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5-HTTLPR, DRD4 GENE, COLLEGE STUDENTS' PSYCHOLOGICAL CHARACTERS AND ACADEMIC PERFORMANCE.

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Abstract

The purpose of this study, “Genetic basis of Academic Performance,” is to evaluate associations between the 5-HTTLPR, the DRD4 gene, psychological characteristics including metacognition and depression, and academic performance as reflected in SAT scores. We discovered that participants with 2-repeat or 7-repeat alleles of the DRD4 gene have significantly lower scores on the Metacognition tests (P=0.022) and two subclades of metacognition, “Cognitive Self-Consciousness” (P=0.021) and “Need to Control Thoughts” (P=0.040), as compared to those without 2-repeat or 7-repeat alleles. 7-repeat allele DRD4 gene carriers have significantly higher scores for alcohol use disorders than those without the 7-repeat variant (P=0.018). People carrying the S/S variants of the 5-HTTLPR gene have significantly higher scores of the Metacognitions subclade, “Cognitive Confidence,” than those with S/L alleles (P=0.028). Many participants took the SAT more than once. We only used their highest scores. The highest SAT reading score of participants is negatively associated with their score on the metacognition test (p=0.046), specifically the metacognition subclades “Positive Beliefs about Worry” (P=0.030) and “Need to Control Thoughts” (P=0.020), The highest SAT math score is negatively associated with the score of the Metacognition test (P=0.029) and the Metacognition subclade “Need to Control Thoughts” (P=0.010). The highest SAT score is negatively associated with the Metacognition subclade “Need to Control Thoughts” (P=0.046) and weakly negatively associated with Metacognition (P=0.075).

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Chapter 1:
Introduction and Background

1.1 History of examinations

Academic performance is commonly measured procedural knowledge such as skills or declarative knowledge though examinations (Ward et al., 1996). The history of examinations can be traced back to ancient times; imperial examinations have been applied to Ancient China for more than 1000 years, to select candidates for the state bureaucracy. The main parts of Ancient Chinese imperial examinations are standardized written examinations (Ebrey 1996). Influenced by Ancient Chinese imperial examinations, England had adopted imperial examinations in 1806 to select specific candidates for positions in Her Majesty's Civil Service (*Chinese ideas in West* 1948). In United of Kingdom, the Northcote–Trevelyan Report of 1854 made four principal recommendations including that recruitment of civil servants should be on the basis of merit determined through standardized written examinations (Kazin et al., 2009).

The examination system for civil service was later applied to education. The industrial revolution led to an increasing complexity and specialization of jobs. In order to educate the general population to meet the minimal job demands, the modern education system was introduced in Europe and North America (Martin 2008). Individual careers became less predefined by social class background but depended more on demonstrated ability and skill (Von Stumm et al., 2011).

Only a small proportion of the population extended their education beyond elementary school prior to World War 1. College entrance examinations were not popular, and even Ivy League universities such as Harvard and Yale could admit all their applicants without requiring examinations at that time (Hubin 1989; Lehmann 2000). However, as more and more people sought higher education, universities and colleges had to select competitive students from among all the applicants, and, as a result, prior academic performance and college entrance examinations became the gatekeeper to higher education and a key to future employment (Chamorro-Premuzic & Furnham, 2010).

Nowadays, in most countries, students usually take standardized tests to apply for a position in a school of higher education. For example, in the US, secondary school students usually take the American College Testing (ACT) or Scholastic Assessment Test (SAT) to apply for a position in a University or college. Undergraduate students often take Graduate Record Examinations (GRE) to apply for graduate studies.

1.2 Factors affecting academic achievement

There are two main categories that can influence academic performance, cognitive factors and non-cognitive factors. Cognitive factors indicate a person's capabilities, such as intelligence, memory, attention, and reasoning, etc. (Hannon 2014). Non-cognitive factors include attitudes, behaviors, strategies, strategies as well as social-economic factors (Gutman & Schoon 2013; Heckman et al., 2006). I will discuss the cognitive factors first and then discuss non-cognitive factors.

1.2.1 Cognitive factors

Individual differences in academic performance have been linked to the variation of intelligence (von Stumm et al., 2011). Students with higher intelligence scores tend to achieve highly in academic settings. Also, many studies investigating associations between intelligence and academic performance have been undertaken. There is evidence supporting the idea that intelligence is highly associated with academic performance.

A study in India of 614 students from the 9th and 10th grades, showed that there was a significant influence of intelligence on academic performance (Board results of students from School) (Ritu & Sheikh, 2013). In a 3-year longitudinal study of students in Portugal, 284 middle school students' academic grades were collected by the end of 7th grade and 9th grade, and they were given intelligence tests (abstract, numerical, and verbal). One of the main findings showed that intelligence is the best predictor of final academic achievement of 9th graders (Soares et al., 2015). A 5-year prospective longitudinal study of 70,000+ English children analyzed the association between intelligence and national examinations in 25 academic subjects at age 16. That study revealed that General intelligence contributed to success on all 25 subjects (Deary et al., 2007). Also, a meta-analysis suggested that intelligence is the single most powerful predictor of academic performance after doing large-scale meta-analytic reviews of the database PsychINFO. PsychINFO is a world-class resource for abstracts and citations of behavioral and social science research (Von Stumm et al., 2011).

The relationship between Scholastic Assessment Test (SAT) scores and general intelligence was well established by two studies: one utilized 917 participants and the other one utilized 104 participants. The two studies indicated that the SAT test is mainly a test of general intelligence (Frey & Detterman, 2004).

However, how strongly intelligence can predict academic achievement remains a controversy. Intelligence is not a strong predictor in all fields of academic performance. For example, intelligence was a weaker predictor for grades of religious studies than it was for math and science for 786 high school students in Australia (Heaven & Ciarrochi, 2012). A study examining 256 Portuguese participants concluded that intelligence is only a weak predictor for the final evaluation of academic achievement. It only explained 0.8% of the variance, and tacit knowledge turned out to be a better predictor (Čavojová & Mikušková, 2015). Some regional studies were not able to find associations between intelligence and academic performance. For example, in a study of 153 Iranian undergraduate students in Malaysia, intelligence was shown not to be related to academic achievement (Naderi et al., 2010).

There is some evidence that some other cognitive factors such as memory, attention, and reasoning are associated with academic achievement. Memory affects all important aspects of learning. There is some evidence for the relationship between memory and academic performance. For example, a study of 98 children in the UK showed that children's working memory skills at five years of age were the best predictor of literacy and numeracy six years later (Alloway & Alloway, 2010). Another study showed that complex working memory scores are strongly linked to attainment levels in both mathematics and science, however, not linked to attainment levels in English (Gathercole et al., 2004).

Attention span is another important factor. A few studies indicated that attention span measured in preschool and the elementary school could predict academic performance at least one year later. However, the relationship of attention span and working memory

with academic achievement was significant positive in early childhood, but non-significant or negative in late years (Stipek & Valentino, 2015).

Few studies have been looking at the relationship between reasoning and academic achievement. There is evidence that reasoning abilities can predict academic achievement, as demonstrated by a study of 10th grade students in India (Bhat 2016).

1.2.2 Non-cognitive factors

Non-cognitive factors play as important a role in academic achievement as cognitive factors. "Attitudes, behaviors, and strategies" have significant effects on academic success according to a study of the University of London (Gutman & Schoon, 2013). Self-efficacy is also a predictor of academic performance. College students with high GPAs often present a high level of self-efficacy (Hannon 2014).

Students with high academic performance use intrinsic goals rather than extrinsic ones according to a study of the University of London (Gutman & Schoon, 2013). Furthermore, students with higher academic performance are motivated to improve upon their previous or upcoming performance than the others with lower motivation (Friedman & Mandel, 2011). Some other factors may affect students' motivation; bad dietary habits may cause a lack of motivation to study (Downes 2015). However, the hypothesis that intrinsically motivated students would perform better than extrinsically motivated students in academia was rejected by a study including 199 undergraduates (Lumanisa 2015).

Self-control is the concept similar to self-discipline and self-regulation. Baumeister et al., (2007) defined self-control as "the capacity for altering one's responses. Having a high

locus of control (internal locus of control) has been found to be a predictor of high collegiate GPA, and having a high locus of control means that an individual attributes success to personal decision making and positive behaviors according to a study of 348 students in the US (Hannon 2014). A high or internal locus of control means the individual believes their own actions control the outcomes. A low or external locus of control blames outside events for outcomes.

There is a negative association between MAI (Metacognitive Awareness Inventory) and academic performance (Sperling et al., 2004). Metacognition is "thinking about thinking", students with good metacognition tend to have good academic performance (Coutinho 2007). In addition, depression and anxiety are associated with lower academic performance (Owens 2012).

Alcohol-use behavior is negatively associated with academic performance. Semester academic performance was found to be negatively associated with alcohol use (Thombs et al., 2009).

Participation in school-based extracurricular activities is positively associated with academic performance (Abruzzo et al., 2016). For example, an educational longitudinal study in 2002 in the US concluded that intensity of participation in extracurricular activities in 10th grade predicted math scores, graduate grade point average and educational progress (ie…, how far in school do you think you will get?) (Fredricks 2012). However, even when a link between participation of extracurricular activities and academic performance was established, the practice behind this relationship has not always been clear. Many unrelated factors such as civic engagement, identity development, positive social relationships, and behaviors may affect this relationship

(Mahoney et al., 2005). For example, socio-economic status has been found to be associated with extracurricular activities (Covay & Carbonaro, 2010).

1.2.3 Family socio-eco backgrounds

We should never ignore links between family socio-economic background and academic performance. Students from rich families are more likely to enter top universities than poor families. According to the Harvard Crimson, approximately 45.6 percent of Harvard undergraduates come from the top 3.8 percent of American households in income (Lanning 2012), only about 4% come from the bottom quintile. The median family income of Yale's students is $192,600, and 45% of Yale's students come from top 5% of families in income, only 2.1% them come from poor families (Chetty et al., 2017).

A meta-analysis reviewed literature between 1990 and 2000 including 101,157 students, 6,871 schools, and 128 school districts in the US, and it showed students from higher social economic level families tended to have the higher academic achievement (Sirin 2005). Also, the positive relationship between socio-economic status and academic achievement varies with age. This relationship remains fairly stable from ages 7 to 11 years and increases from the age of 11 to the age of 15 years in Canada (Caro 2009).

Some studies suggest socio-economic status of students reflect their parents' education levels, which can influence students' academic performance through environments and educational investments. Students from highly educated parents tend to have more stimulating learning environments (Magnuson 2007). A study indicated that the relationship quality with parents would influence academic self-efficacy among

adolescent-aged children, which in turn affected their academic performance (Yuin & Yaacob, 2016).

1.2.4 Racial achievement gap

Racial achievement gap infers that there are educational disparities between races. The racial academic achievement gap remains over the past half-century in the United States. Blacks and Hispanics are more likely to receive lower grades on standardized tests than Whites and Asians (Ansell 2011). There is some evidence that racial group differences across admissions tests, such as SAT, ACT, GRE, GMAT, MCAT, and LSAT have been fairly consistent. Since the 1960s, students taking these assessments have become increasingly diverse in racial groups, and the examination of ethnic score differences have been more rigorous (Camara & Schmidt, 1999).

Until the end of 20 century, the largest gaps still exist between white and African American students in the US. On average, African American students performed lower than White students in composite scores (Hedges & Nowell, 1998). On average, Asian Americans performed lower in SAT verbal section and higher in the GRE quantitative test than White students (Camara & Schmidt, 1999). From 2007 to 2008, the achievement gap stayed the same for the majority of states (Vanneman et al., 2009).

1.3 Genetics and academic achievement

1.3.1 Heritability of academic performance

Heritability is used to estimate the degree of variation in a phenotypic trait in a population that is due to genetic variation between individuals in that population (Wray & Visscher, 2008). This concept can also be alternatively expressed in the following

question: “What is the proportion of the variation in a given trait within a population that is not explained by the environment or random chance?” (Gazzaniga et al., 2010).

Many studies about the heritability of academic performance have been undertaken. There is some evidence supporting the idea that academic performance is relatively highly heritable.

A nation-wide twin study in Great Britain including twins born in English and Wales between 1994 and 1996, Children with medical problems, uncertain or unknown zygosity and those whose first language was not English were excluded. After exclusions, the total number of participations for whom General Certificate of Secondary Education (GCSE) data were obtained at age 16 was 11,117. There were 2,008 pairs of monozygotic (MZ) twins, 1,730 pairs of same-sex dizygotic (DZ) twins, and 1,736 pairs of opposite-sex DZ twins. This study found that individual differences in educational achievement are highly heritable. Heritability was substantial for the overall GCSE performance for core subjects (58%) and subfields: English (52%), mathematics (55%) and Science (58%) (Shakeshaft et al., 2013).

In addition to the UK study above which showed high heritability, some other studies had similar conclusions. For example, Twin studies in Australia, the US and Scandinavia have discovered high heritability (77%) for reading at age 8 (Byrne et al., 2009; 615 pairs) and in the US at age 10 (Olson et al., 2011; 489 pairs). A twin study of 12- year-old Dutch children showed a heritability of 60% for a national test of educational achievement (Bartels et al., 2002; 691 pairs).

Genetics influences choice of subjects of students' study as well as their performance. In the UK, after completing compulsory education at age 16, students can choose to continue to study for two years (A-levels) and can chose from different courses to prepare to apply for university training. A study using a representative sample of UK twin pairs (6584) concluded that heritability estimates 44% for the choice of A-level and 52%-80 for the choice of subject (Rimfeld et al., 2016).

1.3.2 Genetic markers

Since we know academic achievement is relatively heritable, a question asked is what genetic markers affect academic achievement? One study indicated that DAT1, DRD2, and DRD4 had been linked to behaviors such as attention regulation, motivation, violence, and cognitive skills. Students who carried particular versions of the three genes were more likely to finish high school and go to college than those who possessed other forms of genes (Beaver et al., 2012).

Recently, some genome-wide association studies have detailed how specific genetic variants have been associated with academic performance. Genome-wide association study is a study of the genome-wide set of genetic variants to discover if any variant is associated with one or more traits (Bush & Moore, 2012).

A recent genome-wide association study (GWAS), which included 101,069 discovery phase samples and 25,490 replication phase samples, identified one genome-wide significant locus (rs9320913, $p = 4.2 \times 10{-}9$) for Edu years (an individual's years of schooling) and two genome-wide significant loci (rs11584700, $p = 2.1 \times 10{-}9$, and

rs4851266, p= 2.2 × 10−9) for college completion. Also, A linear polygenic score accounts for about 2% of

the variance in Edu Years according to all measured SNPs (Rietveld et al., 2013). In another study, a genome-wide polygenic score for education years accounts for up to 5% of the variance in reading performance at age 14 in the UK (Selzam et al., 2017).

1.3.3 Two markers in this study

The purpose of this study, the genetic basis of academic performance, is to learn the genetic mechanisms and psychological characteristics that may influence academic performance levels of college students (such as SAT, ACT, GRE, GMAT and GPA). It is believed that knowledge obtained by this study will improve our understanding of how genetic variation affects academic performance and psychological health. Better understanding the genetic basis of academic performance will help us to develop future tests or drugs that could improve such performance.

The two genetic markers analyzed in the project "Genetic basis of Academic Performance" are 5-HTTLPR and DRDR, both of them have been investigated as candidate genes for modulating a number of approach-related behaviors. I will talk about 5-HTTLPR first and DRD4 second.

The 5-HTTLPR (Serotonin-transporter-linked polymorphic region) is found on chromosome 17 at 17q11.1-17q12 (Ramamoorthy et al., 1993). It contains a 43 bp insertion/deletion polymorphism in the 5' regulatory region of the gene (Heils et al., 1996). The gene codes for the serotonin transporter which is an important neurotransmitter. The ins/del has been associated with variations in transcriptional

activity of serotonin, long allele results in higher serotonin transporter mRNA transcription than short allele (Praschak-Rieder et al., 2007).

The short(S) alleles of 5-HTTLPR have been thought to be related to neuropsychiatric disorders. For examples, A study has indicated that individuals with one to two S alleles expressed more depressive symptoms and suicidality in relation to stressful life events than individuals with two L alleles (Caspi et al., 2003). A meta-analysis concluded that the S allele is associated with an increased risk of developing depression under stress (Karg et al., 2011). However, a 2017 meta-analysis including 31 data sets containing 38,802 European ancestry subjects denied such an association (Culverhouse et al., 2018). A study in China indicated that students carrying two S alleles of 5-HTTLPR is associated with anxiety, however, that association has not been found in female students (Chang et al., 2017).

Some studies indicated that the 5-HTTLPR gene is associated with insomnia. For example, a study in France including 157 patients suffering from insomnia and 827 healthy controls, it found that the short (s-) allele of the 5-HTTLPR was significantly more frequent in patients suffering from insomnia than healthy controls (Deuschle et al., 2010).

5-HTTLPR maybe associated with personality traits. S-allele carriers tend to have slightly higher neuroticism score with the NEO PI-R personality questionnaire on average (Lesch et al., 1996). However, some other studies failed to find this association (Flory et al., 1999).

The 5-HTTLPR gene has been involved in gene-culture coevolutionary studies. Results of a study undertaken by Northwestern University suggested evidence for gene-culture coevolution with the 5-HLLPLR gene. According to their study, which included individuals across 29 nations, increased frequency of S allele carriers predicted decreased anxiety and mood disorder prevalence because of increased collectivistic cultural values. Membership or participation in larger family or societal groups seems to mediate or reduce anxiety and mood disorder. This conclusion seems to be in opposition of some studies indicating S allele carriers tended to have mood disorders. This gene-culture coevolutionary study indicated that collectivism buffers genetically susceptible populations from increased prevalence of affective disorders (Chiao & Blizinsky, 2010).

The 5-HTTLPR gene may play a role in intelligence. For example, one small study showed higher intelligence scores being observed in individuals with two S alleles versus other allele combinations (Volf et al., 2015).

The dopamine receptor D4 is a dopamine D2-like G protein-coupled receptor encoded by the DRD4 gene on chromosome 11 at position 11p15.5 (Van Tol et al., 1991). Like the 5-HTTLPR gene, the DRD4 gene is linked to many psychiatric conditions as well.

The DRD4 gene varies between 2 and 11 repeats of a 48-bp coding region. Worldwide, more than 90% of people carry variants with 2, 4 and/or 7 repeats (Wang et al., 2004). We observed the same in this study, with 2,4, and 7 repeats being the most common.

Biomedical analyses of DRD4 protein have been conducted, the 7-repeat and the 2-repeat tend to react less effectively to dopamine molecules (Wang et al., 2004). DRD4 7R and 2R proteins have blunted responses for cAMP reduction and requiring increase in

dopamine concentration for reductions comparable to the 4R protein. The blunted response of the 7R allele is stronger than the 2R allele, the 2R allele is the midway between 7R and 4R alleles (Wang et al., 2004).

The 7-repeat (7R) variant of DRD4 (DRD4 7-repeat polymorphism) has been linked to a susceptibility for some psychological disorders such as Attention Deficit Hyperactivity Disorder (ADHD) (Wu et al., 2012), alcoholism (Laucht et al., 2007), behavioral disinhibition (Congdon et al., 2008), and pathological gambling (De Castro Pérez et al., 1997). In addition, individuals with 7 or more repeats tend to have sensation-seeking behaviors, including both migration and novelty-seeking (Chen et al., 1999 & Ding et al., 2002). In addition to the 7-repeat allele of DRD4 gene, long alleles (7 or more repeats) are considered to be associated with ADHD with impaired executive attention (Gorlick et al., 2015). According to some studies, the 2-repeat variant has been associated with some psychological disorders (for example ADHD), similar to the 7-repeat variant (Comings et al., 1999). It should be noted that a recent study at the Chinese University of Hongkong found an increased prevalence of the 2-repeat variant among Chinese ADHD children (Leung et al., 2017). However, such associations between DRD4 alleles and psychological disorders (such as ADHD, novelty-seeking and alcohol use) have not always been consistently replicated (Kluger et al., 2002; Paterson et al., 1999). The frequency of DRD4 alleles varies between populations, for example, the 7R allele is more frequent in America than in Asia (Wang et al., 2004). A question has been put forward that since the 7R allele could bring negative emotional consequences, how it had been maintained in the population. Is it somehow being selected for in nature? The 7R allele has been under selection for about 40000 years (Wang et al., 2004). Frequency of the 7R

alleles is higher in nomadic populations than sedentary ones (Chen et al., 1999). According to another study, nomadic Ariaal men with 7R alleles had higher health status than others with other variants, however, sedentary (non-nomadic) Ariaal men with the 7R allele seemed to have lower health status (Eisenberg et al., 2008). As we mentioned before, the DRDR 7R allele is associated with ADHD. However, ADHD is assumed to be an evolutionarily successful behavioral for hunter-gathers or nomadic people. To adapt successfully, individuals must constantly explore the environment for threats and opportunities to adapt successfully, thus, hyperactivity may be useful for some people (Jensen et al., 1997). However, the role of DRD4 gene is much more complex, as it plays a role in intelligence. According to a study in University of Toronto, externalizing behavior (such as ADHD and aggression) was negatively correlated with IQ for participants without the 7-repeat allele. But externalizing behavior and IQ were uncorrelated for 7-allele carriers (DeYoung et al., 2006).

The purpose of the current study is to figure out associations between genetic markers (alleles of the 5-HTTLPR, and DRD4 genes), psychological characters including attention, depression, metacognition, alcohol behavior, procrastination and friendship, and academic performance (SAT, ACT, GRE, GMAT and GPA). The hypothesis is that the 5-HTTLPR and DRD4 genes will be associated with scores of psychological tests of subjects, and these two markers are likely associated with academic performance.

We believe knowledge obtained by this study will improve our understanding of how genetic variation affects academic performance and psychological health. Better understanding the genetic basis of academic performance will help us to develop future tests, drugs or strategies that could improve such performance.

Chapter 2:
Methodology

2.1 Participants

The project "Genetic Basis of Academic Performance" was approved by the Human Subjects Research Review Committee at Binghamton University in May 2017 (IRB Protocol # 4063-17). Participants were recruited for the project at Binghamton University and SUNY Broome Community College. The event was advertised via campus flyers and B-line (an email system at Binghamton University). Each participant was given $5 for participating in this study. All participants were healthy adults (≥18) and were given a written informed-consent document, which they signed, indicating they understood what the project would entail and what (if any) risks they would exposed to by participating in the project.

2.2 Surveys

Participants have been asked to submit academic records from their higher education studies, including SAT or ACT for undergraduate students, GRE or GMAT for graduate students, as well as their Grade Point Average (GPA) in college. The unofficial or official transcripts showing their GPAs were downloaded, screenshotted or photographed from the School website and the SAT/ACT, GRE/GMAT scores were downloaded,

screenshotted or photographed from the appropriate official website. Most Participants have completed some questionnaires including MCQ-30, Beck Depression Inventory II, the alcohol use disorders identification test: Interview version and Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist.

(Part A), Procrastination Scale (Lay, 1986), a very short friendship questionnaire and a demographic questionnaire (e.g., race/ethnicity, gender, religion and parents' occupation). I will explain each of the Psychological tests below:

2.2.1 MCQ-30

Metacognition, or "thinking about thinking", refers to psychological structures, events and knowledge that are involved in the interpretation of thinking itself (Wells & Cartwright-Hatton, 2004). The Metacognitions Questionnaire (MCQ) is a scale measuring an individual's different dimensions of metacognitive beliefs. It was first developed by Sam Cartwright-Hatton and Adrian Wells (1997), and consists of 65 items following the conceptual analysis offered by the Self-Regulatory Executive Function model (the metacognitive model and theory of psychological disorder). It consists of 5-subscales, and the Alpha reliabilities for them range from 0.72 to 0.89. Metacognitive characters measured by the MCQ are positively associated with depression, obsessive-compulsive symptoms and text-anxiety, etc… (Wells & Cartwright-Hatton, 2004).

The Metacognitions Questionnaire 30 is a 30-item version of the MCQ consisting of the five-factor structure: 1) positive beliefs about worry (e.g., "Worrying helps me cope"); 2) negative beliefs about the controllability of thoughts and corresponding danger worry (e.g., "My worrying is dangerous for me"); 3) cognitive confidence (e.g., "I have a poor

memory"); 4) negative beliefs about thoughts in general/need to control thoughts (e.g., "(e.g., "My worrying could make me go mad"); and 5) cognitive self-consciousness (e.g., "I am constantly aware of my thinking"). Participants are asked to complete a four-point scale ranging from 1 (do not agree) to 4 (agree very much). The questionnaire showed good convergent validity and internal consistency (Alpha scores ranged from 0.72 to 0.93), and acceptable to good test–retest reliability (Wells & Cartwright-Hatton, 2004).

2.2.2 Beck Depression Inventory II

Beck Depression Inventory (BDI) was developed by Aaron T. Beck and is a 21-question multiple-choice self-report inventory for measuring the severity of depression. The original version, BDI, first published in 1961 (Beck et al., 1961) and was revised in 1996 as Beck Depression Inventory II(BDI-II) (Beck et al., 1996). BDI-II has a high one-week test–retest reliability (Pearson r =0.93) (Beck et al., 1996) and a high internal consistency (α=.91) (Beck et al., 1996).

2.2.3 The alcohol use disorders identification test: Interview version

The Alcohol Use Disorders Identification Test (AUDIT) is a ten-question test created by the World Health Organization. Several Studies have discovered that AUDIT is a valid tool to identify alcohol abuse problem behaviors. (Donovan et al., 2006).

2.2.4 Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist: Part A

The Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist is a questionnaire used in the diagnosis of adult ADHD, it has 18 questions in two parts: Part A and Part B. Part A has 6 questions. If four or more marks appear in the darkly shaded boxes in Part

A, then the patient has symptoms highly consistent with ADHD. The scale has proven to be a valid and useful tool for diagnosis of adult ADHD with both high internal consistency and high concurrent validity (Adler et al., 2006).

2.2.5 Procrastination Scale

The procrastination scale we used was authored by Lay (1986). It is self-reported five point Likert scale (Extremely uncharacteristic= 1, moderately uncharacteristic= 2, Neutral=3, Moderately uncharacteristic =4 and Extremely uncharacteristic= 5). It consists 20 questions, 10 of them are reversed-keyed items. The scale has high reliability (Saleem and Rafique 2012).

2.2.6 Friendship questionnaire

We asked all participants to complete a friendship questionnaire as follows: it is that 'how many close friends/confidants do you have?' with options being: 'none', '1 or 2 friends', '3 to 5 friends', '6 to 9 friends', '10 or more friends' (Ebstein et al., 2015).

In addition, participants have been asked a demographic questionnaire including race/ethnicity, gender, religion and parents' occupation.

2.3 Lab work

DNA samples were collected by cheekswab, which is a non-invasive sample collection that has no known risk for adults. The Lab work had been undertaken in Dr. Merriwether's Molecular Anthropology DNA Lab in SUNY Binghamton. Sample collection, DNA extraction, PCR, DNA quantification, DNA analysis through gel electrophoresis had been all ongoing. DNA extractions were done using QIAamp DNA

Mini Kits following manufacturer's instructions. The two genetic markers I have analyzed are 5-HTTLPR and DRD4, the 43bp insertion/deletion polymorphism of 5-HTTLPR and variable number tandem repeat (VNTR) polymorphisms have been identified through gel electrophoresis.

Polymerase chain reaction (PCR)-amplification of the 5-HTTLPR was carried out with the primers, Forward: 5'- ATG CCA GCA CCT AAC CCC TAA TGT - 3', Reverse: 5'- GGA CCG CAA GGT GGG CGG GA - 3' (Gelernter et al., 1999), each PCR was in a total volume of 25 µl solution containing 5 µl genomic DNA, 2.50 µl 10x PCR Buffer, 12.88 distilled (DI) water, 0.50 µl 10mM dNTP, 1.25 µl each of the forward and reverse primers, 1.50 µl 25mM $MgSO_4$ and 0.13 µl Platinum Taq polymerase (Invitrogen). The thermo cycles was taken as follows: 95˚C for 15 minutes, 35 cycles (95°C for 1 minute, 65°C for 1 minute, 72°C for 1 minute), 72 ˚C for 4 minutes, and 4 ˚C~.

Polymerase chain reaction (PCR)-amplification of the DRD4 gene was carried out with the primers, DRD4: 5′ GCG ACT ACG TGG TCT ACT CG 3′, 5′AGG ACC CTC ATG GCC TTG 3′(Dreber et al., 2009). Each 2 µl template DNA was mixed with 8 µl solution of master mix containing 2.0 µl 10X PCR Buffer, 6.9 µl dH_20, 2.0 µl dITP/dNTPs, 1 µl 25mM Mg_2SO_4 , 4 µl Q solution, 0.10 platinum Taq, and 1.0 µl for each Forward and Reverse primer. The thermo cycles was taken as follows: 95˚C for 15 minutes, 40 cycles (95°C for 1 minute, 56°C for 1 minute, 72°C for 1.5 minutes), 72 ˚C for 10 minutes, and 4 ˚C~.

Both markers have been identified through gel electrophoresis through 2% agarose gels stained with ethidium bromide.

2.5 Statistical analysis

We used One-Way analysis of Variance (One-Way ANOVA) and One-Way Multivariate analysis of Variance (One-Way MANOVA) to evaluate the relationships between the 5-HTTLPR and DRD4 genes with the psychological characteristics we measured. Post-hoc t-tests were adjusted for multiple comparisons using the Bonferroni method. The associations between Psychological characteristics and Academic performances were determined using Pearson Product-Moment Correlation Coefficients (The Pearson Correlation Coefficient). Statistical significance was set at $p<.05$. The statistical analysis was conducted using IBM SPSS Statistics 22.0.

Chapter 3

Results

3.1 With and without 2-repeat and 7-repeat alleles of the DRD4 gene

We use the same abbreviations for metacognitions in this paper throughout: MetaCC: MCQ-30 subclade “Cognitive confidence”. MetaPB: MCQ-30 subclade “Positive beliefs about worry”. MetaCS: MCQ-30 subclade “Cognitive self-consciousness”. MetaNB: MCQ-30 subclade “Negative beliefs about the controllability of thoughts and corresponding danger worry”. MetaNC: MCQ-30 subclade “Negative beliefs about thoughts in general/need to control thoughts”.

91 participants have the data of DRD4 gene and completed MCQ-30. Table 1 shows the DRD4 VNTR polymorphisms of these 91 participants, the different combinations of alleles (One allele from father and another one from mother) of participants.

Table 1: Genetic variants of the participants

DRD4 Allele frequencies. Total number is 91.

DRD4 VNTR	2R/2R	2R/3R	2R/4R	3R/4R	4R/4R	4R/7R	3R/3R	7R/7R
Numbers Of Participants	6	1	10	4	48	18	2	2

We divided DRD4 VNTR polymorphism into two groups as the table 2 shows,

Participants without 2-Repeat and 7-Repeat alleles are grouped into group 1 (these are 3-repeat or 4-repeat carriers).

Each participant in Group 2 carries either or both of 2-Repeat alleles and 7-Repeat alleles. We chose this grouping because 2-Repeat alleles and 7-Repeat alleles have blunted responses for cAMP reduction (Wang et al. 2004), and these two variants have been found to be associated with psychological disorders like ADHD (Wu et al., 2012).

Table 2: Descriptive Statistics: With and without 2-repeat and 7-repeat alleles of the DRD4 gene
DRD4 Descriptive Statistics. 1:00: Group 1, Group without 2-repeat and 7-repeat alleles. DRD4 2:00: Group 2, Group with either of 2-repeat and 7-repeat alleles, or both.

	DRD4	Mean	Std. Deviation	N
MCQ-30	1.00	61.8704	13.11638	54
	2.00	55.5405	12.07061	37
	Total	59.2967	13.01409	91
MetaCC	1.00	10.4815	4.16971	54
	2.00	9.9189	3.56977	37
	Total	10.2527	3.92596	91
MetaPB	1.00	12.1481	4.53251	54
	2.00	10.6757	4.10321	37
	Total	11.5495	4.40016	91
MetaCS	1.00	17.0370	4.42959	54
	2.00	14.9459	3.79287	37
	Total	16.1868	4.28670	91
MetaNB	1.00	10.8889	3.89323	54
	2.00	10.0541	4.06848	37
	Total	10.5495	3.96446	91
MetaNC	1.00	11.3704	3.39976	54
	2.00	9.9459	2.88623	37
	Total	10.7912	3.26094	91

As Table 3 “Pairwise Comparisons” shows, after One-Way Multivariate Analysis of

Variance (One-Way MANOVA) with Bonferroni adjustment, we discovered participants without 2-Repeat and 7-Repeat alleles (Group 1) have significantly higher overall scores in MCQ-30 than those with 2-Repeat or 7-Repeat alleles or both alleles (Group 2), The standard error is 2.711 and P =0.022. For the MCQ-30 subclade "cognitive self-consciousness", Group 1 has significant higher score than Group 2, the standard error=0.893, P=0.021. And for the MCQ-30 subclade "Negative beliefs about thoughts in general/need to control thoughts", Group 1 has significantly higher scores than Group 2, with a standard error=0.683, P=0.040. The DRD4 gene is not significantly associated with other Metacognitions subclades.

Table 3: Pairwise Comparisons: With and without 2-repeat and 7-repeat alleles of the DRD4 gene
DRD4 1.00/Group 1: Group without 2-repeat and 7-repeat DRD4exon III 48-bp VNTR Polymorphism.
DRD4 2.00/Group 2: Group with 2-repeat or 7-repeat.

Dependent Variable	(I) DRD4	(J) DRD4	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
MCQ-30	1.00	2.00	6.330*	2.711	.022	.943	11.717
	2.00	1.00	-6.330*	2.711	.022	-11.717	-.943
MetaCC	1.00	2.00	.563	.840	.505	-1.107	2.232
	2.00	1.00	-.563	.840	.505	-2.232	1.107
MetaPB	1.00	2.00	1.472	.931	.117	-.378	3.323
	2.00	1.00	-1.472	.931	.117	-3.323	.378
MetaCS	1.00	2.00	2.091*	.893	.021	.317	3.865
	2.00	1.00	-2.091*	.893	.021	-3.865	-.317
MetaNB	1.00	2.00	.835	.846	.327	-.847	2.516
	2.00	1.00	-.835	.846	.327	-2.516	.847
MetaNC	1.00	2.00	1.424*	.683	.040	.067	2.782
	2.00	1.00	-1.424*	.683	.040	-2.782	-.067

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni

3.2 4R/4R, 2-repeat and 7-repeat alleles of the DRD4 gene

Since the 4-repeat allele is associated with some psychological characters, for example, carriers have been reported to have higher GPA reward dependence (RD) than non-carriers (Ham et al., 2006). And 4R/4R carriers had higher internet addictions than those with either or both of 2-repeat and 3-repeat alleles (Sun et al., 2016). In order to test whether having 4R/4R is associated with Metacognition, we grouped 4R/4R carriers in one group, and other participants with either or both of 2-Repeat and 7-Repeat alleles are grouped into group 2, same with group 2 in table 3.

As Table 4 and Table 5 show, after One-Way MANOVA with Bonferroni adjustment, we discovered participants without 4R/4R alleles (4-repeat homozygous) (Group 1) have higher overall scores in the MCQ-30 than those with 2-Repeat or 7-Repeat alleles or both alleles (Group 2), the association is not statistically significant, but is close to significance, standard error is 2.740 and p=0.078. For the MetaCS, Group 1 has significant higher score than Group 2, the standard error=0.920, P=0.039. And for the MetaNC, Group 1 has higher score than Group 2 but not statistical significant, the standard error=0.686, P=0.084.

Table 4: Descriptive Statistics: 4R/4R, 2-repeat and 7 repeat alleles of the DRD4 gene

DRD4 1:00: Group 1. DRD4 2:00: Group 2.

	DRD4	Mean	Std. Deviation	N
MCQ-30	1.00	60.4375	12.86411	48
	2.00	58.0233	13.21343	43
	Total	59.2967	13.01409	91
MetaCC	1.00	10.1875	3.89028	48
	2.00	10.3256	4.01023	43
	Total	10.2527	3.92596	91
MetaPB	1.00	11.7500	4.16418	48
	2.00	11.3256	4.68900	43
	Total	11.5495	4.40016	91
MetaCS	1.00	16.8750	4.49409	48
	2.00	15.4186	3.95349	43
	Total	16.1868	4.28670	91

Continued Table 4

MetaNC	1.00	11.1458	3.31335	48
	2.00	10.3953	3.19329	43
	Total	10.7912	3.26094	91

Table 5: Pairwise comparisons: 4R/4R, 2-repeat and 7 repeat alleles of the DRD4 gene

DRD4 1:00: Group 1. DRD4 2:00: Group 2.

Dependent Variable	(I) DRD44	(J) DRD4	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
MCQ-30	1.00	2.00	4.897	2.740	.078	-.553	10.347
	2.00	1.00	-4.897	2.740	.078	-10.347	.553
MetaCC	1.00	2.00	.269	.821	.745	-1.365	1.902
	2.00	1.00	-.269	.821	.745	-1.902	1.365
MetaPB	1.00	2.00	1.074	.905	.239	-.726	2.875
	2.00	1.00	-1.074	.905	.239	-2.875	.726
MetaCS	1.00	2.00	1.929*	.920	.039	.100	3.758
	2.00	1.00	-1.929*	.920	.039	-3.758	-.100
MetaNB	1.00	2.00	.488	.801	.545	-1.106	2.082
	2.00	1.00	-.488	.801	.545	-2.082	1.106
MetaNC	1.00	2.00	1.200	.686	.084	-.164	2.564
	2.00	1.00	-1.200	.686	.084	-2.564	.164

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

3.3 3-repeat and non-3 repeat of the DRD4 gene

Very few studies have been conducted looking at 3-repeat allele carriers of the DRD4 gene, because the large majority of people carry variants with 2, 4 and/or 7 repeats (Wang et al., 2004). We grouped 3-repeat carriers in group 2, the others in Group 1. We have seven 3-repeat allele carriers in total as table 1 and table 6 show.

As Table 7 shows, After One-Way ANOVA, we discovered that participants without 3-repeat alleles (Group 1) have significant higher overall scores in the MCQ-30 than others (Group 2), with a standard error of 5.000 and p=0.023. Group 1 has a non-significant (but close to be significant) higher score than Group 2 in MetaNB, standard error=1.540 and p=0.071.

Table 6: Descriptive Statistics: 3-repeat and non-3 repeat alleles of the DRD4 gene
DRD4 1:00: Group 1. DRD4 2:00: Group 2.

	DRD4	Mean	Std. Deviation	N
MCQ-30	1.00	58.4048	12.73182	84
	2.00	70.0000	12.38278	7
	Total	59.2967	13.01409	91
MetaCC	1.00	10.1071	3.74171	84
	2.00	12.0000	5.80230	7
	Total	10.2527	3.92596	91
MetaPB	1.00	11.3452	4.13185	84
	2.00	14.0000	6.83130	7
	Total	11.5495	4.40016	91
MetaCS	1.00	16.0119	4.30884	84
	2.00	18.2857	3.63842	7
	Total	16.1868	4.28670	91
MetaNB	1.00	10.3333	3.67123	84
	2.00	13.1429	6.38823	7
	Total	10.5495	3.96446	91
MetaNC	1.00	10.6429	3.18749	84
	2.00	12.5714	3.86683	7
	Total	10.7912	3.26094	91

Table 7: Pairwise Comparisons: 3-repeat and non-3 repeat alleles of the DRD4 gene

DRD4 1:00: Group 1. DRD4 2:00: Group 2.

Dependent Variable	(I) DRD4	(J) DRD4	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
MCQ-30	1.00	2.00	-11.595*	5.000	.023	-21.529	-1.661
	2.00	1.00	11.595*	5.000	.023	1.661	21.529
MetaCC	1.00	2.00	-1.893	1.540	.222	-4.953	1.167
	2.00	1.00	1.893	1.540	.222	-1.167	4.953
MetaPB	1.00	2.00	-2.655	1.718	.126	-6.068	.759
	2.00	1.00	2.655	1.718	.126	-.759	6.068
MetaCS	1.00	2.00	-2.274	1.679	.179	-5.609	1.062
	2.00	1.00	2.274	1.679	.179	-1.062	5.609
MetaNB	1.00	2.00	-2.810	1.540	.071	-5.869	.250
	2.00	1.00	2.810	1.540	.071	-.250	5.869
MetaNC	1.00	2.00	-1.929	1.274	.134	-4.459	.602
	2.00	1.00	1.929	1.274	.134	-.602	4.459
Attention	1.00	2.00	.583	.647	.370	-.702	1.869
	2.00	1.00	-.583	.647	.370	-1.869	.702
Depression	1.00	2.00	-3.476	3.049	.257	-9.535	2.583
	2.00	1.00	3.476	3.049	.257	-2.583	9.535
Alcohol	1.00	2.00	.536	1.242	.667	-1.932	3.003
	2.00	1.00	-.536	1.242	.667	-3.003	1.932

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

3.4 DRD4 gene and Alcohol use disorders

There are 92 participants who have completed the alcohol use disorders identification test (AUDIT): Interview version, and their DRD4 gene alleles have been successfully analyzed. As the table 8 shows.

Table 8: Genetic variants of participants

Total number is 92.

DRD4 VNTR	2R/2R	2R/3R	2R/4R	3R/4R	4R/4R	4R/7R	3R/3R	7R/7R
Participants	6	1	11	4	48	18	2	2

Since the 7-repeat allele of DRD4 has been reported to be associated with many Psychological disorders (Wu et al., 2012), and 7-repeat alleles have blunted responses for cAMP reduction. We divided our participants into two groups, as the Table 9 shows, Group 1 is the group without 7-repeat Allele, and Group 2 is with 7-Repeat Allele.

After taking One-Way ANOVA with Bonferroni adjustment, we found that 7-repeat allele carriers have significantly higher scores of AUDIT than those without the 7-repeat allele, as the table 10 shows.

Table 9: Descriptive statistics of alcohol use
DRD4 1:00/Group 1: Group without the 7-repeat DRD4exon III 48-bp VNTR Polymorphism. DRD4 2:00/Group 2: Group with 7-repeat Allele.

		N
DRD4 Groups	1.00	72
	2.00	20

Table 10: Pairwise Comparisons: DRD4 gene and Alcohol use
DRD4 1:00/Group 1: Group without 7-repeat DRD4exon III 48-bp VNTR Polymorphism. DRD4 2:00/Group 2: Group with 7-repeat Allele.

Dependent Variable: The alcohol use disorders identification test: Interview version						
					95% Confidence Interval for Difference[b]	
(I) DRD4	(J) DRD4	Mean Difference (I-J)	Std. Error	Sig.[b]	Lower Bound	Upper Bound
1.00	2.00	-1.856*	.770	.018	-3.385	-.326
2.00	1.00	1.856*	.770	.018	.326	3.385

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

However, Total scores of 8 or more are considered as an indicator of hazardous and harmful alcohol use (Barbor et al., 2011). So, we divided participants into two groups with regards to alcoholism: Group 1 has a score of less than 8, Group 2 has a score greater or equal to 8. After taking Cross tabulation through IBM SPSS 22.0, we found that 7-repeat DRD4 VNTR polymorphism does not play a role in whether harmful alcohol use or not occurs, as the table 11 and table 12 show.

Table 11: Case Processing Summary: DRD4 gene and alcohol use

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Alcohol * DRD4	92	98.9%	1	1.1%	93	100.0%

Table 12: Chi-Square Tests: DRD4 gene and alcohol use

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.199[a]	1	.138		
Continuity Correction[b]	1.160	1	.282		
Likelihood Ratio	1.935	1	.164		
Fisher's Exact Test				.216	.141
Linear-by-Linear Association	2.175	1	.140		
N of Valid Cases	92				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.17.

b. Computed only for a 2x2 table

3.5 DRD4 gene and ADHD

Since the 2-repeat allele has a blunted response (Wang et al., 2004) for cAMP reduction and has been linked to ADHD (Leung et al., 2017), we divided participants into two groups, 2-repeat allele carriers (Group 2) and non-carriers (Group 1), as table 13 shows:

Table 13: Number of participants

DRD4 1:00: Group 1. DRD4 2:00: Group 2.

	Number of Participants	
DRD4 Groups	1:00	74
	2:00	18

After One-Way ANOVA, we discovered participants with 2-repeat alleles (Group 2) have significantly higher overall scores in the "Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist: Part A" than others (Group 1), Standard error=0.424, p=0.011. As Table 14 shows.

Table 14: Pairwise Comparisons: DRD4 gene and ADHD

DRD4 1:00: Group 1. DRD4 2:00: Group 2.

Dependent Variable: Attention

(I) DRD42	(J) DRD42	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
1.00	2.00	-1.105*	.424	.011	-1.948	-.263
2.00	1.00	1.105*	.424	.011	.263	1.948

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

For ASRS-V.1.1, According to Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist instructions from the World Health Organization 2003, it is considered consistent with ADHD in adults when four or more marks appear in the darkly shaded boxes. We divided participants into two groups: Group 1 consists of those participants who have less than four markers appearing in the darkly shaded boxes of ASRS-V.1.1: part A; Group 2 consists the participants with four or more markers appear in the boxes. We have 72 participants in Group 1 and 20 participants in Group 2, As table 15 shows:

After taking Cross tabulation through IBM SPSS 22.0, DRD4 with the 2-repeat allele is significantly associated with ASRS.V.1.1. In another words, participants with 2-repeat alleles are more likely to be associated with ADHD. As table 16 shows.

Table 15: DRD4 * ASRS.V.1.1. Crosstabulation

DRD4 1.00: Group 1. DRD4 2.00: Group 2.

			ASRS.V.1.1.		
			1.00	2.00	Total
DRD4	1.00	Count	62	12	74
		Expected Count	57.9	16.1	74.0
		% within DRD4	83.8%	16.2%	100.0%
		% within ASRS.V.1.1.	86.1%	60.0%	80.4%
		% of Total	67.4%	13.0%	80.4%
	2.00	Count	10	8	18
		Expected Count	14.1	3.9	18.0
		% within DRD4	55.6%	44.4%	100.0%
		% within ASRS.V.1.1	13.9%	40.0%	19.6%
		% of Total	10.9%	8.7%	19.6%
Total		Count	72	20	92
		Expected Count	72.0	20.0	92.0
		% within DRD4	78.3%	21.7%	100.0%
		% within ASRS.V.1.1.	100.0%	100.0%	100.0%
		% of Total	78.3%	21.7%	100.0%

Table 16: Table Chi-Square Tests: DRD4 * ASRS.V.1.1

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.781[a]	1	.009		
Continuity Correction[b]	5.223	1	.022		
Likelihood Ratio	6.010	1	.014		
Fisher's Exact Test				.021	.014
Linear-by-Linear Association	6.707	1	.010		
N of Valid Cases	92				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.91.

b. Computed only for a 2x2 table

3.6 5-HTTLPR and Metacognitions

Another genetic marker we have tested is 5-HTTLPR that contains a 43 bp insertion/deletion polymorphism in the 5' regulatory region of the gene (Heils et al., 1996). We have two different alleles, short allele (S) and long allele (L), and three combinations, S/S, S/L and L/L. Three groups have been categorized, Group 1(S/S), Group 2(S/L) and Group 3(L/L). 90 participants have the data of 5-HTTLPR and have taken the MCQ-30, as table 17 shows:

Table 17: Between-Subjects Factors

Total participants=90

		N
5-HTTLPR Group	1:00	28
	2:00	44
	3:00	18

After applying One-Way MANOVA with Bonferroni adjustment, the association between 5-HTTLPR alleles and the Metacognition subclade "cognitive confidence" has been established. S/S carriers have significant higher scores of Metacognition subclade "cognitive confidence" than S/L carriers, Standard error=0.928 and P value=0.028, there is no significant association between group 2 and group 3, Group 1 and group 3. As table 18 shows:

Table 18: Pairwise Comparisons: 5-HTTLPR and Metacognition

5-HTTLPR 1:00: Group 1 "S/S". 5-HTTLPR 2:00: Group 2 "S/L". 5-HTTLPR 3:00: Group 3 "L/L".

Dependent Variable	(I) 5-HTTLPR	(J) 5-HTTLPR	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
MCQ-30	1.00	2.00	5.630	3.141	.230	-2.038	13.298
		3.00	3.690	3.926	1.000	-5.893	13.274
	2.00	1.00	-5.630	3.141	.230	-13.298	2.038

Continued Table 18

	3.00	1.00	-3.690	3.926	1.000	-13.274	5.893
		2.00	1.939	3.636	1.000	-6.936	10.815
MetaCC	1.00	2.00	2.471*	.928	.028	.205	4.737
		3.00	1.802	1.160	.372	-1.030	4.633
	2.00	1.00	-2.471*	.928	.028	-4.737	-.205
		3.00	-.669	1.074	1.000	-3.292	1.954
	3.00	1.00	-1.802	1.160	.372	-4.633	1.030
		2.00	.669	1.074	1.000	-1.954	3.292
MetaPB	1.00	2.00	1.604	1.061	.402	-.985	4.193
		3.00	1.036	1.325	1.000	-2.200	4.271
	2.00	1.00	-1.604	1.061	.402	-4.193	.985
		3.00	-.568	1.227	1.000	-3.564	2.428
	3.00	1.00	-1.036	1.325	1.000	-4.271	2.200
		2.00	.568	1.227	1.000	-2.428	3.564
MetaCS	1.00	2.00	.305	1.036	1.000	-2.224	2.834
		3.00	1.992	1.295	.383	-1.169	5.153
	2.00	1.00	-.305	1.036	1.000	-2.834	2.224
		3.00	1.687	1.199	.489	-1.240	4.614
	3.00	1.00	-1.992	1.295	.383	-5.153	1.169
		2.00	-1.687	1.199	.489	-4.614	1.240
MetaNB	1.00	2.00	1.942	.943	.128	-.361	4.244
		3.00	-.536	1.179	1.000	-3.413	2.341
	2.00	1.00	-1.942	.943	.128	-4.244	.361
		3.00	-2.477	1.091	.077	-5.142	.187
	3.00	1.00	.536	1.179	1.000	-2.341	3.413
		2.00	2.477	1.091	.077	-.187	5.142
MetaNC	1.00	2.00	-.584	.796	1.000	-2.528	1.359
		3.00	-.496	.995	1.000	-2.925	1.933
	2.00	1.00	.584	.796	1.000	-1.359	2.528
		3.00	.088	.921	1.000	-2.161	2.338
	3.00	1.00	.496	.995	1.000	-1.933	2.925
		2.00	-.088	.921	1.000	-2.338	2.161

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

3.7 Pearson correlations between SATs and Metacognitions

Some of participants provided multiple SAT scores (they took the SAT more than once). We chose the highest scores including the highest overall scores, highest reading scores, highest math scores and highest Writing scores. Some participants took the *New SAT* which was administrated for the first time in 2016 (Lewin 2014). We converted *New SAT* scores to old ones through "SAT Concordance Tables for Higher Education" released in 2016 by CollegeBoard. We have SAT data including 55 highest scores of overall SAT and SAT Math, 54 highest scores of SAT Reading and Writing. As the Table 19 shows:

Table 19: Descriptive Statistics: SATs and Metacognitions

	Mean	Std. Deviation	N
SAT	1846.9091	222.63467	55
SAT Math	634.9091	77.31304	55
SAT Reading	620.1852	81.22856	54
SAT Writing	611.1111	91.64465	54
MCQ-30	59.4022	12.98186	92
MetaCC	10.2717	3.90858	92
MetaPB	11.5652	4.37853	92
MetaCS	16.1957	4.26393	92
MetaNB	10.6196	3.99957	92
MetaNC	10.7826	3.24402	92

After applying "Pearson Product-Moment Correlation Coefficient" The SAT overall score is negatively associated with MetaNC, Pearson correlation coefficient (r)=-0.271, P=0.046. And SAT overall score is almost negatively associated with MCQ-30 overall score, r=-0.242, p=0.075.

SAT math is negatively associated with MCQ-30 overall score (r=-0.294, p=0.029), MetaNC (r=-0.343, p=0.010). SAT reading is negatively associated with MCQ-30 (r=-0.273, p=0.046), MetaPB (r=-0.295, p=0.030) and MetaNC (r=-0.316, p=0.020). The other correlations are not statistical significant, Results as the table 20 shows:

Table 20: Correlations: SATs and Metacognitions

		SAT	SAT Math	SAT Reading	MCQ-30	MetaNC	MetaPB
SAT	Pearson Correlation	1	.856**	.826**	-.242	-.271*	-.235
	Sig. (2-tailed)		.000	.000	.075	.046	.085
	N	55	55	54	55	55	55
SAT Math	Pearson Correlation	.856**	1	.588**	-.294*	-.343*	-.239
	Sig. (2-tailed)	.000		.000	.029	.010	.080
	N	55	55	54	55	55	55
SAT Reading	Pearson Correlation	.826**	.588**	1	-.273*	-.316*	-.295*
	Sig. (2-tailed)	.000	.000		.046	.020	.030
	N	54	54	54	54	54	54
MCQ-30	Pearson Correlation	-.242	-.294*	-.273*	1	.688**	.707**
	Sig. (2-tailed)	.075	.029	.046		.000	.000
	N	55	55	54	92	92	92
MetaNC	Pearson Correlation	-.271*	-.343*	-.316*	.688**	1	.494**
	Sig. (2-tailed)	.046	.010	.020	.000		.000
	N	55	55	54	92	92	92
MetaPB	Pearson Correlation	-.235	-.239	-.295*	.707**	.494**	1
	Sig. (2-tailed)	.085	.080	.030	.000	.000	
	N	55	55	54	92	92	92

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

3.8 Association between Metacognition and Depression

Another important finding as the table 21 shows, MCQ-30 subclade "cognitive self-consciousness" is positively associated with BDI-II, as the Table 21 shows, r=0.241 and p=0.020.

We will discuss this finding in the Discussion section.

Table 21: Correlations: Metacognition and Depression

Meta CS: MCQ-30 subclade "cognitive self-consciousness. Depression: BDI-II.

		Depression	MetaCS
Depression	Pearson Correlation	1	.241*
	Sig. (2-tailed)		.020
	N	93	92
MetaCS	Pearson Correlation	.241*	1
	Sig. (2-tailed)	.020	
	N	92	92
*. Correlation is significant at the 0.05 level (2-tailed).			

Chapter 4

Discussion, Conclusions and Limitation

We discovered that the DRD4 and 5-HTTLPR genes did not play a direct role in SAT performance, however, individuals lacking both the 2-repeat and 7-repeat DRD4 alleles are positively associated with Metacognition, and Metacognition is negatively associated with scores of SAT (our longest allele is 7-repeats).

At first, we discuss associations between psychological characteristics and psychological tests, and then these tests and SATs. The majority findings for this part are associations between DRD4 alleles and Metacognition.

4.1 Why Participants with 2-repeat and 7-repeat DRD4 alleles have significantly lower scores on Metacognition?

Participants with 2-repeat and 7-repeat DRD4 alleles have significant lower scores on the Metacognitions questionnaire-30(MCQ-30), two subclades of MCQ-30, “Cognitive Self-Consciousness” and “Need to Control Thoughts” than those without 2-repeat and 7-repeat alleles.

Previous studies have indicated that metacognition is associated with some psychological disorders, especially anxiety and depression (Matthews et al., 1999; Papageorgiou & Wells, 2003). For the MCQ-30, the total score of the MCQ-30 and four subclades: “positive beliefs about worry (MetaPB, negative beliefs about worry concerning uncontrollability and danger (MetaNB), cognitive confidence (MetaCC) and need to control thought (MetaNC) were found to be positively and significantly correlated with depression and anxiety (Tajrishi et al., 2011). According to another study in the UK, MetaNB and MetaCC explained significant variance in both anxiety and depression

(Fisher et al. 2016). In addition, we found a significant and positive association between MetaCS (MCQ-30 “Cognitive Self-Consciousness”) and the overall score of Beck Depression Inventory II(BDI-II).

We have demonstrated that the L allele (7 or more repeat) and the 2-repeat variants of the DRD4 gene are positively associated with many psychological disorders, especially ADHD in the introduction section of this document (Wu et al., 2012; Leung et al., 2017; Gizer & Waldman, 2012; Bidwell et al., 2011; Gizer et al., 2009; Munafò et al., 2008). The question remains why are these two variants negatively associated with Metacognition? Why do these two “bad” variants become “good” in Metacognition? We will explain it in two different ways as follows:

4.1.1 Attentional bias

2-repeat and 7-repeat (or greater) alleles may not necessarily serve as “risk” genes, even they are associated with ADHD. Attentional deficit may help in some addictive behaviors. According to a regional study, Carriers of 2-repeat and 7 repeat variants are more likely to experience reduced durations of internet use, protecting them from internet overuse (Sun et al. 2016), following this logic, one possible way to explain this finding is that the two variants maybe associated with reduced biased attention.

Biased attention, or attentional bias is the tendency that a person’s perception to be affected by his/her recurring thoughts (Bar-Haim et al., 2007). In another words, Biased attention is the attention focused on disorder-relevant information, which is important for maintenance of some psychological disorders. For example, individuals with social anxiety demonstrate biased attention for socially threatening information (Schultz &

Heimberg, 2008), and individuals with depression demonstrate biased attention for sad faces (Gotlib et al. 2004).

There are associations between Biased attention, Anxiety and depression (Pfabigan & Tran, 2015). As I mentioned before, 2-repeat and long allele (7 or more repeats) carriers of the DRD4 exon III VNTR tend to have Attention Deficit Hyperactivity Disorder (ADHD). They are more likely to have reduced level of biased attention as well. This reduced biased attention may be negatively associated with depression and anxiety. Since I mentioned metacognition is positively associated with anxiety and depression, it may explain why participants with either or both of 2-repeat and 7-repeat variants (the longest alleles of our participants are 7-repeats) have significant lower scores in the MCQ-30 than others.

4.1.2 DRD4 gene is a plasticity gene

Some studies have demonstrated that the 7-repeat allele of the DRD4 gene exon III is positively associated with impaired attention, such as ADHD (Wang et al., 2012), but other studies showed that 7-repeat is positively associated with heightened attention, such as addictive problems, for example, emotional stimuli (Wells et al., 2012) and smoking related cues (Munafò et al., 2008). Also, associations between DRD4 and psychological disorders (Such as ADHD, novelty-seeking and alcohol use) have not always been consistently replicated as we mentioned before (Kluger et al., 2002; Paterson et al., 1999).

Heightened attention does not always lead to psychological disorders, such as alcohol or drug use, but may bring positive effects. A study indicated that carriers of 7 or more

repeats in exon III of the DRD4 gene demonstrated heightened selective attention to high-priority items in the environment, and as result, they scored well in categorical learning tasks and working memory learning tasks (both rely on heightened attention).

As mentioned in the introduction section of this document, externalizing behavior and IQ were uncorrelated for 7-allele carriers but correlated for participants without 7-repeat (DeYoung et al., 2006).

As result, DRD4 is a plasticity gene that plays very complex roles. 2-repeat and 7 repeat variants do not always play negative roles in mental health, the two alleles maybe associated with positive beliefs about thinking and memory and associated with metacognition.

The two explanations are not contradictory to each other. As a plasticity gene, DRD4 2-repeat or 7-repeat carriers may demonstrate attentional deficit in some areas, but also demonstrate heightened attention in some other areas (such as addictive behaviors and working memory mentioned previously). If they demonstrate attentional deficit in attentional bias, they are unlikely to have anxiety and depression, as anxiety and depression are positively associated with Metacognition. This may explain why DRD4 2-repeat and 7-repeat carriers demonstrated high scores in Metacognition.

We have one suggestion for future studies. Six 3-repeat variant carriers were recruited in this study, they have higher scores in metacognitions than others, as Tables 6 and 7 show, and 4R/4R carriers (4-repeat homozygous) have higher scores in metacognitions than those with 2-repeat or 7-repeat or both alleles. 3-repeat and 4-repeat alleles together may play an important role in metacognition. As Table 3 shows, participants without 2-repeat

and 7-repeat alleles (these are all 3-repeat and 4-repeat carriers in this study) have significantly higher scores in metacognition. We suggest that 3-repeat and 4-repeat alleles together play a role in metacognition. Since there are really no studies about 3-repeat variant of DRD4 gene, we suggest that more studies about 3-repeat allele should be undertaken.

4.2 Genetic markers and some psychological characters other than Metacognition

These findings are consistent with previous studies, as follows:

7-repeat DRD4 gene carriers have significant higher scores for alcohol use disorders, but after crosstab analysis, it does not play a role in whether harmful alcohol use or not. A previous study has indicated that 7-repeat allele of the DRD4 gene is linked to alcoholism (Laucht et al., 2007).

Individuals carrying the DRD4 2-repeat allele are significantly associated with ASRS.V.1.1 (Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist: Part A), and after taking Cross tabulation, 2-repeat carriers have more chance to mark 4 or more dark boxes in ASRS.V.1.1 part A, which is a sign to be highly consistent with ADHD. A recent study has indicated that the 2-repeat allele is prevalent among ADHD children (Leung et al., 2017).

The S/S variant carriers of the 5-HTTLPR gene have significantly higher scores of MCQ-30 subclade “Cognitive Confidence” than S/L allele carriers. Because S allele has been discovered to be linked to negative emotions such as anxiety and depression (Caspi et al., 2003). As I mentioned before, MCQ-30 subclade “Cognitive confidence” is positively associated with depression (Tajrishi et al., 2011; Fisher et al. 2016).

4.3 SATs and Metacognitions

We discovered that the SAT highest overall score is negatively associated with MetaNC, And SAT highest overall score is almost negatively associated with MCQ-30 overall score, p=0.075. SAT highest math is negatively associated with MCQ-30 overall score and MetaNC. SAT reading is negatively associated with MCQ-30 overall score, MetaPB and MetaNC.

Some previous studies have identified there is association between metacognition and academic performance. As we mentioned in the introduction section, Sperling et al. (2004) found a negative association between MAI (Metacognitive Awareness Inventory) and academic performance. Students with good metacognition scores tend to have good academic performance (Coutinho 2007). Higher scores of metacognitions that are indicators for having a higher level of unhelpful thoughts and negative thinking about cognition, can lead to negative effects on academic performance. Negative associations between metacognition and academic performance can also be explained by the fact that metacognition is positively associated with depression and anxiety, and both depression and anxiety are negatively linked to academic performance (Owens et al., 2012), so higher scores of the MCQ-30 and its subclades lead to lower scores of SATs.

In conclusion, we didn't find a direct correlation between two genetic markers (the 5-HTTLPR and DRD4 genes) and SATs, but we discovered an indirect association between the DRD4 gene and SATs though metacognition. Participants with either or both of 2-repeat and 7-repeat alleles of the DRD4 gene have lower scores on the MCQ-30, and MCQ-30 is negatively associated with SATs. We suggest that 2-repeat and 7-repeat

alleles of the DRD4 gene may play a more positive role in higher scores of SATs than other variants of the DRD4 gene.

We do note that 91 participants have the data of DRD4 gene and completed the MCQ-30, but only 53 participants have the data for the DRD4 gene and SATs (Overall scores and Math, Reading and Writing). The smaller sample size may play a role in why we didn't find a direct association between theDRD4 gene and SAT scores. We suggest a larger sample size study to more accurately test for any association between the DRD4 gene and SAT scores.

Table 22: Descriptive Statistics.
All SATs are highest scores of Participants

	DRD4CC	Mean	Std. Deviation	N
SATHWACT	1.00	1831.0000	237.49192	30
	2.00	1893.0435	191.34535	23
	Total	1857.9245	218.88141	53
SATHM	1.00	629.0000	74.80319	30
	2.00	652.6087	74.11400	23
	Total	639.2453	74.72640	53
SATHR	1.00	608.0000	87.70641	30
	2.00	640.0000	69.08493	23
	Total	621.8868	81.02840	53
SATHWWACT	1.00	611.6667	91.31542	30
	2.00	614.3478	94.09019	23
	Total	612.8302	91.63845	53

4.4 Limitation

The major limitation is that the most of participants were recruited at Binghamton University, 90 out of 93 participants are current students at Binghamton University (BU). However, students entering BU need to pass a certain level of admission criteria, the

differences in SATs of these participants are not big enough to establish a statistical association between SAT scores and other factors, and the results of this study may not be representative in general, but rather the specific situation at Binghamton University.

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