not be a prime focus for the future but minimizing negative interactions with our modern environment could be one of the future avenues of research. In conclusion, understanding the evolutionary origins of mental disorders is essential for a thorough understanding of the problem and its possible solutions.

Acknowledgements

I would like to express my deep and sincere gratitude to Dr. Ronald L. Mumme for giving me the opportunity to write a research paper on a topic of my interest. I am extremely grateful for his support and guidance at every step of the way, without which I could not have completed this project.

References

Andersen I, Thielen K, Bech P, Nygaard E, Diderichsen F. 2011. Increasing prevalence of depression from 2000 to 2006. Scandinavian Journal of Public Health 39(8):857–863. doi:10.1177/1403494811424611.
Andrews PW, Thomson JA. 2009. Depression's evolutionary roots. Scientific American. https://www.scientificamerican.com/article/depressions-evolutionary/.

Bateson .M, Brilot B, Nettle D. 2011. Anxiety: An evolutionary approach. The Canadian Journal of psychiatry. 56(12):707–715. doi:10.1177/070674371105601202.
Bethune S. 2019. Gen Z is more likely to report mental health concerns. https://wwwapaorg. https://www.apa.org/monitor/2019/01/gen-z.
Compton WM, Conway KP, Stinson FS, Grant BF. 2006. Changes in the prevalence of major depression and comorbid substance use disorders in the United States between 1991–1992 and 2001–2002. American Journal of Psychiatry 163(12):2141–2147. doi:10.1176/ajp.2006.163.12.2141.
Durisko Z, Mulsant BH, McKenzie K, Andrews PW. 2016. Using evolutionary theory to guide mental health research. The Canadian Journal of Psychiatry 61(3):159–165. doi:10.1177/0706743716632517.
Gilbert P, McEwan K, Bellew R, Mills A, Gale C. 2009. The dark side of competition: How competitive behaviour and striving to avoid inferiority are linked to depression, anxiety, stress and self-harm. Psychology and Psychotherapy: Theory, Research and Practice. 82(2):123–136. doi:10.1348/147608308x379806.
Guffanti G, Gameroff MJ, Warner V, Talati A, Glatt CE, Wickramaratne P, Weissman MM. 2016. Heritability of major depressive and comorbid anxiety disorders in multi-generational families at high risk for depression. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. 171(8):1072–1079. doi:10.1002/ajmg.b.32477.
Hagen EH. 2011. Evolutionary theories of depression: A critical review. The Canadian Journal of Psychiatry. 56(12):716–726. doi:10.1177/070674371105601203.
Hidaka BH. 2012. Depression as a disease of modernity: Explanations for increasing prevalence. Journal of Affective Disorders 140(3):205–214. doi:10.1016/j.jad.2011.12.036.
Hyman S. 2000. The genetics of mental illness: implications for practice. https://www.who.int/bulletin/archives/78(4)455.pdf.
Keller MC, Miller G. 2006. Resolving the paradox of common, harmful, heritable mental disorders: Which evolutionary genetic models work best? Behavioral and Brain Sciences 29:385-452.
Kinney DK, Tanaka M. 2009. An evolutionary hypothesis of depression and its symptoms, adaptive value, and risk factors. The Journal of Nervous and Mental Disease. 197(8):561–567. doi:10.1097/nmd.0b013e3181b05fa8.
Kwong ASF, López-López JA, Hammerton G, Manley D, Timpson NJ, Leckie G, Pearson RM. 2019. Genetic and environmental risk factors associated with trajectories of depression symptoms from adolescence to young adulthood. JAMA Network Open. 2(6):e196587. doi:10.1001/jamanetworkopen.2019.6587.
McGuffin P, Katz R, Watkins S, Rutherford J. 1996. A hospital-based twin register of the heritability of DSM-IV unipolar depression. Archives of General Psychiatry. 53(2):129–136. doi:10.1001/archpsyc.1996.01830020047006.
Nabeshima T, Kim H-C. 2013. Involvement of genetic and environmental factors in the onset of depression. Experimental Neurobiology. 22(4):235. doi:10.5607/en.2013.22.4.235.

Nesse R. 1999. Testing evolutionary hypotheses about mental disorders. In Stearns SC, editor. Evolution in health and disease, Oxford University Press. p. 260-266.
Nesse RM. 2000. Is depression an adaptation? Archives of General Psychiatry. 57(1):14.doi:10.1001/archpsyc.57.1.14
Penckofer S, Kouba J, Byrn M, Estwing Ferrans C. 2010. Vitamin D and depression: Where is all the sunshine? Issues in Mental Health Nursing 31(6):385–393. doi:10.3109/01612840903437657.
Price JS. 2003. Evolutionary aspects of anxiety disorders. Dialogues in Clinical Neuroscience. 5(3):223–36. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181631/.
Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. 1990. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA. 264(19):2511–2518.
Sloman .L, Farvolden P, Gilbert P, Price J. 2006. The interactive functioning of anxiety and depression in agonistic encounters and reconciliation. Journal of Affective Disorders. 90(2-3):93–99. doi:10.1016/j.jad.2005.12.001.
World Health Organization. 2021. Depression. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression.