# CONCEPTUAL ADVANCES IN PSYCHIATRY: PRACTICAL APPLICATIONS TO TREATMENT BRAD BOWINS, M.D.

# CENTRE FOR THEORETICAL RESEARCH IN PSYCHIATRY & CLINICAL PSYCHOLOGY

- Addresses the need for high quality theoretical research, and the current lack of balance between empirical and theoretical approaches in psychiatry and clinical psychology
- Promotion
- Guidelines
- Assistance
- "There is nothing so practical as a good theory." (Kurt Lewin)
- <u>www.psychiatrytheory.com</u> or <u>www.theorypsychiatry.com</u>

#### PUBLISHED RESEARCH ARTICLES

- Depression: Discrete Or Continuous? Psychopathology, In Press
- Cognitive Regulatory Control Therapies. American Journal of Psychotherapy, 2013; 67(3): 215-236
- Therapeutic Dissociation: Compartmentalization & Absorption. Counselling Psychology Quarterly, 2012; 25(3): 307-317
- Psychosis: A Synthesis Of Motivational And Defect Perspectives. The American Journal of Psychoanalysis, 2012; 72: 152-165
- Augmenting Behavioural Activation Treatment With The Behavioural Activation And Inhibition Scales. Behavioural and Cognitive Psychotherapy 2012; 40: 233-237
- A Cognitive Regulatory Control Model Of Schizophrenia. Brain Research Bulletin, 2011; 85: 36-41
- Repetitive Maladaptive Behavior: Beyond Repetition Compulsion. The American Journal of Psychoanalysis, 2010; 70: 282-298

#### PUBLISHED RESEARCH ARTICLES

- Personality Disorders: A Dimensional Defense Mechanism Approach. American Journal of Psychotherapy, 2010; 64(2): 153-169.
- Motion Sickness: A Negative Reinforcement Model. Brain Research Bulletin, 2010; 81: 7-11.
- Hypomania: A Depressive Inhibition Override Defense Mechanism. Journal of Affective Disorders, 2008; 109: 221-232.
- How Psychiatric Treatments Can Enhance Psychological Defense Mechanisms. The American Journal of Psychoanalysis, 2006; 66 (2): 173-194.
- Psychological Defense Mechanisms: A New Perspective. The American Journal of Psychoanalysis, 2004; 64(1): 1-26.
- Delusions and Self-Esteem (B Bowins & G. Shugar). Canadian Journal of Psychiatry, 1998; 43: 154-158.

#### **WORKSHOP FORMAT**

- Mental illness: Discrete Or Continuous?
- A Conflicted World: Research Bias
- What Is Mental Illness?
- These topics link together in intriguing ways
- Questions & Discussion

#### MENTAL ILLNESS: DISCRETE OR CONTINUOUS?

- Nature tends to be organized continuously
- Continuums provide for trait variation crucial for natural selection
- We prefer discreteness trading accuracy for simplicity
- Kinsey (1948 & 1953): "The living world is a continuum in each and every one of its aspects" and "It is a characteristic of the human mind that tries to dichotomize in its classification of phenomena"
- Continuum Principle: Natural phenomena tend to occur on a continuum, and any instance of hypothesized discreteness requires unassailable proof
- How well do discrete models of mental illness stand up?

- 100 years of research and no accurate characterization.
- Endogenous/melancholic, reactive/neurotic, major, minor, and dysthymic constitute some of discrete types proposed
- Major diagnostic systems (DSM and ICD) rely on a discrete model, but the precise types shift over time
- For example, DSM-IV-TR Major, Minor, and Dysthymic; DSM 5 Minor dropped and Persistent Depressive Disorder replaces Dysthymia
- Major depression somewhat equivalent to endogenous/melancholic

- Consistent with the disease model the proposed types should have different etiologies, symptom profiles, courses, and responses to treatment
- No consistent differences in etiology, for example BDNF, TNF, adinopectin, IL-6, all implicated in depression, no difference between reactive, major, and bipolar depression (Su et al, 2011)
- Course such as relapse risk, suicide, and readmission no differences
- Symptom profiles-Despite decades of research Parker and colleagues have failed to clearly distinguish melancholic depression
- Response to treatment no overall difference, Parker's finding of ECT and TCA's apply more to older people regardless of depression type

- Some support for melancholic depression, such as psychomotor impairment, anergia, anhedonia, agitation, fewer anxiety symptoms, higher cortisol levels and failure to suppress with dexamethasone
- How to resolve this quandary?
- Based on continuum principle the evidence for discrete types is insufficient
- Concept-Discrete and continuous models not fully distinct
- Continuous quantitative variation yields qualitative variation as an emergent property
- Non-melancholic and melancholic continuous-Melancholic symptoms emerge with increasing severity (Schotte et al, 1997)

- Model-Depression continuum characterized by dimensions of duration and severity
- 3 levels on each dimension, applying the product of duration X severity
- Example,  $1 \times 1 = 1$  quantitatively and qualitatively much different than  $3 \times 3 = 9$
- Indicate level on each dimension as different combinations can give the same numeric value (e.g moderate duration X high severity and long duration X moderate severity, both 6)
- Ratings and product to be listed for each episode of depression
- 3 levels of severity supported by ICD mild, moderate, and severe; risk of suicide and relapse increases with each level (Kessing et al, 2004)

- Duration dimension in time units, perhaps short 1-3 months, moderate 3-6 months, and long > 6 months
- Severity dimension more challenging; suggest depression inhibition concept proposed by Kraepelin with revisions: Inhibition of mental, emotional, social, and physical behaviour
- Supported by motivational parameters of Behavioural Activation System (BAS) and Behavioural Inhibition System (BIS), with low BAS and high BIS characterizing depression; depressive inhibition not to be confused with BIS though
- Measurement techniques can be devised for each component of depressive inhibition; the sum giving a score for severity dimension
- Treatment strategies tailored to each component should improve the outcome, and behavioural activation treatments applied to BIS & BAS

- Issues to address-depression related to specific circumstances and comorbidity
- Accounting for depression related to specific circumstances, such as social stressors, physical illness, and stimuli relevant to BIS and BAS
- Specific circumstances activate or trigger the depression continuum
- In some instances reversal of the circumstances can de-activate or reduce depression
- In other instances depressive inhibition is too established and other treatment interventions are required

- How to incorporate anxiety, hypomania-mania, psychosis, and personality issues with depression-comorbidity?
- Factor analytic research by Parker and colleagues, and also Cochrane (1977), finds melancholic/endogenous and non-endogenous factors
- Non-melancholic a mixture of anxiety, personality, psychosis, etc
- Placement on the same dimension? Polar opposites trade off and the mid-level less intense symptoms than the extremes
- Logically, there must be separate continuums for the various conditions and interfacing of the continuums occurs with comorbidity
- The power of conceptual reasoning and practical applications

#### HYPOMANIA-MANIA: DISCRETE OR CONTINUOUS?

- Hypomania: A Depressive Inhibition Override Defense Mechanism (Journal Of Affective Disorders, 2008)
- Continuum: Subthreshold hypomania-hypomania-subthreshold mania-mania
- Hypomania typically improves functioning in the moment relative to depression; overriding or interrupting depressive inhibition
- Mania maladaptive as with psychosis
- Regulatory mechanism proposed-When costs > benefits the process is deactivated or dampened; intact regulation BPII and deficient BPI
- Hypomania not a problem to treat, but a treatment for depression; actually encourage hypomania via increase cognitive, social, and physical activity-Increased BAS, reduced BIS

#### PSYCHOSIS: DISCRETE OR CONTINUOUS?

- A Cognitive Regulatory Model Of Schizophrenia (Brain Research Bulletin, 2011)
- Psychotic thought content (cognitive distortions), thought form, and sensory perceptual experiences on a continuum; an extensive range derived from the evolution of human intelligence
- The more extreme portion of the range is reality incongruent impairing adaptive functioning in the conscious and awake state
- A regulatory process blocks psychotic level expressions from the conscious and awake state; during sleep psychotic equivalents expressed in dreams due to relaxed regulation
- The schizophrenic disease process/s producing negative symptoms, damages or impairs the cognitive regulatory processes resulting in psychosis; treatment strategies follow from this model

### PERSONALITY DISORDERS: DISCRETE OR CONTINUOUS?

- Personality Disorders: A Dimensional Defense Mechanism Approach (American Journal Of Psychotherapy, 2010)
- Widely accepted that normal and abnormal personality are continuously organized, but cannot get from normal personality (e.g Big 5) to abnormal personality
- Psychological defenses that are adaptive in a mild form become maladaptive in a severe and persistent form (example of Avoidant Personality Disorder)
- Normal personality dimensions might influence the defensive style a person adopts; for example, closed to experience-avoidant defense
- Stress likely to intensify the severity and persistence of the defense
- Treatment goal is to reduce defense use to normal range

#### RESEARCH BIAS: THE MODERN DAY DRUG COMPANY ERA & MARKETING SUCCESS

- Simple and easy to follow stories sell; discrete models fit well
- In 2010 antipsychotics and antidepressants placed in the top five "bestsellers" generating \$16.9 and \$16.1 billion, respectively, in that year alone!
- Research funding has shifted since the 1980's from public to industry-Bayh-Dole Act, U.S.A., was very influential in this shift
- Research outcomes are expected to both generate and market product
- Marketing starts with discovery of a compound: "Creating evidence and establishing consensus" (Healy, 2003)
- Marketing departments recruit academics; "making friends"

#### RESEARCH BIAS: THE MODERN DAY DRUG COMPANY ERA & MARKETING SUCCESS

- Evidence for a product derived from a minority of studies; FDA typically only 2 positive result studies required for approval
- Trial data proprietary; the pharmaceutical industry funds the vast majority of product relevant research
- Ghostwritten papers a major issue; researcher "ornamental"
- International Committee of Medical Journal Editors decided that from July, 2005 only registered trials can be published
- Clinical Trial Registry by US National Library Of Medicine
- Problems: Access to full data of non-published papers can be challenging, meta-analytic research is usually based on published papers, and medication usage relies on peer-reviewed publications

#### RESEARCH BIAS: PANIC DISORDER

- The pharmaceutical industry insider term for Panic Disorder was "Upjohn Illness"
- In 1964 a study by Donald Klein proposed panic as a discrete illness that could be treated with medication (funding by Geigy, and Smith & Kline & French); discreteness and marketing connection evident
- Klein's influence on the DSM-III Anxiety and Dissociative Disorders subcommittee led to Panic Disorder in DSM-III (1980)
- Prior to this change panic was logically seen as a more extreme expression of anxiety-Anxiety Neurosis, "characterized by anxious over-concern extending to panic and frequently associated with somatic symptoms" (DSM-II)
- In 1981 Upjohn marketed Xanax (alprazolam) for Panic Disorder, despite its own research showing little support for a separate illness

#### RESEARCH BIAS: SCIENTISM

- Scientism defined in terms of improper science has replaced good science according to Edward Shorter (A History of Psychiatry, 1997)
- "As often happens in medicine, the availability of a treatment leads to an increase in recognition of the disorder that might benefit from that treatment" (David Healy)
- The Upjohn Illness is such an example, and even more so is the extension of SSRI treatment to virtually everything including mild anxiety and dysphoria
- The current push to apply second generation antipsychotics to the treatment of anxiety disorders, depression, and sleep disturbances is a major concern
- Research bullying-Evident with research raising concerns about genetically modified organisms; time for a time-out?

#### RESEARCH BIAS: ORIGINS & SOURCES

- Human social cognition emphasizes reciprocity-95% of our 200,000 year evolution occurred in hunting-gathering societies where reciprocity was crucial
- Funding establishes a motivation to reciprocate producing bias, as for example defining the public good as product generation noted with biotechnology research involving genetically modified organisms (Busch et al, 2004)
- "Publish or perish" leads to "distort or despair" for researchers, contributing to research bias
- Sources of research bias: Statistical, reporting and publication, funding and conflict of interest
- Theory applied to empirical research can counter these sources of bias

#### RESEARCH BIAS: STATISTICS

- The crucial significance of "a priori" probability
- The probability of a research result being true prior to testing guides the interpretation of positive results (John Ioannidis, Plos Med, 2005)
- If the a priori probability of an outcome being true is low, then a positive result only measures bias!
- Ioannidis believes that most medical research results (even top tier)
  are false given their low a priori probability of being true; research by
  industry confirms it
- Bayer 64% (43/67) of the most promising oncology, women's health, and cardiovascular disease research not replicable (Prinz et al, 2011)
- Amgen 89% of prominent cancer results not replicable (Begley & Ellis, 2012)

#### RESEARCH BIAS: STATISTICS

- Transitivity: If drug A is better than drug B, and drug B is better than drug C, how can drug C be better than drug A? The a priori probability issue applies
- Research comparing drugs of the same class such as SSRI's incur transitivity, but research funding and marketing efforts are often oriented to such comparisons
- Data mining-"If you torture the data long enough it will confess"commercial data mining packages available
- Effect size and generalizability trade-off; the use of "pure" subjects increases effect size but reduces generalization
- What if subjects are aware of active drug/placebo status in RCT's? Reduced impact if placebo and enhanced impact if active drug

#### RESEARCH BIAS: REPORTING & PUBLICATION

- Erick Turner et al (2008) examined 12 antidepressants approved by the FDA between 1987-2004, the studies involving 12,564 patients
- 51% of the studies were deemed to be positive, and all but one was published
- Of the 49% deemed not positive, 11 were published as positive, 22 were not published, and only 3 published as not positive
- In addition, reported effect sizes exceeded that derived from FDA reviews by an average of 32%, and these studies used "pure" subjects known to amplifying the effect size
- Kirsch et al (2008) meta-analysis found that 40% of SSRI trials were not published (2X average), and these failed to show a benefit resulting in a calculated placebo response of 82%

#### RESEARCH BIAS: REPORTING & PUBLICATION

- Academic journals owned by a handful of publishing corporations
- Success derived from the impact factor and reprint sales
- Impact factor based on cited items over the prior 2 years; positive result medication studies tend to have higher citations
- Reprint sales the driving financial force for most journals, and positive result medication studies yield very high reprint orders (by pharmaceutical companies)
- High reprint order studies are significantly more likely to be funded by the pharmaceutical industry (Handel et al, 2012)

# RESEARCH BIAS: FUNDING & CONFLICT OF INTEREST

- Funding bias influence on conferences-Sen & Prabhu (2012) examined 278 medication trial abstracts presented at the APA 2009 and 2010 conferences: 97.4% of industry sponsored trial abstracts were positive towards the medication, 2.6% mixed, and none negative
- 100% of the DSM-IV Mood Disorder and Schizophrenia and Other Psychotic Disorders panel members had one or more financial link to the pharmaceutical industry (Cosgrove et al, 2006); the same applies to DSM-5
- BPA safety example (Baker, 2008)-176 studies, 13/13 industry funded, no harm; 152/163 studies no industry funding, harmful
- Industry funding can lead to biasing influences, such as inappropriate comparison doses, exaggerated effect sizes, and publication bias (Lexchin et al, 2003)

# RESEARCH BIAS: FUNDING & CONFLICT OF INTEREST

- Academia shifted from "public trusts" to businesses from the 1980's onward; bias is inevitable because products > true results
- Financial thresholds for relevance have often been in the \$10,000-\$20,000 range above annual income!
- Pharmaceutical industry funding not only for research, but for speaker's bureau engagements, advisory committees, conference attendance, honorarium to speak at conference, consulting contracts
- KEY POINT: Ideal of product research is low risk/high benefit, but in our entropy driven world this is infrequent; unless very high risk/very low benefit, positive spins (e.g. marketing) come into play
- Trust in science is eroding over time

#### EVIDENCE-BASED MEDICINE & TREATMENT FADS

- Medical treatments derived from biased research constitute biased evidence-based medicine
- Example of the "robust" evidence in favour of SSRI's driving medication > psychotherapy
- Meta-analyses typically rely on published research studies
- Treatment guidelines and diagnostic protocols are set by academics commonly receiving funds from pharmaceutical companies
- Medication fads follow as with SSRI's in past, and currently second generation antipsychotics for anxiety and depression
- Marketing for off-label uses advances fads, such as second generation antipsychotics for sleep problems

# RESEARCH BIAS: CONCEPTS & PRACTICAL APPLICATIONS

- Psychiatry is essentially a "captured" discipline due to pharmaceutical company funding
- Sound conceptual reasoning applied to empirical research can promote true research outcomes, what it SHOULD be all about!
- Recommend independent and objective product approval and testing centres be established for all pharmaceutical products, genetically engineered organisms, and new chemicals
- Best 2/3 studies conducted in these centres is the basis for approval,
   with publication of each trial in a not-for-profit open access journal
- Industry funds the studies but has no control; if a rare condition public funds can be used
- See A Conflicted World: Research Bias chapter (self-destruction.ca)

# How to Save Us From Self-Destruction

**Brad Bowins, M.D.** 

Collectively we are engaging in self-destructive behavior, compromising our present and jeopardizing our future. Rampant greed, irregular regulation, unrestrained urban and resource development, out of control global warming, biased pharmaceutical and biotechnology research, and lethal levels of obesity, are all severely damaging us. Dr. Bowins drills down exposing these forms of selfdestruction, and shows why we might be setting ourselves up for widespread revolution and devastation. Also revealed is how our psychological defense ironically perpetuate major forms of self-destructive behavior. We have reached the tipping point, but the solutions proposed can save us from self-destruction, if we take action.

Dr. Bowins is a psychiatrist and researcher heading the Center For Theoretical Research in Psychiatry & Clinical Psychology. As a theoretical researcher he has published novel theories, and as a clinician has treated many forms of selfdestructive behavior. From extensive experience with patients negatively impacted by the global economy, exposure to many environmental concerns, and in-depth research, it became evident that we are all engaging in self-destructive behavior. In line with his clinical experience, Dr. Bowins provides solutions that can save us from self-destruction, and motivates each of us to take action because significant change starts with the individual.

\$24.95

**Brad Bowins, M.D** 

# How to Save Us From Self-Destruction DEAD TIPPING POINT **Brad Bowins, M.D.**

#### WHAT IS MENTAL ILLNESS?

- The discrete/continuous debate and research bias issues are critical considerations when it comes to the question of, what is mental illness?
- Application of these considerations:
- 1). Mental illness definition/s should NOT be based on pharmaceutical company marketing agendas that favour discrete diagnoses
- 2). Given the Continuum Principle and evidence for the mental health conditions covered, continuums apply
- 3). Appreciating that qualitatively different states can arise from quantitative variation as an emergent property, assists in placing varying expressions within a continuous framework

#### WHAT IS MENTAL ILLNESS?

- Discrete entities or "zones of rarity" an illusion
- Distinct continuums for mental health disorders almost certainly apply (e.g depression, psychosis); can interface with one another
- Robert Spitzer's (1973 & 1981) definition requires suffering or disability; instrumental in removing homosexuality from DSM
- Jerome Wakefield (1992) argues that disorders are "harmful dysfunctions"-A negatively valued outcome caused by failure of some internal mechanism to perform a naturally selected biological function
- "Harmful dysfunction" problematic in that difficult to assess the naturally selected biological function and appropriate level
- Useful in that it highlights the importance of impairment

#### WHAT IS MENTAL ILLNESS?

- Suggest simplifying to impairment in functioning, such as impaired cognitive, emotional, social, and/or physical functioning for depressive inhibition
- Threshold on a continuum applies in that once functional impairment occurs this point identifies mental illness; below normal variation
- Entails some challenge in identifying "functional impairment" for a given person; fine, as there will always be "fuzziness" in nature
- Suffering, distress, or related forms of "harm" not useful-Examples of blood pressure and high cholesterol where biological dysfunction, but frequently no "harm" when assessed
- Can treat "normal variation" not considered to be disorders, as for example a person with dysphoric mood who shows no impairment in functioning; no diagnosis of depression though

#### THEORY IN PSYCHIATRY

- DARE TO THINK!
- CHALLENGE THE STATUS
  QUO
- THIS IS HOW SCIENCE &
  KNOWLEDGE ADVANCES

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