Biological traits and psychophysiological substrates of anxiety and somatic symptoms

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Anxiety as an emotion: from adaptive to excessive anxiety

**Anxiety** is an emotion characterized by feelings of tension, worried thoughts and physical changes like increased blood pressure that interact.

(American Psychological Association, 2014)

**High state anxiety and Anxiety Disorders:**
- multiple and inter-related factors involved in the development and maintenance of pathological anxiety.

- Symptoms: emotional, cognitive, behavioural and physical.
- Somatic symptoms are usually key features (acute activation of sympathetic nervous system)

(Barlow, 2002; Clark & Wells, 1995; Clark et al., 1997; Olesen, Gustavsson, Svensson, Wittchen & Jönsson, 2012; Sansone & Sansone, 2010).
Mind-body interaction models of emotion creation and anxiety

Clark and cognitive-perceptual models’ vs Damasio’s Somatic Marker Hypothesis
Cognitions retain a central role in shaping the perception and interpretation of bodily sensations of arousal

Cognitive models have enlightened the understanding of anxiety disorders and enabled treatment improvements (Clark & Beck, 2010; Hilchey, & Clark, 2014)

n=168 (Panic Disorder, PD)
Internal bodily state exerts pervasive influences on brain function and mental activity

“Mental processes and their neural substrates are intimately linked to the homeostatic control of internal bodily state. There are a set of distinct interoceptive pathways that directly and indirectly influence brain functions.”

“The majority of visceral signals that shape behavior, cognition, and, arguably, emotion go unnoticed.”
Mind-body interaction models of emotion creation and anxiety

Attentional focus to the body senses and the capability to be aware of these sensations

Vulnerability trait and a potential marker for hypochondriasis, anxiety and somatization
Cognitive attitude characterized by an exaggerated focus on physical symptoms, rumination and magnification ("somatosensory amplification")

Body senses

PROPIOCEPTION
EXTEROCEPTION
INTEROCEPTION

(Bekker, Croon, van Balkom & Vermee, 2008; Kirmayer & Looper, 2006; Abramowitz, Schwartz & Whiteside, 2002; Sherrington, 1906; Laskowski, 2000)
INTEROCEPTION

• Ability to perceive changes in the physiological state of the body
• Constitutional trait of an individual
• Essential to the generation of emotional feeling states
• Associated with higher levels of anxiety and Anxiety Disorders

Interoceptive constructs

Interoceptive sensibility
Interoceptive accuracy

(Damasio, 1996; Clark, 1986; Parkin et al., 2013; Garfinkel et al., 2015)
Interoceptive sensibility assessment (I)

Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al., 2012)- http://www.osher.ucsf.edu/maia/  
Spanish validation (Chile)  
Evaluates: Noticing, non-distracting, not-worrying, attention regulation, emotional awareness, self-regulation, body-listening, trusting
Interoceptive accuracy (I)

Heartbeat counting tasks (Schandry 1982): “Mental tracking task”
- “count silently each heartbeat felt (without manually checking)”
- 6 cued intervals.
- time-windows of 25, 30, 35, 40, 45 and 50s
- presented in randomised order.

Heart beat perception/discrimination tasks (Brener and Jones, 1977; Katkin 2001)
- “Is the tone synchronised with your heartbeat?”
- Paradigm example: 15 different blocks of 10 tones (at 440 Hz and 100ms duration).
- Tones triggered by the participant’s heartbeat.
- Tones timed to coincide with systole or to occur delayed.

Pulse-oximetry signal from the left index finger

(Katkin et al., 2001; Schandry,1981)
Interoception and its role in anxiety

Studies report a significant association between interoceptive sensitivity and higher levels of anxiety:

• Non clinical samples: evidence for increased cardiac interoceptive sensitivity in anxiety related phenotypes (trait anxiety, AS..)

• Clinical samples (PD, SAD, ...): it might rather be linked to clinical anxiety per se than to selected anxiety disorders
<table>
<thead>
<tr>
<th>Anxiety phenotype</th>
<th>Author</th>
<th>Sample</th>
<th>Method</th>
<th>Interoceptive sensitivity (ES = d)</th>
<th>Self-report anxiety (ES = d)</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety sensitivity</td>
<td>Sturges and Goetsch (1996)</td>
<td>29 high and 30 low AS undergraduate female students</td>
<td>Perception of heartbeats (Schandry Task) after stressful mental arithmetic and caffeine challenge</td>
<td>Arithmetic: High AS &gt; Low AS (0.44)</td>
<td>High AS &gt; Low AS</td>
<td>Mental Arithmetic: High AS &gt; Low AS (statistical trend: p &lt; 0.06)</td>
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<td></td>
<td>Sturges et al. (1998)</td>
<td>12 high and 12 low AS undergraduate female students</td>
<td>Perception of heartbeats (Schandry Task) during and after a hyperventilation challenge</td>
<td>Caffein: High AS = Low AS (0.05)</td>
<td>High AS &gt; Low AS</td>
<td>High AS = Low AS</td>
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<td>Richards and Bertram (2000)</td>
<td>18 high and 18 low AS participants</td>
<td>Detection of changes in pulse transition time (PTT) during ten different tasks</td>
<td>Perception of PTT: High AS &gt; Low AS (1.79)</td>
<td>–</td>
<td>Overall sympathetic activity: High AS = Low AS</td>
</tr>
<tr>
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<td>Stewart et al. (2001)</td>
<td>15 high and 15 low AS undergraduate female students</td>
<td>Perception of heartbeats (Schandry Task) during a stressful mental arithmetic/spelling task</td>
<td>High AS &gt; Low AS (1.65)</td>
<td>–</td>
<td>Baseline: High AS = Low AS</td>
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<td>Eley et al. (2004)</td>
<td>34 male and 45 female school children, qualified as good (7) or poor (72) heartbeat perceivers</td>
<td>Perception of heartbeats (Schandry Task) during three differing intervals</td>
<td>AS-scores higher for good compared to poor heartbeat perceivers (0.47)</td>
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<tr>
<td>State anxiety</td>
<td>Schandry (1981)</td>
<td>Sample of 39 HC, qualified as good (17) and poor (17) heartbeat perceivers</td>
<td>Perception of heartbeats (Schandry Task) during given time interval</td>
<td>–</td>
<td>STAI-state: Good perceivers &gt; bad perceivers (0.96)</td>
<td>Good perceivers = bad perceivers</td>
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<td>Ludwig-Rosenthal and Neufeld (1985)</td>
<td>61 undergraduate students, qualified as good and poor heartbeat perceivers</td>
<td>Perception of heartbeats (interoceptive and exteroceptive tracking task)</td>
<td>–</td>
<td>STAI-state: Good perceivers &gt; bad perceivers (0.57)</td>
<td>Good perceivers &gt; bad perceivers</td>
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<td>Naring and van der Staak (1995)</td>
<td>13 HC low and 11 participants high in state anxiety (SA)</td>
<td>Heart rate perception as indicated by two items of a self-report inventory during various tasks</td>
<td>High SA &gt; Low SA (0.79)</td>
<td>–</td>
<td>High SA = Low SA</td>
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<td>Trait anxiety</td>
<td>Stepstoe and Voge (1992)</td>
<td>30 female participants</td>
<td>Perception of heartbeats (self-report) during three stressful tasks</td>
<td>High TA = Low TA (0.18)</td>
<td>–</td>
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<td>DePascalis et al. (1984)</td>
<td>9 high participants with high and 7 with low anxiety (SA)</td>
<td>McFarland Task combined with biofeedback</td>
<td>Negative correlation between TA and heart rate perception (1.09)</td>
<td>–</td>
<td>High TA = Low TA</td>
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<td></td>
<td>Richards and Bertram (2000)</td>
<td>18 high and 18 low state and trait anxiety participants</td>
<td>Detection of changes in pulse transition time (PTT)</td>
<td>Perception of PTT: High TA &gt; Low TA High SA (0.28; 0.12)</td>
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<td>Pollatos, Gramann, et al. (2007)</td>
<td>18 male participants, characterized as high (9) versus low (9) responders to the stress task</td>
<td>Perception of heartbeats (Schandry Task) and isometric handgrip exercise</td>
<td>Correlation between trait anxiety and interoceptive awareness (1.01)</td>
<td>–</td>
<td>STAI-trait: High responder &gt; low responder</td>
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<td>Pollatos, Herbert, et al. (2007)</td>
<td>102 students</td>
<td>Perception of heartbeats (Schandry Task) and rating of 60 affective pictures</td>
<td>Correlation between trait anxiety and interoceptive awareness (0.58)</td>
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<td>Karsdorp et al. (2009)</td>
<td>44 HC and 36 participants with congenital heart disease (CHD) characterized concerning high, medium or low trait anxiety</td>
<td>Physiological and subjective responses to false heart rate feedback in two exercise tasks</td>
<td>Low and Medium TA: HC = CHD (0.5; 0.36)</td>
<td>–</td>
<td>HC = CHD</td>
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<td>High TA: HC &lt; CHD (1.27)</td>
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</table>

Note: AS = Anxiety Sensitivity; CHD = Congenital Heart Disease; HC = Healthy Controls; PTT = Pulse Transition Time; SA = State Anxiety; TA = Trait Anxiety; STAI = State Trait Anxiety Inventory; Cohen’s d were calculated from a) means and standard deviations or odds ratios based on the comparison between participants with high compared to low anxiety scores or b) transformed from r based on the association between anxiety and heartbeat perception.
Mind-body interaction models of emotion creation and anxiety

Pre-existing psychological traits

Biological and psychological vulnerabilities & Environmental stimuli and influences

Pre-existing physiological traits

Stress and challenges

Cognitions: conceptual knowledge

Top-down

Knowledge, expectations or beliefs

Mismatch

Sensory and somatic physiological signals

Bottom-up

Actual body state

Behavioural, cognitive and emotional response

Anxiety, somatic symptoms and Anxiety disorders

Mind-Body Interactions in Anxiety and Somatic Symptoms

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Somatic vulnerability phenotypes to anxiety?

• Some medical conditions are highly related to the expression of anxiety and autonomic abnormalities:
  – Postural Tachycardia syndrome (PoTS)
  – Joint Hypermobility Syndrome (JHS)

- 50% of PoTs patients express JHS.

- 70% of JHS patients manifest autonomic symptoms and/or PoTS.
Joint Hypermobility Syndrome

- Inherit collagen condition characterized by an increased joint mobility in passive and active movements.
- Strong genetic component with autosomal dominant pattern. Women/men ratio (3:1).
- Estimated prevalence of JH in general population: 10-15%; in anxiety disorder: 70%

Connective tissue protein component of multiple body constituents (bone, cartilage, tendon, blood vessels...).

Can cause a wide range of symptoms & it is considered a systemic multisystem affection.

(Ross & Grahame, 2011; Bravo & Wolff, 2006; Beighton & Grahame, 2012)
Joint Hypermobility Syndrome: clinical features

Articular and extra-articular features

✓ widespread musculoskeletal pain
✓ multiple soft tissue lesions and fragility of supportive connective tissue and skin.
✓ increased incidence of mitral valve prolapse and high elasticity of the aortic wall
✓ hypotension
✓ asthma
✓ gastro intestinal problems (reflux, irritable bowel syndrome)
✓ autonomic symptoms
✓ functional illnesses such as fibromyalgia and chronic pain and fatigue
✓ anxiety disorders (particularly panic, agoraphobia and social phobia)

Interoception and Joint Hypermobility Syndrome

Neuroimaging and psychophysiological investigation of the link between anxiety, enhanced affective reactivity and interoception in people with joint hypermobility

Núria Mallorquí-Bague, Sarah N. Garfinkel, Miriam Engels, Jessica A. Eccles, Guillem Pailhez, Antonio Bulbena, and Hugo D. Critchley

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• No further associations were found between the body awareness subscales and state anxiety.

Note: * = p< 0.05
Mediation analysis of interoception in JH and anxiety

Graphic showing the regression coefficients, with the coefficients ($\beta$) for the effect of hypermobility on state anxiety with the latter (when entering interoception into the model) in parentheses.

Note: $^*$ = $p<0.05$; $^{**}$ = $p<0.01$
Postural Tachycardia Syndrome (PoTS)

- Multifaceted disorder of the autonomic nervous system that profoundly impacts physical functioning.
- PoTS is characterized by tachycardia on standing.
- Many patients develop situational anxiety that causes reduced activity level.
- No established guidelines for the psychological treatment of POTS.
Intervention techniques in PoTS and JHS

• Symptomatic treatments

• Psychological approaches:
  - JHS: CBT for pain and anxiety management suggested for treatment (there is a need of studies).
  - PoTs: CBT elements (in-vivo exposure and symptom discrimination) and Mindfulness.
Mind-body interaction models of emotion creation and anxiety

Conclusions and Clinical implications

- Psychophysiological mechanisms contribute to anxiety disorders.
- Affective traits (AS, trait anxiety) and constitutional physiological traits are important dimensions that are implicated in the development and maintenance of anxiety and somatic symptoms.
- Treatment models framed on mind-body interaction models are needed.
- Could interoception be an adaptive trait? (MF, Biofeedback)
THANK YOU FOR YOUR ATTENTION

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