Predicting antidepressant response to transcranial magnetic stimulation with heart rate variability

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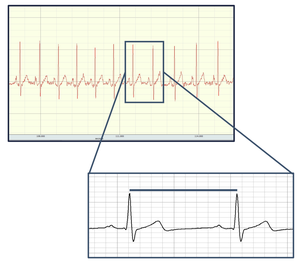
Introduction

- Treatment resistant depression (TRD): a form of depression where patients do not respond to ≥ 2 antidepressant treatments. Occurs in ~20% of people with depression.
- Repetitive transcranial magnetic stimulation (rTMS) is an effective intervention for TRD (~40% efficacy).
- We are unable to predict treatment outcome. This would allow for a personalized-medicine approach to treat TRD.
- Heart rate variability (HRV) measures the balance between sympathetic and parasympathetic nervous system processes because by measuring the temporal variability between successive heart beats (Figure 1).

Figure 1



- Greater HRV is associated with greater parasympathetic weight.
- Lower HRV is associated with greater sympathetic weight and sudden cardiac death in cardiovascular disease patients[1].
- Lower HRV is reported in patients with depression[2], similar to heart transplant patients[3].
- Goal: Understand HRV's predictive ability for TMS treatment response.

Hypothesis

- Baseline HRV would increase following successful rTMS treatment.
- HRV would be inversely correlated with depression scores.
- Baseline and HRV reactivity would predict subsequent treatment outcome.

Methods

- Present analysis: 17 individuals with TRD receiving rTMS treatment at UIHC between 2018 and 2020. Demographics are displayed in Tables 1 and 2.
- Participants sat at rest for 5 minutes and while watching a clip from Funniest Home Videos while electrocardiogram data was collected with BIOPAC MP150 before and after a full clinical treatment course of TMS.

$$RMSSD = \sqrt{\frac{\sum_{i=1}^{N-1}(RR_i - RR_{i+1})^2}{N-1}}$$

- HRV Reactivity = Happy RMSSD - Rest RMSSD.
- Patient Health Questionnaire-9 (PHQ-9) was self-reported by the participants.
- Treatment response: ≥ 50% reduction in PHQ-9 scores.

Results

Figure 2 Rest HRV

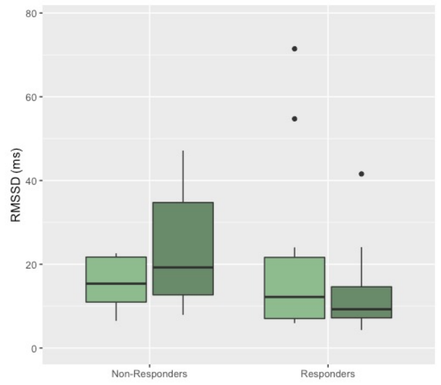


Figure 4 Rest HRV

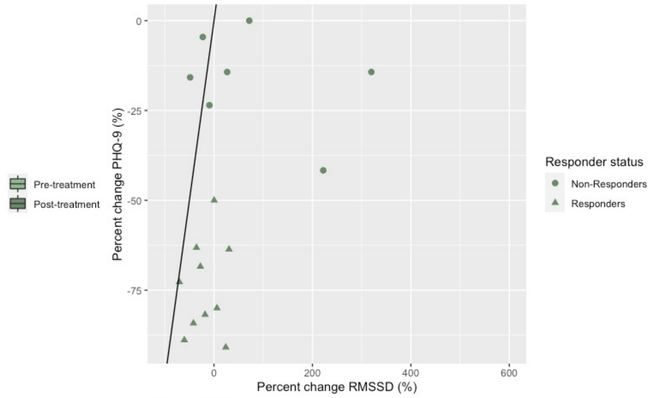


Figure 3 Happy HRV

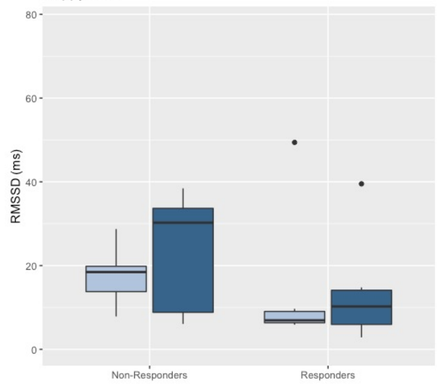


Figure 5 Happy HRV

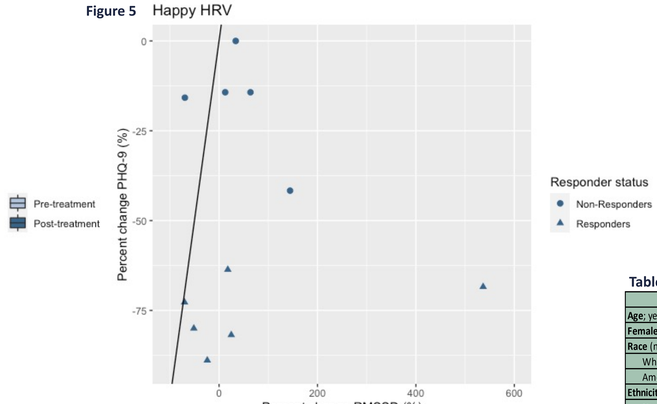


Figure 2 and 3: No significant changes in Rest or Happy RMSSD before and after treatment for treatment non-responders and responders. Figure 4 and 5: No significant correlations between percent change in Rest or Happy RMSSD and percent change PHQ-9. Their regression lines are plotted. Figure 6: There was a significant difference in pre-treatment Reactivity between responders and non-responders; non-responders had greater HRV Reactivity. There was also a significant decrease in HRV reactivity from pre to post treatment in non-responders, and no significant change for responders. Figure 7: No significant relationship between percent change in Reactivity RMSSD and PHQ-9 scores.

Figure 6 HRV Reactivity

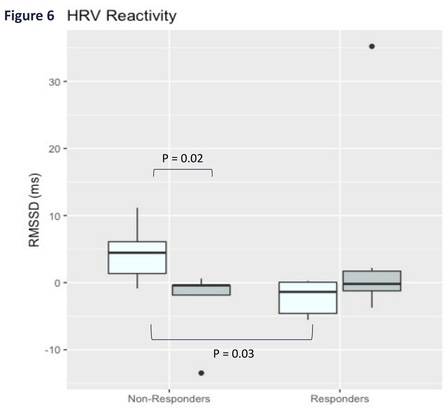
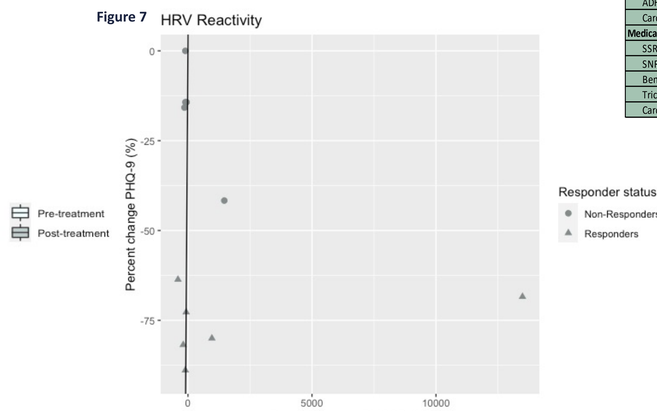


Figure 7 HRV Reactivity



Discussion

- In contrast to expected outcomes, Rest and Happy HRV was not significantly associated with depression scores or treatment response.
- Low HRV may be a trait, rather than state marker of depression and may not be a useful predictor of treatment response.
- Greater Reactivity was found in non-responders compared to responders.
- High pre-treatment Reactivity may indicate a subsequent treatment non-responder, contradicting our expected results.
- A preliminary power analysis indicates that these analyses are extremely underpowered.
- Concurrent medications such as SSRIs, tricyclics, and benzodiazepines may drive most of the relationships between depression and HRV[2].
- Over 40% of our participants were taking these medications and had comorbid cardiovascular conditions.
- A meta-analysis suggests that there may not be a change in HRV after antidepressant treatment[4], possibly due to heterogenous sample characteristics and HRV measurements between studies.
- In conclusion, the relationship between depression treatments and HRV remain unclear.
- Going forward, we will assess the effects of demographics, comorbidities, and medications on these relationships, as well as other measures of HRV.

Table 1

Resting HRV Dataset N = 17	
Age; years (SD)	55.5 (14.9)
Female (n, %)	9, 52.9%
Race (n, %)	
White	16, 94.1%
American Indian/Alaska Native	1, 5.8%
Ethnicity (n, %)	
Non-Hispanic	17, 100%
Baseline Patient Health Questionnaire-9 Score; mean (SD)	17.5 (4.0)
End of treatment Patient Health Questionnaire-9 Score; mean (SD)	8.6 (6.4)
Responders (n, %)	10, 58.8%
Type of TMS treatment (n, %)	
10 Hz	7, 41.2%
iTBS	10, 58.8%
Comorbidities (n, %)	
Anxiety disorders	12, 70.6%
PTSD	3, 17.6%
OCD	2, 11.8%
Personality disorders	3, 17.6%
ADHD	5, 29.4%
Cardiovascular comorbidities	7, 41.2%
Medications (n, %)	
SSRIs	8, 47.1%
SNRIs	6, 35.2%
Benzodiazepines	9, 52.9%
Tricyclics	2, 11.8%
Cardiovascular medications	6, 35.3%

Table 2

HRV Happy Dataset N = 11	
Age; years (SD)	60.8 (9.7)
Female (n, %)	6, 54.5%
Race (n, %)	
White	10, 90.9%
American Indian/Alaska Native	1, 9.1%
Ethnicity (n, %)	
Non-Hispanic	11, 100%
Baseline Patient Health Questionnaire-9 Score; mean (SD)	17 (4.3)
End of treatment Patient Health Questionnaire-9 Score; mean (SD)	8.6 (6.3)
Responders (n, %)	6, 54.5%
Type of TMS treatment (n, %)	
10 Hz	5, 45.5%
iTBS	6, 54.5%
Comorbidities (n, %)	
Anxiety disorders	5, 45.5%
PTSD	1, 9.1%
OCD	1, 9.1%
Personality disorders	2, 18.1%
ADHD	3, 27.2%
Cardiovascular comorbidities	6, 54.5%
Medications (n, %)	
SSRIs	7, 63.6%
SNRIs	3, 27.2%
Benzodiazepines	7, 63.6%
Tricyclics	2, 18.1%
Cardiovascular medications	4, 36.4%

References

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