Neuroscience of psychosomatic medicine: cardiovascular risk

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Psychosomatic medicine research

• Delineate biological mechanisms whereby psychological, behavioural and social factors influence health outcomes

• Use this information to optimise healthcare

• Apply current methods in human neuroscience to understand mind-body links to disease pathogenesis
Figure 1. Schematic illustration conveying the notion that aspects of socioeconomic position (SEP) over the lifecourse can come to affect health and disease states via neurobiological pathways. Affective, cognitive, behavioral, and physiological factors linking different dimensions of SEP to health and disease states can be viewed as bidirectionally related to multiple brain networks, amenable to study by neuroimaging approaches. The links between dimensions of SEP and the function and structure of different brain networks can be further conceptualized as subject to effect modification and mediation by environmental, social, and individual-level factors that can influence downstream pathways to health and disease.
Stress

Wikipedia:

• Physiological stress - stressor upsetting the homeostasis
• Psychological stress is a feeling of strain and pressure
• Stress is a response to a stressor
  – body's method of reacting to a challenge
  – sympathetic nervous system activation
  – negative condition or a positive condition with impact on mental & physical well-being.
• ‘Allostatic overload’
Allostasis

Maintaining stability through change
Active adjustment to both predictable and unpredictable events...

Allostatic load - the cumulative cost to the body of allostasis
Allostatic overload - a state in which pathophysiology occurs
Levels of analysis: ABCD

A = Mind
B = Behaviour
C = Information transfer system
    - autonomic, neuroendocrine, immune
D = End organ e.g. heart
Cardiovascular disease

• Leading cause of mortality
• Primacy to cardiovascular health
• Compromised by psychological or physical challenges

• Strategies to understand:
  experimental description of brain centres engaged by challenges
  and predicting CV response
Examples

• Exercise and mental effort
• Blood pressure reactivity
• Social evaluative threat
• Inflammation

ABC
Correlates of cardiovascular arousal

- Effortful isometric exercise
- Effortful mental arithmetic
- Effortless isometric exercise
- Effortless mental arithmetic

Sensory-motor areas + autonomic areas = inner-speech/cognitive areas + autonomic areas

- Blood pressure (mmHg)
- Heart rate (beats/min)

Mental arithmetic:

- Blood pressure
- Heart rate
Effortful isometric exercise & Effortful mental arithmetic

Effortless isometric exercise & Effortless mental arithmetic

= sensory-motor areas + autonomic areas

= inner-speech/cognitive areas + autonomic areas
Activity covarying with BP mean age 35 yrs

Critchley et al., J Neurosci 2000
523, 259-70
A  
1-back task  
2-back task  

Isometric exercise tasks  

B  
RR interval (secs)  
Grip pressure (kPa)  

Motor responses during experiment
Activity attributable to increased low-frequency (sympathetic) power influencing HRV
Cognitive appraisal
dorsolateral & lateral prefrontal

Sensory-motor
somatomotor parietal

Motivation
ventromedial prefrontal
orbitofrontal
medial temporal hypothalamus

sympathetic
parasympathetic

Critchley 2004 PNAS
Cardiac risk

• Enhanced cardiovascular response

• Psychosocial conditions
  – Grief, depression, bereavement, personality

• Socio-economic factors
  – Social standing
    (Marmot: e.g. Whitehall studies, Black reports)
  – infection, nutrition
(A) Stroop Task

Example Incongruent Condition Trials

- Red
- Green
- Blue
- Yellow

Variable SOA (1-5 sec)

Example Congruent Condition Trials

- Blue
- Green
- Yellow
- Red

Fixed SOA (mean incongruent)

(B) MSIT

Example Incongruent Condition Trials

- 2 3 2
- 3 3 1
- 1 1 2

Variable SOA (1-5 sec)

Example Congruent Condition Trials

- 3 3 3
- 2 2 3
- 1 2 1

Fixed SOA (mean incongruent)

Sheu et al., 12

Gianaros et al., 2009
Depression, bereavement, grief

- Physiological marker: vagal withdrawal
- Rumination, anhedonia
- Neural substrates: Subgenual cingulate cortex
- Hyperactivity: reduced volume

- Complicated grief
Perceived social standing

A

Where do you stand?
“Best Off” >

“Worst Off” >

B

Perigenual ACC

C

pACC Volume vs. Ladder Ranking

Gianaros et al., 2007 SCAN
INFLAMMATION

• Sickness behaviours
  – Fatigue confusion
  – Depression, social withdrawal
  – Sensory sensitivity

• Cardiovascular and cerebrovascular risk
  – Sticky vessels
  – Autonomic changes HRV
Viewing emotional facial expressions

Mood response to vaccination

Correlations with inflammation associated mood change

<table>
<thead>
<tr>
<th>Side</th>
<th>Region</th>
<th>MNI</th>
<th>Z score</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>R + L</td>
<td>sgACC</td>
<td>-2 22 -8</td>
<td>3.29</td>
<td>0.55</td>
</tr>
<tr>
<td>L</td>
<td>Amygdala</td>
<td>-14 -8 28</td>
<td>3.39</td>
<td>0.57</td>
</tr>
</tbody>
</table>

- Mayberg et al. 2005
- Harrison et al., 2009

Harrison et al., 2009
Central autonomic network mediates cardiovascular responses to acute inflammation: Relevance to increased cardiovascular risk in depression?

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a Institute of Medical and Veterinary Biosciences, University of Edinburgh, Edinburgh, UK
b Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
c Institute of Health & Wellbeing, University of the West of Scotland, Paisley, UK
Graph A: Mean IL-6 levels comparing Placebo and Inflammation groups.

Graph B: Mean diastolic blood pressure comparing Placebo and Inflammation groups.

Graph C: Mean LF/HF ratio comparing Placebo and Inflammation groups.

Diagram:
- Heart rate variability
  - LF/HF Ratio
    - Path a: Inflammation to Heart rate variability
      - 0.35 (0.12) p = 0.01
    - Path b: Inflammation to Blood Pressure
      - 6.39 (2.53) p = 0.022
- Inflammation
- Diastolic Blood Pressure
  - Path c: Inflammation to Diastolic Blood Pressure
    - 3.70 (1.53) p = 0.026
A. Path a: Inflammation response

B. Path b: dBP correlates

Path a

Brain regions

Path b

Inflammation

Path c

Diastolic Blood Pressure

Legend

- 0.001
- 0.005
- 0.010
- 0.001
- 0.005
- 0.010
PSYCHOPHYSIOLOGICAL TRIGGERS
Evidence that really matters

The NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Cardiovascular Events during World Cup Soccer

Ute Wilbert-Lampen, M.D., David Leistner, M.D., Sonja Greven, M.S., Tilmann Pohl, M.D., Sebastian Sper, Christoph Völker, Denise Güthlin, Andrea Plasse, Andreas Knez, M.D., Helmut Küchenhoff, Ph.D., and Gerhard Steinbeck, M.D.

ABSTRACT

BACKGROUND
The Fédération Internationale de Football Association (FIFA) World Cup, held in Germany from June 9 to July 9, 2006, provided an opportunity to examine the relation between emotional stress and the incidence of cardiovascular events.
The FIFA World Cup 2006 in Germany started on June 9, 2006. The 2006 World Cup matches with German participation are indicated by numbers 1 through 7: match 1, Germany versus Costa Rica; match 2, Germany versus Poland; match 3, Germany versus Ecuador; match 4, Germany versus Sweden; match 5, Germany versus Argentina; match 6, Germany versus Italy; and match 7, Germany versus Portugal (for third-place standing). Match 8 was the final match, Italy versus France.
Hypothesized links between acute emotional triggers and cardiac events mediated through physiological responses and pathophysiological effects.

From Bhattacharyya and Steptoe (2007): Emotional Triggers of Acute Coronary Syndromes

Progress in Cardiovascular Diseases, 49:353-364
All strokes 90%:
- hypertension (OR 2.64)
- smoking (2.09)
- waist-to-hip ratio (1.65)
- diet (1.35)
- physical activity (0.69)
- diabetes (1.36)
- alcohol (1.51)
- psychosocial stress (1.30)
- depression (1.35)
- cardiac causes (2.38)
- ratio of apolipoproteins B to A1 (1.89)

Unadjusted ORs for patients exposed to potential triggers during the 2 hours before the stroke compared to the same 2 hours the preceding day

<table>
<thead>
<tr>
<th>Triggering factor</th>
<th>The day of the stroke only</th>
<th>The day before only</th>
<th>Both periods</th>
<th>No exposure</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one of seven potential triggers*</td>
<td>76</td>
<td>9</td>
<td>13</td>
<td>102</td>
<td>8.4 (4.5–18.1)</td>
</tr>
<tr>
<td>At least one of three potential triggers†</td>
<td>57</td>
<td>4</td>
<td>2</td>
<td>137</td>
<td>14.3 (5.3–54.2)</td>
</tr>
<tr>
<td>Negative emotions</td>
<td>29</td>
<td>2</td>
<td>2</td>
<td>167</td>
<td>14 (4.4–89.7)</td>
</tr>
<tr>
<td>Anger</td>
<td>14</td>
<td>1</td>
<td>1</td>
<td>184</td>
<td>14 (2.8–253.6)</td>
</tr>
<tr>
<td>Sudden posture change in response to a startling event</td>
<td>24</td>
<td>1</td>
<td>1</td>
<td>174</td>
<td>24 (5.1–428.9)</td>
</tr>
<tr>
<td>Sudden temperature change</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>194</td>
<td>5 (0.8–95.8)</td>
</tr>
<tr>
<td>Positive emotions</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>188</td>
<td>4 (1.0–26.5)</td>
</tr>
<tr>
<td>Heavy eating</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>189</td>
<td>4 (1.0–26.5)</td>
</tr>
<tr>
<td>Heavy physical exertion</td>
<td>15</td>
<td>7</td>
<td>0</td>
<td>178</td>
<td>2.1 (0.9–5.6)</td>
</tr>
</tbody>
</table>

* Sudden posture change in response to a startling event, negative emotions, anger, sudden temperature change, positive emotions, heavy eating, heavy physical exertion.
† Sudden posture change in response to a startling event, negative emotions, anger.

• Emotional arousal esp negative emotion
• Autonomic reactivity
• Inflammatory context
• Abnormal cardiovascular context
• Psychological vulnerability
• Psychosocial socioeconomical vulnerability
LATERALITY / ASYMMETRY HYPOTHESIS

Sudden autonomic discharges to heart can trigger arrhythmia:

- Emotional challenge
- Epilepsy
- Stroke
- ACH

At cortex, autonomic drive appears lateralized

Emotional processing largely lateralized

Heart rate variability / vagal tone reduced in chronic stress and depression
Simple model of arrhythmogenesis

Left-right autonomic innervation of ventricles

Sympathetic activity acts on repolarization

Repolarization & electrical recovery: QTi, T wave morphology

Arrhythmia from inhomogeneity of repolarization


TCRT - Local homogeneity

Critchley et al., 2004 Brain
Laterality index of midbrain activity

(T-L)/(T+L) adjusted data

TWR - Local inhomogeneity

Right lateral midbrain correlating with TWR
Laterality predicts proarrhythmic changes

A  TCRT

Change in TCRT homogeneity
(x10^-3)

Effortless Effortful Effortless Effortful

Subjects
3, 6, 7, 9, 10
1, 2, 4, 5, 8
NO LATERALIZATION LATERALIZED

B  TWR

Change in TWR inhomogeneity
(x10^-5)

Effortless Effortful Effortless Effortful

Subjects
3, 6, 7, 9, 10
1, 2, 4, 5, 8
NO LATERALIZATION LATERALIZED
Role of neuroscience in psychosomatic medicine

• Understanding interactions between mental and physical health

• Novel target mechanisms

• Central importance to psychiatry
  – Risk factors to depression same as CVD
  – Psychosis 12-25 yrs shorter life expectancy
Relevant concepts

• Allostasis

• Stress

• Psychoneuroimmunology