HERETIC's GUIDE

to neural substrates of sexual dysfunction

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A part of the nervous system that underlies a specific behavior or psychological state.

**neu·ral sub·strate**

/ˈn(y)oorəl ˈsəbˌstrāt/

*noun*

A part of the nervous system that underlies a specific behavior or psychological state.
Optimal sexual function requires that an organism can:

1. Identify **attractive others** in the environment
2. Orienting **attention** to potential mate
3. Detect sensory information about **incentive value**
4. Motor engagement to **physically approach** (and return!)
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See, smell, taste, move
TRPV-IR nerve ending
(vulvar lamina propria, *mus musculus*)
phrenology

/noun/

The detailed study of the shape and size of the cranium as a supposed indication of character and mental abilities.
phrenology /freɪˈnɛlədʒi/  

noun

The detailed study of the shape and size of the cranium as a supposed indication of character and mental abilities.
Human Connectome Project’s New Brain Map

- Sensory/Motor
- Visual
- Auditory
- Task Positive
- Task Negative
The Resting Brain
What kind of *network* is the brain?
What kind of network is the brain?

A Regular  B Small-World  C Random  D Hierarchical Small-World  E Disrupted in Chronic Pain

More Sparsely Connected Node  More Densely Connected Node

Increasing information exchange between node and rest of brain

Primary Visual Cortex  Thalamus
What kind of network is the brain?
Do we have “sexual” brain networks?
This is adaptive—preferentially orients us to threats, facilitates action/escape, etc as well as rewards.
Common to All Conditions

Physical Contact Specific

Touch Specific

Auditory Specific

Visual Specific
Can the body detect threat before it contacts the body?
The **position of body in space** modulates perception of pain.

Pain perception increases as threats approach.

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Bucchari et al., 2016
The position of body in space modulates perception of pain.

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Bucchari et al., 2016
Peri-personal space determines perceived pain intensity

Sensitive to: Approaching threats, rules of gravity, and the importance of the head
Blink responses were recorded when the shocked hand was **4-60 cm** from Drake’s face.

Increased blink response at **20 cm** in those with high anxiety.
Defensive Peripersonal Space
Our internal states are, in part, defined by the space we inhabit.
The perceived boundaries of our bodies—which define internal / external—can change.

Ex. “Body Matrix” (Moseley, Gallace, & Spense, 2012)
By sharing peri-personal space with lovers, they may impact perception of body boundaries.
How do we know this is *sexually relevant*?

**Intranasal oxytocin**……

- Facilitates female *approach behavior* to male confederates (*double-blind RCT*).

- Mediates physical distance from an attractive female confederate in monogamous *but not single* men.
Perceived threat is positively correlated with EMG vaginal activity in women with and without vaginismus. 

(Van der Velde & Everaerd, 2001)
Anxiety mediates altered subcortical circuitry in men with UCPS_{sex}.

Greater communication* between fronto-limbic and temporal regions.

*measured as link-count functional connectivity

Farmer et al., In Preparation
Men and women with bladder pain syndrome/interstitial cystitis show symptom-related changes in axonal microstructure.
Take home messages

- Internal perception is dependent on the body’s position in space,
- Measure of fitness? An astute nervous system is evolutionarily adaptive
- Anxiety can amplify peri-personal defensive space and reorganize brain networks in men with ejaculation-related pain
- An underappreciated dimension of sexuality to assess and target
neural substrate

noun

The surface or material on or from which an organism lives, grows, or obtains its nourishment.
Methods

1. **Functional connectivity** defined in 2 ways:

(a) Pearson correlation between two regions’ BOLD time courses (*standard*); and

(b) Voxel-wise link count (# of significant inter-regional correlations, where $r > 0.3$), for 10% most connected regions (e.g., *10% connection density*)

   - Note this method controls for known site differences in resting state fMRI by extracting an equal # of data points from each brain that relative to

2. Two-way **ANOVA**: Main effects for gender, sex-related pain (+/-) & their interaction;

3. Significant regions were examined individually and within spatially-defined neural networks (frontolimic, sensorimotor, temporo-occipital)

4. **Hub disruption** was examined in relation to UCPPS-specific networks
Two measures of neuroplasticity: *function and structure*

**Function**
- assessed via fMRI
- extracted in relation to a task (e.g., pain rating) OR as correspondence of activity in two regions (e.g., resting state)
- short-term plasticity vulnerable to change

**Structure**
- assessed via T1-weighted anatomical scanning AND diffusion tensor imaging
- tissue types segmented based on magnetic properties
- used to infer loss/gain of function based on anatomical abnormalities
- longer-term plasticity