Symptoms in Sync: Visualizing Change Patterns of Treatment Resistant Major Depressive Disorder across rTMS

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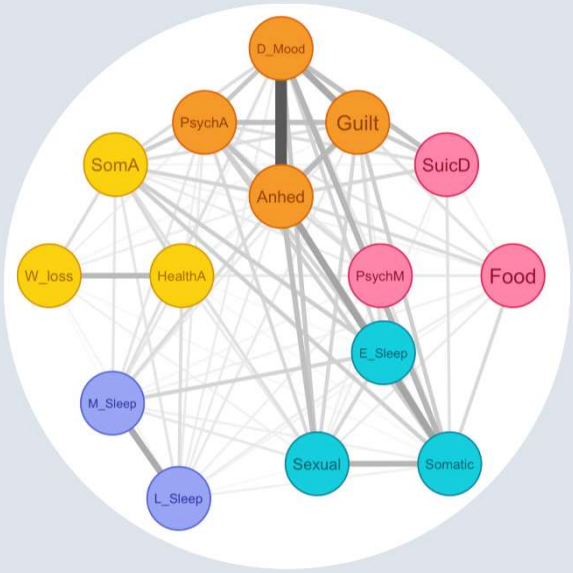
Non-Responders

Average HRSD-17 improvement: -1%

n=118

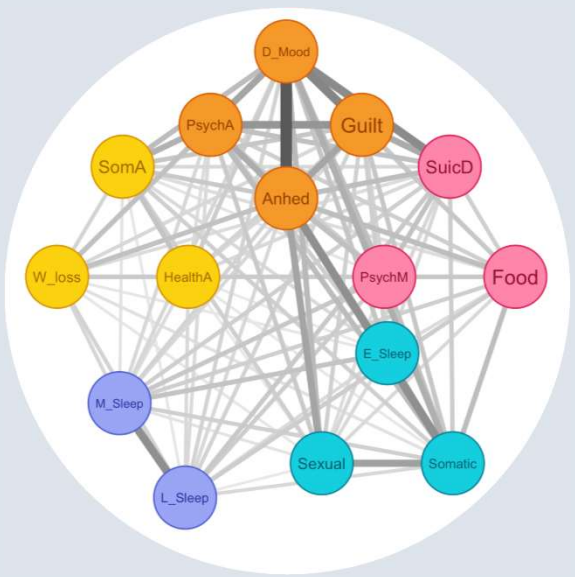


Average Distance between Symptoms: 5.14

Moderate Responders

Average HRSD-17 improvement: 34%***

n=196

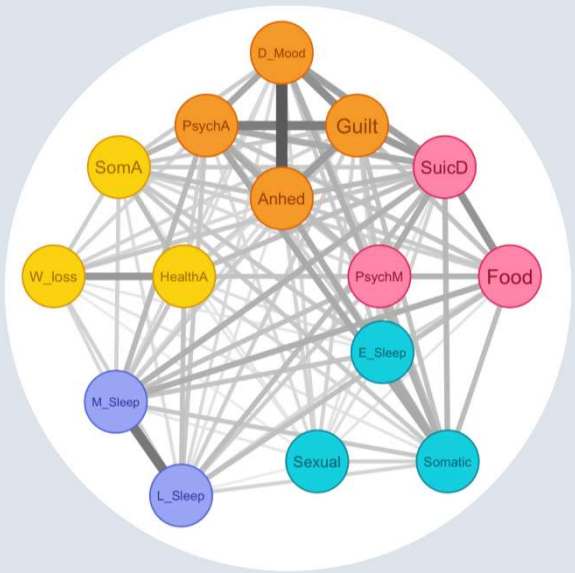


Average Distance between Symptoms: 4.89

High Responders

Average HRSD-17 improvement: 64%***

n=247



Average Distance between Symptoms: 4.46

* *p*=<.05
*** *p*=<.001

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Symptoms that change in similar ways across time have a smaller **distance** between them.

There appeared to have a dose-response relationship; the average distance between symptoms was *smallest* in those who responded *well* to rTMS treatment (symptom changes were more closely related/alike to one another). Those who did *not* respond to rTMS treatment had the largest average distance (a sparser network with more weakly-related symptoms).

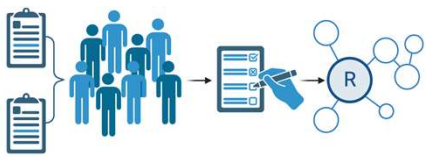
← References, supplement, and online copy

Does the similarity in the way symptoms change over time reveal meaningful differences between those who respond to rTMS and those who do not?

Background

- Repetitive Transcranial Magnetic Stimulation (rTMS) is a safe and effective neurostimulation depression treatment even for those whose do not respond to medication.[1]
- It is unclear why some people respond to treatment and why some do not [2]
- Current approaches are insufficient in considering the inter-causal relationships among depressive factors.[3,4]

Methods



Data was combined from two past studies, THREE-D[5] (*n*=386) and CARTBIND[6] (*n*=175). All participants failed at least 1 medication trial in the past. Depression was measured using the HRSD-17[7] on baseline and treatment days 10, 15, and 20.

Group participants by treatment response (% change from baseline to day 20 of rTMS)	***K*-means clustering**[8]
Determine how similarly symptoms change throughout treatment (their "distance")	**Dynamic Time Warping**[9]
Visually model symptom distances	**Network analysis**[10]
Group symptoms based on the similarity of their distances	**Hierarchal clustering**[11]

Legend

	Core Depressive Symptoms
D_Mood	Depressed Mood
Guilt	Feelings of Guilt
Anhed	Anhedonia (Pleasure in Work/Activities)
PsychA	Psychic Anxiety
	Vegetative Symptoms
SuicD	Suicide
Food	Somatic Symptoms, Gastro-intestinal
PsychM	Psychomotor Change (Slowing + Agitation)
	Autonomic/Homeostatic Dysregulation
E_Sleep	Insomnia, Early in the Night
Somatic	General Somatic Symptoms
Sexual	Genital Symptoms
	Insomnia, Staying Asleep
M_Sleep	Insomnia, Middle of the Night
L_Sleep	Insomnia, Early Hours of the Morning
	Somatic Symptoms
SomA	Somatic Anxiety
HealthA	Hypochondriasis
W_loss	Weight Loss

Discussion

- Because the symptoms of high responders change in ways that are similar to one another, it may be that a positive change in one symptom then "reverberated" throughout the network, ultimately leading to global illness improvement
- *Why* symptom networks appear the way they do could be due to unique neurobiological origins
  - Some studies using fMRI show greater levels of functional connectivity (FC) in treatment responders[12,13]
  - FC may increase over a course of rTMS[14]
- Future studies may compare antidepressant and rTMS non-responders directly

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