Effect of propranolol on facial processing in autism spectrum disorder

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social interaction deficits, communication impairments, and restricted, repetitive behaviors (1). ASD, with estimates of incidence as high as 1 in 88 individuals, has a largely unknown etiology (2). Pharmacological intervention is currently being explored to improve symptoms of ASD, including those in the social domain (3,4). Social interaction deficits in this population may include facial processing abnormalities, such as reduced eye contact, and increased fixation on less socially-salient facial regions, such as the mouth (5). However, there is variability in the degree of these deficits in the current literature (6). Additionally, it has been previously hypothesized that stress mediates poor facial processing in individuals with ASD (7,8). This pilot study examines the effect of propranolol, a nonselective beta-adrenergic antagonist anxiolytic, on facial processing in individuals with ASD and typically developing controls.

Methods

Individuals with ASD (n = 12, mean age = 18.25 ± 2.67 (SD) years, mean WASI IQ = 103.50 ± 13.04 (SD)) and age/IQ/gender-matched controls (n = 12) participated in two study sessions. Propranolol (40 mg) and placebo were administered in a double-blinded, counter-balanced manner. Heart rate and blood pressure was recorded pre- (0 min) and post-drug administration (60 and 150 min). Drugs were administered 1 hour prior to testing to allow for peak drug effects during testing.

Eye movements were recorded using an Eye-Trac R6 remote eye movement monitor with video head tracking (Applied Sciences Laboratories, Bedford, MA). The eye movement monitor was calibrated for each participant at the start of each recording session. Dynamic video stimuli of 16 novel human (8 male, 8 female) faces were presented for 10 seconds each at each session. Participants were instructed to view the images naturally.

For data analysis, video stimuli were converted into image frames, with 1 image frame captured at each 500 ms time segment, resulting in 20 image frames for each video clip. Areas of interest (AOIs) corresponding to the eyes, nose, and mouth were designated *a priori* and fixation data was mapped onto the images using EyeNal and FixPlot programs. Visual fixation time spent on the eyes, nose, and mouth regions for each second of video clip was extracted from the EyeNal data. 2 x 2 ANOVAs and paired sample *t*-tests were used to compare average visual fixation time for each AOI across drug conditions (propranolol and placebo) within each group (ASD and control). Simple linear regression models were used to evaluate relationships between ASD symptomatology, as measured by ADI-R subscale scores, and fixation time on AOIs.

Acknowledgements

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Effect of Propranolol vs. Placebo

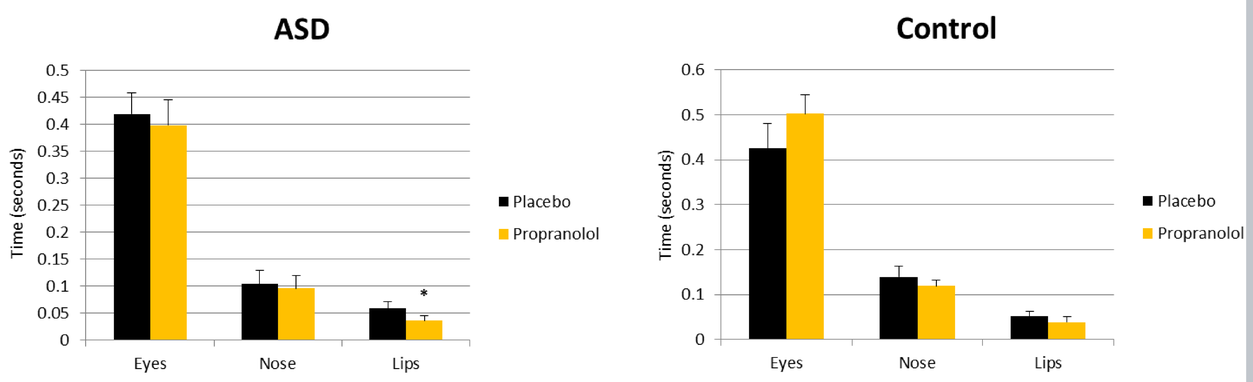

Figure 1. Average time spent fixating on each AOI per second of video segment for both ASD and control subjects. Bars represent S.E.M. * p < 0.05

Heart Rate and Blood Pressure

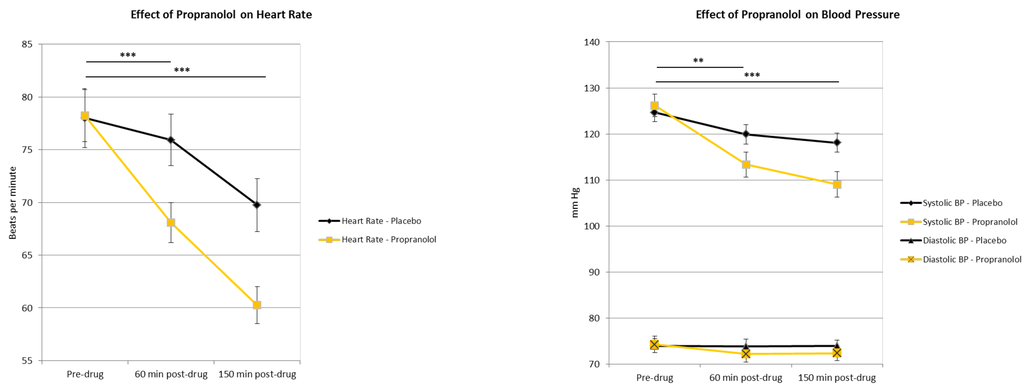

Figure 2. Effects of propranolol on both heart rate and blood pressure across all participants at 0, 60, and 150 minutes post-drug administration. Bars represent S.E.M. ** p < 0.01; *** p < 0.001

Mouth Fixation and Symptomatology

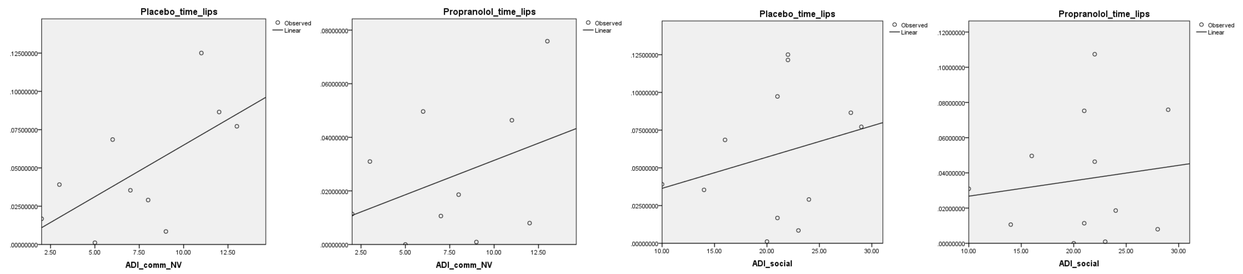

Figure 3. Linear regression models for time spent fixating on the lips in each drug condition and ADI-R non-verbal communication and social interaction subscale scores. $p < 0.05$ for time spent fixating on the lips in the placebo condition and non-verbal communication.

Results

- A significant main effect of drug was found in a 2 x 2 ANOVA for time spent fixating on the lip region ($F(1,22) = 7.410$, $p = 0.012$) with no drug x group interaction and no main effect of group.
- Paired *t*-tests revealed a significant decrease in the time the ASD participants spent fixating on the lip region in the propranolol condition, as compared to the placebo condition ($t(11) = 2.873$, $p = 0.015$).
- No significant differences were found between drug conditions for time spent on the eye or nose regions in the ASD group. Additionally, no significant differences were found between drug conditions for time spent on any of the AOI regions in the control group.
- As expected, propranolol led to significant decreases between baseline and the time of testing (60 minutes post-drug) in heart rate ($t(23) = 6.852$, $p = 0.001$) as well as systolic blood pressure ($t(23) = 7.108$, $p < 0.001$), across all participants.
- Linear regression models showed a positive relationship between ADI-R non-verbal communication scores and time spent fixating on the lips in the placebo condition ($\beta = 0.007$, $t(8) = 2.325$, $p = 0.049$), but not in the propranolol condition.

Conclusions

- These initial findings indicate a potential benefit from propranolol in reducing the time individuals with ASD spend looking at the mouth.
- A positive relationship between non-verbal communication deficits and time spent looking at the lips in the placebo condition further suggests mouth fixation as a target for pharmacological intervention.
- The older and high-functioning nature of the participants in the present study may have contributed to a lack of other facial processing abnormalities in the placebo condition, as behavioral therapy for ASD often emphasizes skills such as eye contact.
- Future studies with larger sample sizes are needed to further delineate the characteristics of facial processing in ASD and the effects of pharmacological intervention.

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