Emotion, Cognition, and the Serotonin 2A Receptor Gene

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Introduction

Cognition

- Cognitive control, or the ability to manage and regulate cognitive processes, is important to everyday life and life outcomes (Nower, et al., 2004)
- Antisaccade task measures cognitive control through the capacity to stop a reflexive response (Everling & Fisher, 1998)

Serotonin and Emotion

- Emotional cues can affect performance on cognitive tasks (West, et al., 2011; Kissler, & Keil, 2008) and cause increased activity in the amygdala and medial prefrontal cortex (Dolcos & McCarthy, 2006)
- Serotonin neurons project to brain areas involved in cognitive control such as the PFC and amygdala, which suggests that serotonin plays a role in cognitive control (Von dem hagan, 2010; Fisher, et al., 2009; Fisher, et al., 2011)

Genetics

- The rs6313 is a single nucleotide polymophism of the 5-HT2A receptor gene that affects the expression of 5-HT2A receptors. C allele homozygotes show lower levels of 5-HT2A receptor protein and mRNA (Polesskaya & Sokolov, 2002).
- C/C genotype of the rs6313 associated with poorer performance than the T/C or T/T on cognitive tasks (Vyas, 2012; Stoltenberg, et al., 2012)

Present Study

- This is the first study to examine rs6313 with the emotional antisaccade task
- **Hypothesis:** The rs6313 genotype will be associated with differences in antisaccadic response time in an emotional antisaccade task

Materials and Method

Participants

Undergraduate students (N=144) (64.3% female, 85.3% White) with a mean age of 20.23 years (SD=4.63)

Eye tracking

- Two blocks of 72 trials:
  - Instructional cue (red=look toward stimulus, green=look away from stimulus)
  - Emotional face (angry, happy, or neutral) from NimStim set of facial expressions (Tottenham, et al., 2009)
  - Target stimulus (black dot on either left or right side of screen)
  - Face present during presentation of target stimulus in no gap condition, absent before target in gap condition

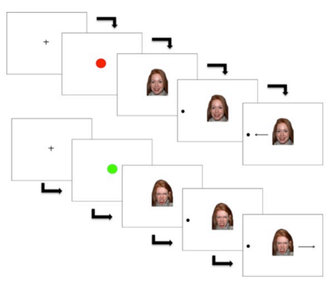

Figure 1: Example trials for prosaccade and antisaccade in gap condition.

Genotyping

- rs6313 SNP of the 5-HTR2A gene genotyped using a StepOnePlus Real-Time PCR system and Taqman SNP Genotyping Assay (Applied Biosystems, Foster City, CA.) Genotype found using ABI Sequence Detection Software v1.2.3 (Applied Biosystems)
- Components consisted of 5 uL mixture prepared using 20 ng DNA, 1X Taqman Master Mix and 2X Taqman primers/probes
- PCR cycling: denaturation at 95 °C for 10 minutes, 40 cycles of denaturing at 95°C for 15 seconds alternating with annealing/extension at 60 °C for one minute
- Gene frequencies in line with the HAPMAP CEU population (Allele frequencies: C=61%, T=39% and genotype frequencies: C/C=39%, C/T=44%, T/T=17%), and in Hardy Weinberg equilibrium ($\chi^2 = 0.71$, p>.05)

Results

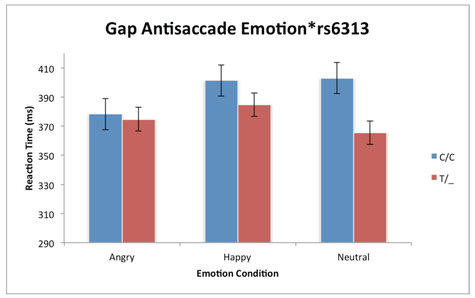

Figure 2: Mean Reaction Times of the Antisaccade in the Gap Condition +/- SE of groups defined by genotype. Significant interaction between emotion and genotype; C/C performs better in angry than happy or neutral. ("C/C" N = 44, "T/_" N = 78) (p=0.019)

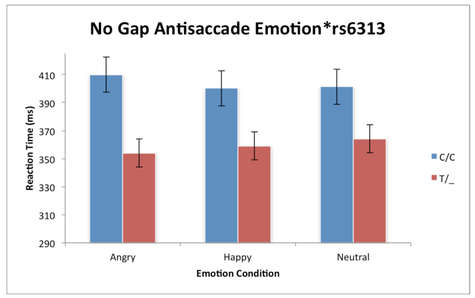

Figure 3: Mean Reaction Times of the Antisaccade in the No Gap Condition +/- SE of groups defined by genotype. Significant difference between genotypes in all emotional conditions; C/C shows slower reaction times. ("C/C" N = 44, "T/_" N = 75) (p=0.353)

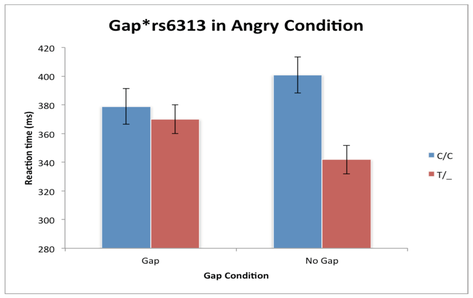

Figure 4: Mean Reaction Times of the Antisaccade in the Angry Condition +/- SE of groups defined by genotype. Significant difference between genotypes in no gap condition; no difference in gap condition. ("C/C" N = 45, "T/_" N = 79) (p=0.013)

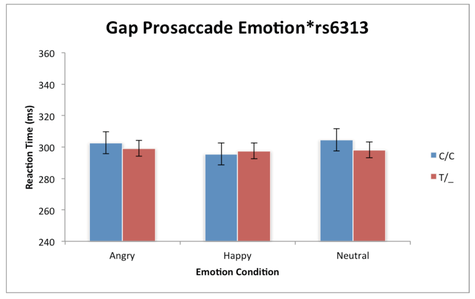

Figure 5: Mean Reaction Times of the Prosaccade in the Gap Condition +/- SE of groups defined by genotype. No significant difference between genotype in any emotional condition. ("C/C" N = 45, "T/_" N = 79) (p=0.594)

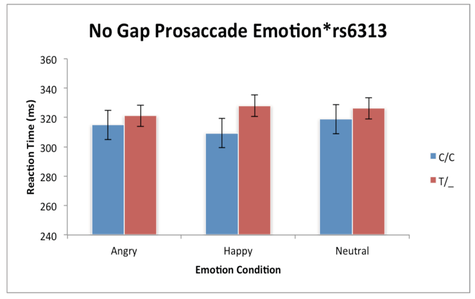

Figure 6: Mean Reaction Times of the Prosaccade in the No Gap Condition +/- SE of groups defined by genotype. No significant difference between genotype in any emotional condition. ("C/C" N = 44, "T/_" N = 78) (p=0.308)

Discussion

- Significantly better performance during the gap than the no gap of C homozygotes on the antisaccade in the angry condition
  - C homozygotes can better disengage from the negative emotional stimulus if the face is no longer present when the target stimulus appears
- C homozygotes perform worse overall than those with T/_ genotypes on antisaccade in gap and no gap
  - T/_ have better cognitive control than C homozygotes overall
- No significant difference between means in prosaccade
  - Emotion and genotype influence the executive functioning used during the antisaccade
  - Differences between conditions is not due to individual differences in overall speed of response, but differences in antisaccade are due to cognitive control
- Results from the gap versus no gap conditions suggest that behavioral treatment in learning to disengage from negative emotions could help C homozygotes who have problems dealing with emotional stressors.
- Differences in means between C/C and T/_ genotypes suggest that impulsivity medications that target the serotonin system could help to regulate the response to emotion that could be interfering with impulse control.
- Further analyses could be conducted to examine the possible influence of gender on antisaccadic reaction time, based on previous evidence of an interaction between the rs6313 and gender on the Barratt Impulsiveness Scale (Stoltenberg, et al., 2012).
- A similar study could be conducted utilizing functional magnetic imaging to examine whether response to different emotions stems from different areas, or varying levels of arousal in the same areas.

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