Autonomic Nervous System Modulation During TMS in Patients with Depression

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Methods

Participants: 15 subjects in a clinical trial of TMS for treatment-resistant depression

Measures: Heart rate and HRV (the root mean square of successive differences [RMSSD] and the standard deviation of NN intervals [SDNN])

Procedure: A 30-day trial of repetitive TMS, with electrocardiograms collected before and during four of the 30 TMS treatment sessions

Analysis: Measures from these timepoints (before vs during TMS) were compared using paired-sample t-tests to see whether they change during TMS. Additionally, mixed model regression analysis was used to assess the relationship between pre- and during-TMS measures for each variable.

Results

Baseline heart rate and SDNN were negatively associated with their calculated change scores from baseline to TMS. There was no association for RMSSD.

In terms of absolute change, there was a positive association between baseline heart rate and change to heart rate during TMS, but the results for both HRV measures were not statistically significant.

Linear mixed model results

<table>
<thead>
<tr>
<th>Measure</th>
<th>β</th>
<th>95% CI</th>
<th>Random Effect (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>-0.237</td>
<td>[-0.358, -0.105]</td>
<td>1.396 (1.263)</td>
</tr>
<tr>
<td>RMSSD</td>
<td>-0.266</td>
<td>[-0.367, -0.165]</td>
<td>330.8 (18.09)</td>
</tr>
<tr>
<td>SDNN</td>
<td>-0.280</td>
<td>[-0.381, -0.179]</td>
<td>529.7 (23.00)</td>
</tr>
</tbody>
</table>

T-test results

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>During TMS</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>805.1</td>
<td>863.2</td>
<td>6.75, p &lt; .001</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>29.1</td>
<td>44.8</td>
<td>5.43, p &lt; .001</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>45.1</td>
<td>54.5</td>
<td>9.40, p &lt; .001</td>
</tr>
</tbody>
</table>

Discussion

↑ baseline heart rate was associated with reductions in heart rate and larger overall changes to heart rate during the first minute of TMS.

↑ baseline SDNN was associated with reductions in SDNN during TMS, and vice versa

There was no relationship between baseline RMSSD and change to RMSSD during TMS

All 3 heart metrics changed in the expected directions during TMS

- TMS may exert an initial rapid modulation of the autonomic nervous system

The present study shows that pre-existing heart rate and HRV may determine the degree to which they are affected by TMS in subjects with treatment resistant depression, but that this varies by HRV measure.

It is possible that subjects with lower baseline heart rates had better autonomic regulation that was less amenable to external modulation by TMS, or that people who were nervous had elevated heart rates that quickly went back down. Future studies with larger sample sizes should clarify this possibility. Further, future analysis should assess whether baseline cardiac measures relate to treatment response after a course of TMS.

Introduction

Transcranial magnetic stimulation (TMS) is a non-invasive treatment for Major Depressive Disorder (MDD). TMS seems to modulate the autonomic nervous system, reflected as changes to Heart Rate Variability (HRV) and heart rate during stimulation.

HRV ↑ and heart rate ↓ during TMS, possibly due to a connection from the prefrontal cortex to the autonomic nervous system, and this may relate to clinical outcomes.

Between-subjects differences in the magnitude of these changes are purportedly due to variation in treatment administration. However, the present study examines the role of patients’ pre-existing cardiac characteristics by comparing baseline HRV and heart rate to changes in HRV and heart rate during TMS.