Baseline Skin Conductance Level as a Predictor of Response to Propranolol for Anxiety and Other Clinical Outcomes in Autism Spectrum Disorder

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Introduction

- Autism Spectrum Disorder (ASD) is a neurodevelopmental condition indicated by deficits in social and communication skills, restricted interests, and repetitive behaviors.
- A meta-analysis found that anxiety is comorbid in up to half of the individuals studied (Van Steensel, 2011), with other studies seeing anxiety in up to 84% of individuals with ASD (Santosh & Singh, 2016). This demonstrates the prevalence of co-occurring anxiety is very high in ASD patients.
- Currently there is no diagnostic biomarker nor any proven pharmacological means of treating the hallmark features of ASD. Furthermore, the effectiveness of pharmaceutical agents for mood disturbances in ASD are unclear, thus more research is necessary to find evidence supporting a standard treatment for anxiety in ASD.
- Research suggests that anxiety correlates with increased sympathetic tone. Because sweating is solely controlled by sympathetic activity, as sweat gland activity rises, it can be quantified by a rise in electrical skin conductance levels (SCL), which may indicate higher levels of anxiety.
- Propranolol, a beta-adrenergic antagonist, blocks the physiologic effects of sympathetic tone and is widely used for its anxiolytic effects in those without ASD. However, more research is needed to better understand its use for anxiety in ASD. We are interested to know whether higher SCL might act as a biomarker to predict a patient's response to propranolol use for anxiety in ASD patients.
- **We hypothesize that individuals within the ASD population with higher SCL experience increased anxiety, and that greater changes in SCL from baseline to the end of the study may predict a greater response to propranolol use for anxiety in autistic patients.**

Methods and Materials

- 16 high functioning ASD patients ages 7-24 were examined in this study's initial analysis. Anxiety, repetitive behavior and several additional behavioral subdomains (social, aberrant, verbal, nonverbal, hyperactive, sensory, restrictive, and overall behavioral abnormalities) were observed and evaluated using the clinician rated Clinical Global Impression of Severity (CGI-S).
- SCL and other indicators of sympathetic activity were measured at baseline and week 12 of an open-label extension (OLE) of a propranolol trial. Propranolol was titrated based on patient weight. CGI-S ratings were completed before and after the 12-week trial.
- Two electrodes were placed on the palm of the nondominant hand. Skin sweat, quantified by SCL, weas recorded for a total of 8 minutes, where the first 3 minutes served as an acclimation period and the remaining 5 minutes of data were analyzed.
- Skin conductance data was obtained using a BIOPAC MP150 Data Acquisition System with an GSR100C amplifier (BIOPAC Systems, Inc., Goleta, CA.). The SCL data was recorded in and obtained from Acqknowledge 4.1 software.
- Windows Excel software was used for data analysis.

Results

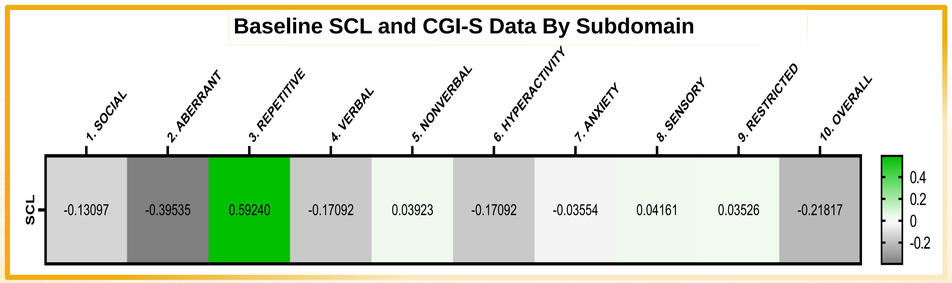

Figure 1. This heat map depicts the correlation coefficient of baseline SCL measurement with change in CGI-S subdomains for core behaviors in ASD. While the null hypothesis was retained for the other measures, a significant positive correlation was seen between changes in baseline SCL and severity of repetitive behavior.

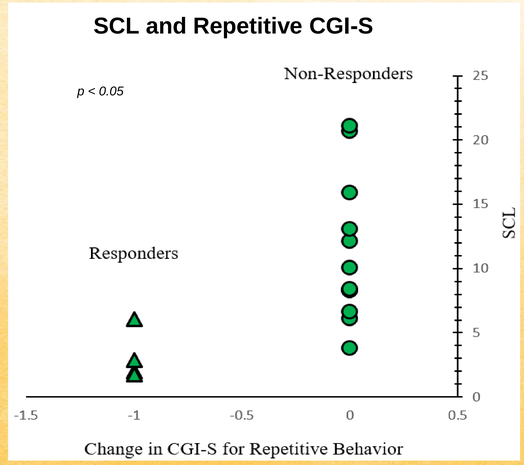

Figure 2. A two-tail t-Test shows significant (**p = 0.0046)* improvement in the CGI-S for repetitive behaviors with an average SCL difference of 7.976 between responders and non-responders.

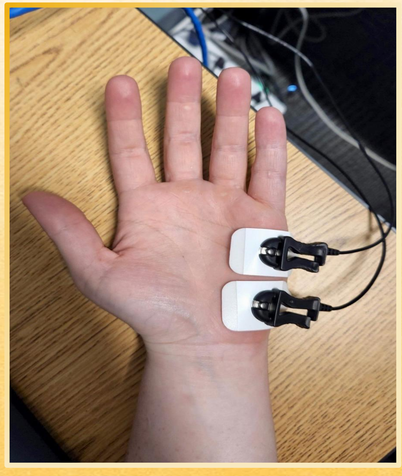

Figure 3. Placement of electrodes on the non-dominant hand while the patient was sitting at rest.

Discussion

- The aim of this initial analysis was to observe whether SCL have a positive association with changes in CGI-S measures in several common features of ASD (i.e., anxiety, repetitive behaviors, etc.).
- Because of propranolol's history of successfully treating anxiety in patients *without* ASD, we wanted to learn more about whether its effects may indicate which subjects might have the greatest behavioral response to propranolol based on changes in SCL and CGI-S ratings in individuals with ASD.
- **Our results did not support our hypothesis and thus we did not find evidence that SCL is a predictor of patient response to propranolol use for anxiety.**
- **We did, however, find a significant positive correlation between changes in SCL and CGI-S measures of repetitive behaviors, which allows for further investigation into the mechanism of this association**.
- We recognize that the small sample size of patients with good SCL data may have limited these findings.

Future Directions

- Establishing biomarkers of core features of ASD may be useful in identifying propranolol as a preferred pharmaceutical therapeutic agent in this population.
- Future data analysis would allow us to look at other possible biomarkers of sympathetic tone. In addition to SCL, we have collected data on heart rate variability and pupillary light response.
- Data analysis from this study is ongoing and further research is warranted to identify which ASD patients might benefit most from propranolol therapy.
- Increasing the number of participants in future trials would help to address issues with sample size.
- Our hope is that further analysis of our data may impact future clinical decision making when treating anxiety and other features associated with ASD.

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