Depression's Biological Underpinnings, as a Shutdown Mechanism for Overloads

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From: law and psychology discussion list [mailto:PSYLAW-L@listserv.unl.edu] On Behalf Of Tyler Carpenter
Sent: Monday, December 07, 2009 06:36
To: PSYLAW-L@listserv.unl.edu
Subject: [PSYLAW-L] OR (of relevance to our recent threads on models, methods and the relationship of science to practice :-) -Fwd: Depression: An Update on Our Most Common Emotional Disorder: An Evolutionary Perspective]

This may be of relevance to our recent threads on models, techniques and the relationship of science to practice.

Enjoy.

Tyler

Summary

This talk summarizes a lengthy review article co-authored with Jaak Panksepp (PDF available upon request). We argue that depression is an evolutionarily conserved mechanism in mammalian brains, selected as a shutdown mechanism to terminate protracted separation distress (a prototype mammalian emotional state), which, if sustained, would be dangerous for infant mammals. However, this fundamental shutdown mechanism remains available to more mature mammalian and hominid brains, particularly those with certain polymorphisms in genetic endowment, early loss/separation trauma, or other predisposing factors, which can promote reactivation in relationship to almost any chronic stressor, including classic dominance conflicts. Social stress models involving dominance conflicts, along with separation models, remain perhaps the two most heuristic testing grounds for depression research using preclinical animal models. Such evolutionarily selected shutdown mechanisms could become hyper-trophied, and released from normal adaptive control mechanisms in vulnerable individuals, to potentially yield the full spectrum of depressive illness.

Depression remains a challenging puzzle of neurobiological correlates, involving changes in many biogenic amine and neuro-peptide systems and alterations in neuro-endocrine and immune function. We show how these core factors, rather than acting in isolation, form an interactive and even synergistic depressive matrix, which argues against any single-factor theory. This includes core contributions from stress cascades, pro-inflammatory cytokines, and multiple neuro-peptide and monoamine systems. Indeed, virtually every modulatory system studied shows alterations in depression, arguing that the notion of a specific locus of control for any chemical imbalance notion remains highly illusive, if not simply illusory. Our review suggests active synergisms between factors, as well as a recursive (looping) control architecture regulating both entry into and exit from depression. Such an interactive matrix of factors may help explain why such an enormous multiplicity of potential treatments are antidepressant, ranging from psychotherapy and social support, to exercise, to multiple drugs, Vagal (Vegas Nerve) and deep brain stimulation, and ECT.

Traditional biological psychiatric perspectives (particularly those emphasizing single factors)

are mostly bottom-up (neglecting relationships between depression and social connection vs. social stress) and typically cannot explain why depression is such a pervasive problem, or why evolution could have ever selected for such a mechanism. Linking depression to protracted separation distress provides a heuristic potential integration of findings, particularly between long-standing psychotherapy and psychodynamic perspectives and emerging neuroscience insights. This hypothesis yields various testable predictions at both clinical and neuroscience levels.

Recent work is summarized that in particular raises serious questions about the current trend away from using psychotherapy for the treatment of most depressions, including evidence that the efficacy of most aminergic antidepressants has been significantly overstated, if not actively misrepresented. Overall, the bottom-up reductionism of contemporary psychiatry, in which Big Pharma has virtually unrestrained influence, is highly motivated to continue promotion of a fragmented molecular concept of depression (recycling some version of a chemical imbalance concept), instead of more heuristic affective or psychological concepts. This economically motivated distortion of basic neuroscience is likely to maintain practice trends in the current direction, to the detriment of patient care and long term well being. Recent scandals around the financial relationships between prominent psychiatrists to Big Pharma only underline these concerns, suggesting that much tighter control over potential conflict-of-interest situations and their unholy influence (over both clinical research and emerging practice trends) is required.

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