Should we be treating temperament instead of anxiety and depression?

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DSM IV
Anxiety and Mood Disorders

- Substantial phenotypic overlap
- High comorbidity
- Necessity of NOS diagnoses (mostly GAD)
- Subthreshold presentations (mostly OCD, MAD & SAD)
DSM IV

“Zenith of splitting” (reliably identified but narrow slices of psychopathology)

DSM-5

“Return to lumping” (based on the deepening knowledge of underlying dimensions of psychopathology and supporting brain circuitry)
Anxiety Disorders

Separation Anxiety Disorder
Selective Mutism
Panic Disorder
Agoraphobia
Specific Phobia
Social Anxiety Disorder (Social Phobia)
Generalized Anxiety Disorder
Substance-Induced Anxiety Disorder
Anxiety Disorder Attributable to Another Medical Condition
Anxiety Disorder Not Elsewhere Classified
Panic Attack
Metastructure of DSM 5

Obsessive-Compulsive and Related Disorders

Obsessive-Compulsive Disorder
Body Dysmorphic Disorder
Hoarding Disorder
Trichotillomania (Hair-Pulling) Disorder
Excoriation (Skin-Picking) Disorder
Substance-Induced Obsessive-Compulsive, or Related Disorders
Obsessive-Compulsive, or Related Disorder Attributable to Another Medical Condition
Obsessive-Compulsive, or Related Disorder Not Elsewhere Classified
Metastructure of DSM 5

Trauma- and Stressor-related Disorders

Reactive Attachment Disorder
Disinhibited Social Engagement Disorder
Acute Stress Disorder
Post-traumatic Stress Disorder
Adjustment Disorders
Trauma- or Stressor-Related Disorder Not Elsewhere Classified
Higher Order Dimensions: (Temperaments)

- Neuroticism: (Introversion) – Eysenck
- Behavioral Inhibition System: Behavioral Activation System (BIS-BAS) – Gray
- Behavioral Inhibition – Kagan
- Negative Affect: Positive affect (NA-PA) --Tellegen, Clark, Watson
- Trait anxiety –(Barlow, 1988; Cattell, 1963)
Higher Order Dimensions: (Temperaments)

- Trait Anxiety / Neuroticism / Behavioral Inhibition
- Behavioral activation / Positive Affect
Neuroticism

- Tendency to experience frequent, intense negative emotions (e.g. anxiety, depression, anger and irritability) associated with a sense of uncontrollability (the perception of inadequate coping) in response to stress.
Temporal Course of Temperamental Dimensions

- $N = 606$
- 75% treated at CARD followed for 2 years whether treated or not.
- Principal DX: Unipolar Mood, GAD, Social Anxiety
- Broad patterns of comorbidity

Brown, T. A., 2007
Generalized Anxiety Disorder

Model-Implied Trajectories of *DSM-IV* Disorder Constructs as a Function of Neuroticism/Behavioral Inhibition. *Note.* N/BI = Neuroticism/Behavioral Inhibition. (N=606).

Brown, T. A., 2007
Some results and future questions

Largest effect size for N/BI

Disorder effect sizes intermediate

More severe N/BI is associated with smaller tx effects

Do changes in N/BI mediate overall change?
Origins of Trait Anxiety/Neuroticism

Triple Vulnerability Theory

Independent Vulnerabilities

**Biological Vulnerability**
(heritable contribution to negative affect)

- “Glass is half empty”
- Irritable
- Driven

**Specific Psychological Vulnerability**
(e.g., physical sensations are potentially dangerous)

- Hypochondriac?
- Nonclinical panic?

**Generalized Psychological Vulnerability**
(sense that events are uncontrollable/unpredictable)

- Tendency towards lack of self-confidence
- Low self-esteem
- Inability to cope
Generalized Biological Vulnerability
Polygenic Model of Vulnerability

“Gene discovery… is, on its own, unlikely to allow us to carve nature at its joints.”
(Kendler, 2006)

“Susceptibility genes… represent particular allelic variations of common genes.”
(Rutter, Moffitt, & Caspi, 2006)

Heightened reactivity in emotion generating structures (amygdala hyperexcitability)
Generalized Psychological Vulnerability
Generalized Psychological Vulnerability

Early disruptive experiences produce a (permanent) sense (schema) of unpredictability, uncontrollability, and an inability to cope with potentially threatening events through a process of sensitization and kindling. “Experimental Neurosis” – Pavlov, Masserman, Liddell (Mineka & Kihlstrom, 1978).

These experiences are associated with stable change in brain structure and function, including gene expression. (Sapolsky 2007; Gillespie & Nemeroff, 2007; Spinelli, Chefer, Suomi, Higley, Barr, & Stein, 2009.)

Disruptive early experiences are not restricted to early trauma – other experiences such as certain parenting styles induce diminished sense of personal control. (Chorpita & Barlow, 1998.)

Consequence is not any one specific disorder.
Stress is associated with loss of control, lack of prediction, no outlets for frustration, chronic threats, and social subordination. These factors lead to increased corticotrophin-releasing factor, which in turn can lead to hypercortisolism, deficient hippocampal neurogenesis, and damage and exacerbation of insults. The glucocorticoid cascade is further complicated by reduced inhibitory feedback.

From Sapolsky, 1992; 2007; Sapolsky et al., 1997.
Common Neurobiological Syndrome

- Hyperexcitability of limbic structures (amygdala overactivation).
- Inefficient or dysregulated cortical inhibition of amygdala responding.
- Deficient pattern separation.

Found in:
- SAD (Phan et al., 2006), GAD (Etkin et al. 2010), PTSD (Shin et al., 2005), Depression (Holmes et al., 2012) and neuroticism itself (Keightly et al., 2003).
Phenotypic Expression

GENERAL BIOLOGICAL VULNERABILITY

DYSREGULATED STRESS RESPONSE

GENERAL PSYCHOLOGICAL VULNERABILITY

NEUROTICISM

GAD

DEP.

LOW PA
+ LOW RESILIENCE
Mediating Stressful and Emotional Experiences in Genesis of Specific Emotional Disorders
Panic Attack
Means and Standard Deviations for Stimulus-Naïve Participants on Measures of Emotional Appraisal and Regulation during the First Emotion Induction

<table>
<thead>
<tr>
<th>Measure</th>
<th>Clinical Participants</th>
<th>Nonclinical Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>MES-A</td>
<td>23.37 (5.22)</td>
<td>26.26 (2.74)*</td>
</tr>
<tr>
<td>MES-C</td>
<td>22.67 (5.43)</td>
<td>24.04 (4.72)</td>
</tr>
<tr>
<td>SUPP</td>
<td>3.50 (2.17)</td>
<td>2.11 (2.03)*</td>
</tr>
<tr>
<td>MRS-R</td>
<td>12.28 (5.50)</td>
<td>11.96 (5.57)</td>
</tr>
<tr>
<td>MRS-M</td>
<td>15.52 (5.03)</td>
<td>15.67 (4.30)</td>
</tr>
<tr>
<td>SELF</td>
<td>5.07 (2.64)</td>
<td>6.33 (2.18)**</td>
</tr>
<tr>
<td>WILL</td>
<td>5.72 (2.46)</td>
<td>6.36 (2.30)</td>
</tr>
</tbody>
</table>

Note. Values are mean scores with standard deviations in parentheses.
MES-A = Meta Evaluation Scale-Acceptability; MES-C = Meta Evaluation Scale-Clarity;
SUPP = Suppression Rating; MRS-R = Meta Regulation Scale-Repair;
MRS-M = Meta Regulation Scale-Maintenance; SELF = Self Efficacy Rating;
WILL = Willingness Rating.

* p < .02
** p < .05

Model of the Persistence of Emotional Distress Featuring Perceived Unacceptability of Emotions and Resulting Emotional Suppression/Avoidance

- Negative affect
  - Emotion perceived as intolerable/unacceptable
    - Efforts to suppress
      - Suppression Fails
  - Emotion perceived as tolerable/acceptable
    - No suppression
      - Mood recovers naturally

Associated constructs reflecting these functional relationships
(Negative reactivity and perceptions of lack of control of intense emotion)

- Increased anxiety sensitivity
- Decreased mindfulness
- Experiential avoidance (emotional suppression, worry, rumination)
- Negative appraisals and attributions
# Examples of Avoidance Strategies

## Behavioral and Interoceptive Avoidance

### Avoidance Strategy

<table>
<thead>
<tr>
<th>Situational avoidance/escape</th>
<th>Disorder Often Associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidance/escape from phobic situations (e.g., crowds, parties, elevators, public speaking, theaters, animals)</td>
<td>PD/A, SOC, SPEC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subtle behavioral avoidance</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidance of eye contact (e.g., wearing sunglasses)</td>
<td>SOC</td>
</tr>
<tr>
<td>Avoidance of sensation-producing activities (e.g., physical exertion, caffeine, hot rooms)</td>
<td>PD/A</td>
</tr>
<tr>
<td>Avoidance of “contaminated” objects (e.g., sinks, toilets, doorknobs, money)</td>
<td>OCD</td>
</tr>
<tr>
<td>Perfectionistic behavior at work or home</td>
<td>GAD, SOC, OCD</td>
</tr>
<tr>
<td>Procrastination (avoidance of emotionally salient tasks)</td>
<td>GAD, DEP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Repetitive or ritualistic behaviors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Compulsive acts (e.g., excessive checking, cleaning)</td>
<td>OCD</td>
</tr>
</tbody>
</table>
Examples of Avoidance Strategies
Cognitive and Emotional Avoidance

<table>
<thead>
<tr>
<th>Avoidance Strategy</th>
<th>Disorder Often Associated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognitive avoidance/escape</strong></td>
<td></td>
</tr>
<tr>
<td>Dissociation (depersonalization, derealization)</td>
<td>PDA, PTSD</td>
</tr>
<tr>
<td>Distraction (e.g., reading a book, watching television)</td>
<td>GAD, DEP, PD/A</td>
</tr>
<tr>
<td>Avoidance of thoughts or memories about trauma</td>
<td>PTSD</td>
</tr>
<tr>
<td>Effort to prevent thoughts from coming into mind</td>
<td>OCD, PTSD</td>
</tr>
<tr>
<td>Worry</td>
<td>GAD</td>
</tr>
<tr>
<td>Rumination</td>
<td>DEP</td>
</tr>
<tr>
<td>Thought Suppresion</td>
<td>All Disorders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety Signals</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrying a cell phone</td>
<td>PD/A, GAD</td>
</tr>
<tr>
<td>Holding onto “good luck” charms</td>
<td>OCD</td>
</tr>
<tr>
<td>Carrying water or empty medication bottles</td>
<td>PD/A</td>
</tr>
<tr>
<td>Having reading materials always on hand</td>
<td>SOC, GAD</td>
</tr>
<tr>
<td>Carrying self-protective materials (e.g. mace, siren)</td>
<td>PTSD</td>
</tr>
</tbody>
</table>

Present Status: A Crossroad

- Effective treatment, but plenty of room for improvement
- Too many distinct protocols—manuals
- Protocols still relatively complex—restricting disseminations
Development of a Transdiagnostic Unified Treatment
Multi-dimensional emotional disorders inventory (MEDI)

Intrusive-Social-Depressed ($n = 22, 9.7\%$)
Unified Protocol: A Modular Approach

Module 1: Motivation Enhancement for Treatment Engagement  
(1 session)

Module 2: Psychoeducation and Treatment Rationale (1-2 sessions)

Module 3: Emotional Awareness Training (1-2 sessions)

Module 4: Cognitive Appraisal and Reappraisal (1-2 sessions)

Module 5: Emotion Driven Behaviors (EDBs) and Emotional Avoidance (1-2 sessions)

Module 6: Interoceptive Awareness and Tolerance (1-2 sessions)

Module 7: Situational Exposures (3-6 sessions)

Module 8: Relapse Prevention  (1 session)  
Barlow et al., 2011
ADIS-IV Principal Diagnosis

$F(1,30) = 23.18, \ p = <.001, \ \eta_p^2 = .436, \ d = 1.76$
### Proportion Achieving Responder Status and High End-State Functioning: ADIS-IV Principal Diagnosis CSR

<table>
<thead>
<tr>
<th>Study Condition</th>
<th>Post- Treatment / WL</th>
<th>6-Month Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%Treatment Responders</td>
</tr>
<tr>
<td>UP Treatment</td>
<td>22</td>
<td>55%</td>
</tr>
<tr>
<td>WL Control</td>
<td>10</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Note: HES Fx= High End-State Functioning.*
Effects on NA – UP Version 2.0

- Significant effect of time on NA ($F_{1,13}=10.55$, $p<.001$)
- Clinical significance of change in NA:
  - Pre-treatment – 27% patients achieved scores within normal range
  - Post-treatment – increased to 67% (as compared to 56% in study 1)
  - 6-month follow-up – increased further to 82%

Ellard et al., 2012
Associated constructs reflecting these functional relationships
(Negative Reactivity and Perceptions of lack of control of intense emotion)

- Increased anxiety sensitivity—(UP–interoceptive exposure)
- Decreased mindfulness—(UP–mindful emotional awareness)
- Experiential avoidance (emotional suppression, worry, rumination) –UP –countering EDP and emotional avoidance
- Negative appraisals and attributions— (UP–cognitive reappraisal)
Efficacy Evaluation of UP

NIMH R01: 2010 – 2015,
N=250
UP: N=100
SDP (GAD, PDA, SOC, OCD): N=100
Waitlist: N=50
Non inferiority (equivalence) trial
Increasing PA

- Individuals with a range of anxiety disorders or symptoms exhibit a decreased tendency to “savor” or maintain positive emotions as well as an increased tendency to “dampen” or minimize positive emotions.

- Treatment module in development to target specific disturbances in positive emotion regulation (Carl in progress).
Positive Affect

- In MDD—dose-response relationship between exercise and increase in PA (Mata et al., 2012).
- Increases in neurogenesis (after exercise in animals) (Speisman et al., 2012)
Take Home Messages

“Splitting” no longer supported empirically or clinically

Higher-order temperaments better account for:
- Description of emotional disorders
- Origins of Emotional Disorders

Developing treatments distill common principles to treat transdiagnostic temperamental features
Thank You

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