The Breakdown of Cross-Frequency Coupling Between Brain and Body Rhythms in Clinical Conditions

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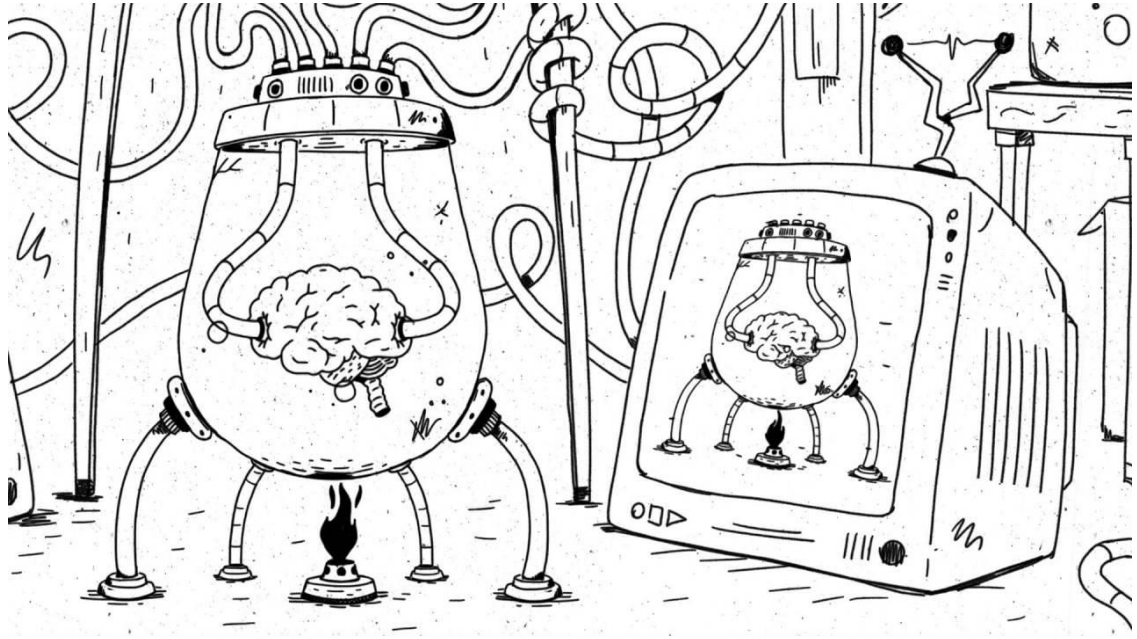
The Proverbial Brain-in-a-Vat: Consciousness Detached from its Neuroanatomical Foundations?

Common thought experiment for proposing or deposing theories of consciousness

Ultimately does not matter. The vatted brain, if we do provision a capacity for phenomenal experience, likely possesses a consciousness that varies drastically from that which we possess in our physiologically-entangled nervous systems



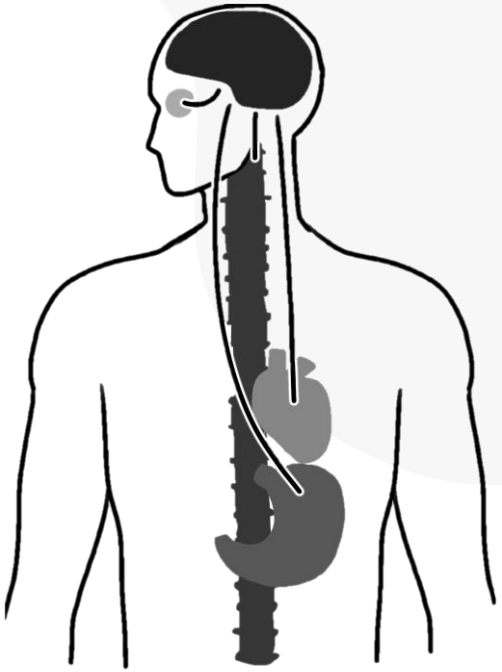
The Embodied and Enactive Neuroscientific Position

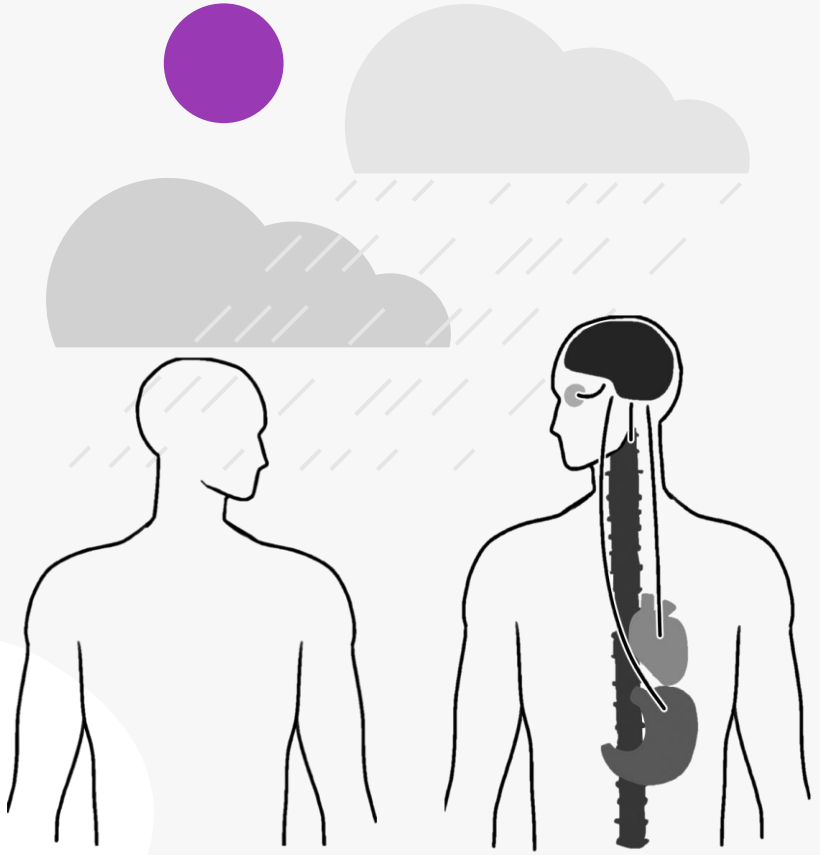
"This approach aims to map the neural substrates of consciousness at the level of large-scale, emergent and transient dynamical patterns of brain activity (rather than at the level of particular circuits or classes of neurons), and it suggests that the processes crucial for consciousness cut across the brain–body–world divisions, rather than being brain-bound neural events" (Thompson & Varela 2001)

"Whatever we may conjecture about a fictitious brain-in-a-vat, the most reasonable would be that in order to create the illusion of a self and a world, the device would need to duplicate not only homeostatic regulation but all brain–body–environment interactions, and thus it would require a vat that is nothing else than a living body engaged in the world" (Fuchs 2009)

"The body intrinsically constrains, regulates, and shapes the nature of mental activity. Call this view the embodiment thesis about cognition" (Foglia & Wilson 2013)

Brain-Body-World Divisions





Intuitive Example: Respiration

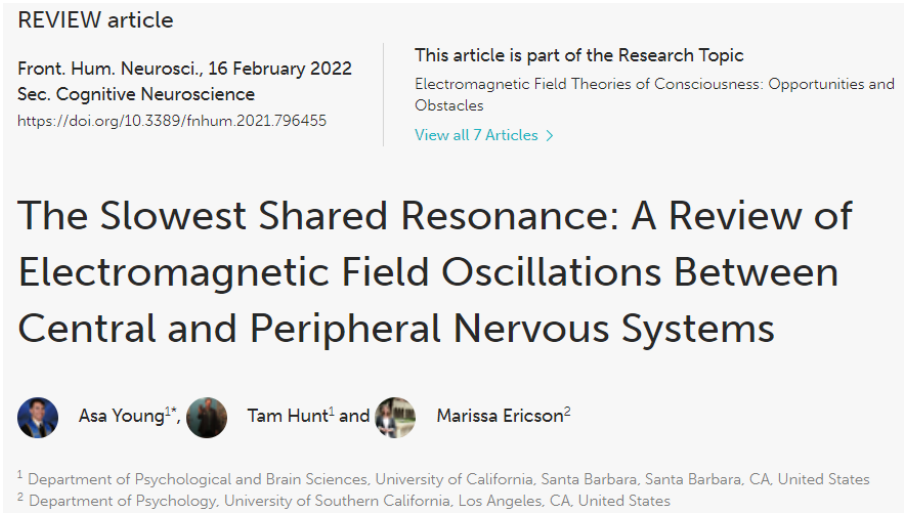
Human (nasal) respiratory cycles, occurring at 0.16-0.33 Hz, entrain cortical activity in the piriform cortex and limbic system (Zelano et al. 2016)

- slow activity (0.1-0.6 Hz) in the piriform cortex is synchronized to the respiration rate; delta and theta are entrained to the onset of inspiration (inhalation)
- Delta, theta, and beta activity are inspiration-locked in the hippocampus, and delta is entrained in the amygdala

The respiratory entrainment of limbic structures infers an influence in emotional processes and this is confirmed by an enhanced detection of fearful faces during nasal inspiration

A Quantifiable Model of Embodied Cognition

"The capacity for phenomenal experience that we attribute to the brain's rhythmic neural hierarchy is, rather, a product of the larger, spatially distributed hierarchy of brain-body rhythms extending from the ultraslow peristaltic cycles to the higher frequency EEG bands and those rhythms that fall between" (Young et al., in progress)



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Electromagnetic Field Theories of Consciousness: Opportunities and Obstacles
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The Slowest Shared Resonance: A Review of Electromagnetic Field Oscillations Between Central and Peripheral Nervous Systems

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Cardiac-Brain Synchrony

"The heart, as the most powerful generator of rhythmic information patterns in the body, acts effectively as the global conductor in the body's symphony to bind and synchronize the entire system" (McCraty et al. 2009)

Heartbeat Evoked Potential (HEP)

Heart Rate Variability (HRV)

Heartbeat Evoked Potential (HEP)

The heartbeat evokes a cortical response and the amplitude of this signal is positively correlated with the perception of one's own heartbeat (Pollatos & Schandry 2004)

It additionally evokes inter-region synchrony in the theta band across a cortical region primarily composed of the left inferior temporal gyrus, left parahippocampal gyrus, and left fusiform gyrus (Kim & Jeong 2019)

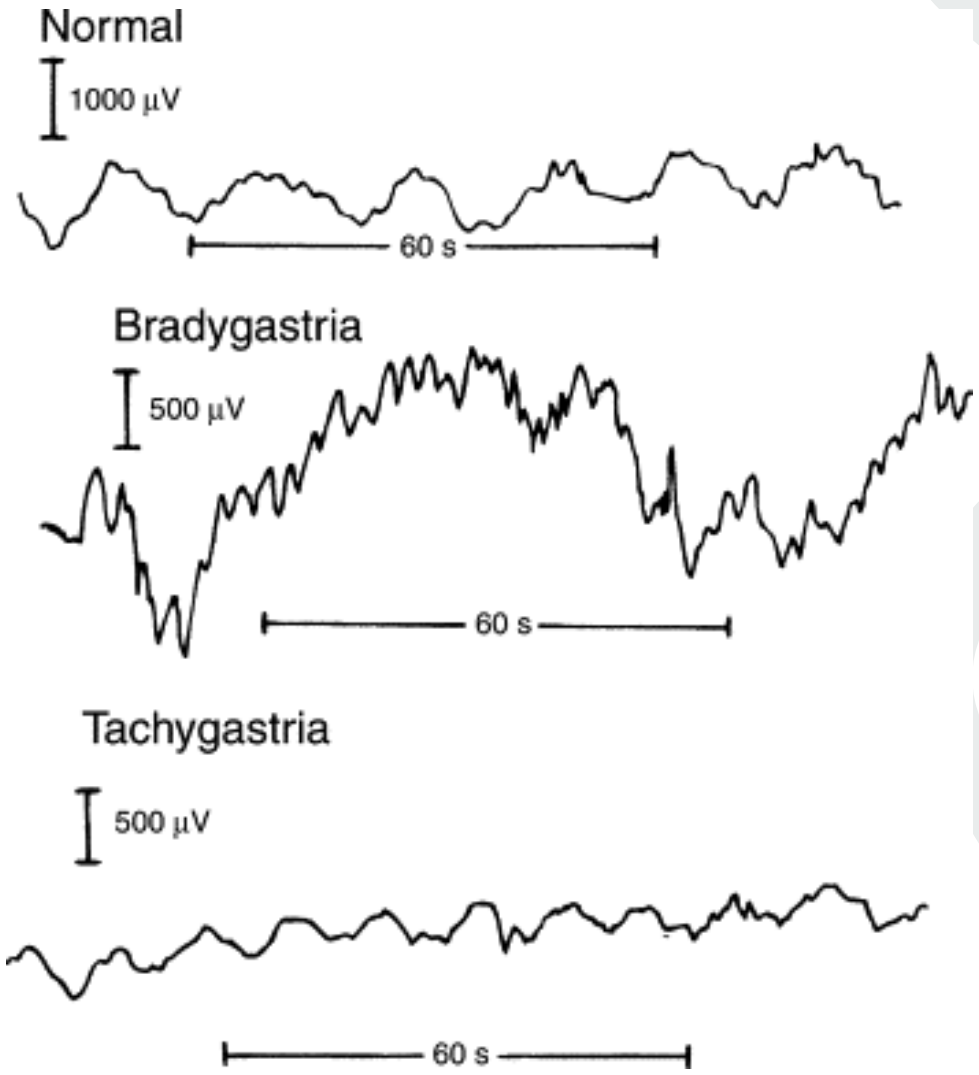
These regions are involved in memory and visual processing, specifically of faces, and this is demonstrated by an enhanced detection of fearful faces in-phase of the heartbeat (Garfinkel et al. 2014)

Heart Rate Variability (HRV)

Variability in the heartbeat, produced in the heart-brain efferent-afferent loops, is a low frequency endogenous rhythm nested within the heartbeat signal (McCraty et al. 2009; Shaffer et al. 2014) that appears to, per preliminary data, be coupled to the BOLD signal (Pfurtscheller et al. 2017)

HRV is the complex and dynamic relationship between the sympathetic and parasympathetic branches of the autonomic nervous system, which create the variability of beat-to-beat changes in the heartbeat (McCraty et al. 2009; Shaffer et al. 2014)

Healthy cardiorespiratory systems exhibit high HRV, but unhealthy systems do not (Chalmers et al. 2014) and brain-dead individuals have functionally zero HRV (Schwerdtfeger et al. 2020)



Gastric-Brain Synchrony

The gut-brain axis is implicated as a central component in state regulation wherein digestive and socioemotional processes are coupled, rooted in the evolutionary history of the organism (Kolacz et al. 2019)

Early vertebrates, when threatened, first initiated shut-down by reducing metabolic activity. This threat response was then supplemented by fight-or-flight mechanisms Mammalian social behavioral networks evolved atop the older ANS fight-flight-freeze mechanisms that emerged from the early gut-brain connection

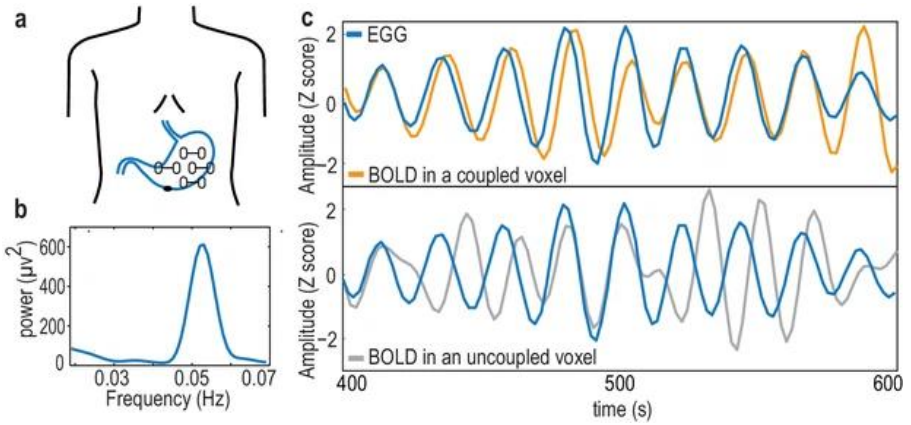
The observer, in hindsight, may follow the development of the human social animal as a step-by-step staircase of evolution with integral ties between the gastric basal system to the higher-order socioemotional controls.

Gastric Basal Rhythm

Measured with the electrogastrogram (EGG), the peristaltic organs, primarily the stomach, emit a central frequency of 0.05 Hz

The gastric basal rhythm entrains alpha activity in a distributed network of cortical and subcortical structures, specifically the right anterior insula, involved in somatotopic organization and interoception (Richter et al 2017; Rebollo et al. 2018)

Blood-oxygen-level-dependent (BOLD) signal, reflective of oxygenated blood-flow to active brain regions, shares 12-17% of variance with the gastric basal rhythm per Lachaux's phase-locking value (Rebollo et al. 2018)



The Function of Brain-Body Synchrony

The brain, a predictive machine, resorts to entrainment for aligning cortical oscillations to the phase dynamics of external stimuli (Lakatos et al. 2019). Endogenously, the entraining oscillations of the peripheral system couple the brain's higher frequency activity to the time-scales of homeostasis (Shalev et al. 2019)

The **neural subjective frame**, the "I" in the statement "I hear/see/smell/feel/taste something," is rooted in the constant stream of afferent information that is recurrently feeding referential maps, a necessary but not sufficient condition to the emergence of the superordinate agent that pilots the entire system (Park & Tallon-Baudry 2014)

In a neurotypical individual, it is expected to observe the gastric basal rhythm synchronized to EEG and BOLD signal, a heart-beat evoked potential and inter-region coherence among other brain-body synchronicities. In the Alzheimer's patient or trauma survivor, we will find a deficiency in one or all the brain-body couplings

Gastric-Brain Dysrhythmia

Alzheimer's Disease and Gut Inflammation

The nascent understanding of AD etiology is centered on the progressive destruction of the gut microbiota (Sochocka et al. 2019; Liu et al. 2020)

The onset of gut inflammation, typically chronic, suppresses the immunological role of the microbiota and leaves the rest of the body susceptible to pathogens that may compromise the blood-brain barrier and the neurons it guards

Richter et al. (2017) and Rebollo et al.'s (2018) reports on resting state gastric-alpha coupling prompted some authors to consider this oscillatory link as a viable route through which the microbiota may influence the brain in a more direct manner (Palacios-Garcia & Parada 2020)

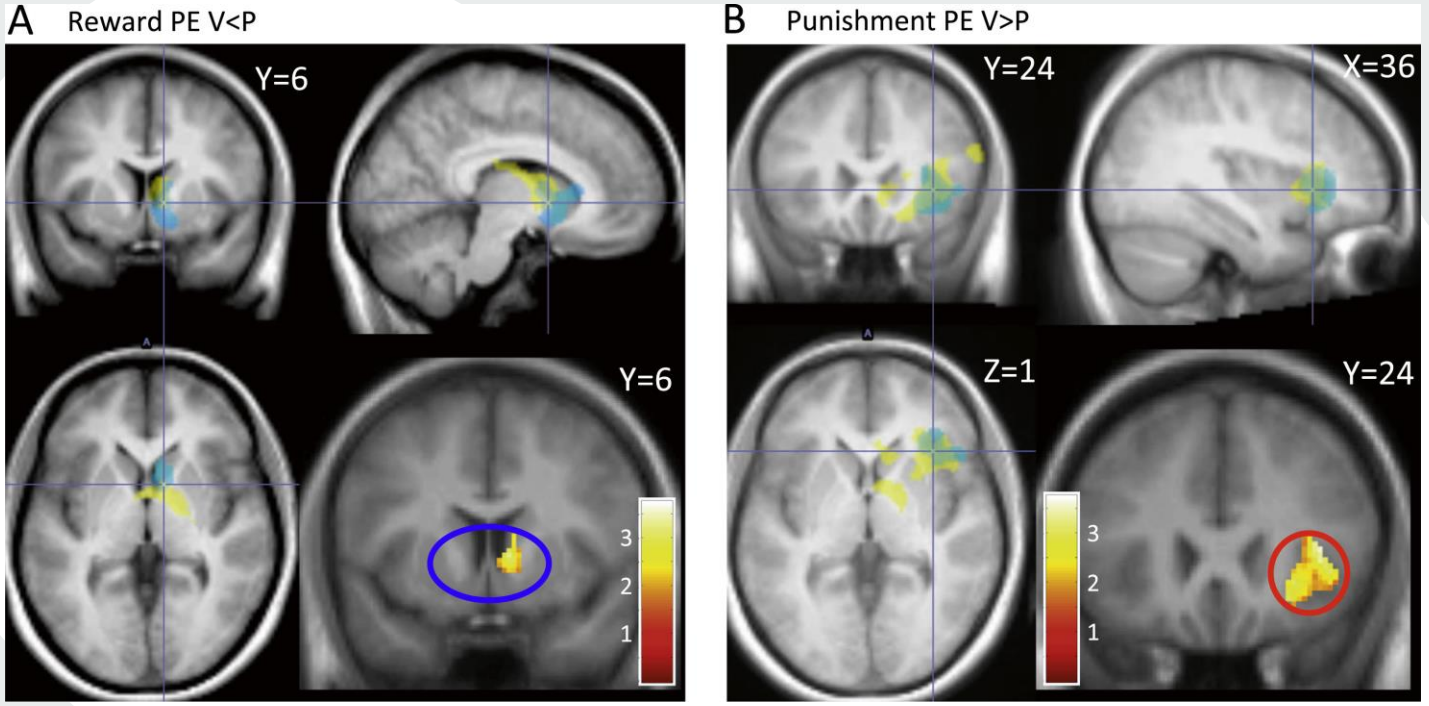
Your Brain on Gut Inflammation

- The onset of gut inflammation precedes the development of a gastric basal dysrhythmia (Mazur et al. 2007)
- Healthy controls exhibit a gastric basal rhythm between 0.025 Hz and 0.060 Hz, but individuals afflicted with ulcerative colitis, an inflammatory bowel disease, possess a rhythm between 0.009 Hz and 0.052 Hz (Sharma et al. 2015)
- Impairment of reward-related behavior in the form of enhanced punishment versus reward sensitivity coincides with the experimental induction of gut inflammation (Harrison et al. 2016)
- fMRI analysis indicated a negative correlation between punishment prediction error and anterior insula activation

Connecting the Dots

We can observe a bodily illness (gut inflammation) disrupting an endogenous rhythm (gastric basal dysrhythmia) that, through its brain-body synchronous relationship (gastric-BOLD coupling at the anterior insula), adversely affects the superordinate agent (impaired reward-related behavior)

Chronic gut inflammation canonical to AD indicates an impairment of the gut-brain axis and severely limited ability to monitor the internal content/state of the body



B, Bottom Right: "Right insula region demonstrating significantly increased correlation with punishment prediction error following inflammation (compared with placebo)" (Harrison et al. 2016)

Gut Inflammation & Mental Illness

Depression, Anxiety, and Traumatic Stress Disorders: Anxiety, depression, and trauma disorders are frequently comorbid with enteric disorders (Kolacz et al. 2019)

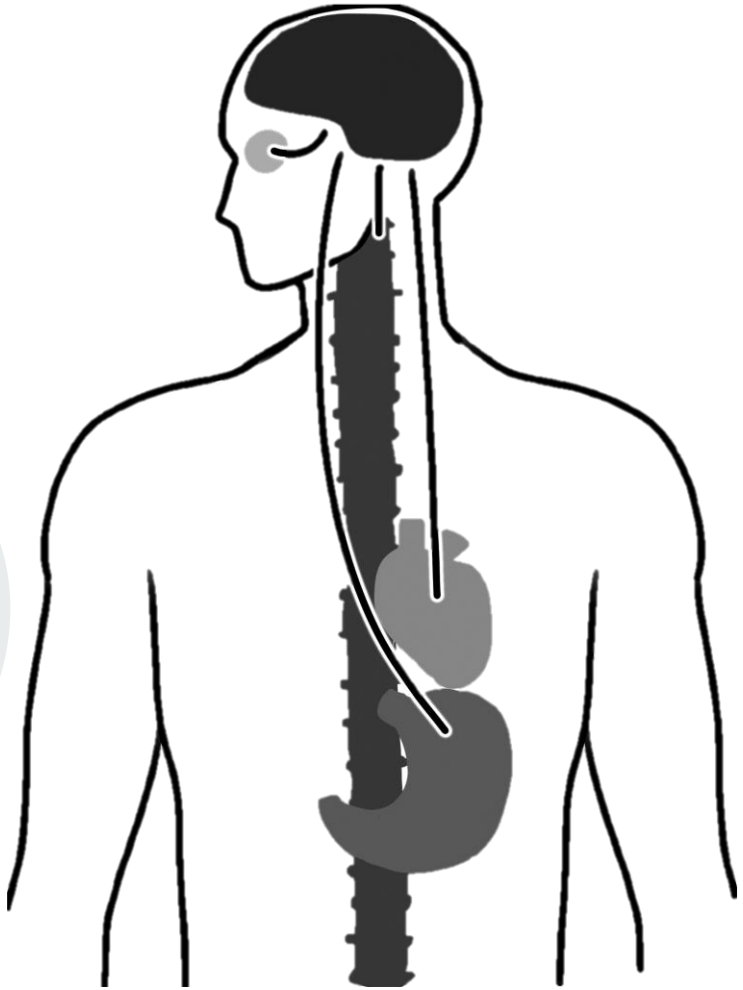
Individuals with IBS exhibit higher levels of anxiety and depression than healthy controls and the authors of the cited study recommend the systematic examination and treatment of these *psychological symptoms of IBS* (Fond et al. 2014)

However, the authors also include discussion concerning 2 cohort studies that conclude, conversely, anxio-depressive symptoms *precede IBS symptoms* (Talley et al. 2001; Goodwin et al. 2013). The converse claim is supported by evidence indicating individuals that have sustained early adverse life events (Bradford et al. 2012), histories of sexual and physical abuse (Drossman et al. 1990), or war trauma (Drossman 2011) are at greater risk for later developing IBS

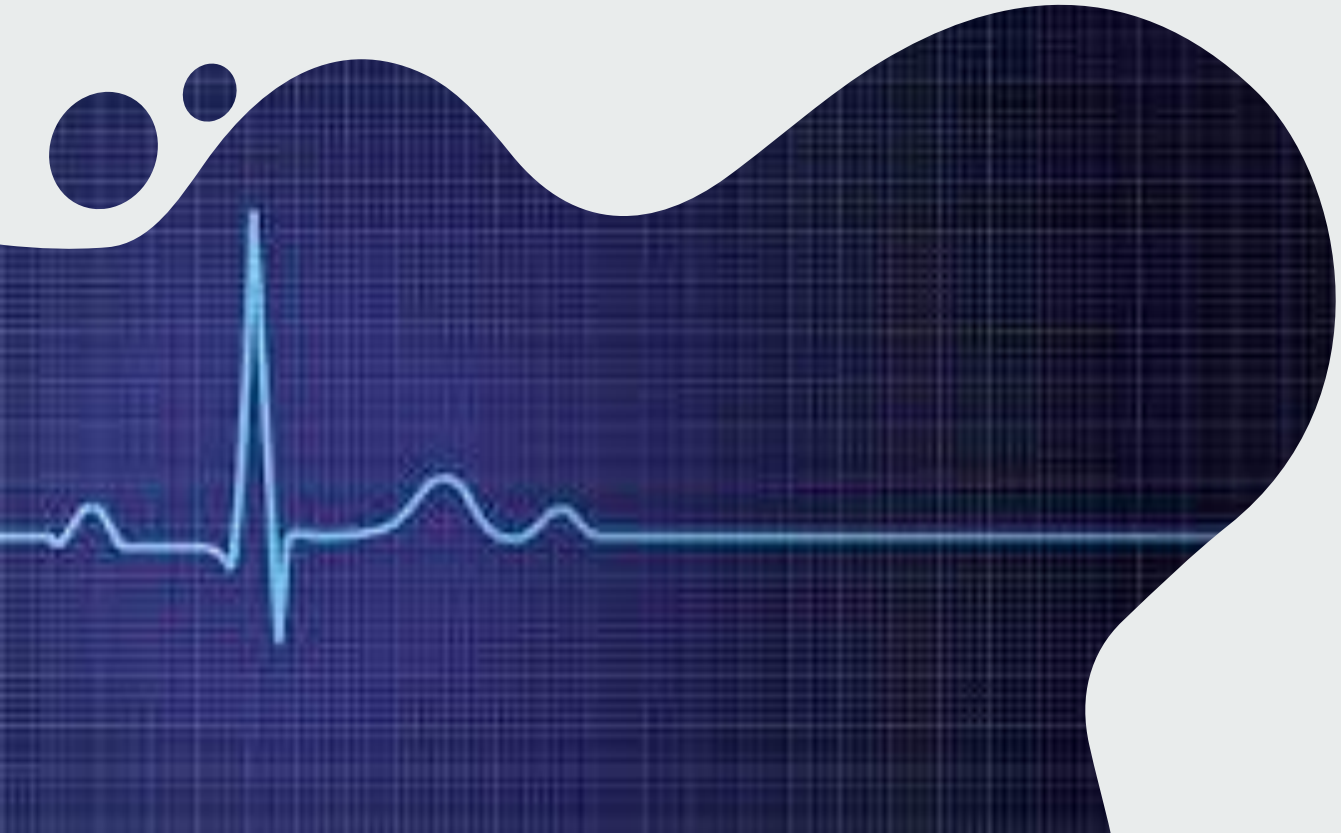
Principle 1: Bi-Directionality of Brain-Body Oscillopathy

Earlier it was claimed the development of gastric dysrhythmia and the undermining of the brain-body spatiotemporal hierarchy was one, among many, factors that contribute to the etiology of AD. Here, in discussing psychological disorders and IBS, we observe a reversal in directionality

The juxtaposition is brought to attention as it is representative of the bi-directional nature of the brain-body spatiotemporal hierarchy. Disruption at one end of the rhythmic correspondence will alter the other



Heart-Brain Dysrhythmias



Decreased Heart Rate Variability (HRV)

Perturbed Sensitivity to the Heartbeat Evoked Potential (HEP)

Decreased HRV

HRV, representative of and product of autonomic activity, is reduced in anxiety disorders (Chalmers et al. 2014), clinical depression (Kemp et al. 2010), traumatic stress disorders (Whitehouse & Heller, 2008), and AD (Zulli et al., 2005)

Low HRV is associated with poor cognitive performance, hypothesized to be an effect of the autonomic system's failure to regulate the brain's blood supply (Elias & Torres 2018)

Sensitivity (or lack thereof) to the Heartbeat

- Behavioral variant frontotemporal dementia presents a HEP of **significantly more negative amplitude** in the insula, amygdala, somatosensory cortex, hippocampus, and anterior cingulate cortex as compared to healthy controls (Birba et al. 2022).
- Individuals diagnosed with obsessive compulsive disorder exhibit **larger HEP** amplitudes (Yoris et al. 2017).
- Depressed patients are less accurate at perceiving their own heartbeat, a result of a significantly **reduced HEP** (Terhaar et al. 2017).
- Borderline personality disorder is likewise linked to a **reduced HEP** (Muller et al. 2015; Flasbeck et al. 2020).

Principle 2: Spectrum of Normative Coupling

When comparing the former 2 and latter 2 examples, we can denote a general disruption in the cardiac-brain synchrony links concurrent with mental illness but, more interestingly, the varying nature of the dysfunction dependent on the sensitivity (or lack thereof) to the cardiac signal

- The former 2 citations reveal a **hyper-embodiment** within which the superordinate agent is engaged in an overactive monitoring of the internal state (Yoris et al. 2017) that compromises the ability to properly react to environmental demands (Birba et al. 2022)
- The latter 2 citations indicate a **disembodiment** of the agent that impairs the ability to perceive the internal state to such an extent that it is hypothesized to underlie the condition of alexithymia, the inability to identify or describe the emotions experienced within one's self (Terhaar et al. 2017; Flashbeck et al. 2020)

Normative Coupling Continued

The disembodiment-hyper-embodiment discussion highlights a probable inference: there is a spectrum of functional brain-body coupling and the neurotypical individual maintains a position in the relative center

Consciousness is widely regarded to be a product of cortical electrodynamics poised near or at a critical point (Carhart-Harris 2018; Toker et al. 2022)

> This critical point rests between stability and chaos, hypo- and hyper-synchrony. At one pole, the brain will descend into a coma and the superordinate agent dissolved; at the other, the brain will be locked in a seizure and the superordinate agent dissolved

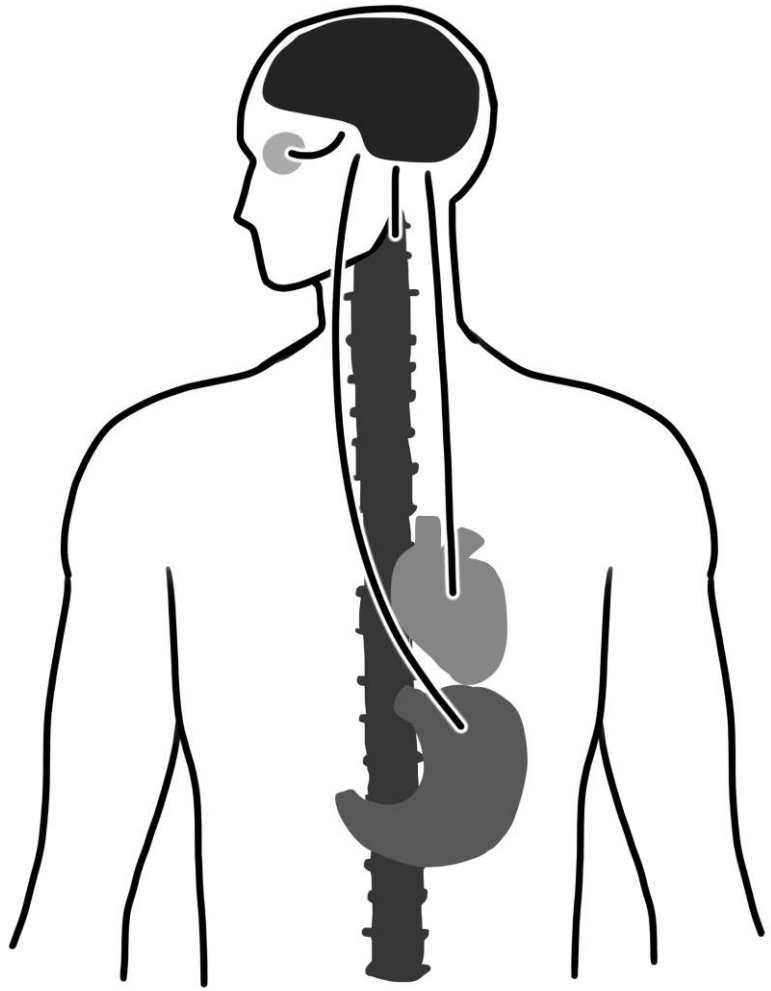
Conclusions and Claims

I. Cognitive and conscious processes, we propose herein, are grounded in the stacked resonance hierarchies extending from the ultra-slow gastric rhythms to the faster frequency EEG bands, and those rhythms in between (Young et al. 2022)

II. The health and integrity of the system is tied to the maintenance of this rhythmic hierarchy

III. Disruption to the rhythmic correspondence, at either end, will result in a disruption at the other

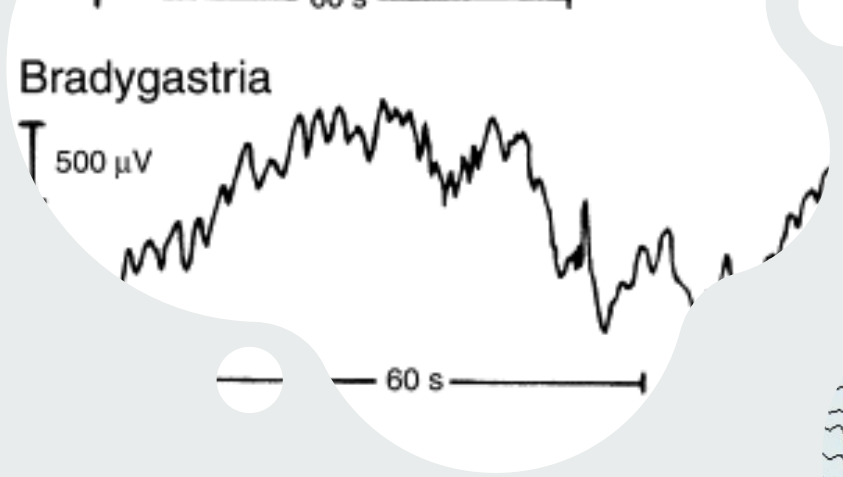
IV. Disruption in either direction, towards scarcity or excess, will manifest an adverse outcome

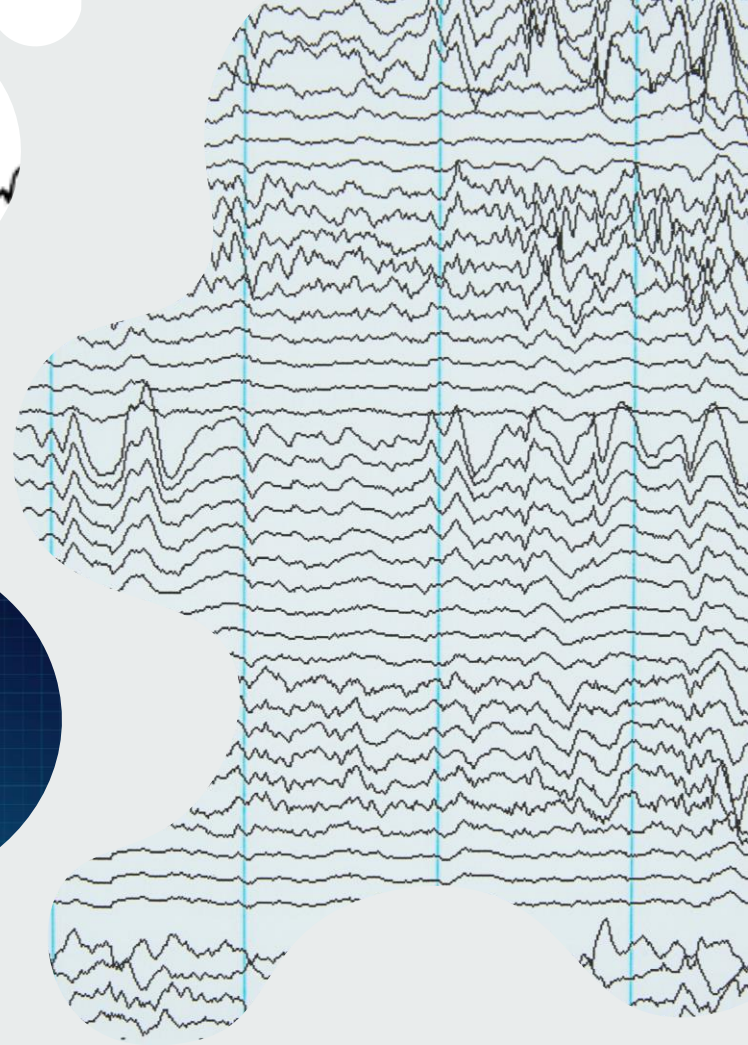


Next Steps: The Construction of Neurotypical and Clinical Profiles of Brain-Body Coupling

Concurrent examination of EEG, EKG, and EGG in neurotypical and clinical populations

The study of oscillopathies may be extrapolated to the entire organism and a broader description of mental illness may be derived

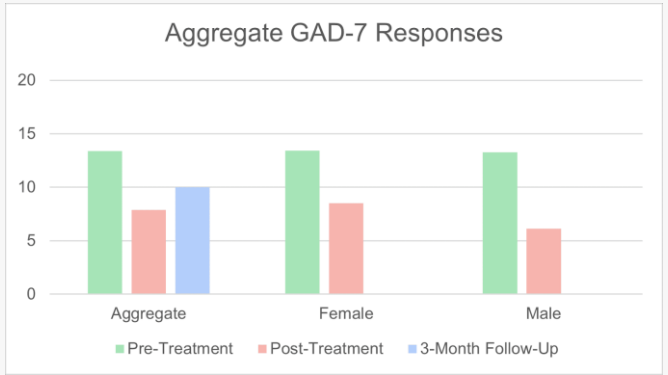


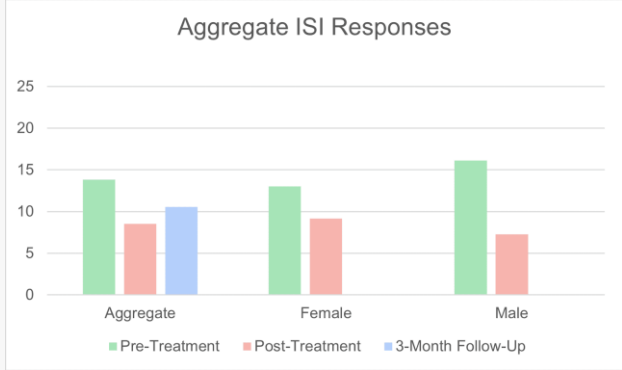


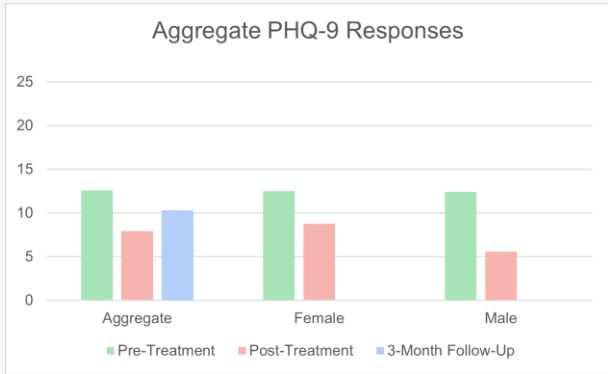
Mimicking Afferent Information with Artificial Devices

Administration of transcranial alternating current stimulation (tACS) to the mastoid processes at 0.14-0.4 Hz in anxious populations (Thompson et al., under review)

Mastoid processes targeted for their proximity to the vagus nerve







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