Syracuse University
Maxwell School of Citizenship & Public Affairs
Lerner Center for Public Health Promotion & Population Health

ISSUE BRIEF #61
January 24, 2023

The End of the "Chemical Imbalance" Theory of Depression - What Now?

Austin McNeill Brown

KEY TAKEAWAYS

- A recent review of neurochemical research and depression finds no evidence that serotonin is related to depression.
- These recent findings add to several other studies which challenge the idea that depression is an individualized illness defined by a "chemical imbalance."
- Medications for depression involving selective serotonin re-uptake inhibitors (SSRI) comprise a billion-dollar industry.
- Health professionals should use this opportunity to consider how market influence has shaped our definition of health and the science of health.

For decades, those diagnosed with depression have been told they suffer from a "chemical imbalance." This explanation involves neurotransmitters, such as serotonin, thought to be the main neurochemical responsible for major depressive disorders. Yet a recent University College of London study[1] has challenged this theory of neurochemical "imbalances" as the cause of depression. While the London study is not the first to question the validity of the theory, it summarizes the results of all pertinent previous studies in an effort to weigh the overall evidence regarding the role of serotonin in depression.

While those working in the fields of neuropsychology and professional therapy have been moving away from chemical imbalance theory, informally and over time, there has never been consensus by mental health practitioners calling for an outright rejection of the theory. The theory remains popular among prescribers such as physicians,[2] and the difference in opinion is often attributed to the differences between psychiatrists (who prescribe medication to treat mental issues) and psychologists (who provide therapy and counselling).

The evidence challenging the theory has mounted over time. Doubt has built up as a result, creating significant professional therapeutic concerns about the validity of the chemical imbalance theory to explain depression. As such, when weighed against the cost/benefit of telling a patient they have an organic neurochemical flaw, many

clinicians have forgone the theory out of concern for how it may be viewed from the patient's perspective.[2]

This brief summarizes the College of London study's main findings, including evidence against the theory that depression is caused by a chemical imbalance. I discuss how and why ideas about chemical imbalance are used by prescribers to help patients understand their conditions and argue that this may not always serve the patient's best interests.[2] I conclude with considerations for patients and health professionals who may be thinking, "What now?"

A Brief History of Depression

Major Depressive Disorder (MDD) is a psychological condition defined by experiencing at least two weeks of near-daily depressed mood, loss of interests or pleasure, weight loss or gain, physical or cognitive impairment, thoughts of suicide, and unreasonable senses of guilt or worthlessness.[3] Nationally representative studies of disease estimate that between 15% and 20% of the U.S. population suffers from clinical depression over their lifetime.[4] Yearly estimates from the same sample cite approximately one in 10 people will struggle with depression in the next 12 months.[4] Depression is considered to be medically treatable, and screening and diagnosis are available in most medical settings, such as the family doctor.[5] Ideal treatment involves a combination of medication and/or therapy.[5] Most diagnosed cases (69%) in the U.S. receive treatment, with over half of those diagnosed receiving at least one medication.[4]

What is the Chemical Imbalance Theory of Depression and What did the College of London Study Find?

The chemical imbalance theory of depression was introduced in the 1960s but rose to prominence in the 1990s alongside the introduction of new medications known as Selective Serotonin Reuptake Inhibitors (SSRI). These drugs prevent the reuptake (or recycling) of serotonin, which is a neurotransmitter associated with positive feelings. These neurotransmitters carry specific signals between brain cells, serving as a sort of ferry system from one cell to the next across what is known as the synaptic gap. Neurotransmitters ensure communication between brain cells so they can all work together.

In layperson's terms, chemical imbalance theory suggests that the ferrying action of mood elevating neurotransmitters, such as serotonin, may be inadequate due to low concentrations in the brain, leading to feelings of depression. Less serotonin ferrying between cells in the synaptic gap reduces the capacity to transmit positivity from one cell to the next. Imagine having a lot of positive letters and delightful packages needing to get across the synaptic gap, but there are only a few serotonin molecules available to ferry them. Since serotonin specializes in this kind of mail delivery, without more serotonin, all that positive mail will be delayed in crossing. This is the general problem that SSRIs seek to solve. The goal of SSRIs is to increase the number of neurotransmitters ferrying across so more mail and packages (sense of positivity) can get across at one time. This concept is the basis of SSRI prescriptions. More ferries mean more positive mail can get to where it needs to go.

With the invention of SSRI drugs and chemical imbalance theory, the number of depression diagnoses began to rise worldwide, from 172 million in 1990 to 258 million in 2017 (Fig. 1). It is no surprise that the rate of prescribing SSRIs rose after the 1990s as new SSRI medications were patented and marketed. In the U.S., by 2015 more than 2

out of 3 of the 25 million people diagnosed with depression received at least one prescription drug.[6] Additional medications, such as benzodiazepines (an anti-anxiety medication), are often co-prescribed in nearly one in five of these cases.[6] Figure 1 shows the total number of diagnoses of MDD from 1996-2015 in grey. Each set of bars shows the composition of prescriptions used to treat the condition. As the figure demonstrates, the number of depression diagnoses has grown over time, and the use of medications to treat depression has become increasingly common.[6]

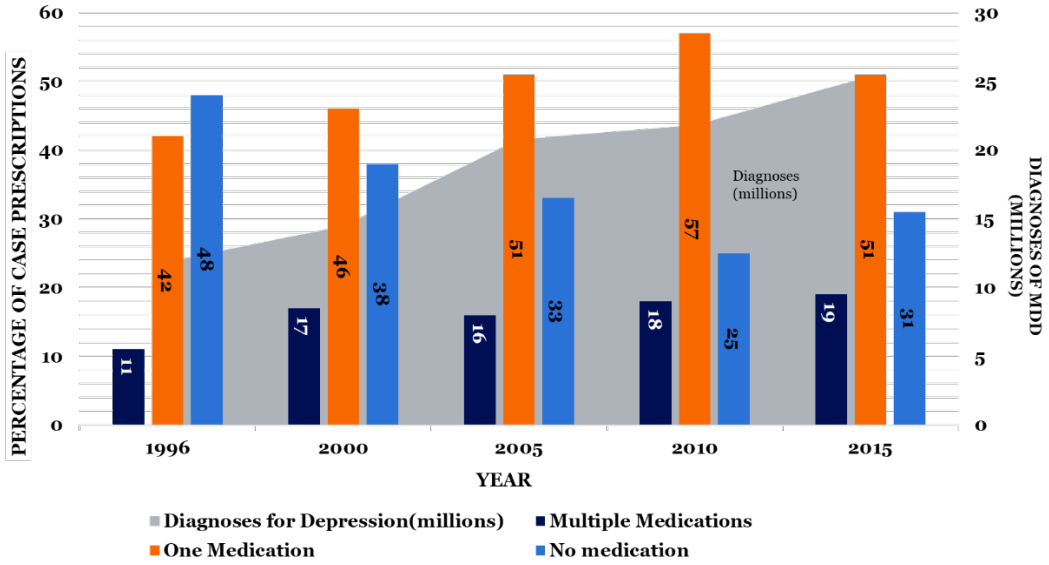

Figure 1. Distribution of Prescription for Diagnoses Cases of Depression, 1996-2015
Data Source: Data for chart is adapted from Luo et al., 2020

SSRI Drugs are Very Profitable for Pharmaceutical Companies

The study from the College of London concluded that: "there is no convincing evidence that depression is associated with, or caused by, lower serotonin concentrations or activity."[1] This is quite a revelation considering not only the sheer number of depression diagnoses since the 1990s, but the ensuing prescriptions which have arisen from such diagnosis. Pharmaceutical companies have amassed trillions of dollars treating depression with SSRI drugs. Assuming the College of London findings are reinforced by future research, the best-case scenario is that SSRIs technically work but that the target (serotonin) has no relation to depression. However, a more critical view might see SSRIs as a profit-making scheme, with pharmaceutical companies widely promoting a class of drug that do little to nothing to treat the condition for which the drugs are prescribed.

Taken together, rising diagnoses, increasing prescriptions, and the incorporation of chemical imbalance theory all merge into a cultural narrative about depression and treatment which raises tough questions about interests, markets, and science. Given the growing body of evidence and lawsuits that showcase the unethical business practices of for-profit pharmaceutical companies,[7] there is reason to suspect profit interests play a definitive role in encouraging the diagnosis of depression and subsequent prescriptions to treat it.[8] There is a lot of money at stake. For example, Prozac™ (fluoxetine), an SSRI approved in 1987, is considered the "best selling drug of all time." It was one of the first "blockbuster" drugs, reaping in $21 billion in profits while under patent, accounting for a third of the company's profit by 2001.[9]

When the results of the College of London study are combined with recent long-term and patient-centered studies exploring the outcomes for SSRI prescribing, the rationale for prescribing SSRIs as a long-term solution may be in serious doubt. Long-term, patient quality-of-life appears to initially improve but then decline in SSRI treatment.[10, 12] Other studies on long-term patient experiences with SSRI note multiple negative side-effects ranging from emotional blunting to sleep problems and sexual dysfunction.[11] About half of those on long-term SSRI are able to taper off them without relapse of depression. However, withdrawal from SSRIs is acute and must be managed under the care of a physician.[12] *Abrupt discontinuance of any prescribed medication should not be attempted without a doctor's oversight*.

We Need a Broader Understanding of Depression

How should we view the theory of chemical imbalance? First, we should recognize that our desire to individualize illnesses like depression is culturally informed and decidedly fashioned by markets. In our acceptance of chemical imbalance theory, we let culture and markets, rather than science influence our opinions. In accepting the theory, we accepted the idea that regardless of context, social issues, or material factors, the individual and their body chemistry was the fundamental cause of illness. The suffering is turned against the sufferer and then monetized, while also masking the realities of social inequities.[15] We have known that as social animals, humans have deeply complex social needs which rely on relational and contextual factors to promote self-worth, self-esteem, and positivity.[14] Positive selfhood is a communal and social production that uses systems of meaning between humans and the social world around them. Culture, community, material conditions, and close relationships have far more to do with how one feels about themselves than any singular or individual deficiency.[15] If we are going to insist on a society that is defined by individualism and consumerism, we should at least recognize that consumption of medications will have only limited usefulness in addressing social problems.

Health professionals may need ask harder questions about the roles of meaning, community, and capital on health. There are a range of questions that would be useful in understanding the lives of patients with depression. What meaningful activities or relationships does the patient have? How do they feel about their jobs, finances, their future? Do they feel like they belong? Do they have hope? What are the sources of material or social insecurity? Do low wages, family stress, or lack of time represent the major contributing factors? Are there enduring psychological burdens, trauma, or shame?

Both psychological and contextual factors (e.g., economic security, meaningful work, and social connections) must be addressed, but in separate ways. Medication, even if it is effective, cannot treat more than the body. *Health professionals should see depression as a social and shared problem that is best addressed in social and shared ways of care and community.* Health professionals should ask what they can do to help people by understanding the conditions in which their patients live, work, and interact and then help them to address the challenges related to these conditions through meaningful activities, accessing material supports, and facilitating community engagement. Finally, health professionals may need to reconsider their own acceptance of theories like "chemical imbalance" and the professional desire to individualize social problems. This is a moment for professional self-reflection.

For many, the coronavirus pandemic highlighted exactly how far out of balance their work and family lives truly were. The disruption allowed people to see how jobs took

precedence over family, social connections, and even their own sense of meaning. Health professionals should consider these recent phenomena as evidence that much of the dissatisfaction and depression in society may have to do with modern lifestyles. This idea is neither new, nor controversial. In short, depression is unlikely to be a purely individual problem, and treating depression must be socially comprehensive. This historic moment presents an opportunity to think differently about how we evaluate the relationship between meaning and health.

Now What?

There are two main considerations moving forward. First, individuals who may be prescribed medications for their depression should involve their prescriber in any decisions regarding such medication or changes to medication. An important feature of SSRIs is that some people feel these medications have helped them, and they are generally safe. Subjective sense of improvement is still a positive result. Today we simply know a bit more about depression than in the past, and individuals should familiarize themselves with the latest research so that they can have informed dialogue with their physicians. These recent finding in no way disqualify the personal experience of depression. It is a debilitating condition.

Second, for health professionals, these findings join the growing science challenging the marketized version of health science that is promoted by the pharmaceutical industry. It is time to reevaluate how much of health science is influenced by the quasi-scientific rhetoric of marketeers. Our direct-to-consumer system of medication promotion leaves health professionals to fill the information gap with the latest science. Translating and communicating science to the public is a significant part of being a health professional. This responsibility has been neglected in recent years. In closing, health professionals should inquire as to the complex conditions of people lives, exercise skepticism in medical silver bullets, and work to establish more holistic solutions to complex problems like depression.

References

1. Moncrieff, J., Cooper, R. E., Stockmann, T., Amendola, S., Hengartner, M. P., & Horowitz, M. A. (2022). The serotonin theory of depression: a systematic umbrella review of the evidence. *Molecular Psychiatry*, 1-14.
2. Kemp, J. J., Lickel, J. J., & Deacon, B. J. (2014). Effects of a chemical imbalance causal explanation on individuals' perceptions of their depressive symptoms. *Behaviour Research and Therapy*, *56*, 47-52.
3. Diagnostic and Statistical Manual (DSM-V)
4. Hasin, D. S., Sarvet, A. L., Meyers, J. L., Saha, T. D., Ruan, W. J., Stohl, M., & Grant, B. F. (2018). Epidemiology of adult DSM-5 major depressive disorder and its specifiers in the United States. *JAMA* psychiatry, 75(4), 336-346.
5. Cuijpers, P., Oud, M., Karyotaki, E., Noma, H., Quero, S., Cipriani, A., ... & Furukawa, T. A. (2021). Psychologic treatment of depression compared with pharmacotherapy and combined treatment in primary care: a network meta-analysis. *The Annals of Family Medicine*, 19(3), 262-270.
6. Luo, Y., Kataoka, Y., Ostinelli, E. G., Cipriani, A., & Furukawa, T. A. (2020). National prescription patterns of antidepressants in the treatment of adults with major depression in the US between 1996 and 2015: a population representative survey-based analysis. *Frontiers in Psychiatry*, *11*, 35.
7. Michaels, D. (2019). The denial playbook: How industries manipulate science and policy from climate change to public health. *Congressional Testimony before the House Natural Resource Committee*, February 26, 2019.

8. Greenslit, N. P., & Kaptchuk, T. J. (2012). Antidepressants and advertising: Psychopharmaceuticals in crisis. *The Yale Journal of Biology and Medicine*, *85*(1), 153.
9. McLean, B. (2001). A Bitter Pill Prozac made Eli Lilly. Then along came a feisty generic maker called Barr Labs. Their battle gives new meaning to the term" drug war.". *Fortune-European Edition*, *144*(3), 56-63.
10. Almohammed, O. A., Alsalem, A. A., Almangour, A. A., Alotaibi, L. H., Al Yami, M. S., & Lai, L. (2022). Antidepressants and health-related quality of life (HRQoL) for patients with depression: Analysis of the medical expenditure panel survey from the United States. *PloS One*, 17(4), e0265928.
11. Cartwright C, Gibson K, Read J, Cowan O, Dehar T. Long-term antidepressant use: patient perspectives of benefits and adverse effects. *Patient Preference & Adherence*. 2016 Jul 28;10:1401-7.
12. Hengartner, M. P. (2020). How effective are antidepressants for depression over the long term? A critical review of relapse prevention trials and the issue of withdrawal confounding. *Therapeutic Advances in Psychopharmacology*, 10, 2045125320921694.
13. Fornaro, M., Cattaneo, C. I., De Berardis, D., Ressico, F. V., Martinotti, G., & Vieta, E. (2023). Antidepressant discontinuation syndrome: A state-of-the-art clinical review. *European Neuropsychopharmacology*, *66*, 1-10.
14. Pyszczynski, T., Greenberg, J., Solomon, S., Arndt, J., & Schimel, J. (2004). Why do people need self-esteem? A theoretical and empirical review. *Psychological Bulletin*, *130*(3), 435.
15. Holmes, M., & McKenzie, J. (2019). Relational happiness through recognition and redistribution: Emotion and inequality. *European Journal of Social Theory*, *22*(4), 439-457.

Acknowledgements

The author would like to thank Alexandra Punch and Shannon Monnat for providing feedback and edits on prior versions of this brief.

Recommended Citation

Brown, Austin. (2023). The End of the "Chemical Imbalance" Theory of Depression - What Now? *Lerner Center Population Health Research Brief Series*. 206. https://surface.syr.edu/lerner/206

About the Author

Austin Brown (abrown48@syr.edu) is a PhD student in the Social Sciences program and a Research Assistant with the Lerner Center for Public Health Promotion and Population Health in the Maxwell School of Citizenship and Public Affairs at Syracuse University.

SYRACUSE UNIVERSITY LERNER CENTER FOR PUBLIC HEALTH PROMOTION & POPULATION HEALTH RESEARCH BRIEF SERIES

Series Editor - Shannon M. Monnat
426 Eggers Hall | Syracuse | New York | 13244
syracuse.edu | lernercenter.syr.edu
To access all our briefs, visit: https://surface.syr.edu/lerner/

The mission of the Syracuse University Lerner Center for Public Health Promotion & Population Health is to improve population and community health through research, education, and outreach focused on the social, spatial, and structural determinants of physical, mental, and behavioral health and health disparities.