

Serotonin Transporter Gene Polymorphism,
Response Inhibition, Auditory Attention and
Emotional Variations: An investigation of the link
between behaviors and genotypic polymorphism.

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Serotonin levels appear to play a role in sensitivity to aversive outcomes

- ▶ The Serotonin transporter gene *SLC6A4* may relate to the evaluation of risk (Nomura et. al., 2015).
- ▶ Conway et. al., (2012) found that short allele carriers who showed a variation in the promoter region of 5-HTT LPR demonstrated increased probability of aggression in response to chronic stress.
- ▶ Kilpatrick et. al. (2015) found that, following exposure to an unpleasant visceral experience, healthy males with a serotonin transporter gene polymorphism showed differential levels of connectivity in emotional arousal centers

Serotonin levels correlate with impulsivity

- ▶ Polymorphisms in the serotonin-transporter gene may have a relationship to impulsivity in both rodents and humans (Bavilaqua & Goldman, 2013).
- ▶ Sonuga-Barke et. al. (2011) found that carriers of the 5-HTLPR s-allele were more averse to the delay of gratification.
- ▶ Men with the short S' allele of the 5-HTTLPR showed higher impulsivity levels on the CPT (Walderhaug, Herman, Magnusson, Morgan, & Landre, 2010).

Methods

	Reliability Coefficients	Validity Coefficients
Brief Test of Attention (Schretlen, 1989); Auditory Divided Attention	Alpha coefficient $r = .82-.91$ (Schretlen, Bobholz, Brandt, 1996)	Digit Span Backwards $r = .53$ Trails B: $r = -.55$ Stroop Color-word Naming: $r = .67$ No gender differences Education & Age do predict scores
Stroop Color-Word Test (Stroop, 1935; Jensen, 1965; Smith & Borg, 1964; Jensen & Rohwer, 1966)	Test-retest reliability for color-word task: $r = .71$ (Jensen, 1965)	Correlates with executive functioning, age, education (Elst, Boxtel, Brenkelen, Jolles, 2006)
Halstead-Reitan (1955) Trailmaking A & B	Test-tetest reliability: Trails A = .75; Trails B = .85 (Giovagnoli et. al, 1996)	Performance correlates with Raven's Progressive Matrices; Education & Age, but not gender
Barratt Impulsivity Scale (Patton & Barratt, 1995)	Internal consistency reliability = .79-.83	Scores correlate with measures of disinhibition & sensation-seeking, Differentiated clinical from control
Costello Anxiety and Depression Scale (Costello & Comrey, 1967)	Split Half reliability depression scale: .90; Anxiety scale; .70; Test-retest reliability .72 & .70	Correlates with Taylor Manifest Anxiety Scale; Depression scale of MMPI

Methods

- Buccal swabs were taken for the purposes of isolating genomic DNA (Küchler, et al., 2011).
- The DNA will be used to determine the 5-HTTLPR genotype of the study participants (McDougle, et al., 1998).
- Ss also completed the psych battery in a single sitting

Demographics (n =49)

Gender	Ethnicity	Religious Affiliation	Age	Sample
92% Female	12% Latino	99.6% Non-denominational Christian	Mean: 21 yrs	Undergraduate students at Christian University
8% Male	.4% Pacific Islander 87.6% Caucasian	.4% Baptist	Range: 19-32 yrs	Psychology and Health Science majors Offered extra credit in exchange for volunteering

Pearson Correlation Coefficients I

	Inattention	Motor Impulsivity	Low Self-Control	Low Cognitive Complexity	Low Perseverance	Cognitive Instability
Motor Impulsivity	0.30					
Low Self-Control	0.37	0.60				
Low Cog Complexity	0.27	0.21	0.30			
Low Perseverance	0.18	0.16	0.11	0.27		
Cognitive instability	-0.07	0.02	-0.14	-0.17	0.10	
Depression	0.22	0.05	0.29	-0.06	0.01	0.17
Anxiety	0.10	0.11	0.26	-0.07	0.11	0.35
Reading speed	0.03	0.25	0.17	-0.09	0.13	0.02
Color interference	0.05	0.09	0.00	-0.24	-0.07	-0.13
Errors Stroop	0.09	0.02	0.14	0.16	0.10	-0.08
Trail A speed	0.17	0.17	0.17	0.00	0.14	-0.07
Trail B (shifting)	0.10	0.27	0.12	0.06	-0.03	-0.12
BTA (auditory attn.)	-0.16	0.02	-0.08	-0.02	-0.17	-0.02

Pearson Correlation Coefficients II

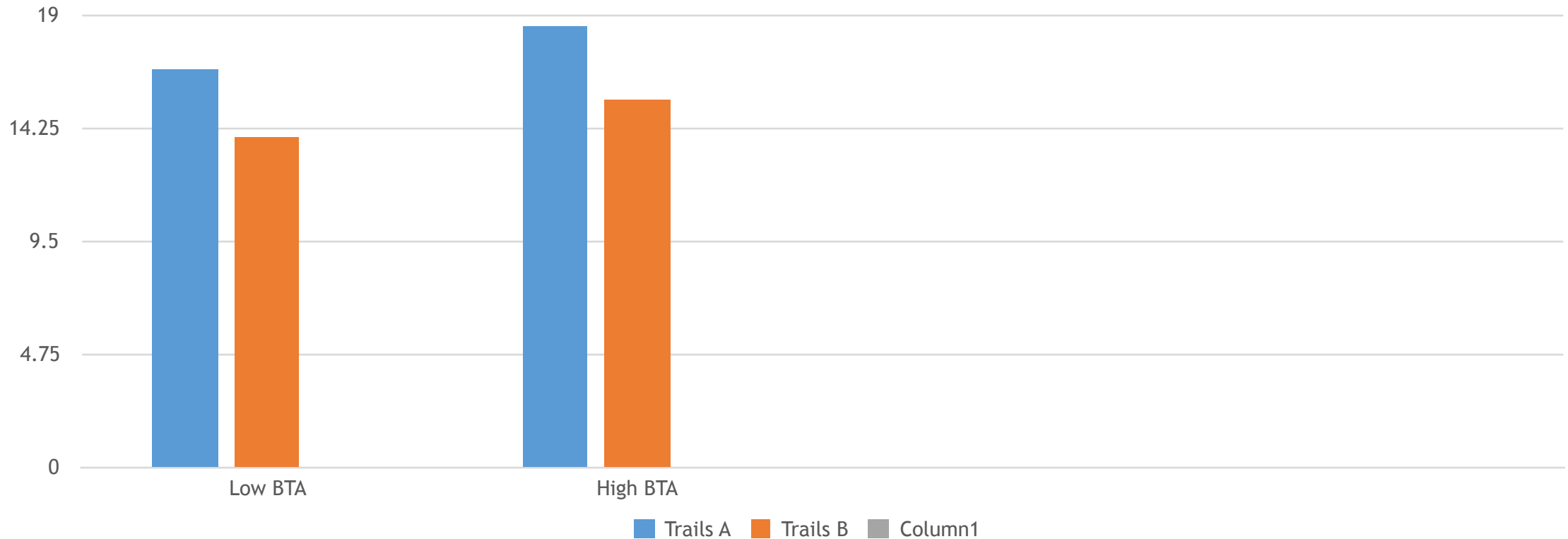
	Depression	Anxiety	Reading Speed	Color-word interference	Errors Stroop	Trail A: Sequencing	Trail B: Mental shifting
Anxiety	0.58						
Reading Speed	-0.01	0.10					
Color Interference	-0.08	0.01	0.65				
Errors Str	0.01	-0.21	-0.10	-0.16			
Trail A	0.06	-0.08	0.30	0.09	0.08		
Trail B	-0.10	-0.08	0.19	0.21	0.04	0.47	
BTA (Auditory attention)	-0.01	0.03	-0.01	0.06	-0.06	0.22	0.30

Two-Factor ANOVA with Replication: No Interaction Effect: Main Effect for A vs B



Two-Factor Anova with replication: Main effect for Trails A vs B; No interaction

Brief Test of Attention (Auditory Working Memory) scores by Trailmaking A and B (sequencing and mental shifting)



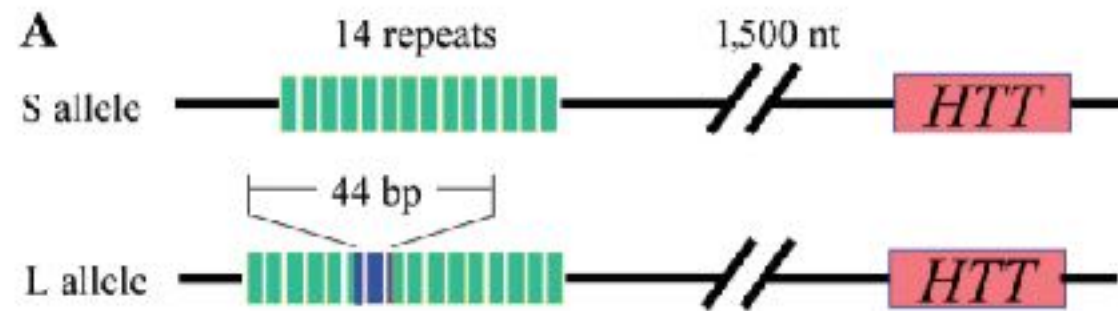
Future Directions and Limitations

- ▶ Enlarge sample size
- ▶ Recruit more male participants
- ▶ Seek more ethnic diversity in the sample
- ▶ Review training with interns re: administration methods; provide supervision
- ▶ Do a reliability and validity check on group administration methods for BTA, Stroop and Trails; Compare against traditional, individual administration via correlation
- ▶ Perhaps add a priming trial for affective induction
- ▶ Counterbalance scales to avoid order effects

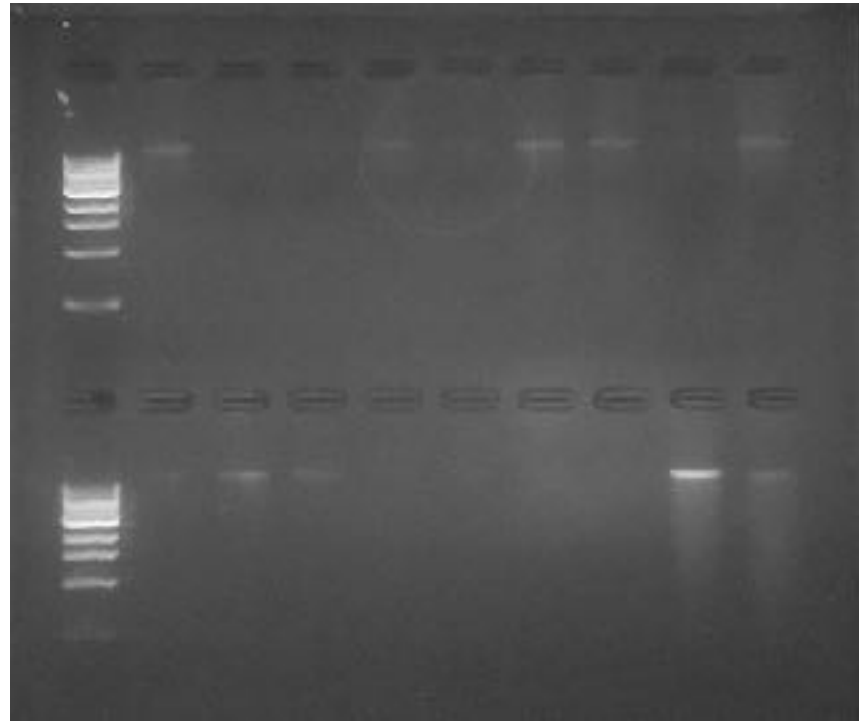
SLC6A4

- ▶ Serotonin Transporter protein
- ▶ Functions at synapses to regulate Serotonin Signaling
- ▶ Target of SSRI's including fluoxetine/Prozac
- ▶ Multiple Polymorphisms in humans.

5-HTTLPR Biallelic genotype



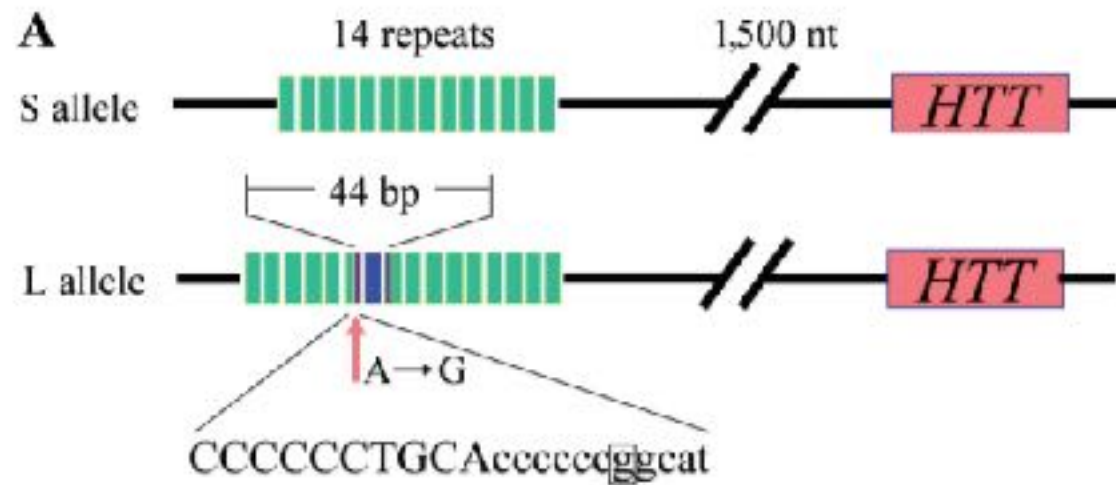
Genomic DNA Isolation



PCR Genotyping Feasibility



5-HTTLPR A/G Triallelic Genotype



SLC6A4 Expression by Genotype

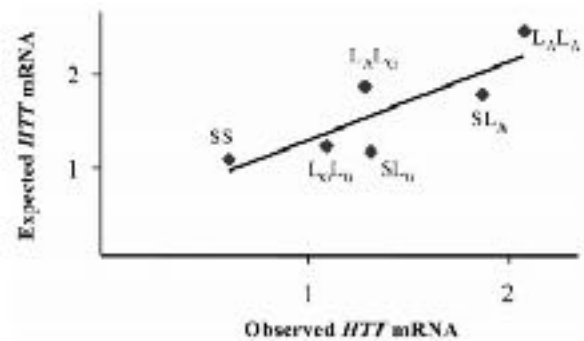


Figure 5 Codominance of *HTT* mRNA expression. The codominance of *HTT* mRNA expression normalized to 18S mRNA was observed in 62 lymphoblastoid cell lines representing the six *HTT*LPR genotypes. Expression values represent the means of 7–15 cell lines per genotype. Observed expression is plotted versus the expression expected on the basis of the codominant model and of computed allele-expression values 0.50 for S, 0.57 for L_{A1} and 1.16 for L_{S1} . For observed vs. expected, $r = 0.84$ and $P = .038$.

Future Directions

- ▶ Worthwhile and feasible with minor alterations:
 - ▶ Further Purification of gDNA prior to PCR?
 - ▶ Use of commercial Buccal Cell DNA Isolation kits?
 - ▶ Post-PCR digestion to determine A/G genotype?
 - ▶ Next Generation Sequencing for Genotyping?

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