Psychology Today

Why Is Depression Always a Lifetime Battle?

What still perplexes experts about the leading cause of disability

Posted Dec 12, 2019

Ben Spielberg, M.S.
The Moody Brain

Pervasive and insidious, Major Depressive Disorder is one of the most common mood disorders in the United States, afflicting upwards of 17 million adults each year. The global impact is, by some accounts, larger than the entire population of the United States. It is characterized by a combination of overwhelming feelings of sadness and/or guilt, lack of energy and motivation, insomnia or hypersomnia, anxiety, agitation, and difficulty concentrating.

Sometimes these symptoms follow a diurnal pattern, such that they worsen in mornings and evenings. Ultimately, these symptoms are so debilitating in so many people that depression is the leading cause of disability worldwide.

We normally think of talk therapy and antidepressant medication as the “gold standard” of treatment for depression. Unfortunately, the research shows that this is more of a temporary band-aid affixed to an underlying issue, as

opposed to a treatment for the root cause. Longitudinal research suggests that over the lifetime, at least 73% of individuals diagnosed with Major Depressive Disorder will endure future episodes, while 90% of individuals with at least three previous episodes will endure more (Mueller et al., 1999; Hollon et al., 2006; Wojnarowski et al., 2018; Solomon et al., 2000). Additionally, this has a multiplicative effect, such that each depressive episode significantly raises the probability for a future depressive episode, regardless of whether traditional treatments were utilized (Solomon et al., 2000).

We have known for many years that stress—in the form of acute life stressors or developmental trauma—can increase the likelihood for further depressive episodes, and this theory is called the kindling hypothesis (Maletic et al., 2007).

According to the kindling hypothesis, every time individuals with depression undergo some stressor, their threshold for withstanding the stressor before entering a depressive episode decreases. The kindling hypothesis was a favored theory in 1992, but most researchers now feel that it doesn't provide an accurate definition (Monroe & Harkness, 2005).

De-mystifying Major Depressive Disorder is an uphill struggle in itself. Although one would hope that more modern research may provide us with additional clarity, that does not seem to be the case. A recent meta-analysis examined a number of different traits that may be associated with multiple recurrences of depression, but only found that residual depressive symptoms

and the number of prior episodes were correlated—even after treatment with cognitive-behavioral therapy (Wojnarowski et al., 2018).

The next subject that may provide some clarity into why depression recurs so often are biomarkers via neuroimaging, hormone levels, or genotyping. A new meta-analysis (Kennis et al., 2019) combed through over 600 peer-reviewed articles to examine whether brain volume (specifically of the prefrontal cortex, hippocampus, and amygdala), inflammatory cytokines, and hormones such as cortisol are related to recurrence of depressive episodes. Although there are some methodological issues due to a general lack of standardization among biomarker studies for Major Depressive Disorder, Kennis' group only discovered that there was but one significant predictor of future depressive episodes: cortisol. And cortisol, of course, is higher in individuals with more life stressors.

It is almost the end of 2019, and it seems that we still know just as little about why depression so pervasively persists throughout the lifetime as we did in 1992. We have made huge strides in neuroimaging, created much more cohesive and integrative theories for depression, but are still relatively clueless about this issue.

Future biomarkers should hopefully provide further clarity, especially as we begin to understand the powerful neuroplastic effects of non-first line treatments such as Transcranial Magnetic Stimulation and ketamine.

Furthermore, it’s likely that the aforementioned treatments may decrease—or at the very least, slow down—future recurrence rates.

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