



8th Annual

**Yale NEA-BPD Conference**  
*Impulsivity, Aggression, and Legal Involvement*  
Friday, May 4, 2012; 8:30 AM - 4:45 PM

**BORDERLINE PERSONALITY DISORDER:  
IMPULSIVITY, AGGRESSION, & LEGAL INVOLVEMENT**

**FRIDAY MAY 4, 2012**

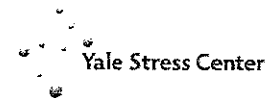
**8:30 AM - 4:45 PM**

Mary S. Harkness Memorial Auditorium, Sterling Hall of Medicine

333 Cedar Street, New Haven, CT

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**Psychopharmacology of Impulsivity and Agression:  
Creating Space for Treatment**

**Haleh Ghanizadeh MD MPH**

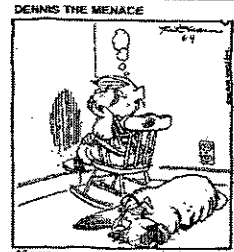
## Impulsivity and Aggression: Creating Space for Treatment

Haleh Ghanizadeh, M.D., M.P.H.

8th Annual Yale NEA-BPD Conference

Borderline Personality Disorder: Impulsivity, Aggression, and Legal Involvement  
May 4, 2012

## Impulsivity:



"actions that are poorly conceived, prematurely expressed, unduly risky, or inappropriate to the situation and that often result in undesirable consequences"

## Aggression:

Moysa, K. B. The Physiology of Violence. (Madison, Chicago, 1971)

"overt behaviour that has the intention of inflicting physical damage on another individual"



<http://www.emotion.com/section/aggression>

## BPD

"...an emergent phenotype principally reflective of a complex interaction involving diminished positive emotion in relation to increased negative emotion, in interaction with diminished activity of the modulatory constraint system and exaggerated reactivity of the fear system." Depue and Lenzenweger

## APA Practice Guidelines

Affective Dysregulation / Impulsive-Behavioral Dyscontrol

Antidepressants: Fluoxetine  
Mood stabilizers: Valproic Acid, Phenytoin, Carbamazepine  
Antipsychotics: Olanzapine, Aripiprazole

Cognitive-Perceptual Symptoms

Antipsychotics: Olanzapine

New, A. S. et al. Fluoxetine increases relative metabolic rate in the prefrontal cortex in impulsive aggression. *Psychopharmacology (Berl.)* 176, 451-458 (2004).

- Individuals who rated highly for impulsive aggression had reduced activation of the prefrontal cortex (PFC)
- SSRIs reduced their ratings of aggression.
- Twelve weeks of SSRI treatment increased baseline activation in the PFC, and PFC activation was negatively correlated with ratings of aggression.

Personal speaker feeds minimally  
affective

**Dialectical Behavior Therapy Plus Olanzapine for Borderline Personality Disorder (8 Weeks)**

Solar J et al. Am J Psychiatry 2005; 162:1221-1224

- ↓ in depressive symptoms according to Hamilton depression scale
- ↓ in clinical anxiety according to Hamilton Anxiety Scale
- ↓ in the frequency of impulsivity/aggressive behavior than the placebo plus dialectical behavior therapy group
- ↓ self-injuring behavior/suicide attempts was nonsignificant

**Antiepileptic drugs for treating recurrent aggression**

Husband N, Fiedler M, Kistner P, Jansen H. Antiepileptics for aggression and associated impulsivity. Cochrane Database of Systematic Reviews 2010, Issue 2. Art. No.: CD007489.

Contradictory data from 14 studies/672 participants

Sodium valproate/divalproex:

- outpatient men with recurrent impulsive aggression,
- impulsively aggressive adults with cluster B personality disorders
- youths with conduct disorder
- not for children and adolescents with pervasive developmental disorder

**Carbamazepine**

reducing acts of self-directed aggression in women with borderline personality disorder, but not in children with conduct disorder.

- Oxcarbazepine
  - verbal aggression and aggression against objects in adult outpatients.
- Phenytoin
  - was superior to placebo on the frequency of
  - aggressive acts in male prisoners and in
  - outpatient men including those with personality disorder, but
  - not on the frequency of 'behavioral incidents' in delinquent boys.

**Combining DBT and Medications**

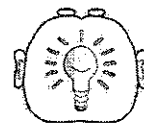
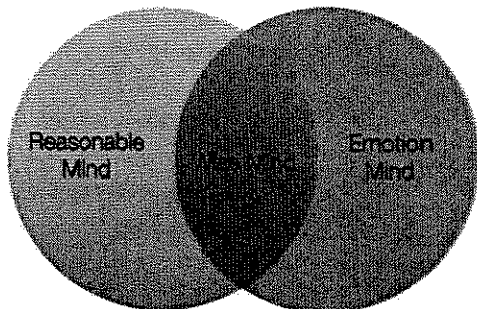
*Accurately assess critical links in behavioral chain*

Mindfulness to increase awareness

Skills to accurately experience and express emotion

Goals/values/self-concept to direct therapy

Meds to maintain focus and attention during intense emotions



*moments that need to be handled*

## Targeting Links

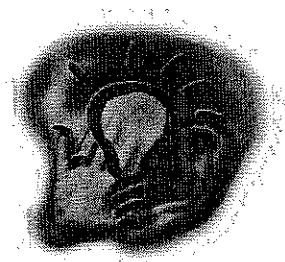
- \* "I can't stand this!"
- \* "Fuck it."
- \* "I give up."
- \* "It doesn't matter."
- \* "I am never..."
- \* "Whatever."

## What do we know?

The frontal cortex provides inhibitory inputs to circuits in the hypothalamus and amygdala

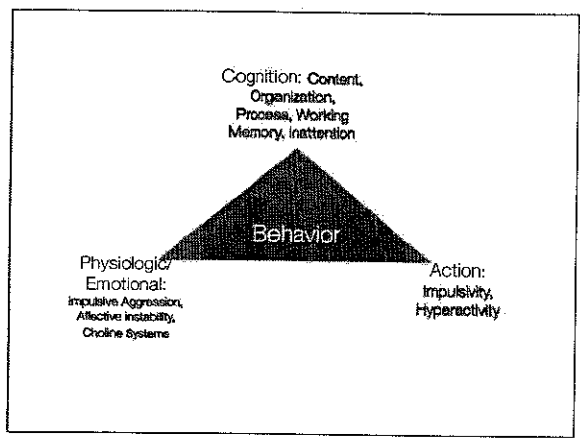
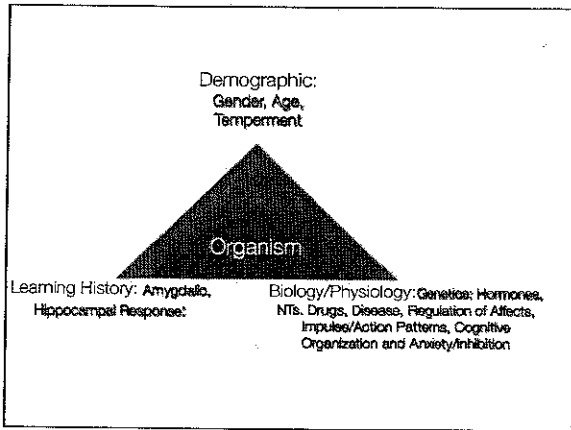
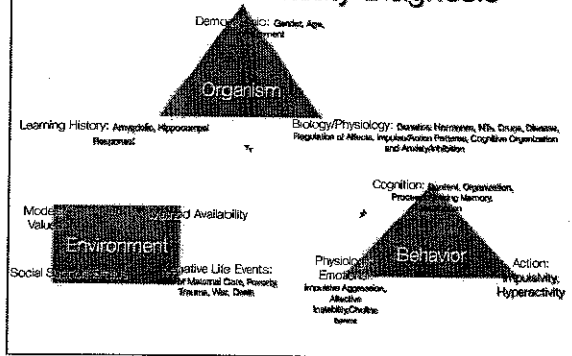
Suppression of negative memories leads to rumination and lowered mood and higher anxiety

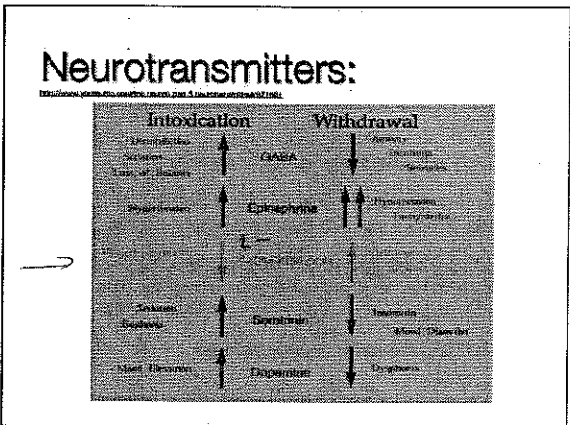
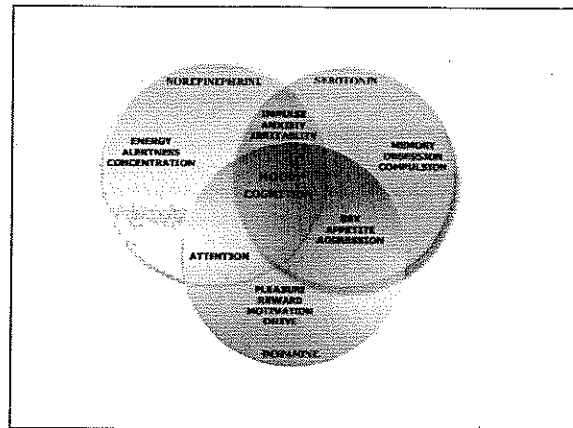
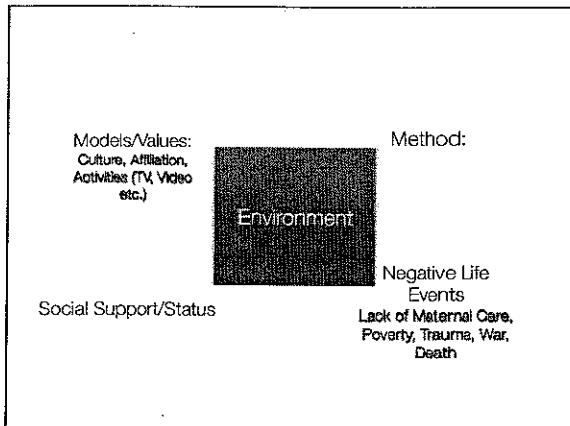
In pts with BPD and heightened activation of limbic circuitry, painful stimuli provided relief to emotional distress



[https://workpowered.files.wordpress.com/2008/07/learning\\_logo1.jpg](https://workpowered.files.wordpress.com/2008/07/learning_logo1.jpg)

## Borderline Personality Diagnosis





Glutamate (excitatory) excess overstimulates brain cells, leading to neuronal loss and atrophy... mood disorders may be regarded as fundamentally atrophic (ie stemming from brain cells in physical distress) rather than symptomatic.

- GABA A (inhibitory) receptors regulate excitability and anxiety, panic, and stress, and are the targets of benzodiazepines such as Ativan, as well as alcohol.
- Low GABA in occipital cortex measured in melancholic depression

**Focus on Emotion Regulation vs. Cognitive Processing**

- Decrease Physiological Arousal
- Re-Orient Attention
- Inhibit Mood Dependent Action

*Re-appraise distally  
choose value/self-concept  
Approach n/skill*

The neuropsychological correlates of borderline personality disorder and suicidal behaviour. *J Child Psychol Psychiatr*. 2006 Mar;51(3):131-42.

Impaired executive function and disinhibitory processes, primarily associated with dorsolateral prefrontal cortical regions may represent a dominant executive pathway to suicide attempt.

- A primary motivational inhibitory pathway involving conflictual, affective, and reflexive decision-making processes associated with orbitofrontal brain regions, in combination with significant cognitive rigidity, may influence the repetitive expression of self-harm or low-lethality suicidal behaviour.

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## $\alpha$ 2 adrenergic catecholamines

→ ↑ regulation of attention and behavior, cognition, and impulsivity by the prefrontal cortex by balancing the emotions from the amygdala/limbic system and "top-down" control.

## $\alpha$ 2 Agonists: more commonly used for hypertension, hot flashes during menopause, tics from stimulants, opioid withdrawal

- vasodilation of arteries; vasoconstriction of coronary arteries and peripheral veins
- modulate noradrenergic tone in the PFC
- influence behavior, cognition and impulsivity
- an essential component of their utility in specific domains of ADHD
- guanfacine > clonidine in specificity to the postsynaptic alpha 2A receptor in the PFC

*Cool blood in Exercentic*

## "Valerie" Quotes

- \* Don't get drop in my stomach anymore
- \* My thoughts are less focused on loss with regard to girls. I don't feel like things are ending for me.
- \* I'm no longer lost in sadness even though I didn't have much to be sad about. (But also distracting from one's relationship end with thoughts about another.)
- \* I feel less impulsive...maybe because....

## Beta Blockers

- No direct effect on anxiety, but diminish patients' preoccupation with their physical state by reducing tremor and the cardiac response to anxiety, which lowers frustration and aggression
- Relax blood vessels and slow heart rate to improve blood flow and decrease blood pressure

## Propranolol

- 5-HT1A antagonist and a 5-HT1B agonist
- Used for aggression
  - organic brain syndromes in children and adults
  - Korsakoff's psychosis
  - schizophrenia
  - severe mental retardation
  - adult autism

## Pindolol

Blocks 5-HT<sub>1A</sub> autoreceptors in the Dorsal Raphe Nucleus to enhance serotonin transmission

- Blocks  $\beta_1$  and  $\beta_2$  adrenergic receptors, ↓ epinephrine and norepinephrine
- $\beta_1 \rightarrow$  ↓ HR and BP slightly
- $\beta_2 \rightarrow$  ↓ renin/angiotensin II  $\rightarrow$  ↓ vasoconstriction (may occur independently as well). Also found in lung and uterus
- bronchial and uterine and GI contractions

Pindolol augmentation in aggressive schizophrenic patients: a double-blind crossover randomized study  
Cassol, N.A.; Micali, L.A.; Bank, P.A.; Washburn, A.A.; Zislesky, H.; Hirschmann, S.; Pitner, M.S.D. *International Clinical Psychopharmacology*  
March 2001 - Volume 15 - Issue 2 - pp 111-115

OAS scores were significantly reduced for number of aggressive incidents towards objects and other persons during pindolol treatment (0.59 versus 1.40,  $F = 6.06$ ,  $P < 0.02$ ; 1.96 versus 3.26,  $F = 4.17$ ,  $P < 0.05$ , respectively).

- ↓ severity of incidents (0.89 versus 3.58,  $F = 19.42$ ,  $P < 0.0001$ ; 2.89 versus 6.85,  $F = 10.11$ ,  $P < 0.004$ , respectively).
- Influence on severity may be associated with a 5-HT<sub>1A</sub> antagonistic effect.

## "Sarah" on Pindolol

- \* Others can get a word in
- \* Doesn't rage, scream
- \* Relationships improved - son will allow her to see him.
- \* No longer "goes off"

The role of serotonergic mechanisms in inhibition of isolation-induced aggression in male mice. Sánchez-G. Am. J. Hyatt J., Molteni ES. *Psychopharmacology (Berl)*. 1998;140(1-2):53-59

The role of serotonergic (5-HT) receptor subtypes in mediation of aggressive behaviour in isolated male mice has been studied. Increases of attack latency was used as a simple measure of antiaggressive behaviour.

- 5-HT<sub>1A</sub> agonists (gaspiron; buspirone) completely inhibit the aggressive behaviour irrespective of their intrinsic activities.
- The mixed 5-HT<sub>1A</sub> and beta-adrenoceptor antagonists (-)alprenolol and pindolol are ineffective discriminative stimulus.
- The selective 5-HT uptake inhibitor citalopram does not inhibit aggressive behaviour.
- Prazosin (alpha 1-adrenoceptor antagonist), clonidine (alpha 2-adrenoceptor agonist), clonitrolol (beta-adrenoceptor agonist), ketanserin (5-HT<sub>2</sub> receptor and alpha 1-adrenoceptor antagonist), clozapine and (-)-ocetodiphen (topiramine (DA), 5-HT<sub>2</sub> receptor and alpha 1-adrenoceptor antagonist) all show an antiaggressive effect.

In conclusion, 5-HT<sub>1A</sub> receptors are involved in mediation of isolation-induced aggressive behaviour in mice.

## AZAPIRONES: Buspirone

Partial serotonin 1A agonist. Lithium too

- No significant effects on seizures, has no muscle relaxant effect and their anti-anxiety action is delayed for some two to three or four weeks.

## Buspirone: Open Pilot Studies

Buspirone 10-25 mg per day reduced aggression, irritability and impulsivity in nonorganic patients

- Low doses may correspond with a presynaptic Serotonin 1A agonism with a feedback loop producing overall postsynaptic antagonism at all serotonin receptors.
- Non-vertiginous dizziness



## Out with the Old?

Affective Dysregulation      Impulsive-Behavioral Dyscontrol

Partial 5-HT<sub>1A</sub> Agonist: Buspirone, Pindolol  
5-HT<sub>1A</sub> antagonist and a 5-HT<sub>1B</sub> agonist: Propranolol  
Alpha-1 adrenoceptor antagonist: Prazosin  
Alpha-2 Agonist: Clonidine, Guanfacine

Cognitive-Perceptual Symptoms

Glutamate inhibitor: Lamotrigine  
Alpha-2 Agonist: Clonidine, Guanfacine

## Couple: task is for husband to pay wife a compliment

### Vulnerabilities

- Feeling fat and undesirable
- History of husband not noticing me
- Major flood in kitchen, exhausted, but went out with husband and his friends night before

"Let's go out (for breakfast)."

- "No"
- "Why is it that we do everything you want to do and you constantly ignore what I want?"
- "I don't want to go out."
- "Did you happen to notice that I got dressed up last night and once again, you failed to pay me a compliment about how I looked?"

"Am I that ugly or undesirable that you can't ever notice me?"

- "Oh, just relax."
- "I'm sick of this! What would it take for you to notice me?"
- I was filling a water bottle at the sink, twisted it and threw it against the sink, and ran upstairs screaming

"I am sick of this! I can't take it anymore!"

- "What do I have to do to get your attention?"
- I thought if I have bruises maybe he'll see that I'm in pain
- I was just screaming and started hitting my legs
- "...I'm taking you to the hospital."

Sweat dripping from my head, crying uncontrollably

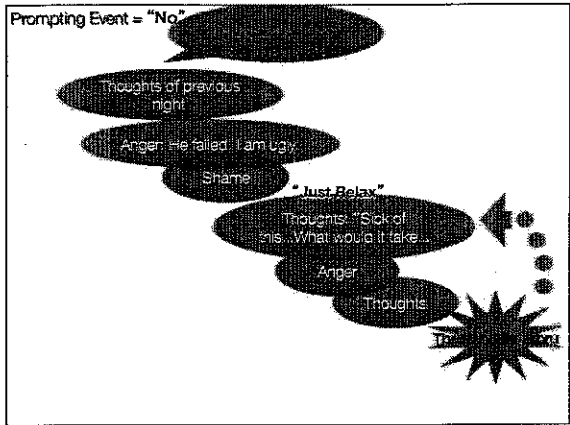
- "Why are you with me? Don't you care about me? Maybe you'd be happy with someone prettier."
- Pounding my legs
- He screamed, "Stop it!"

He squeezed my wrists hard and grabbed me to hug me

- I just kept crying
- He said, "Go take a shower."
- We then went out

### What are critical patterns?

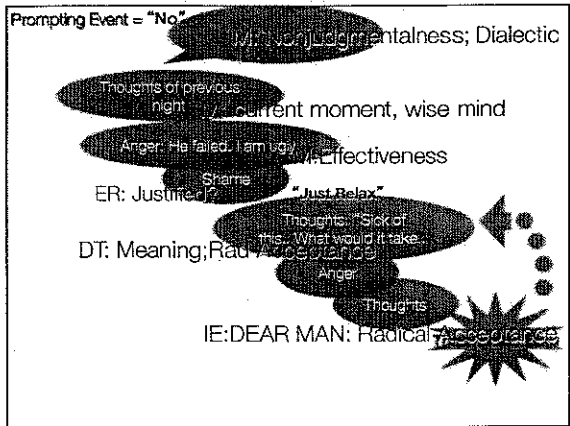
- Vulnerability to negative emotions
- Underlying unworthiness
- Bringing past event into current "offense"
- Inability to utilize radical acceptance of not being noticed
- Operant conditioning of behavior
- Reinforcement of behavior



### Restraining impulsivity....

What's the impulse?

- Where is attentional control needed?
- What skills would you teach?
- What emotional exposure would you pursue?



### Tasks in emotion modulation (Gottman & Katz, 1990)

- Observe that emotion is occurring (tolerate it)
- Decrease (or increase) physiological arousal associated with emotion
- Re-orient attention
- Inhibit mood-dependent action
- Organize behavior in the service of external, non-mood dependent goals

## Self-Concept

- \* Values:
- \* Core Beliefs
- \* Objectives/Daily Goals
- \* Location Perspective

## Obstacles

- \* Self-Concept
- \* Lack of mindfulness practice
- \* Inhibited grief
- \* Reinforcement of maladaptive behavior

## De-escalation Behavioral Tech. MME.

Focus on Emotion Regulation vs. Cognitive Processing

- Decrease Physiological Arousal
- Re-Orient Attention
- Inhibit Mood Dependent Action

## De-escalation Cont.

Specific Strategies

- Cue Removal
- Validation
- Skills Coaching
- Physiological Interventions (breathing, willing hands, exercise, half smile)
- Shift attention until emotion goes down