NIH Blueprint for Neuroscience Research

Sleep Research Society®

Beyond the Symptom: The Biology of Fatigue

September 27 – 28, 2021

‘Psychomotor slowing’

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Disclaimer and Disclosures

Disclaimer
This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of the NIH.

Disclosure
This certifies that I, Hugo Critchley, have no financial relationship that is relevant to the subject matter of this presentation.

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Definitions

Psychomotor slowing
Retardation
Dysexecutive syndrome
Abulia
Avolitional
Amotivation
Detachment
Apathy
Anergia
Flattened / blunted affect
Resource limitation
Diminished self-efficacy
Negative symptoms
Catatonia with akinetic mutism
Obsessional slowness
Preoccupation

Motor activity
Decreased activity (actimetry)
Slowed reaction times
Lower velocity
Reduced amplitude of limb movements
Latency and accuracy of eye-movements

Speech
Decreased speech production
Increased speech pause time
Prosody articulation

Cognition
Reduced psychomotor speed (reaction time on cognitive tasks)
Fluency impairments (self-generated items)

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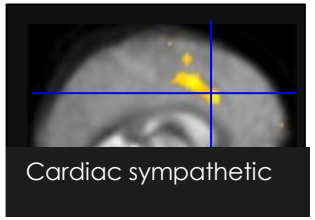
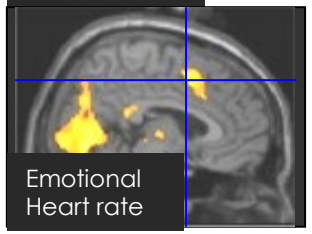
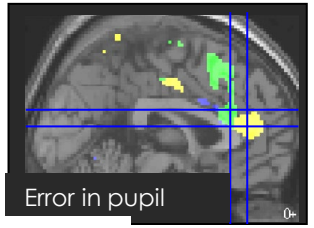
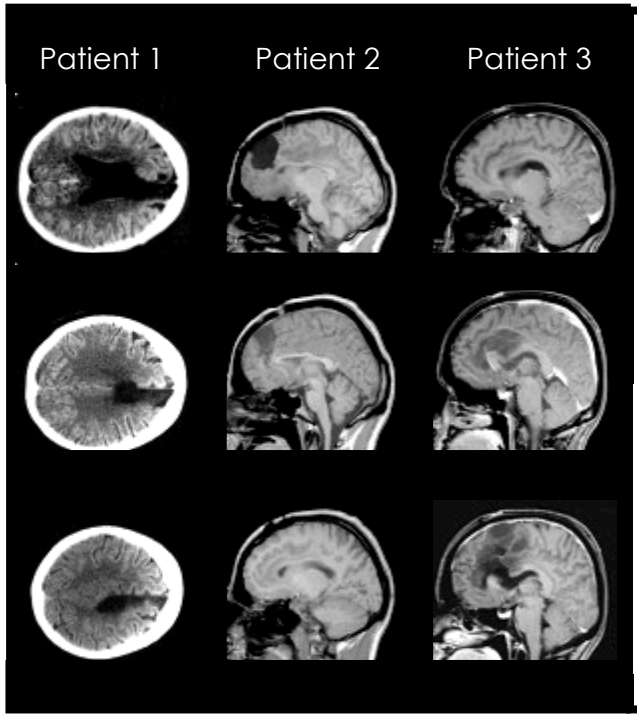
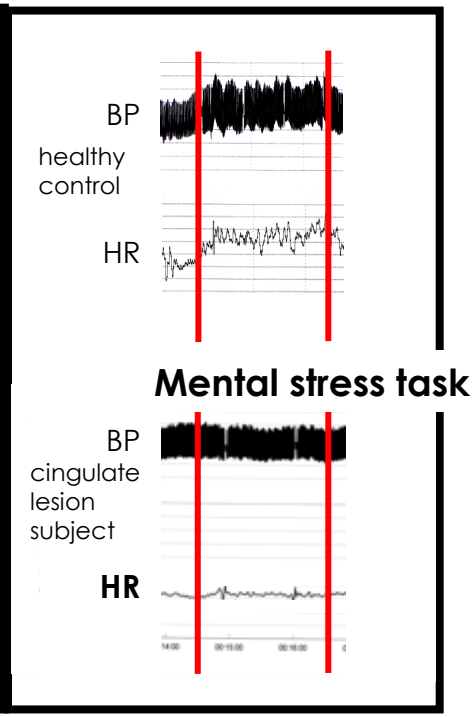
Adaptive autonomic engagement

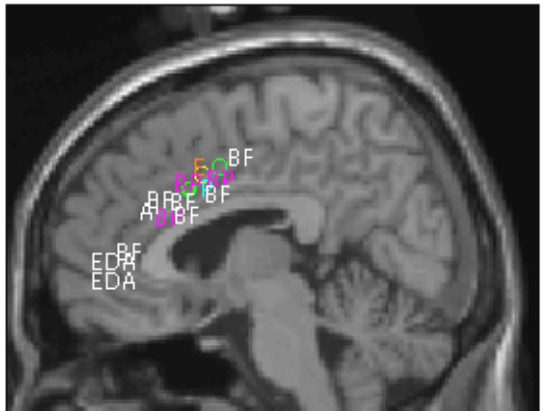


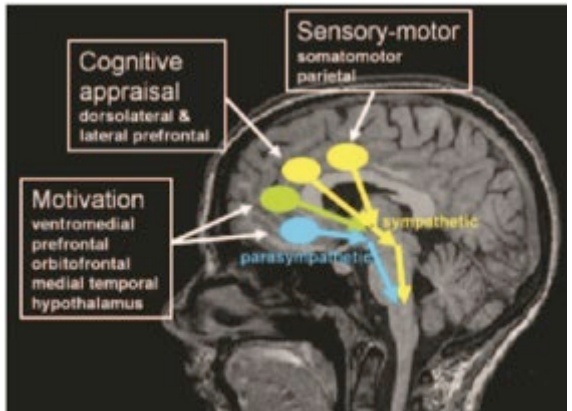


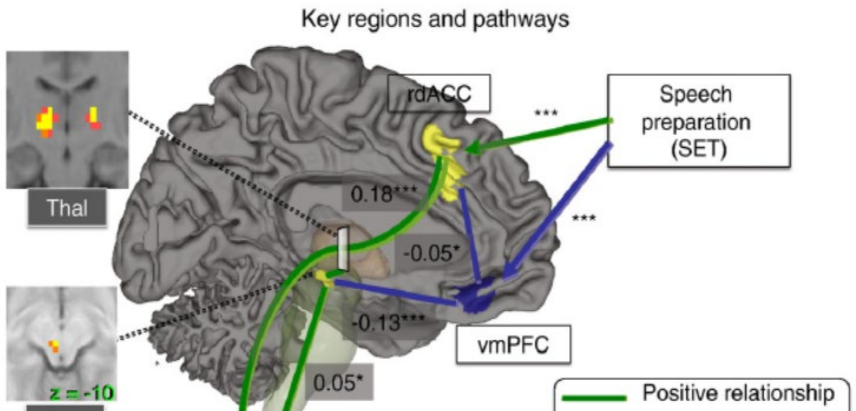






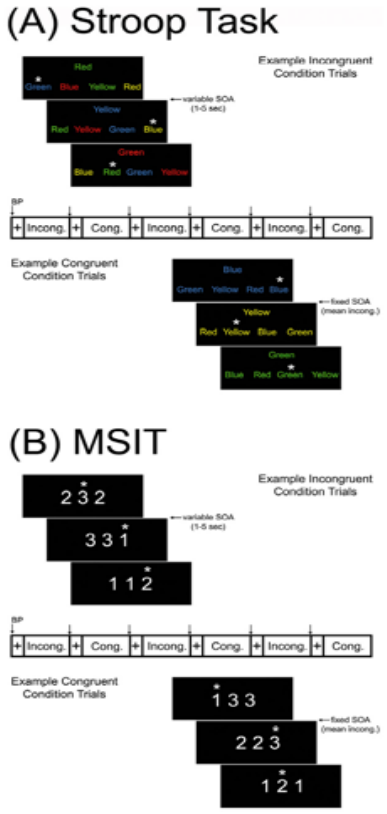


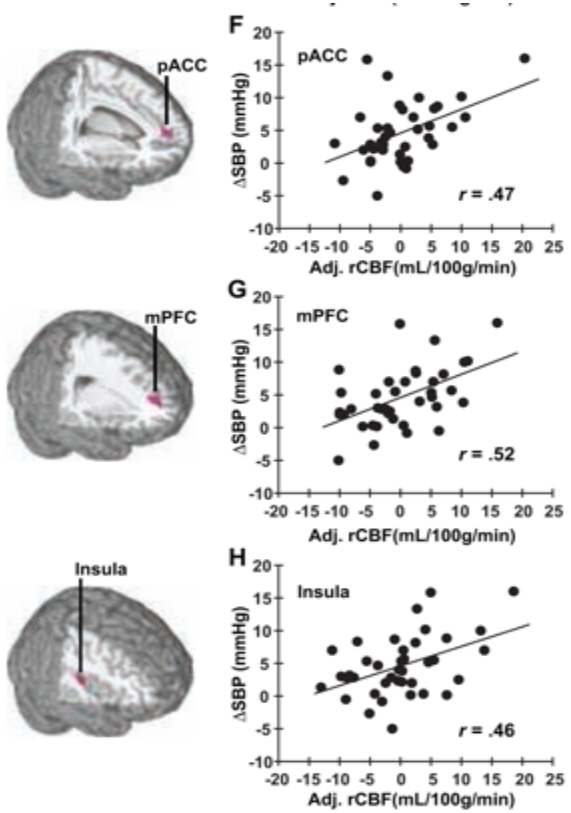


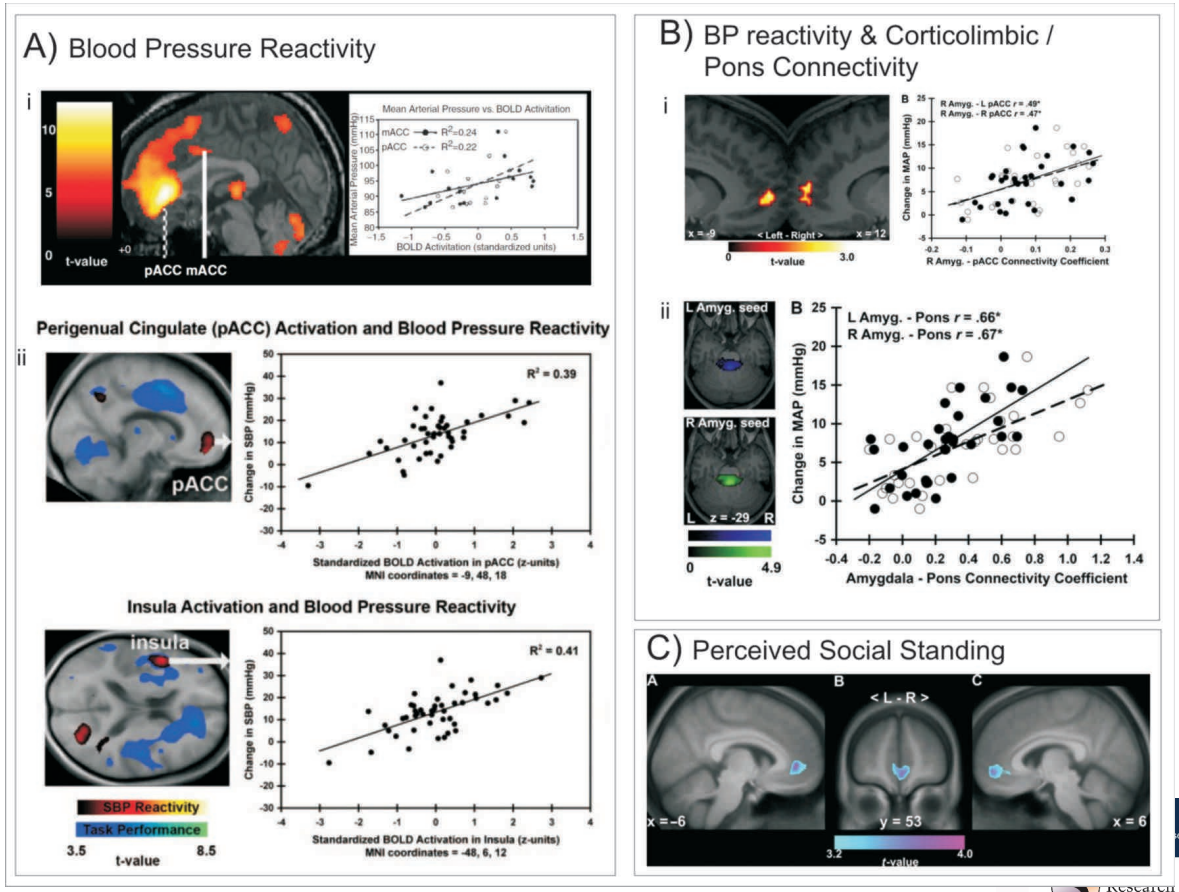


Individual differences

GREEN



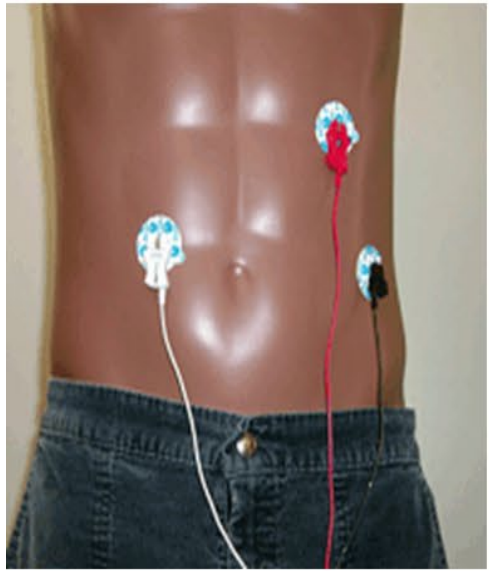




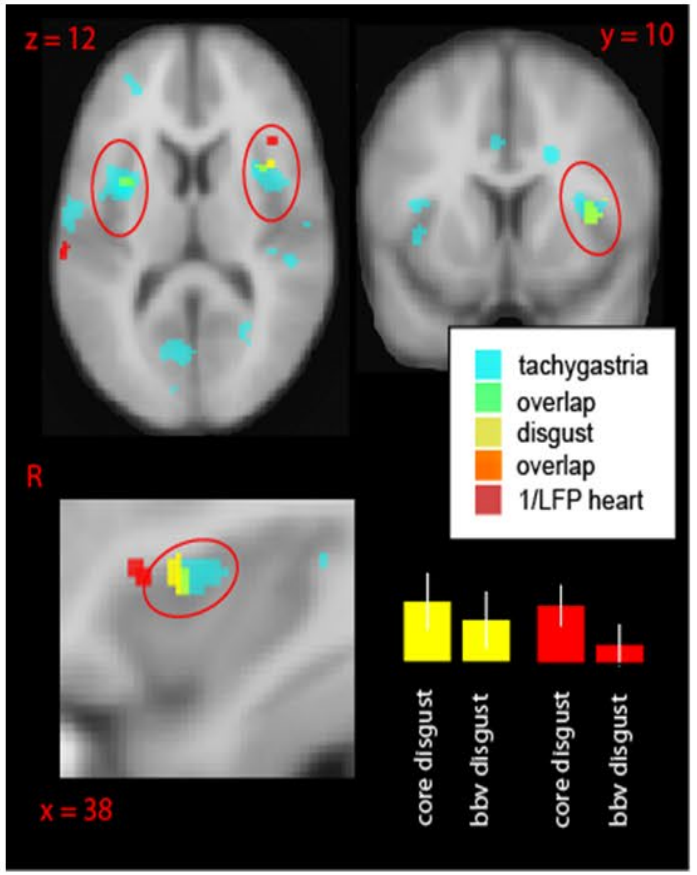
Gianaros et al. 2007, 2008, 2009, 2017

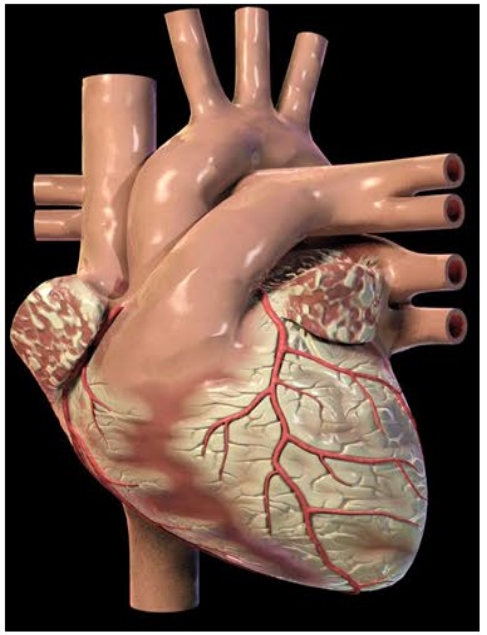
Interoceptive access via insula

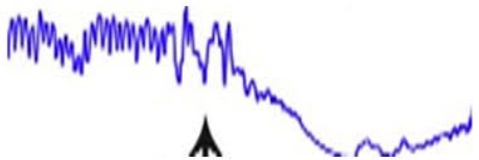
insular cortical regions: viscerosensory cortex, conscious access,

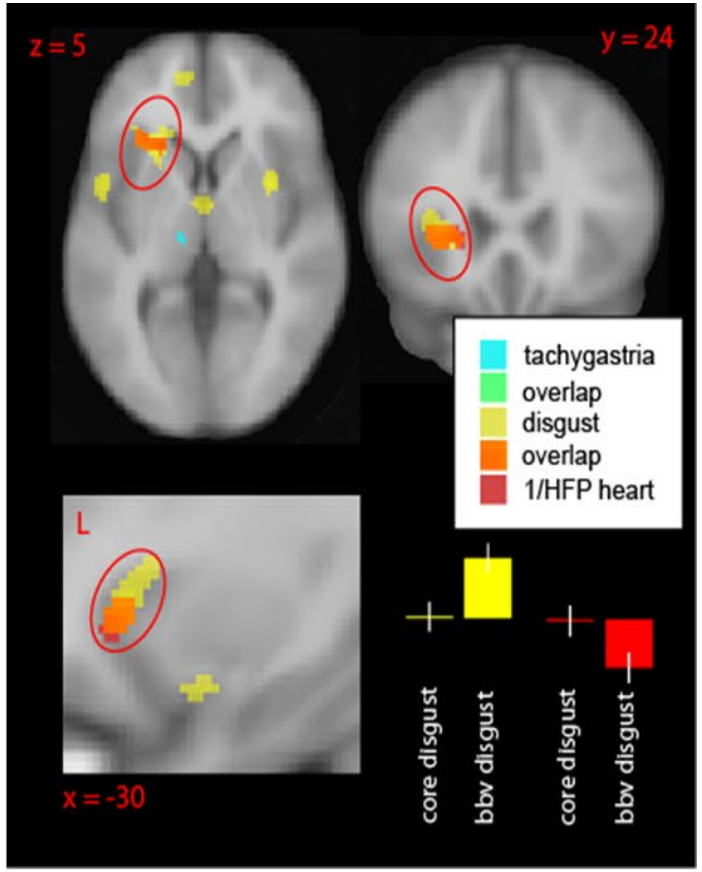


Controls & PAF









Interoceptive predictive coding

THE JOURNAL OF COMPARATIVE NEUROLOGY 493:154–166 (2005)

Neural Mec
Affective, an

Wellcome Department of Imagin
London (UCL) Autonomic Un
University College London Hos
Square, Lo

Influential theoretical model
body in the expression of emotic
states of bodily arousal influence
making. Functional neuroimagin
nisms that generate changes in a
to internal feedback signals to i
cingulate cortex is implicated in g
tal cortices may be specialized in
prefrontal cortex is recognized to
inate in states of rest and diseng
dynamic interactions with the env
of these cortical regions in auton
control, forward (efference copies) and inverse models are proposed to enable prediction and correction of action and, by extension, the interpretation of the behavior of others. It is hypothesized that the neural substrate for these processes during motivational and affective behavior lies within the interactions of anterior cingulate, insula, and orbitofrontal cortices. Generation of visceral autonomic correlates of control reinforce experiential engagement in simulatory models and underpin concepts such as somatic markers to bridge the dualistic divide. J. Comp. Neurol. 493:154–166, 2005.

Opinion

Cell PRESS

A common role of ins
empathy and uncertai

Tania Singer[1,2], Hugo D. Critchley[3] and Kerstin

[1] Laboratory for Social and Neural Systems Research, University of Zuric
[2] Institute for Empirical Research in Economics, University of Zurich, Swi
[3] Clinical Imaging Sciences Centre, Brighton and Sussex Medical School,

Although accumulating evidence highlights a crucial role of the insular cortex in feelings, empathy and processing uncertainty in the context of decision making, neuroscientific models of affective learning and decision making have mostly focused on structures such as the amygdala and the striatum. Here, we propose a unifying model in which insula cortex supports different levels of representation of current and predictive states allowing for error-based learning of both feeling states and uncertainty. This information is then integrated in a general subjective feeling state which is modulated by individual preferences such as risk aversion and contextual appraisal. Such mechanisms could facilitate affective learning and regulation of body homeostasis, and could also guide decision making in complex and uncertain environments.

Behavioral and Brain Sciences

Extending predictive processing to the body: Emotion as interoceptive inference

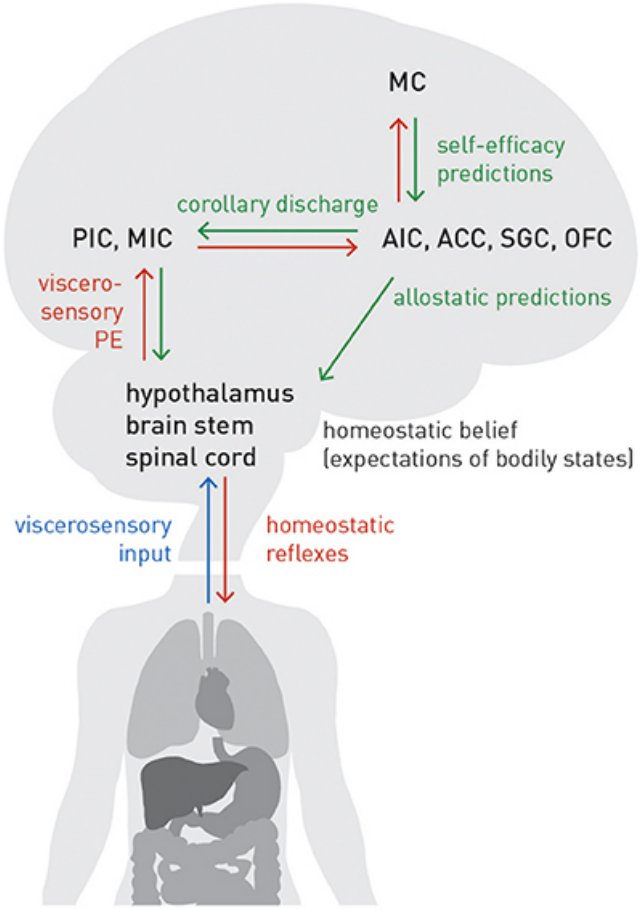
Published online by Cambridge University Press: **10 May 2013**

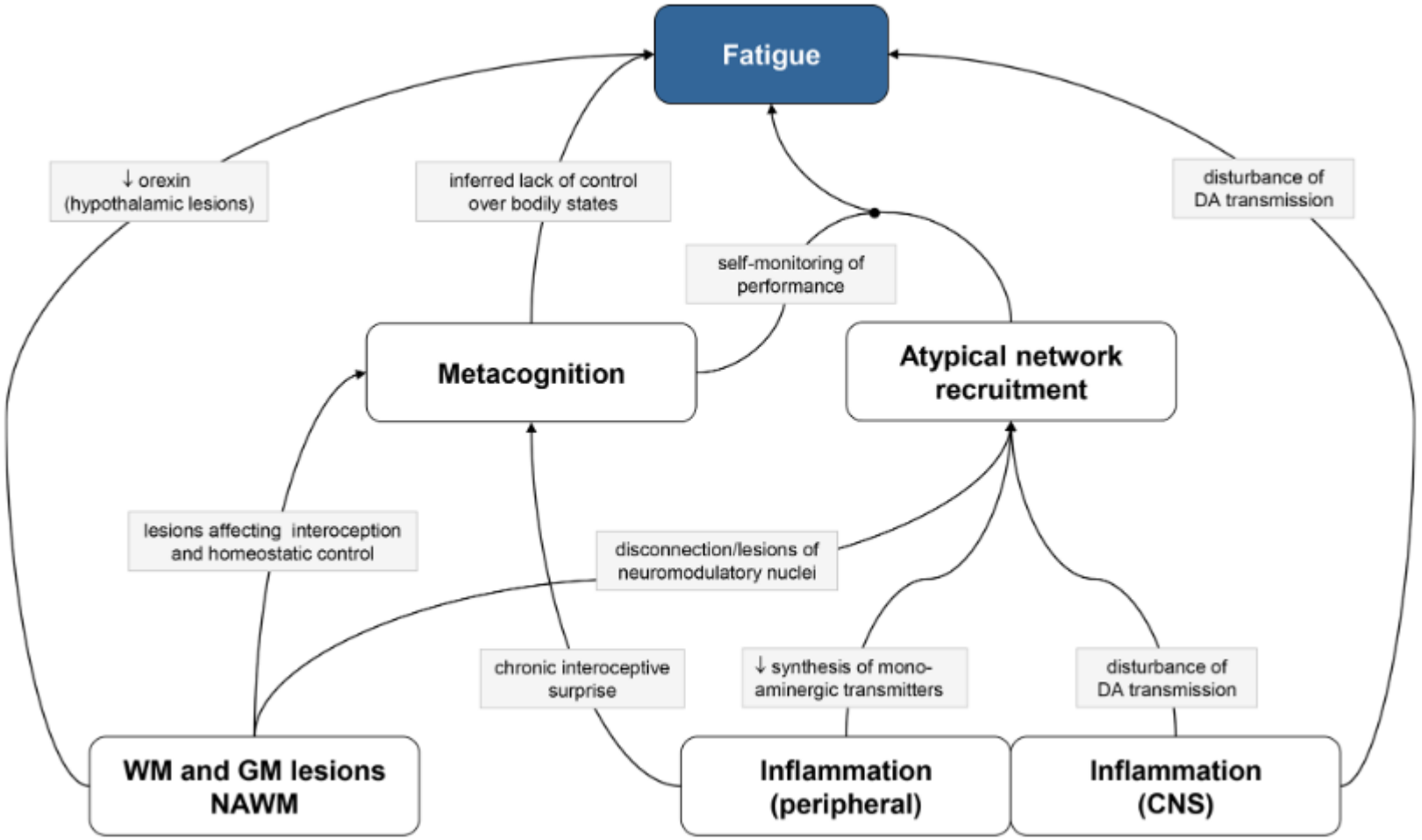
Anil K. Seth and Hugo D. Critchley

Abstract

The Bayesian brain hypothesis provides an attractive unifying framework for perception, cognition, and action. We argue that the framework can also usefully integrate *interoception*, the sense of the internal physiological condition of the body. Our model of "interoceptive predictive coding" entails a new view of emotion as interoceptive inference and may account for a range of psychiatric disorders of selfhood.

Metacogntion: allostatic self-efficacy





Stephan et al. **Allostatic Self-efficacy: A Metacognitive Theory of Dyshomeostasis-Induced Fatigue and Depression** *Front Hum Neurosci 2016*

Z Manjaly et al. **Pathophysiology and cognitive mechanisms of fatigue in MS** *JNNP 2019*

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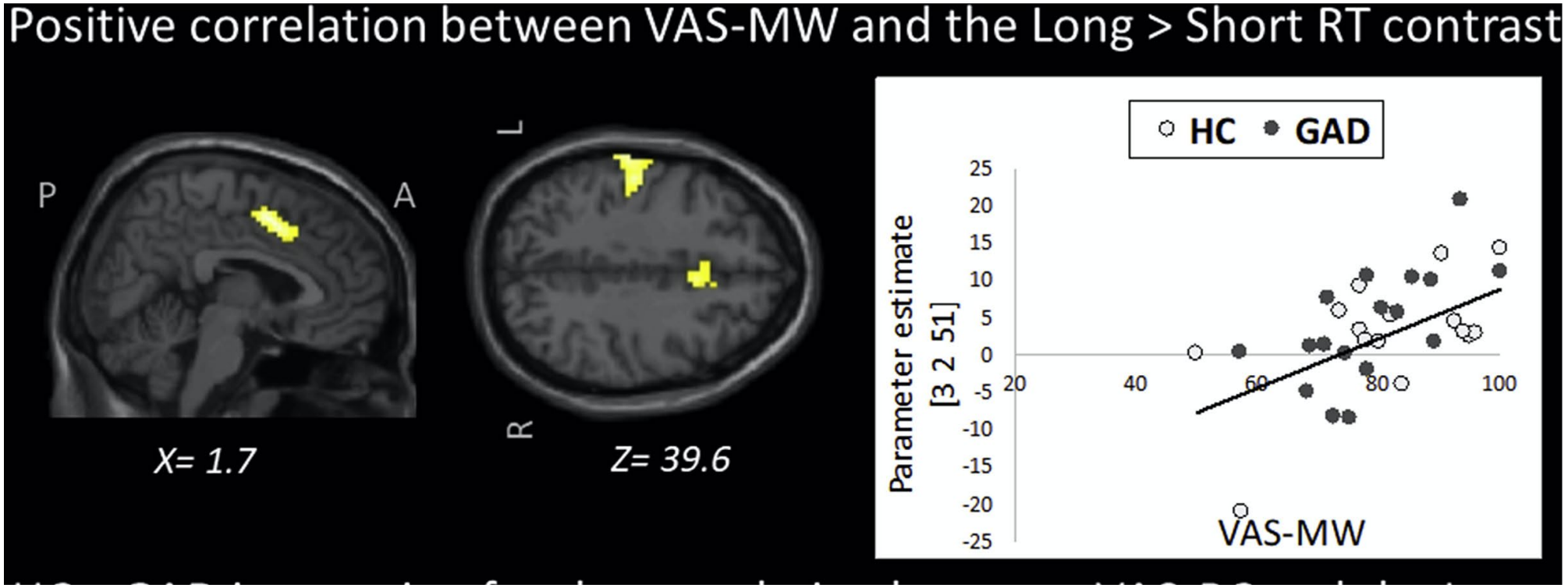
Affective distraction



Pupllometry
HRV anxiety Induction

Network connectivity

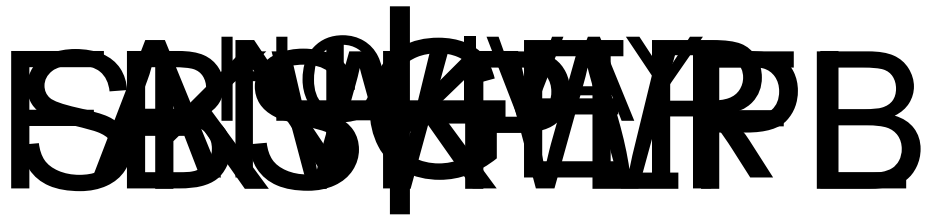
Makovac et al Neuroimage 2019

Affective priming

1 Subliminal word presentation '**ANGER**' or '**RELAX**' (*Hull et al., 2002*)

2 Letter string > word / non-word judgement

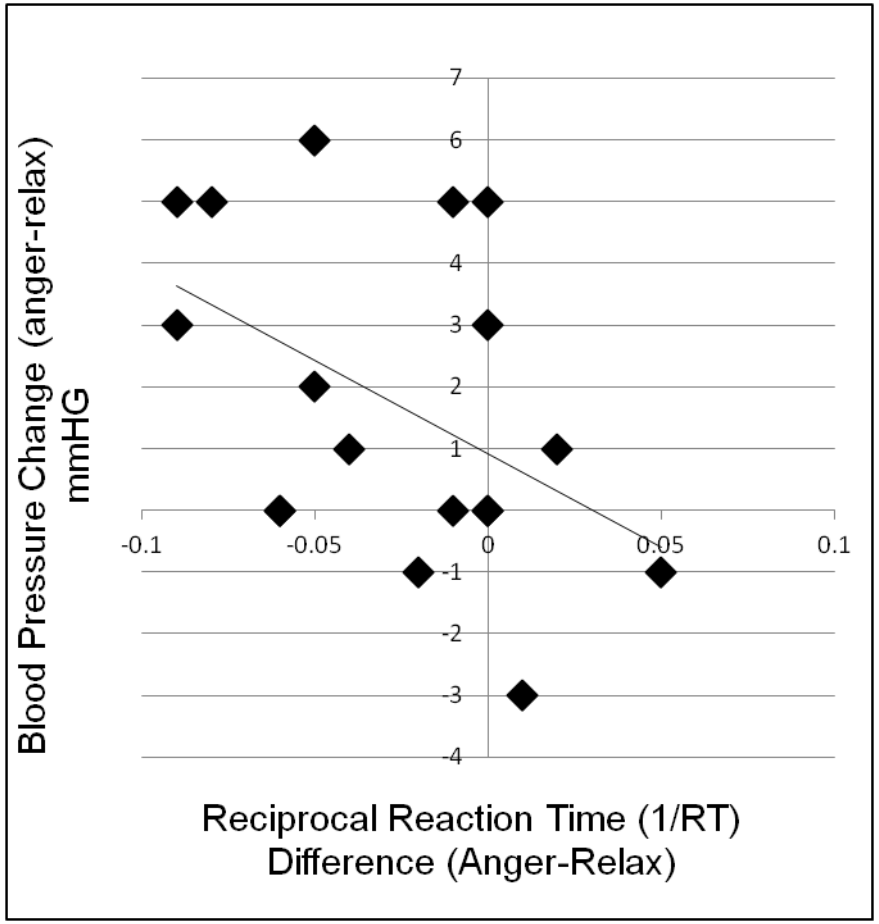
- Reaction times
- Within-participant design

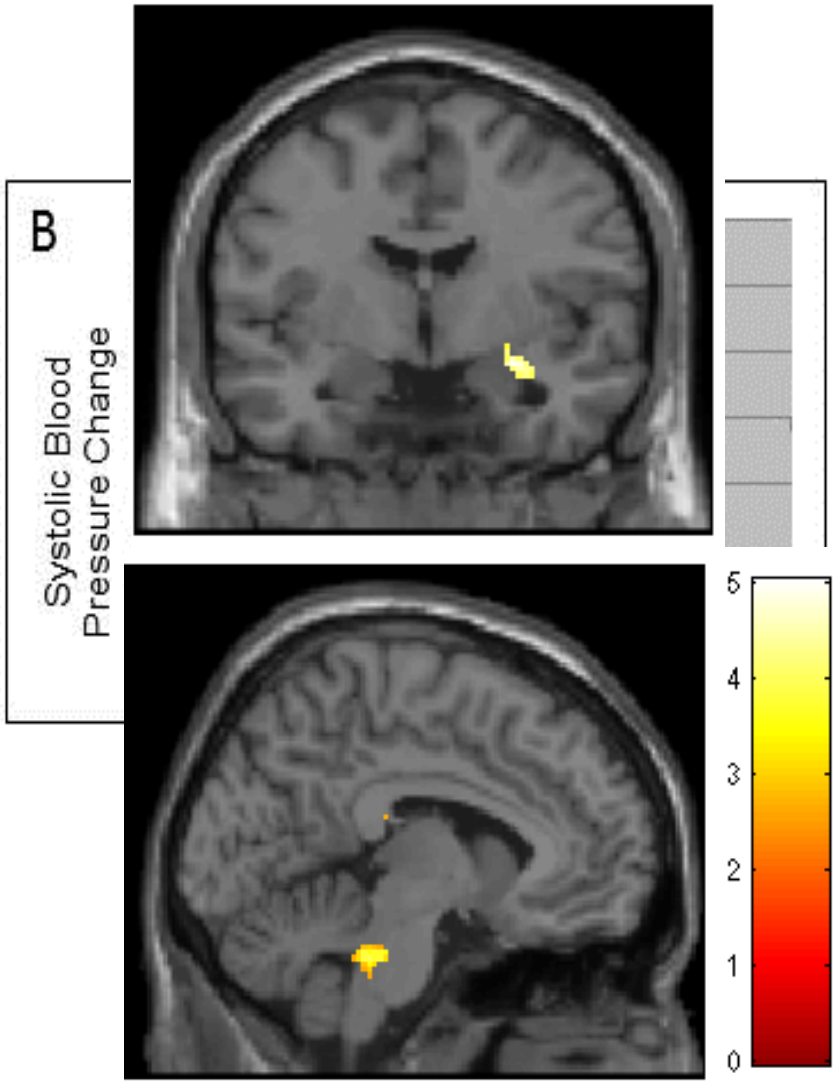


Word / non-word?

Garfinkel et al., SCAN 2015

Affective priming





Garfinkel et al., SCAN 2015

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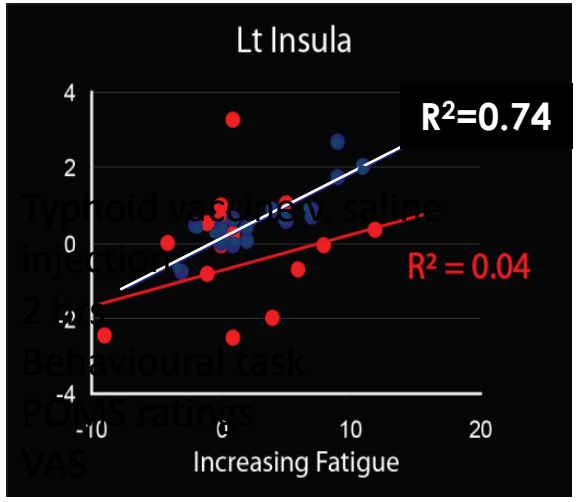
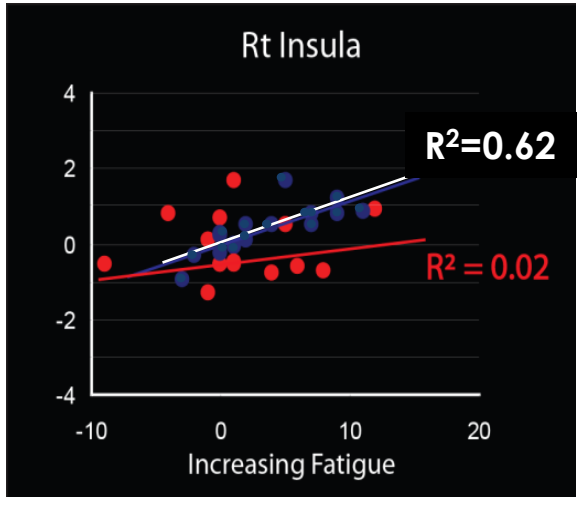
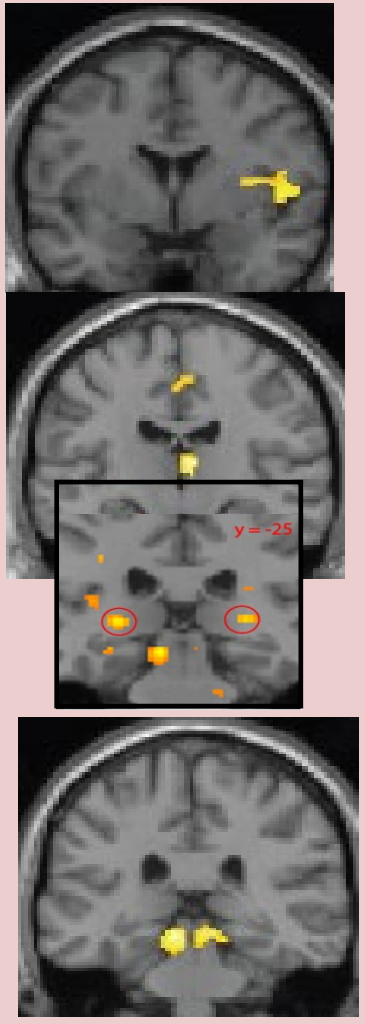
Inflammatory feelings

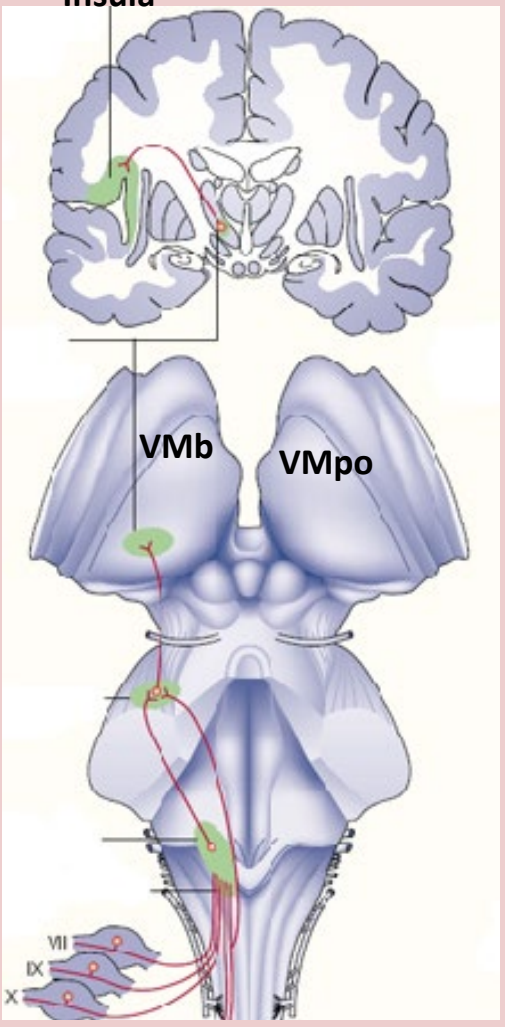


Typhoid vaccine v saline injection
2 hrs
Behavioural task
POMS ratings
VAS

vaccine placebo







Harrison et al. Biol Psych 2009

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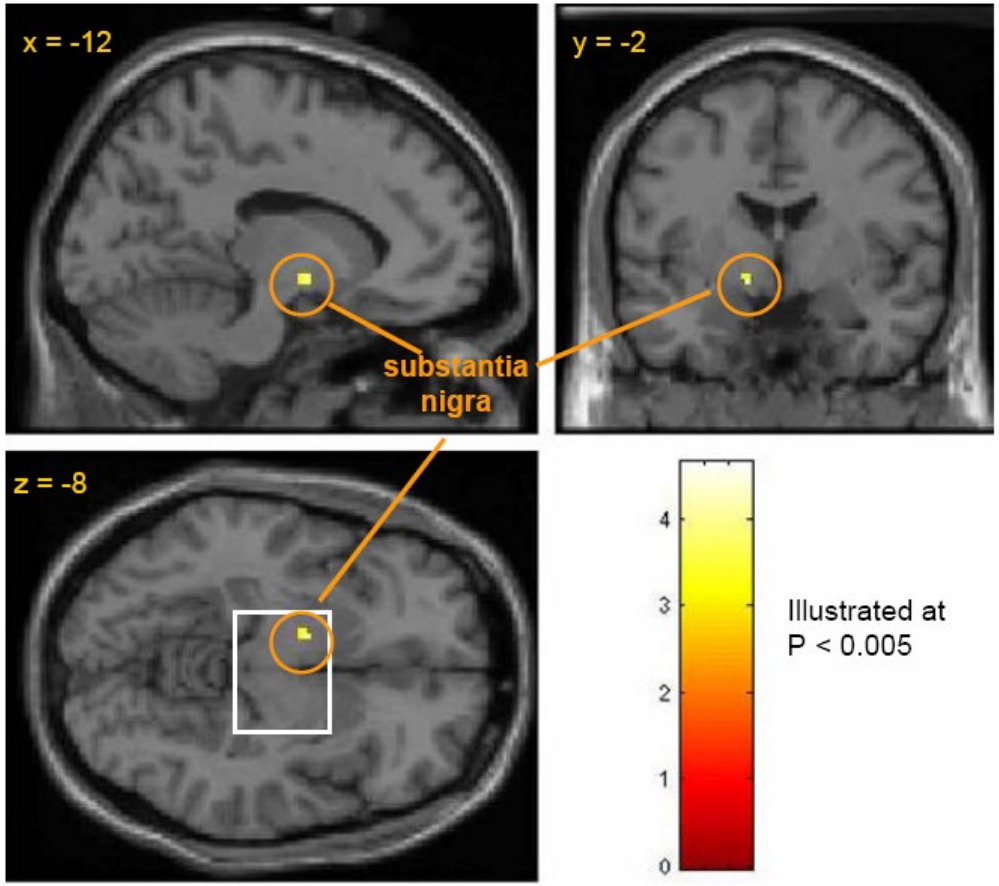
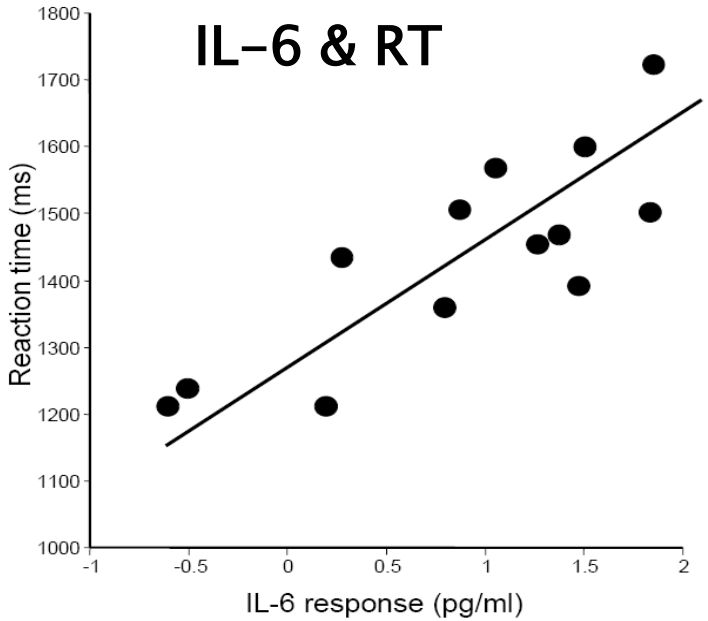
Inflammation and response

Typhoid vaccination
Correlations with response time



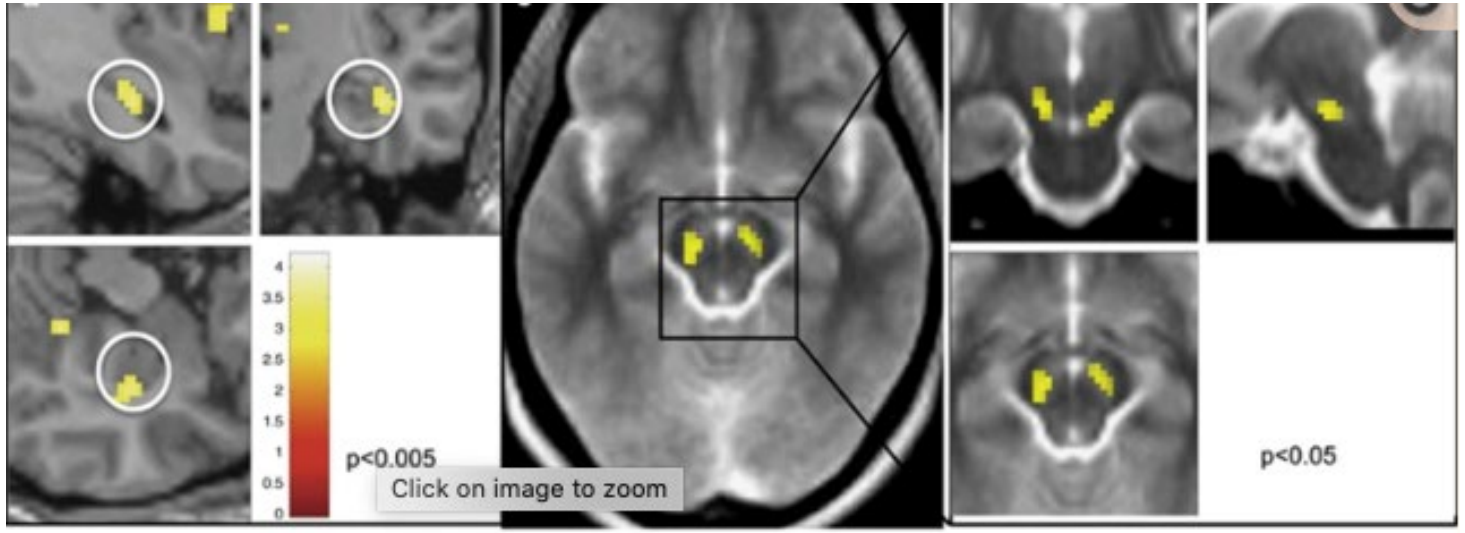


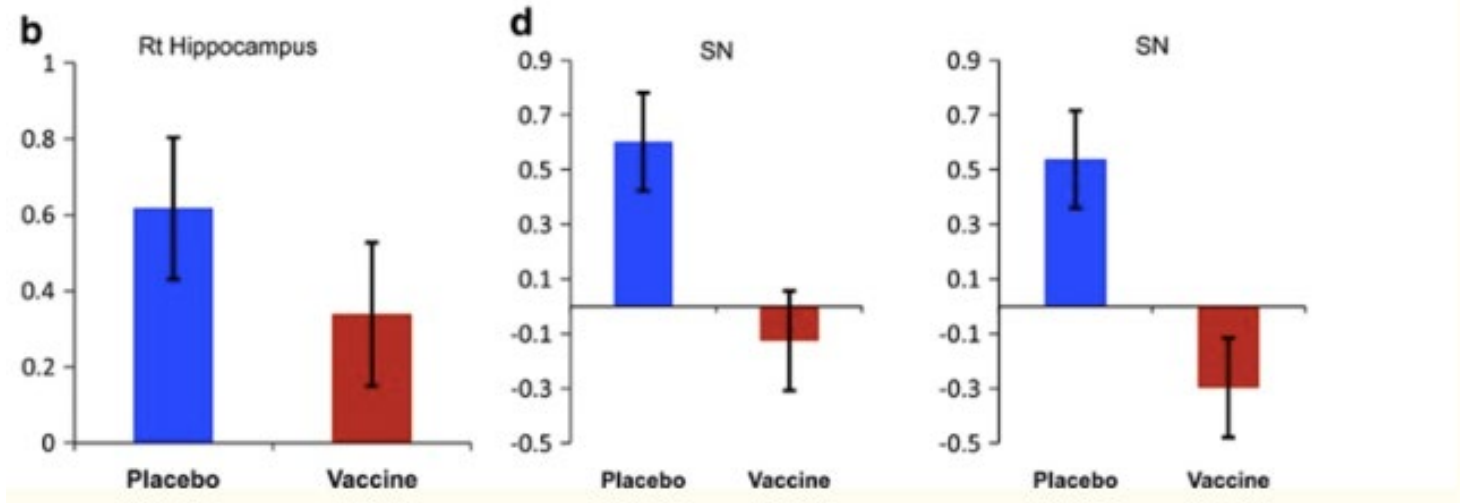
red

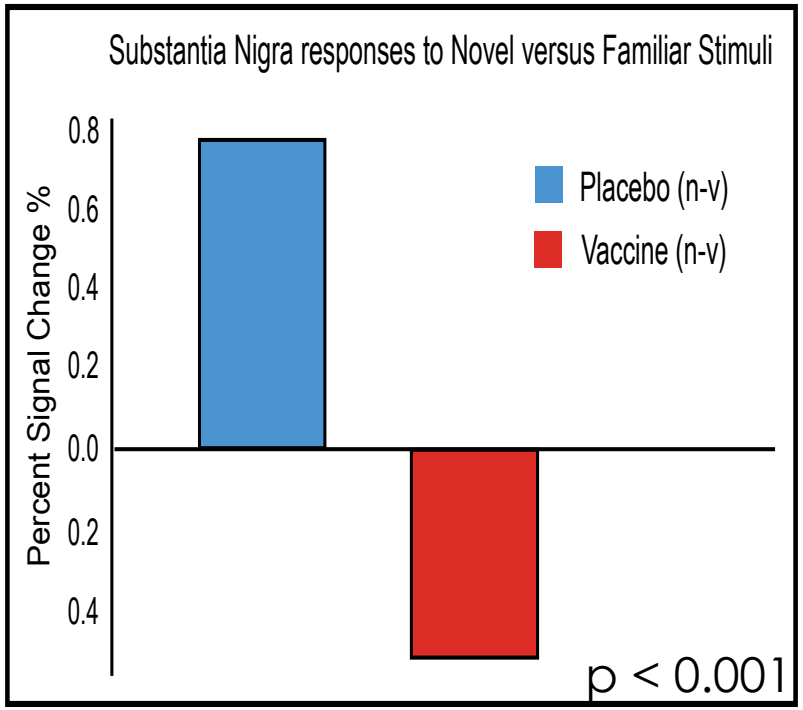
blue yellow red green

Brydon et al. Biological Psychiatry 2008

Inflammation and response







Harrison et al. Neuropsychopharmacology 2015

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Fatigue as value of rest

The temporal dynamics of opportunity costs: A normative account of cognitive fatigue and boredom. **Agrawal M, Mattar MG, Cohen JD, Daw ND.** **Psychol Rev. 2021 Aug 12. doi: 10.1037/rev0000309.**

Fatigue

- Not consumption and diminution of resources
- Value of offline internal computation of values for future benefit
- (cf boredom value of changing external behavior to gather more information)
- Explore / exploit
- Delay for 'active rest' to produce more accurate evaluations (e.g. hippocampal replay)

Model can be applied to allostatic interoceptive control
Inflammotion and hippocampus
Replay can be rumination
Unconscious rumination and non-restful sleep (e.g. Broschott)

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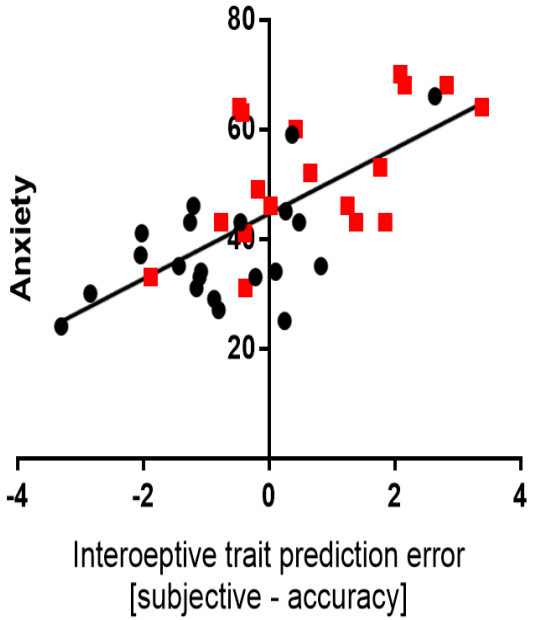
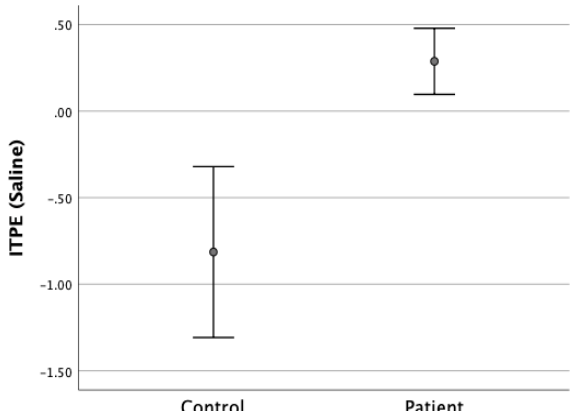
Interoceptive trait prediction errors





Dimensional level	Nature
Executive	Behavioural
Metacognitive	Correspondence between subjective self-report and objective performance accuracy
Sensibility	Subjective self-report
Accuracy	Objective behavioural performance score
Preconscious impact on other processes	Behavioural, neural
Afferent signal	Neural

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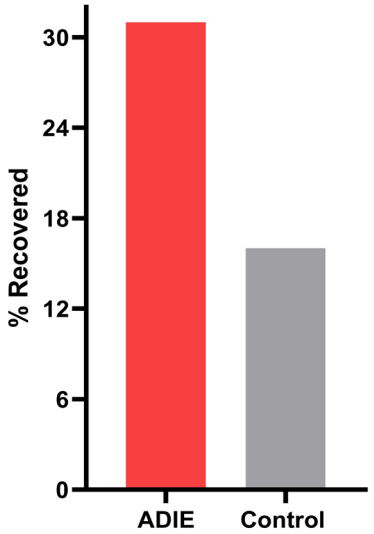
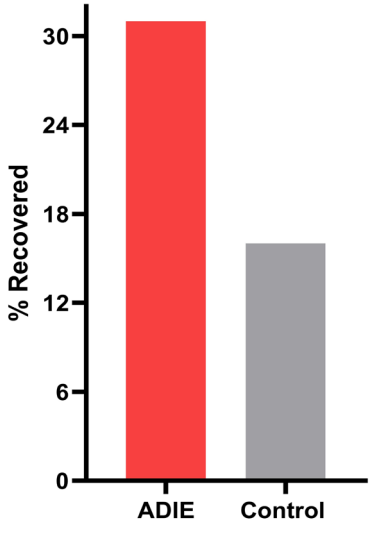
journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Interoceptive training to target anxiety in autistic adults (ADIE): A single-center, superiority randomized controlled trial

Lisa Quadt[a,b,*], Sarah N Garfinkel[a,c], James S Mulcahy[a], Dennis EO Larsson[a,d,e], Marta Silva[f], Anna-Marie Jones[b], Clara Strauss[b,d], Hugo D Critchley[a,b,g]

[a] Department of Neuroscience, Brighton and Sussex Medical School,Trafford Centre, University of Sussex Brighton, United Kingdom
[b] Sussex Partnership NHS Foundation Trust Brighton, United Kingdom
[c] Institute for Cognitive Neuroscience, University College London, London, United Kingdom
[d] School of Psychology, University of Sussex, Brighton, United Kingdom





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Further work

- Fatigue
- Dysautonomia
- Joint hypermobility
- Fibromyalgia
- Inflammation
- Anxiety
- Neurodevelopmental disorders
- Dissociative symptoms
- FND
- MS
- Long COVID

Garfinkel, Eccles, Harrison, Quadt, Amato and many others

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