

Are Anxiety and Depression the Same Disorder?

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Abstract

The issue of co-morbidity in Anxiety and Depression as disorders leads to questions about the integrity of their present taxonomies in mental health diagnostics. At face value the two appear to have discrete differences, yet nonetheless demonstrate a high co-morbidity rate and shared symptoms implying pathological similarities rather than that of chance. Reviewing evidence from behavioural, neural, and biological sources that elaborate on the aspects of these two constructs, helps to illustrate the nature of these apparent differences and similarities. Integrating evidence from the anxiety and depression literature with the pathological process best illustrated by the burnout theory, alongside with support from the neurobiology of anxiety and stress, presents a proposition of a basic and natural anxiety pathology that when excessive, may result in the symptoms psychology has come to know as representative of anxiety and depressive disorders.

Keywords: Depression; Anxiety; Neuroimaging; Stress

The Problem of Comorbidity

Both the Diagnostic and Statistic Manual of Mental Disorders (DSM) and International Statistical Classification of Diseases and Related Health Problems (ICD) categorise anxiety and depression as different types of mental disorder. The ICD-10 categorises anxiety disorders as part of the spectrum of neurotic, stress-related and somatoform disorders, and depression under mood/affective disorders.¹ Although formerly under different sections in earlier versions, the recent DSM-5 places these in a general mental disorder category, with categories specific to depressive disorders and anxiety disorders, and further subdivided into different variations.² Despite terminological differences, the two associate anxiety disorders with anxious and fearful psychological and physiological symptoms, and depressive disorders with low mood, motivation, and negative affect. An estimated quarter of the population of the United States of America are estimated to have been afflicted by an anxiety disorder within

¹ *International Statistical Classification of Diseases and Related Health Problems*, World Health Organisation (Geneva: WHO Press, 2010)

² *Diagnostic and statistical manual of mental disorders*, American Psychiatric Association (Washington, DC: Author, 2013).

their lifetime.³ Sanderson, Di Nardo, Rapee, and Barlow find that up to 90% of people diagnosed with anxiety disorders suffer from another mental disorder.⁴ Amongst anxiety disorders co-morbidity ranges from 10% to 15% with depressive disorders, whilst depressive disorder's co-morbidity with anxiety disorders range from 15% to 75%.⁵ This review shall investigate this apparent problem of co-morbidity and whether they are two taxonomically different pathologies or aspects of a single pathology.

The Behavioural Standpoint

The tripartite model attempts to resolve the co-morbidity issue by suggesting that anxiety and depression are separate disorders that share a significant common factor.⁶ Their reasoning in summary is that anxiety is a hyperarousal disorder and depression is an anhedonic disorder, and that hyperarousal fails to account for depressive symptoms and likewise anhedonia fails to account for anxiety symptoms; therefore negative affective is the common symptom that explains the prevalence of co-morbidity.^{7,8} Rather than negative affect, some researchers prefer the concept of neuroticism as the major common factor.^{9,10} According to Wetherell et al., the results of their longitudinal study imply that anxiety symptoms lead to depression more so than depression symptoms to anxiety, a reflection of the earlier stated rates of depression's co-morbidity with anxiety (15%-75%).¹¹ In this same study, analysis revealed a correlation of .84 between factors of anxiety and depression in young adults and the authors posit neuroticism as the common factor for vulnerability to anxious and depressive disorders. It is important to note that the premise that the disorders are different in such examples is based upon behaviours, as they present polarised core behaviours and are therefore assumed and classed as different.

Neuroimaging Anxiety and Depression

The prefrontal cortex (PFC) is the seat of cognitive and emotional processing.¹² People self-reporting higher levels of behavioural inhibition, which is correlated with avoidance, anxiety, and neuroticism,¹³ demonstrate higher levels of activity in the right dorsolateral PFC

³ R. C. Kessler et al., "Lifetime and 12-month Prevalence of DSM-III-R Psychiatric Disorders in the United States: Results from the National Comorbidity Survey." *Archives of General Psychiatry* 57 (1994).

⁴ W. C. Sanderson et al., "Syndrome Comorbidity in Patients Diagnosed with a DSM-III-R Anxiety Disorder." *Journal of Abnormal Psychology* 99 (1990).

⁵ C. M. Cummings, N. E. Caporino, and P. C. Kendall, "Comorbidity of Anxiety and Depression in Children and Adolescents: 20 Years After," *Psychological Bulletin* 140, no. 3 (2014), doi: 10.1037/a0034733.

⁶ L. A. Clark, and D. Watson, "Tripartite Model of Anxiety and Depression: Psychometric Evidence and Taxonomic Implications," *Journal of Abnormal Psychology* 100, no. 3 (1991).

⁷ Clark and Watson, "Tripartite Model of Anxiety and Depression."

⁸ T. E. Joiner et al., "Physiological Hyperarousal: Construct Validity of a Central Aspect of the Tripartite Model of Depression and Anxiety," *Journal of Abnormal Psychology* 108, no. 2 (1999).

⁹ J. L. Wetherell, M. Gatz, and N. L. Pederson, "A Longitudinal Analysis of Anxiety and Depressive Symptoms," *Psychology and Aging* 16, no. 2 (2001).

¹⁰ L. M. Weinstock, and M. A. Whisman, "Neuroticism as a Common Feature of the Depressive and Anxiety Disorders: A Test of the Revised Integrative Hierarchical Model in a National Sample," *Journal of Abnormal Psychology* 155 (2006), doi: 10.1037/0021-843X.115.1.68.

¹¹ Cummings, Caporino, and Kendall, "Comorbidity of Anxiety and Depression."

¹² K. L. Phan et al., "Functional Neuroanatomy of Emotion: A Meta-Analysis of Emotion Activation Studies in PET and fMRI," *NeuroImage* 16 (2002).

¹³ A. J. Elliot, and T. M. Thrash, "Approach-Avoidance Motivation in Personality: Approach and Avoidance Temperament and Goals," *Journal of Personality and Social Psychology* 82, no. 5 (2002), doi: 10.1037//0022-3514.82.5.804.

(dPFC).¹⁴ In healthy pathologically low anxiety individuals, threatening stimuli increase activity in the PFC, whilst high anxiety participants are less responsive.¹⁵ Despite this lower activity, individuals with generalised anxiety disorder possess higher levels of metabolism in the dPFC.^{16,17} Depression too is associated with reduced activity in the dPFC.¹⁸ Furthermore extensive damage to multiple areas in the PFC is positively associated with depressive symptoms, with damage to the dPFC regions rendering the most severe symptoms.¹⁹

The amygdala modulates fear responses.²⁰ Increased amygdala activity has been linked to decreased dPFC activity in both healthy and depressed individuals.^{21,22,23} However amygdala activity varies amongst depressed individuals, with some possessing above average volume and activity, and others reduced volume and activity compared to healthy individuals, which Sacher et al. propose may signify the respective differences between individuals suffering from first episodes of major depression and those with recurring episodes.²⁴

The hippocampus is known to be the core area of the brain dedicated to memory, having an impact on all memory related cognition.²⁵ Anxiety in general is associated with increased activity in the anterior hippocampus, and state anxiety with the addition of increased connectivity with the PFC.²⁶ State anxiety is the conscious cognitive perception of threats, reflected in PFC activity, whilst the more automatic trait anxiety response is associated with connectivity to the more sensory and unconscious posterior cortical regions of the brain.²⁷ Depression however is associated with atrophy throughout hippocampus.^{28,29}

¹⁴ A. J. Shackman et al., "Right Dorsolateral Prefrontal Cortical Activity and Behavioral Inhibition," *Psychological Science* 20 (2009), doi: 10.1111/j.1467-9280.2009.02476.x.

¹⁵ S. Bishop et al., "Prefrontal Cortical Function and Anxiety: Controlling Attention to Threat-Related Stimuli." *Nature Neuroscience* 7, no. 2 (2004), doi: 10.1038/nn1173.

¹⁶ E. M. Drabant et al., "Experiential, Autonomic, and Neural Responses during Threat Anticipation Vary as a Function of Threat Intensity and Neuroticism," *NeuroImage* 55 (2011), doi: 10.1016/j.neuroimage.2010.11.040.

¹⁷ S. J. Mathew et al., "Dorsolateral Prefrontal Cortical Pathology in Generalized Anxiety Disorder: A Proton Magnetic Resonance Spectroscopic Imaging Study," *American Journal of Psychiatry* 161, no. 6 (2004).

¹⁸ G. J. Siegle et al., "Increased Amygdala and Decreased Dorsolateral Prefrontal BOLD Responses in Unipolar Depression: Related and Independent Features," *Biological Psychiatry* 61 (2007), doi: 10.1016/j.biopsych.2006.05.048.

¹⁹ M. Koenigs et al., "Distinct Regions of Prefrontal Cortex Mediate Resistance and Vulnerability to Depression." *The Journal of Neuroscience* 28, no. 47 (2008), doi: 10.1523/jneurosci.2324-08.2008.

²⁰ Phan et al., "Functional Neuroanatomy of Emotion."

²¹ F. Dolcos, and G. McCarthy, "Brain Systems Mediating Cognitive Interference by Emotional Distraction," *Journal of Neuroscience* 26 (2006), doi: 10.1523/jneurosci.5042-05.2006.

²² Siegle et al., "Increased Amygdala and Decreased Dorsolateral Prefrontal BOLD Responses."

²³ G. J. Siegle et al., "Can't Shake that Feeling: fMRI Assessment of Sustained Amygdala Activity in Response to Emotional Information in Depressed Individuals," *Biological Psychiatry* 51 (2002).

²⁴ J. Sacher et al., "Mapping the Depressed Brain: A Meta-Analysis of Structural and Functional Alterations in Major Depressive Disorder," *Journal of Affective Disorders* 140 (2012), doi: 10.1016/j.jad.2011.08.001.

²⁵ L. Nadel, and M. A. Peterson, "The Hippocampus: Part of an Interactive Posterior Representational System Spanning Perceptual and Memorial Systems," *Journal of Experimental Psychology* 142, no. 4 (2013), doi: 10.1037/a0033690.

²⁶ B. Ajay et al., "Human Anterior and Posterior Hippocampus Respond Distinctly to State and Trait Anxiety," *Emotion* 12 (2012), doi: 10.1037/a0026517.

²⁷ M. S. Fanselow et al., "Are the Dorsal and Ventral Hippocampus Functionally Distinct Structures?" *Neuron* 65, no. 1 (2010), doi: 10.1016/j.neuron.2009.11.031.

²⁸ B. S. McEwen, "Effects of Adverse Experiences for Brain Structure and Function," *Biological Psychiatry* 48, no. 8 (2000).

²⁹ R. M. Sapolsky, "The Possibility of Neurotoxicity in the Hippocampus in Major Depression: a Primer on Neuron Death," *Biological Psychiatry* 48, no. 8 (2000).

The anterior cingulate cortex (ACC) is associated with memory recall.³⁰ In adolescents, rumination was associated with an increased likelihood of developing depression, having had a past depressive episode, and the duration and severity of depressive episodes.^{31,32} Depression often shows greater subgenual ACC activity and metabolism, with correlation to ruminative tendencies.^{33,34,35} Furthermore the degree of ACC responsiveness to social stresses is positively correlated with the onset of depressive symptoms.³⁶ Diminished ACC activity in depression however is negatively correlated with recovery rates.³⁷ Considering anxiety has an earlier age of onset than depression and predicts depression later in life,^{38,39,40} would appear to imply that responsiveness to perceived threats or stresses and the chronic re-experience of these in the form of rumination may play a role in the onset of depression and its ongoing severity.

Thus the behavioural and neurological states are polarised in the disorders of anxiety and depression. However considering there are studies that find anxiety precedes depression and is even predictive of depressive episodes in individuals,^{41,42,43,44} one may propose some relation exists from one to the other. This very hypothesis has been posited indirectly by the occupational burnout hypothesis. The concept of burnout outlines how individuals suffering from anxieties and strains in the form of occupational stress are more likely to be exhausted and develop depressive symptoms.^{45,46} Factors such as neuroticism, gender, financial strain, job satisfaction, domestic issues, chronic medical illness, and depressive symptoms are identified as specific stressors related to the severity of burnout over time.⁴⁷ Bianchi, Schonfeld & Laurent found that 90% of their participants identified as burned out using a

³⁰ Phan et al., "Functional Neuroanatomy of Emotion."

³¹ J. R. Z. Abela, and B. J. Hankin, "Rumination as a Vulnerability Factor to Depression During the Transition From Early to Middle Adolescence: A Multiwave Longitudinal Study," *Journal of Abnormal Psychology* 120, no. 2 (2011), doi: 10.1037/a0022796.

³² L. B. Stone et al., "Co-Rumination Predicts the Onset of Depressive Disorders During Adolescence." *Journal of Abnormal Psychology* 120, no. 3 (2011), doi: 10.1037/a0023384.

³³ D. Mandell et al., "Neural Substrates of Trait Ruminations in Depression," *Journal of Abnormal Psychology* 123 (2014), doi: 10.1037/a0035834.

³⁴ Sacher et al., "Mapping the Depressed Brain."

³⁵ T. Yang et al., "Depressed Adolescents Demonstrate Greater Subgenual Anterior Cingulate Activity," *Neuroreport* 20, no. 4 (2009), doi: 10.1097/WNR.0b013e3283262e10.

³⁶ C. L. Mastein et al., "Subgenual Anterior Cingulate Responses to Peer Rejection: A Marker of Adolescents' Risk for Depression," *Developmental and Psychopathology* 23 (2011), doi: 10.1017/S0954579410000799.

³⁷ D. Pizagalli et al., "Anterior Cingulate Activity as a Predictor of Degree of Treatment Response in Major Depression: Evidence From Brain Electrical Tomography Analysis," *American Journal of Psychiatry* 158, no. 3 (2001).

³⁸ A. Bittner et al., "What Characteristics of Primary Anxiety Disorders Predict Subsequent Major Depressive Disorder?" *Journal of Clinical Psychiatry* 65, no. 5 (2004).

³⁹ M. M. Fichter et al., "Twenty-Five-Year Course and Outcome in Anxiety and Depression in the Upper Bavarian Longitudinal Community Study," *Acta Psychiatrica Scandinavica* 122, no. 1 (2010), doi: 10.1111/j.1600-0447.2009.01512.x.

⁴⁰ L. J. Woodward, and D. M. Fergusson, "Life Course Outcomes of Young People with Anxiety Disorders in Adolescence," *Journal of the American Academy of Child & Adolescent Psychiatry* 40 (2001).

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⁴³ Wetherell, Gatz, and Pederson, "A Longitudinal Analysis."

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⁴⁵ S. M. Jex, T. A. Beehr, and C. K. Roberts, "The Meaning of Occupational Stress Items to Survey Respondents," *Journal of Applied Psychology* 77, no. 5 (1992).

⁴⁶ J. D. McKnight, and D. C. Glass, "Perceptions of Control, Burnout, and Depressive Symptomatology: A Replication and Extension," *Journal of Consulting and Clinical Psychology* 63, no. 3 (1995).

⁴⁷ G. Armon et al., "Joint Effect of Chronic Medical Illness and Burnout on Depressive Symptoms Among Employed Adults," *Health Psychology* 33, no. 3 (2014), doi: 10.1037/a0033712.

psychometric burnout scale met the DSM-IV criterion for depression, and that increased ratings of burnout correlated with increased severity of depressive symptoms.⁴⁸ Thus it is implied according to the burnout theory, that excessive anxiety and stress over time has an influence on the onset depressive symptoms.

Biochemical Evidence of an Anxious Pathology

The evidence that can tie the behavioural and neuroimaged observations, is the role of excitatory neurotransmitters. It is worth noting that the word anxiety itself and its symptoms imply anticipatory psychological and physiological arousal. Vital to this process is glutamate, an excitatory neurotransmitter that stimulates the activity of the sympathetic nervous system and accounts for up to 50-60% of neurotransmission in the brain.⁴⁹ Although essential for basic functioning and survival, the neurotoxicity of excessive glutamate upon neurons is noteworthy.^{50,51,52,53} In rats developmental stresses facilitated and increased glutamate release in the amygdala.⁵⁴ Considering the amygdala's connectivity to various regions of the brain,⁵⁵ such sensitisation may trigger a cascading fear/anxiety response throughout the brain. Furthermore chronic stress also reduces functioning and damages neurons in the hippocampus and PFC, the precise areas found damaged in depressive disorders.^{56,57,58}

Glutamate antagonists are effective as antidepressant medications, and many present antidepressants and anxiety treating benzodiazepines interfere with and reduce glutamate release and uptake.^{59,60,61} It is also noteworthy that many popular informal drugs such as alcohol, cannabis, and non-steroidal anti-inflammatory drugs (e.g. acetaminophen, aspirin, ibuprofen) all either suppress release or suppress uptake of glutamate in the brain,^{62,63,64,65}

⁴⁸ R. Bianchi, I. S. Schonfeld, and E. Laurent, "Is Burnout a Depressive Disorder? A Reexamination With Special Focus on Atypical Depression," *International Journal of Stress Management* 21, no. 4 (2014), doi: 10.1037/a0037906.

⁴⁹ J. M. Wierońska et al., "Depression Viewed as a GABA/Glutamate Imbalance in the Central Nervous System," in *Clinical, Research and Treatment Approaches to Affective Disorders*, ed. M. Jurueña (Rijeka, Croatia: InTech, 2012).

⁵⁰ T. A. Azami et al., "Regional Regulation of Glutamate Signaling During Cuprizone-Induced Demyelination in the Brain," *Annals of Anatomy* 195, no. 5 (2013), doi: 10.1016/j.aanat.2013.03.004.

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⁵² M. Frigo et al., "Glutamate and Multiple Sclerosis," *Current Medical Chemistry* 19, no. 9 (2012), doi: 10.1515/revneuro-2012-0062.

⁵³ A. Lau, and M. Tymianski, "Glutamate Receptors, Neurotoxicity and Neurodegeneration," *Pflügers Archiv* 460, no. 2 (2010), doi: 10.1007/s00424-010-0809-1.

⁵⁴ S. Tzanoulinou et al., "Long-Term Behavioral Programming Induced by Peripuberty Stress in Rats Is Accompanied by GABAergic-Related Alterations in the Amygdala," *PLoS ONE* 9, no. 4 (2014) doi: 10.1371/journal.pone.0094666.

⁵⁵ A. Roy et al., "Functional Connectivity of the Human Amygdala using Resting State fMRI," *Neuroimage* 45, no. 2 (2009), doi: 10.1016/j.neuroimage.2008.11.030.

⁵⁶ McEwen, "Effects of Adverse Experiences."

⁵⁷ Sapolsky, "The Possibility of Neurotoxicity in the Hippocampus."

⁵⁸ M. Popoli et al., "The Stressed Synapse: the Impact of Stress and Glucocorticoids on Glutamate Transmission," *Nature Review of Neuroscience* 13 (2013), doi: 10.1038/nrn3138.

⁵⁹ A. Medina et al., "Glutamate Transporters: a Key Piece in the Glutamate Puzzle of Major Depressive Disorder," *Journal of Psychiatric Research* 47, no. 9 (2013), doi: 10.1016/j.jpsychires.2013.04.007.

⁶⁰ L. Musazzi et al., "The Action of Antidepressants on the Glutamate System: Regulation of Glutamate Release and Glutamate Receptors," *Biological Psychiatry* 73, no. 12 (2013), doi: 10.1016/j.biopsych.2012.11.009.

⁶¹ A. J. Delaney, and P. Sah, "GABA Receptors Inhibited by Benzodiazepines Mediate Fast Inhibitory Transmission in the Central Amygdala," *The Journal of Neuroscience* 19, no. 22 (1999).

⁶² T. M. Brown, J. M. Brotchie, and S. M. Fitzjohn, "Cannabinoids Decrease Corticostriatal Synaptic Transmission via an Effect on Glutamate Uptake," *The Journal of Neuroscience* 23, no. 35 (2003).

giving insight into the prevalence of drug use in anxiety and mood disorders.^{66,67} Thus the neural damage of depression could be caused by an excess of stress related neurochemicals, which although essential for activity and functioning, in excess result in neurological damage. These effects are reflected in visible energy levels, cognitive abilities, and compensatory (e.g. self-medicating) behaviours common to anxiety and depression.

Biomarkers in the blood have been indicated for both anxiety and depression in the form of cholesterol, with heightened levels of high-density lipoprotein (HDL) associated with heightened levels of anxiety and depression, and higher levels of low-density lipoprotein (LDL) with lower levels of anxiety and depression.^{68,69} Curiously the excitatory hormone and neurotransmitter epinephrine significantly increases HDL cholesterol in the bloodstream,⁷⁰ while the similar norepinephrine reduces LDL cholesterol.⁷¹ Thus stress has a direct effect on the prevalence of these biomarkers. Of further interest is cholesterol's essential role in the biosynthesis of testosterone,⁷² and that HDL cholesterol positively associates with testosterone and yet is reduced by its presence.^{73,74,75} The importance of the previous sentence is that when testosterone binds to androgen receptors in the brain, it demonstrates protective and reparative effects.^{76,77} Thus a reasonable suggestion can be made that stress plays an important role in stimulating an increase in HDL cholesterol, effectively increasing testosterone production, of which upon binding to androgen receptors protects and or repairs stress related neurological damage. In an animal studies regarding chronic stress, higher levels of the feminine hormone estradiol resulted in augmented physiological stress, while

⁶³ D. Casper et al., "Ibuprofen Protects Dopaminergic Neurons Against Glutamate Toxicity In Vitro," *Neuroscience Letters* 289, no. 3 (2000).

⁶⁴ M. Pistis et al., "Delta(9)-Tetrahydrocannabinol Decreases Extracellular GABA and Increases Extracellular Glutamate and Dopamine Levels in the Rat Prefrontal Cortex: an In Vivo Microdialysis Study," *Brain Research* 948 (2002).

⁶⁵ M. Roberto et al., "Acute and Chronic Ethanol Alter Glutamatergic Transmission in Rat Central Amygdala: an In Vitro and In Vivo Analysis," *Journal of Neuroscience* 24, no. 7 (2004).

⁶⁶ J. Bolton et al., "Use of Alcohol and Drugs to Self-Medicate Anxiety Disorders in a Nationally Representative Sample," *Journal of Nervous and Mental Disease* 194 (2006), doi: 10.1097/01.nmd.0000244481.63148.98.

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⁶⁸ H. R. Liebermann et al., "Lipid and Other Plasma Markers Are Associated With Anxiety, Depression, and Fatigue," *Health Psychology* 51, no. 2 (2012), doi: 10.1037/a0026499.

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⁷¹ P. A. Edwards, D. Lemongello, and A. M. Fogelman, "The Effect of Glucagon, Norepinephrine, and Dibutyryl Cyclic AMP on Cholesterol Efflux and on the Activity of 3-hydroxy-3-methylglutaryl CoA Reductase in Rat Hepatocytes," *Journal of Lipid Research* 20 (1979).

⁷² M. R. Waterman, and D. S. Keeney, "Genes Involved in Androgen Biosynthesis and the Male Phenotype," *Hormone Research* 38, nos. 5-6 (1992).

⁷³ D. S. Freedman et al., "Relation of Serum Testosterone Levels to High Density Lipoprotein Cholesterol and Other Characteristics in Men," *Arteriosclerosis, Thrombosis, and Vascular Biology* 11 (1991).

⁷⁴ S. T. Page et al., "Higher Testosterone Levels are Associated with Increased Highdensity Lipoprotein Cholesterol in Men with Cardiovascular Disease: Results from the Massachusetts Male Aging Study," *Asian Journal of Andrology* 10, no. 2 (2008), doi: 10.1111/j.1745-7262.2008.00332.x.

⁷⁵ R. Shabsigh et al., "Cardiovascular Issues in Hypogonadism and Testosterone Therapy," *The American Journal of Cardiology* 16, no. 12 (2005), doi: 10.1016/j.amjcard.2005.10.009.

⁷⁶ J. Hammond et al., "Testosterone-Mediated Neuroprotection Through the Androgen Receptor in Human Primary Neurons," *Journal of Neurochemistry* 77, no. 5 (2001).

⁷⁷ R. Hussain et al., "The Neural Androgen Receptor: a Therapeutic Target for Myelin Repair in Chronic Demyelination," *Brain* 136 (2013), doi: 10.1093/brain/aws284.

higher levels of the masculine hormone testosterone attenuated physiological stress.⁷⁸ These observations may offer an explanation towards the demographics in depression where women are around 33% more likely to suffer from depression in their lifetimes than men.⁷⁹ An additional curiosity from animal studies is the related restorative effects of mild exercise upon the neurons of the hippocampus,⁸⁰ and may further suggest the biology of the alleviating effects of physical exercise on both anxiety and depression in human studies.^{81,82}

Conclusion

In conclusion, based on pure observation of behavioural symptoms, anxiety and depression are different disorders. Neuroimaging the two disorders reflects the behavioural interpretation through the mostly polarised activity between normal anxiety responses and severe depression. Yet when one proposes the hypothesis that chronic anxiety leads to neural damage, the disorders then lie upon a spectrum of the severity and duration of anxious cognitions and behaviours and the resulting neurological damage, thus appearing to be a single pathology. The biochemical evidence would support this hypothesis of the two behaviours being of the same biological mechanism, clarifying depression as a later consequence of an anxious psychopathology. The author's personal observation is that the psychophysiological stress response to external threats appears to be similar to what the immune response is to internal threats, and that both in excess enact detrimental effects (see Tisconik et al. for an analogous theory in immunology, i.e. the cytokine storm⁸³).

There is also a curious irony of some research declaring neuroticism as the common factor between depression and anxiety, without acknowledging the physiological effects of neurological stress upon anxiety and depression, as the linguistic morphology of “neuroticism” represents a state inclined towards “neurosis”, meaning anxiety, tension, and arousal of the nervous system. Linguistically therefore, anxious behaviours are essentially manifestations of neurosis and the two terms can be considered interchangeable, as is indicated by the psychophysiological evidence. Yet it is entirely understandable following the empirical strength of behavioural studies in the earlier half of the previous century and to this day, alongside the lack of present technology in the past, that the behavioural symptoms and thence terminology were the primary means of consolidating the present taxonomy of mental illness. Considering this perspective however, unless a strictly behavioural premise for taxonomy is the focus for diagnosis and treatment, the current ICD-10 and DSM-5 diagnostic criteria may misrepresent the psychopathological nature of mental illness in the case of anxiety and more so depression. From a psychopathological standpoint, a reasonable argument can be made that anxiety and depression are part of the same underlying pathology. This single disorder perspective also offers insight into the widespread success of single

⁷⁸ A. Sfikakis et al., “Effects of Testosterone and Estradiol on Stress-Induced Adrenal and Hippocampal Weight Changes in Female Rats,” *Hormones* 13 (2014).

⁷⁹ Kessler et al., “Lifetime and 12-month Prevalence of DSM-III-R Psychiatric Disorders.”

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⁸² S. Toker, and M. Biron, “Job Burnout and Depression: Unraveling Their Temporal Relationship and Considering the Role of Physical Activity,” *Journal of Applied Psychology* 97, no. 3 (2012), doi: 10.1037/a0026914.

⁸³ J. R. Tisconik et al., “Into the Eye of the Cytokine Storm,” *Microrbiology and Molecular Biology Reviews* 76 (2012), doi: 10.1128/mmbr.05015-11.

process therapies upon numerous and supposedly different disorders.⁸⁴ Where considering a possible singular psychopathological model of these disorders would likely be of greatest importance is in refining measures of prevention, intervention, and, when required, recovery oriented medication of mental illness through detailed study and understanding of this underlying anxiety psychopathology.

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