Depression Diagnosis and Treatment: Reformation Required

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ABSTRACT. By the numbers, depression is a staggeringly prevalent mental disorder. 350 million people are depressed worldwide, $11.3 billion is spent on antidepressants annually, and the rate of depression diagnoses has grown 400% since the 1980s. There is a clear necessity for an improvement in current medical practices. Figuring out the root causes, formulating stronger methods of diagnosis, and properly identifying and treating those who suffer from depression is imperative to public health in America and abroad. I propose that advancing scientific quantification of depression by improving the efficacy of research practices and funding will reform the current inadequacy of depression diagnosis and treatment. This proposal is threefold. My first suggestion for reforming depression diagnosis and treatment rests in the publication of all research, studies, and clinical trials associated with the mental disorder. Secondly, we must emphasize a quantitative format for diagnosis and treatment based on the neurobiological specificities of the individual. Finally, we need to consider a system of checks and balances between academic and industrial research to prevent the dissemination of inaccurate information and faulty drugs. It is my hope that advancing neuroscience research through these proposals will elucidate the line between emotion and emotional disorders, helping us treat and diagnose de-

1. Introduction

350 million people are depressed worldwide. $11.3 billion is spent on antidepressants annually, but the rate of depression diagnoses has grown 400% since the 1980s (Ross, 2012). What if this is all wrong? A study by Johns Hopkins reports that 60% of depression diagnoses are in fact misdiagnoses ("Are We as Depressed as We Think," 2013). Misdiagnoses leads to more people thinking they have depression, and more people subsequently purchasing medication to fix it. What if the antidepressants do not work? A 2008 study from Irving Kirsch of Harvard Medical School estimates that 75% of the time, "an antidepressant's effect could have been obtained merely by taking [a] placebo" (Mukherjee, 2012). Where are the mistakes being made? I believe they are being made in the inadequate diagnosis criteria and treatment plans for depressed patients, propagated by the current status of depression research.

Figuring out the root causes, formulating stronger methods of diagnosis, and properly identifying and treating those who suffer from depression is imperative to public health in America and abroad. Insufficient standards for depression diagnosis, uncertainty among clinicians, and deficient knowledge of the depressed brain leads to misdiagnosis and mistreatment of patients. There is a clear necessity for an improvement in current medical practices. Since depression is part of a complex network within human neuroanatomy and genetics, fixing this problem lies in the understanding of depression's neurobiological underpinnings in association with happiness. Improving our cognizance of depression depends on our ability to quantify emotion through neuroscience research. Advancing scientific quantification of depression by improving the efficacy of research prac-

2. Depression and Happiness Share Neurobiological and Genetic Bases

Quantifying emotion in the human body has the potential to improve proper diagnosis of depression and create individualized treatments for patients. Advanced technologies such as functional magnetic resonance imaging (fMRI), positron emission tomog-

fast scan voltammetry (FSV) allow measurement of brain activities and neurotransmitters associated with emotion (Leyton, 2009, 234). For example, these tools have revealed brain regions such as the amygdala, and neurotransmitters such as serotonin, norepinephrine, and dopamine to have a strong correlation with happiness compared to other brain regions and neurotransmitters ("The Neurobiology of Emotion"). Furthermore, certain genes that code for specific proteins, enzymes, and functions unite the brain systems and chemicals connected with emotion. An individual's confluence of neurobiology and genetics dictates normal emotional states, as well as the extent of his or her nonstandard reactions to emotional stimuli.

Depression has a similar basis in the malfunctioning of these systems. The disorder is not simply the abundance or dearth of neurotransmitters interacting with the brain. Instead, the network of neurotransmitters and their relation to the network of the brain creates a working spectrum of emotion. For depression specifically, the newest and most promising research considers the subcallosal cingulate, a bundle of nerve cells that "function as a conduit" between brain regions controlling consciousness and emotion; this bundle of nerve cells depends in part on the proper functioning of the serotonin system, which has strong links to human happiness (Mukherjee, 2012). A malfunctioning of any one system mitigates the chances for another connected system to work properly, leading to disorder.

Understanding and quantifying happiness can illuminate an ensuing disorder in mental states by creating a solid foundation for explicit, objective criteria. According to Professor Morten L. Kringelbach of Oxford (2009), neuroimaging techniques are especially helpful in measuring happiness. He explains, "[self-reported happiness] ratings throughout a human neuroimaging experiment . . . [can be correlated] with changes in activity in the human brain" (p. 204). This technique can be used for measuring happiness,

3. Depression Statistics in the U.S. and Abroad

Unfortunately, depression knows no boundaries. Over 30 million Americans are currently using antidepressant drugs (Ross, 2012). Internationally, a study in the PLOS Medicine journal found that "depression is the second leading cause of years lived with disability," (Ferrari et al., 2013) with 9 percent of the U.S. and 4 percent of the world diagnosed with it. As universal as happiness, "people of all ages, backgrounds, lifestyles, and nationalities" suffer from depression ("Major Depression Facts," 2013). It is a silent and debilitating pandemic. This data indicates an enormous global problem, but researchers have limited knowledge about depression's reliance on the malfunctioning of specific neural pathways associated with emotion.

The increasing frequency in global depression rates and the statistics of depression prevalence and misdiagnosis are monumental causes for concern. Are people getting more depressed, or are doctors getting worse at diagnosing patients? Do antidepressants really work if depression rates are increasing? Answers to these questions have many variables, but the common uniting factor in resolving these problems is researching how depression manifests itself in humans. Depression is detrimental to health, longevity, and productivity; decreasing its rifeness would in-

4. A Global Call for Reform

Domestic and international pervasiveness is the first reason for reform. Improving standards for diagnosis can help doctors identify genuine cases of depression in patients and reduce false positives. In a publication on depression in the journal Health Affairs, the authors announced, "doctors should be better educated on diagnosing depression" (Shute, 2011). Giving the public and the doctors who treat them more precise information about the mental disorder will increase public awareness concerning proper identification and treatment.

Secondly, the medical formulation for diagnosis is qualitative and open to interpretation. The backbone of depression diagnosis rests with the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM). According to the DSM, one must have "five or more . . . symptoms over a two-week period, most of the day, nearly every day" (Nuckols). These symptoms include "depressed mood," "significantly diminished interest . . . in activities," "significant weight loss [or weight gain] when not dieting," "insomnia or increased desire to sleep," "restlessness or slowed behavior," and "fatigue or loss of energy" ("Depression Tests and Diagnosis," 2014). Additionally, the DSM states symptoms can be based on "your own feelings" or the "observations of some-

a subjective medical framework. There are too many opportunities for open interpretations of symptoms in these guidelines. Giving medical care providers leeway for diagnosis engenders misdirected distribution of prescriptions. Improvement lies in the advancement of objective criteria through compelling research.

Finally, refining suitable treatments for depression is essential. Scientists are not completely sure why antidepressants work for some people and not others (Hendriksen, 2014). Additionally, "almost three-quarters of [antidepressant] prescriptions are written without a specific diagnosis" (Shute, 2011). In this current system, over-prescription of drugs leads to the unnecessary propagation of adverse side effects. These include nausea, weight gain, decreased sex drive, insomnia, and anxiety ("Depression Tests and Diagnosis," 2014). Antidepressants seem to produce side effects that are the same as the symptoms of the depression that they are supposed to treat. In fact, the FDA also mandates that all antidepressants carry a "black box" notice: the strictest label warning for prescription drugs due to an increased risk of suicide ("Depression Tests and Diagnosis," 2014). The need for a black box warning indicates a limited understanding of how antidepressants work, but doctors do not often exercise extreme precautions before prescribing. Considering primary care doctors, not psychiatrists, wrote 254 million prescriptions globally in 2010 for mild to moderate depression, we need to reevaluate the usefulness of antidepressants and the basis for which certain drugs are prescribed to prevent the risk of severe side effects due to misdiagnoses (Shute, 2011). There is more; in a report for ABC News, reporter Lauren Cox states that doctors and psychiatrists make their "best guess" in prescribing antidepressants for their patients (2009). Insufficient standards for diagnosis and a limited knowledge of how antidepressants work are to blame. Even if doctors are operating under their best intentions for the

5. What We Currently Know About Depression and Happiness

Finding more concrete evidence showing a physical link to emotion is the first step in moving away from diagnoses and treatments based on guesses. Certain regions of the brain are linked to emotions in greater proportion than others, and the extent to which someone feels sad or happy depends on individual neurobiological idiosyncrasies. Scientific quantification of depression and happiness is made possible through technological advances; for example, connecting humans to various brain scanning machines, emotional reactions can be directly correlated with a change in neural activity documented by an attached computer. Specifically, the hippocampus has garnered attention regarding signals between brain neurons in relation to the subcallosal cingulate, mentioned earlier. Doctor Siddhartha Mukherjee of Columbia University says in his article "Post Prozac Nation" for the New York Times, "In the nondepressed brain, circuits of nerve cells in the hippocampus may send signals . . . to regulate mood," but "when the hippocampus malfunctions . . . emotional pain can be generated and amplified out of context" (2012). Thus, specific brain regions may play certain roles in properly functioning emotions.

We also know that the brain has other chemicals working for it, assisting in emotional response. Analyzing the brain's patterns of activity in conjunction with serotonin, norepinephrine, and dopamine may offer improved ways to describe depression and happiness. These three neurotransmitters transmit signals in the brain. Neuroscientist Susan Greenfield (2000) in her book, The Private Life of the Brain, posits that neurotransmitters act like a "fountain," (p. 41) greatly affecting the brain and causing neurons to generate electrical signals. Mukherjee (2012) adds that neurotransmitters are "dynamic factors that make nerves grow, perhaps forming new circuits." Scientists and researchers agree that these neurotransmitters play a role in emotion, but this is the only consensus that has significant accompanying research. Requiring objective methods to diagnose and treat depressed patients depends on the greater comprehension of known functions and systems related to emotion.

Depression and happiness are also linked innately through genetics. We know there are particular genes associated with increases in happiness. For example, the 5-HTTLPR gene makes a serotonin transporter molecule, but an individual can receive long versions or short versions at birth as a pair of alleles. Of the 2574 teens part of a research study analyzing the effects of 5-HTTLPR, those with the two long versions of the gene were twice as likely to say

different individuals ("Depression Tests and Diagnosis," 2014). Consider two patients sharing the same depression diagnosis under current medical standards. There is a high probability each patient will react differently to antidepressants, psychiatric therapy, or a combination of the two (Mukherjee, 2012). Genetic predispositions may explain inconsistencies in treatment response. Individualizing treatment plans through identification of unique genetic and neurobiological factors properly acknowledges depression's complexity.

6. Depression is a Shape-shifting Disorder

Like a fingerprint, depression symptoms are unique to individuals. The DSM assigns diagnoses by correlating similarities in physical and emotional indicators among patients. Main subtypes of depression include Major Depressive Disorder, Persistent Depressive Disorder, Premenstrual Dysphoric Disorder, Substance and Medication-induced Depressive Disorder, and Disruptive Mood Dysregulation Disorder (Nuckols). The last subtype, updated in 2013, is the DSM's latest attempt at refining diagnosis descriptions; Disruptive Mood Dysregulation Disorder describes abnormal tempers and irritability in children ages six to eighteen exclusively. However, Major Depressive Disorder is the number one psychological disorder in the western world ("Depression," 2011). The National Institute of Mental Health differentiates Major Depressive from Persistent Depressive Disorder by the duration of symptoms, with the latter involving a two-year minimum ("Depression," 2011). Doctors and researchers are strenuously attempting to map a sea of subtypes with limited knowledge of why each is different within an individual.

Even though new versions of the DSM are released with improvements to previous classifications of disorders, the broad statements and generalized characteristics of each subtype currently do not possess proper medical specificity begetting accurate diagnosis and treatment. The official, recognized link among these disorders is "the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that impact function" (Nuckols). In essence, the medically accepted commonality between these subtypes is general sadness and apparent changes in body and brain function: a broad umbrella statement. We can explain roughly how each subtype is different, but we cannot fully explain why. Current research points us to regions of the brain, neurotransmitters, and certain genetic tendencies, but without

7. Treatments Are a Guess and Check

Regardless, depression is still a real and debilitating mental disorder. Treatments aim to alleviate depressive emotions by increasing the likelihood of positive emotions. The entire structure of antidepressant medication hinges upon our current knowledge of which neurobiological factors make people happy and why. It is no surprise that scientists are still not sure how and why antidepressants work ("Depression," 2011). Current research has shown that modern antidepressants increase the concentrations of specific neurotransmitters by preventing reuptake in the brain ("Depression Tests and Diagnosis," 2014). The brain naturally reabsorbs neurotransmitters, and antidepressants block this reabsorption. The belief is that increasing concentrations of "feel-good" neurotransmitters such as serotonin will relieve depression symptoms. The most popular antidepressants created with this notion of a chemical imbalance include serotonin, norepinephrine, and dopamine reuptake inhibitors. Zoloft, Lexapro, and Prozac are three such drugs (Cox, 2009). When doctors prescribe an antidepressant, they make an educated guess based on their experience. The drug could potentially work, or the patient will need to try a different one in two to six weeks because his or her body does not respond to it well.

Are drugs the only option for depressed patients? Anti-drug advocates would say no, claiming there are other methods of treatment that are safer and more effective than medication. These treatments work holistically, healing the connection between the brain and body. Alternatives such as yoga, acupuncture, and physical exercise have been shown to significantly improve mood in individuals with mild to moderate depression (Ross, 2012). These activities work on the same premise as antidepressants, without the side effects: stimulating the release of "feel good" chemicals ("Depression and Exercise," 2014). Supporting the theory of depression as a chemical imbalance, Greenfield maintains that depression is an inappropriate hyperactivity of neurons. She states that neurotransmitters may "involve limitation of neuronal connections activated at any one moment," and antidepressants decrease this excessive "neuronal

not explain why multiple studies show no correlation regarding neurotransmitter concentrations in autopsies of depressed patients (Mukherjee, 2012). Serotonin, norepinephrine, and dopamine may be involved in depression and happiness, but the extent of their involvement is unclear.

8. The Brain Requires Further Mapping

Current theories of how depression works rely on correlative data: therein lies the problem. A higher concentration of neurotransmitters does not always equal a happier person, just as one brain region is not entirely responsible for emotion. Scientists are trying to find specific examples of causality in depression, but are limited by our current understanding of the brain. Even with advanced technologies such as fMRI and PET scans, there is no definitive statistic on how much of the brain we know, only that we do not know a great deal. In a program on the brain for PBS, Kurt Fischer, the director of the Mind, Brain, and Education program at the Harvard Graduate School of Education, lightheartedly says, "we do not know very much!" ("How Much Do We Really Know"). In the same program, UCLA clinical professor Daniel Siegel responds that humans are "just beginning to identify how systems in the brain work together in an integrated fashion to create complex mental processes" ("How Much Do We Really Know"). The brain's system of emotion is integral for quantifying depression, but emotion could also be widely linked to other brain systems. Isolating brain research to specific regions allows in-depth analysis, but to improve depression diagnosis and treatment, researchers will need to focus on breadth as well: connecting the brain's intricacies to form a more detailed picture of human emotional response.

Neuroscience has advanced our understanding of the brain from a center of thought to a sophisticated, hyper-connected assemblage of numerous systems. When the brain malfunctions because of internal or external stimuli in depression, quantifying the ensuing emotional disorder is an impressive feat to undertake. Furthermore, different subtypes of depression may involve a variety of factors. In some people, certain neurotransmitters could have a larger role in emotion than others (Mukherjee, 2012). Im-

9. Reexamining Publications and the Spread of Accurate Information

An advanced knowledge of depression relies on the dissemination of credible academic publications and properly funded research. Academia thrives on this foundation—but unfortunately—many studies are not published on purpose. Hindering the development of reliable treatments are the numerous unpublished studies on antidepressants. Withholding information from the public and academic spheres severely limits the circulation of knowledge for which drugs work and why. Irving Kirsch's (2010) meta-analysis, examining 38 published clinical trials involving more than 3,000 depressed patients, showed that the placebo effect was the cause of most mood improvement. Worse still, upon digging up unpublished depression studies using the Freedom of Information Act, Kirsch (2010) and his colleagues found antidepressants highly ineffective; half of the trials showed no difference between placebo and drug. Inconclusive data or limited sample sizes are valid reasons for unpublished studies, but choosing not to publish clear examples of antidepressant ineffectiveness skews trustworthy "published" information.

If one reads the Federal Drug Administration's guidelines on supporting approval for antidepressant medication, one to two studies providing "substantial evidence" of a drug's efficacy is adequate ("FDA Report: Guidance for Industry," 1998). Putting this guideline into perspective, a laboratory can conduct 10 studies, two of which show a small advantage in taking an antidepressant while the other eight reveal no perceivable benefit, and the drug can receive FDA approval. Kirsch (2010) prudently notes that an antidepressant's effect does not have to be large; "it doesn't have to be clinically significant; it just has to be statistically significant." This system of approval unjustly propagates subpar performance of antidepressants

10. Reforming Data Discrepancy

Requiring only statistical significance perpetuates a culture of approval based on the medication's creator, not the medication's user. The FDA's method of antidepressant approval also allows patients to be prescribed drugs that might not even work. My first suggestion for reforming depression diagnosis and treatment rests in the publication of all research, studies, and clinical trials associated with the mental disorder. This includes all tests conducted on antidepressants, as well as alternative forms of treatment. If

the very least be made accessible to the public. The Freedom of Information Act is a solid foundation for open distribution of knowledge, but it only applies to federal agency records, requires a written request for specific information, and the agencies are not required "to do research for you, analyze data, answer written questions, or create records in response to your request" ("How Do I Make a FOIA Request," 2010). Additionally, if a pharmaceutical company conducts a private clinical trial separate from a federal entity, there is no guarantee that an individual can ask for or acquire the results if they are not submitted to the FDA.

Why would pharmaceutical companies conduct private trials, or refuse to publish certain studies? Consider GlaxoSmithKline's (GSK) involvement in the largest healthcare fraud settlement in U.S. history. GSK failed to report safety data to the FDA, promoted unapproved uses for antidepressants Paxil and Wellbutrin, and bribed doctors to promote and prescribe these medications improperly. In 2012, GSK was required to pay $3 billion dollars and agree to monitoring by the U.S. government for five years ("GlaxoSmithKline," 2012). GSK was worried about its profit, not its patients. The largest U.S. health care scandal in history involved antidepressants, but it is not an isolated incident. Other companies such as AstraZeneca, Novartis, and Bayer (creator of Aspirin) have also been accused of malpractice (Ray, 2014). Transparency is the key to exposing which drugs work. Transparency can be achieved through requiring higher standards for FDA approval, and mandating that all trials and studies are accessible. Without this openness, pharmaceutical companies will per-

11. Shifting From Qualitative to Quantitative Diagnosis

Beyond improving the rate of publication and transparency, my second suggestion for reform emphasizes a quantitative format for diagnosis and treatment based on the neurobiological specificities of the individual. We know there are multiple subtypes of depression, numerous stimuli that cause it, and even more bodily factors that influence it. Diagnosis and treatment will benefit from personalized care that evolves from the greater comprehension of how all these aspects work together. There is no reason for depressed patients to have the same medication if individuals respond differently based on their biological and genetic makeup. Specific treatment plans will develop through further brain and genetic research. For example, assume advanced analysis of a person has shown that his specific neurobiological idiosyncrasies place strong emphasis on serotonin. Recall the long version of the 5-HTTLPR gene as one such idiosyncrasy. If his happiness inordinately depends on serotonin, existing antidepressants that are known to promote increased serotonin concentrations can be used with enhanced specificity. This example draws on the chemical imbalance theory, but knowing how happiness malfunctions in other individuals to cause depression can be instrumental in creating other patient-specific treatment plans. Isolating specific neurobiological pathways in patients is a crucial step towards quantitative and objective medical approaches to depression. Moving away from the qualitative depression diagnosis standards outlined in the DSM requires that doctors have a better knowledge of how depression works. Quantifying the components involved in depression yields the possibility of reducing depression misdiagnoses and decreasing antidepressant prescriptions. Individ-

12. It Is Wise to Invest

Reforming depression diagnosis and treatment as dictated above requires proper investment in brain research concerning human emotion. This must be accomplished by reconciling the relationship between academic and industrial research: my last suggestion for reform. Academic research in this sense pertains to independent studies usually funded by government grants. On the other hand, industrial research is done for pharmaceutical companies funded by these same companies. UC Berkeley's Understanding Science online resource contains an analysis of how research is funded, and it elucidates how science can be used for the benefit of one party. "A pharmaceutical company paying for a study of a new depression medication, for example, might influence the study's design or interpretation in ways that subtly favor the drug that they'd like to market" ("Who Pays for Science," 2014). Differing sources of funding introduce biases based on motives. Therefore, certifying that unaffiliated academic research laboratories test industrial studies will reduce business bias in an effort to improve research as a whole. To make wise

and industrial research to prevent the dissemination of inaccurate information and faulty drugs.

13. Measurable Movements Forward

Investment in research based on the neurobiological and genetic networks linked to depression and the publication of all studies will usher in a quantitative reformation of diagnosis and treatment. I am confident that the initiation of my suggestions will reduce cases of misdiagnoses, domestic and international expenditure on antidepressants, and misinformation on the foundations for emotions in association with mental disorders. Depression's hold on humanity is of egregious scale. If implemented, these reforms could impact mental health globally by improving the way doctors and patients perceive depression. Doctor Siddhartha Mukherjee (2012) aptly explains the wonderment of the brain's complexities with an analogy. "The painter Cézanne, confronting one of Monet's landscapes, supposedly exclaimed: 'Monet is just an eye, but, God, what an eye.' The brain, by the same logic, is still a chemical soup — but, God, what a soup." It is my hope that advancing neuroscience research through these proposals will elucidate the line between emotion and emotional disorders, expanding our perspectives on what it means to be

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