Anxiety and Panic: Drivers of Distress

Steven M. Baskin PhD
New England Institute for Neurology and Headache
Stamford, Connecticut USA
Greenwich Hospital of Yale-New Haven Health
Greenwich, Connecticut USA

World Congress of Neurology
Santiago, Chile
November 1, 2015

Disclosures

- Advisory Boards: Allergan, Depomed, Teva

Learning Objectives

- Participants will be able to outline the symptoms of anxiety, in particular panic, and how they may affect the presentation, progression and outcome of comorbid disease, using migraine as model.
- Attendees will be able to describe various treatment alternatives for the patient who presents with comorbid anxiety.
- Participants will be able to recognize the parallels that exist between fear of somatic sensations (e.g. fear of pain in migraineurs) and the role of interoceptive conditioning and anxiety sensitivity in panic disorder.

Overview

- Anxiety disorders are highly prevalent in the general population and comorbid with numerous neurological disorders and often a significant driver of distress.
- Migraine will be used as a model to show the effect of comorbid anxiety on symptom presentation, adherence to treatment, and chronification of illness.
- There are similarities between episodic disorders with high impairment (such as migraine) and panic disorder where patients develop conditioned fear to somatic sensations.
- Borderline Personality Disorder is an extreme form of emotional dysregulation that may have a catastrophic effect on the management of comorbid emotional and neurologic disorders.

Psychiatric comorbidity

- May complicate differential diagnosis.
- Non-adherence with treatment regimens 3 X more likely if depressed or anxious, across numerous disorders.
- Associated with lower quality of life, more fatigue, and reduced adherence to disease-modifying therapy in multiple sclerosis (MS).
- Poorer drug tolerability
- May increase risk of relapse
- May chronify the course of migraine

Baskin SM. and Smitherman TA. *Neurol Sci*. 2009;30:S61-S65; Blanchard et al., 1985;
Guidetti et al., 1998; Holroyd et al., 1988;
Lanteri-Minet et al., 2005; Bigal ME, Lipton RB 2006; Micieli et al., 1985; Mongini et al., 2003
Waldie & Poulton, 2002; Scher, et al 2008; Marrie, RA, et al. Mult Scler. 2015 Mar; 21(3): 305–317

Association Between Migraine and Anxiety: Community Studies

Odds Ratio

Reference	Panic	GAD	OCD	Phobia
Breslau (1998)				
migraine with aura	10.4	4.1	5.0	2.9
migraine w/o aura	3.0	5.5	4.8	1.8
Swartz et al (2000)	3.4		1.3	1.4
Breslau et al (2001)	3.7			
Merikangas et al (1993)	3.3	5.3		
McWilliams (2004)	3.6			
Saunders et al (2008)	3.6			
Wang et al (2007)	6.6 (chronic migraine)			

Modified from Smitherman, TA et al. *Headache* 2013;53:23-45

Anxiety Disorders

- Symptoms common to most all anxiety disorders:
  - Anxiety-related and danger-related cognitions (fear or worry)
  - Physical symptoms
  - Avoidance behaviors (some are very subtle)

- Assessment of physical symptoms and panic is of particular importance with migraine and other episodic disorders with high impairment.
  - Overestimate the probability of danger (migraine) and perceive it as more unmanageable and threatening than objective reality. Very sensitive to medication side effects and somatic sensations.

Smitherman TA, et al. *Headache* 2013;53:23-45

Headache and Psychiatric Comorbidity (multi-axial examples)

Axis I	Axis I	Axis I
Major Depression	Major Depression	Major Depression
	Panic Disorder	Panic Disorder
Axis II	Axis II	Axis II
No disorder	No disorder	Borderline personality
Axis III	Axis III	Axis III
Episodic migraine	HF Episodic migraine	Chronic migraine

Increasing Complexity and Difficulty

Sheftell FD, Atlas SJ. Headache 2002; 42: 934-944

Anxiety Disorders

- Typically accompanied by fear-based thoughts of danger and vulnerability. Avoidance of feared stimuli reduces discomfort but maintains the danger belief that fear stimuli and anxiety symptoms themselves are harmful. Patients across all anxiety disorders exhibit avoidance behaviors.
- Tend to overestimate the likelihood of the occurrence of a negative event (migraine) and perceive situations as more catastrophic, threatening, and unmanageable than their objective reality.

Generalized Anxiety Disorder

A. Excessive anxiety and worry occurring more days than not for at least 6 months.
B. The individual finds it difficult to control the worry.
C. Anxiety and worry are associated with three or more of the following:

- Restlessness or feeling keyed up on or edge.
- Easily fatigued
- Difficulty concentrating or mind going blank.
- Irritability
- Muscle tension
- Sleep disturbance

Panic Disorder

- A patient must experience unanticipated panic attacks in order to get a diagnosis of PD.
- Panic disorder is diagnosed when an individual has persistent, unexpected attacks with at least 1 month of continual apprehension about their recurrence or a change in their behavior as a result of having panic attacks.
- Leads to extensive use of medical services. Agoraphobia, MDD, personality disorder leads to more persistent symptoms.

Vickers K, McNally RJ. *J Abnorm Psychol* 2004;113:582-591;
Katon WJ, *NEJM*; 2006;354:2360-67;
Pilowsky DJ, et al. *Depress Anxiety* 2006;23:11-16.

Panic Disorder DSM-5
Diagnostic Criteria

A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) symptoms from a list of 13 physical and cognitive symptoms.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.)

Panic Disorder DSM-5

4 or more of a list of 13 symptoms

11 Somatic Symptoms

- Pounding heart
- Sweating
- Shaking/trembling
- Sensations of SOB
- Feelings of choking
- Chest discomfort
- Nausea/abdominal distress
- Feeling dizzy, unsteady
- Paresthesias
- Chills or heat sensations
- Derealization or depersonalization

2 Cognitive Symptoms

- Fear of dying
- Fear of losing control or "going crazy"

Panic Disorder DSM-5

B. At least one of the attacks has been followed by one month (or more) of one or both of the following:

1. Persistent worry about additional panic attacks or their consequences (losing control, “going crazy”, having a seizure, etc.)

2. A significant maladaptive change in behavior related to the attacks (such as avoidance of exercising or unfamiliar places)

Differential diagnosis

- Is the patient afraid of stimulus itself (e.g. heights)? **Specific phobia**
- Is patient afraid of negative evaluation (independent of panic)? **Social Anxiety disorder**
- Is patient afraid of content of obsessive thought? **Obsessive-compulsive disorder.**
- Do the panic attacks only occur in the presence of general worry? **GAD**
- Do panic attacks only occur with post-traumatic stimuli? **PTSD**
- Does patient have recurrent, unexpected PA's and is patient fearful of the somatic sensations? **Panic Disorder**

Migraine/Anxiety relationship

- Panic disorder is a chronic condition similar to migraine with episodic attacks with high impairment and interictal worry about future attacks.
- Anxiety disorders comorbid with migraine or other episodic conditions may increase somatic and anxiety sensitivity, condition fear reactions to those physical sensations, and provoke avoidance behavior.
- This is turn may affect symptom presentation as well as adherence to treatment.

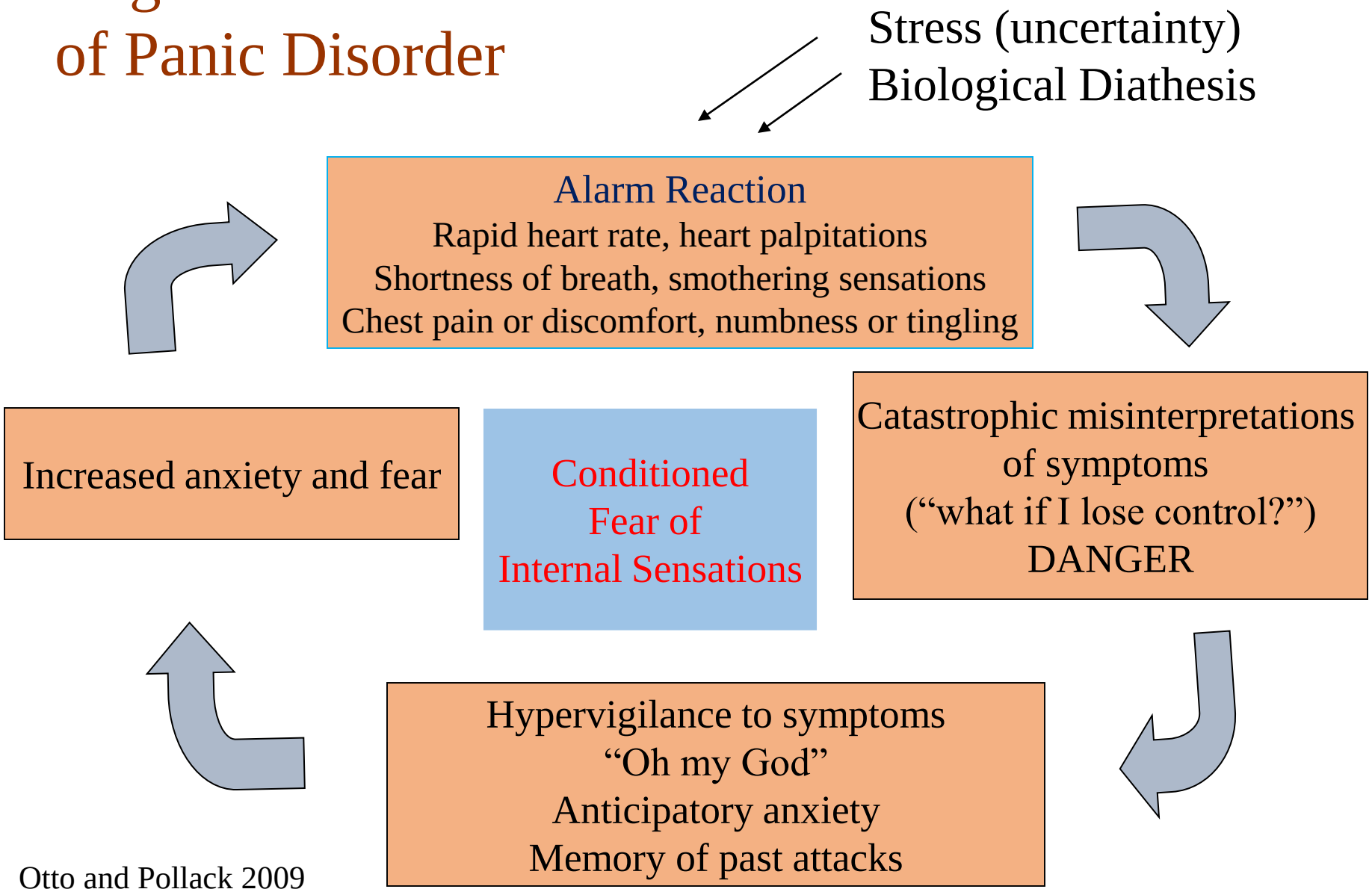
Smitherman, Kalivas & Bailey, *Headache* 2013;53:23-45

Anxiety Sensitivity

- Tendency to notice and fear benign physical sensations due to beliefs that these sensations will have harmful and have possibly catastrophic consequences.
- Positive correlation between anxiety sensitivity and brain activation in anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC) and insula.
- Predicts fear of pain and maladaptive avoidance behaviors in migraine patients.
- Associated with more frequent and disabling headaches as well as greater susceptibility to headache triggers. May be relevant to people with epilepsy, MS, vertigo.

Smitherman TA, et al *Headache* 2013;53:23-45; Norton PJ &Asmundson CJG, *Pain* 2004;111:218-223; Poletti S, et al. *Psychiatry Res.* 2015 Aug 30;233(2):95-101.

Cognitive-Behavioral Model of Panic Disorder



Otto and Pollack 2009

Treatment Options

Pharmacological

- Benzodiazepines
- SSRI's
- SNRI's/SARI's
- TCA's
- MAOI's

Cognitive-Behavioral

- Education
- Self-Monitoring
- Breathing Retraining
- Applied Relaxation
- Cognitive Restructuring
- Exposure (In Vivo and Interoreceptive)

Five classes of medication>placebo

- Tricyclic antidepressants (TCA's)
- Monoamine oxidase inhibitors (MAOI's)
- Benzodiazepines (high potency better data)
- Selective serotonin-reuptake inhibitors (SSRI's)
- Selective serotonin-norepinephrine reuptake inhibitors (SNRI's)

- Start low and go slow, anxiety disorder patients are very sensitive to side effects.
- In primary care setting, adding just one component of CBT significantly improves outcome to meds.
- CBT helps with managing side effects of SSRI's
- Chronic use of benzos leads to poorer outcome in CBT

American Psychiatric Association practice guideline, 2009; Craske MG & Barlow DH, 2008; Marcus SM, et al. *Am J Psychiatry* 2007;164:273-5

Borderline Personality Disorder

The ultimate in emotional dysregulation

- In primary care, 4X the prevalence than in the general population; BPD are frequent users of general medical care. 10% of all psychiatric outpatients.
- Suicidal gestures, self-injury and unstable relationships most useful for correct diagnosis.
- Suicide risk 20-50 X higher than general population.
- More likely to have persistent pain
- PD's affect 26% of inpatients with refractory CM (most BPD).
- More disability
- Lower probability of responding to standard preventative pharmacological therapy in migraine.
- More prone to medication overuse

Davis RE, Smitherman TA, and Baskin SM. *Neurol Sci*. 2013;34(Suppl 1):S7-S10;
Lake A, et al. *Headache*, 2009; Rothrock, et al. *Headache*, 2007
Leichsenring F, et al. *Lancet* 2011;377:74-84.

Anxious Depression

- The presence of anxiety with depression can increase difficulties in diagnosis.
- GAD or PD + MDD additional burden and may increase frequency of depressive episodes and may lead to persistent depressive disorder.
- Comorbid borderline personality disorder has worse prognosis and poorer treatment response in MDD.
- Added anxiety may transform depression to a more chronic state that is more resistant to treatment and may possibly be related to dysregulated activity in brain stem nuclei.

Kupfer, et al. *Lancet* 2012;379:1045-1055; Das-Munshi, J et al. *Br J Psychiatry* 2008;192:171-77; Moffitt TE, et al. *Arch Gen Psychiatry* 2007;64:651-60; Beesdo, et al *Arch Gen Psychiatry* 2007;64:903-12 Michels R. *Am J Psychiatry* 2010;167:487-88

Conclusions

- Anxiety Disorders may complicate comorbid neurological disorders
- Patients may develop conditioned fear to somatic sensations that are similar to fear conditioning in panic disorder
- Interoreceptive awareness and anxiety sensitivity are important factors in both anxiety and migraine
- Psychopharmacological management and cognitive behavioral therapies have a large evidence-base.
- Awareness of these issues may help with the management of the comorbid neurological disease.