THE RELATIONSHIP OF COMT, WORKING MEMORY, AND FLUID INTELLIGENCE IN HUMANS

By

DOUGLAS N ZACHER

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Written under the direction of

Dr. J. W. Whitlow, Jr.

And approved by

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Dr. Sean Duffy

_____

Dr. Mary Bravo

_____

Dr. Robrecht van der Wel

Camden, New Jersey

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THESIS ABSTRACT

The Relationship of COMT, Working Memory, and Fluid Intelligence in Humans

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Thesis Director:

Dr. J. W. Whitlow, Jr.

The role of dopamine in working memory and fluid intelligence is well documented. Dopamine in the frontal cortex is evidenced to exert influence over working memory. Dopamine synthesis is evidenced to be associated with fluid intelligence. Catechol-o-methyltransferase is a gene responsible for large quantities of dopamine in the frontal cortex. The genetic polymorphism on COMT is known to reduce the amount of dopamine that is destroyed through enzymatic degradation in the frontal lobe by four times the normal amount. We hypothesized that the COMT MET allele will be associated positively with increased working memory capacity and fluid intelligence whereas the COMT VAL allele will not be. We also hypothesized that due to the shared neural processes, working memory capacity and fluid intelligence will be correlated with one another. We found significant correlations between the WMC battery and the fluid intelligence measure however we found no relationship between the COMT polymorphisms, working memory capacity, and fluid intelligence.

Dedication

This paper is dedicated to the friends I made and the lessons I learned during my time at Rutgers-Camden. May the memories of my time here continue to shape and guide me to become the person I hope to be.

Introduction

The capacity to manipulate symbols while simultaneously remembering information for brief periods is the domain of working memory (Lewandowsky, 2011). Working memory (WM) is a concept that has captured the attention of cognitive psychologists in recent years due to its relationship with executive functioning and with fluid intelligence (gF). Fluid intelligence is the ability of humans to adapt to a new situation or cognitive task (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008), and measures of gF have been found to be related to performance on various real world tasks. The intent of this study is to examine a potential link between genetic polymorphisms in the gene for catechol-o-methyltransferase (COMT), working memory, and fluid intelligence in humans.

In an attempt to understand the nature of working memory new developments have begun that look to combine genetic variability knowledge with working memory knowledge. Using behavioral genetics studies involving twins, evidence suggests that the genetic heritability is high in areas of executive functioning including but not limited to; working memory, sustained attention, response inhibition, and error processing (Barnes, Dean, Nandam, O'Connel, & Bellgrove, 2011). This knowledge of genetic heritability combined with pharmacological studies can be used to indicate a potential predictor relationship between a specific gene, its polymorphisms, and an area of executive functioning which is in this case, working memory.

Before it is possible to isolate a genetic expression for examination it is necessary to identify a greater process that this gene expression will influence. In this case, the large process concerns the availability of dopamine (DA) in cortical areas. Studies involving

monkeys have demonstrated the powerful influence that DA has on the prefrontal cortex (PFC) in a positive manner (Brozoski et al as cited by Zahrt, Taylor, Mathew, Arnsten, 1997). Increased levels of DA in the PFC of rats predicted a greater ability to shift from one rule to another on a trial-to-trial basis (Frank, Moustafa, Haughey, Curran & Hutchison, 2007). The ability of the rats to switch from the tasks would appear to be a facet of increased executive functioning in accordance with our definition of working memory and executive functioning. In a study done on nematodes, dopamine deficient subjects were impaired in a state-dependent learning condition (Ardiel & Rankin, 2011). This illustrates the opposite side of the story seen in the rat study, namely, when there was a lack of DA the ability to learn in a trial was diminished. This evidence demonstrates the importance of dopamine in learning tasks. Further animal studies done on rats examined how mild stress exposure produced working memory deficits by agents that blocked the DA receptors (Arnsten and Goldman-Rakic as cited by Zahrt et al., 1997). Research also suggests that DA in the PFC of monkeys is among the highest levels of concentration among all cortical areas (Sawaguchi & Goldman-Rakic, 1991). This evidence does two things; it strengthens our evidence in nonhuman animal studies that too little DA is negative for executive functioning and that a lack of DA seems to affect working memory and by association, executive functioning and learning.

Dopamine (DA), has also been shown to play a large role in cognitive processes in humans including, but not limited to, working memory (Cools & D'Esposito, 2011). When subjects were trained for working memory tasks they demonstrated increased DA release post training (Backman, Nyberg, Soveri, Johansson, Andersson, Dahlin, Neely, Virta, Laine, Rinne, (2011). Cools et al., as cited by Landau et al. (2009) found a

relationship between the capacity to synthesize dopamine and working memory capacity in young adults. Being able to synthesize higher amounts of DA would lead to higher executive functioning and learning as well as an increased level of fluid intelligence (Shlagenhauf et al., 2013). One explanation for the role of DA in learning is that bursts of DA fired after unexpected rewards are thought to affect corticostriatal plasticity so that these rewarding actions have a higher rate of being selected in th future (Frank et al., 2007).

This shows the necessity for dopamine as an overarching control mechanism in executive functioning. According to Braver and Cohen (2000) the function of the PFC can be thought of as a control mechanism for working memory. This strengthens the larger process we are trying to analyze by reinforcing the area of the brain that should be focused on. During a delayed epoch of working memory tasks, certain processes allow the brain to hold information in the absence of stimuli. This process appears to engage the dopamine system in humans (Landau, Lal, O'Neil, Baker & Jagust, 2009). Holding information for a period of time without a stimuli fits within our operationalized definition of working memory. This demonstrates at a neuronal level the role that DA is theorized to be performing involving learning.

When administered bromocriptine, a DA agonist, volunteers demonstrated increased performance on working memory tasks (Cools & Esposito, 2011). This evidence adds to the knowledge of the role of DA in working memory. Cools & Esposito (2011) also showed how administration of a DA antagonist, sulpiride, impaired performance on tasks that were sensitive to PFC function. Furthermore, increased ability to be distracted and perseveration are known hallmarks of neurological damage to the

PFC (Damasio as cited by Braver & Cohen, 2000). This evidence along with what we already know about DA from animal studies can be used as a guideline for examining what gene expression to investigate when trying to examine working memory. The criteria for the gene that we are looking to investigate must involve a gene with an effect on the neurotransmitter DA in the PFC.

In a study using the Digit Symbol Substitution subtest of the Weschsler Adult Intelligence Scale-III and the Stroop Color-Word test, researchers failed to find a common genetic variant that would explain large portions of the variation in the complex traits of cognition (Cirulli, Kasperaviciute, Attix, Ge, Gibson & Goldstein, 2010). This finding explains the previous statement about the contribution of individual genes but it also illustrates a failure in explaining the role of genetics in some of the research done previously. With the amount of inter-functional operation of neurological structures the ability to tease apart confounding variables involved in cognition becomes reliant on advanced methodology including, but not limited to, better ways of genotyping. Due to the knowledge of candidate genes for executive processes and their biological substrates, cognitive neuroscience can generate hypotheses involving the relationship between a gene and a specific cognitive process while minimizing the risk of false positive associations (Barnes et al., 2010). While quasi-experimental studies do not imply causation, the knowledge of the timeline of genetic expression and the biological processes they influence lend themselves towards the inference of a causal model which we hope to illustrate in our study.

One of the most promising genes implicated in cognitive functioning is Catechol-O-Methyltransferase (COMT) (Savitz et al., 2006). The COMT gene is responsible for a

functional polymorphism that causes a code substitution of methionine (met) for valine (val) at codon 158 (Malholtra, Kelser, Mazzanti, Bates, Goldberg & Golman 2002). The COMT Met allele expression was associated with greater adjustments in trial-to-trial tasks after a single instance of negative feedback (Frank et al., 2007). This means that while already being linked by empirical studies to some forms of learning there are still gaps in the field of study regarding all of the roles of COMT.

This still leaves open the question, why study COMT compared to the multitude of factors that on a neurological level influence dopamine levels in the brain?

> "The major mechanism by which the synaptic activity of dopamine is terminated is by reuptake, followed by metabolic degradation. Catchol-O-Methyltransferase (COMT) is the major mammalian enzyme involved in the metabolic degradation of released dopamine and accounts for more than 60% of the metabolic degradation of dopamine in the frontal cortex" (Malholtra et al., 2002).

The Met allele is thermolabile and has one fourth the enzymatic activity and subsequent metabolic degradation of the Val allele (Malholtra et al., 2002). With the known area of effect of the COMT gene, the polymorphism would be responsible for the largest amount of DA, in the PFC making it a prime candidate for correlational studies. Individuals with the Val allele typically have high COMT activity and low baseline DA compared to individuals with the Met allele who typically have low COMT activity and high baseline DA (Cools & D'Esposito, 2011). The effect that dopamine has on cognitive functioning relies initial values as dopamine moves through a U shaped pattern of functioning. With the previous knowledge of the role of DA in executive functioning, the Val allele would intuitively be associated with lower WMC and lower fluid intelligence whereas the Met allele would be associated with higher WMC and higher fluid intelligence. In the interest

of being parsimonious this study will focus on one of the genetic polymorphisms which empirically appear to have one of the broadest reaching effects on dopamine in the PFC.

This polymorphism also has the potential to be associated with increased levels of fluid intelligence. Fluid intelligence was associated with increased blood flow to the ventral-striatum which is an area also related to tasks such as complex attention (Schlagenhauf et al., 2013). What makes this interesting is that (Jaeggi et al., 2008) found that improvements on a working memory capacity test also increased fluid intelligence levels in participants. This is where the literature becomes ambiguous in the sense that the causality of such a change is unclear. This change in working memory capacity and subsequently fluid intelligence is theorized to come from two possible ways; through a decrease in the number of cortical dopamine receptors or through the tuning of the brains own dopaminergic transmissions through this training (Klingberg, 2010). With the evidence of dopamine's inverted u-shaped level of functioning on executive processes (Cools & D'Esposito, 2011) it is possible to theorize that this increase in fluid intelligence comes from a potential overlap in neural networks that are modulated by a healthy level of dopamine. However it is possible to hypothesize that having a healthy level of dopamine to begin with will not only result in a more efficient working memory capacity and fluid intelligence levels.

In a study using the Wisconsin Card Sorting Test as a primitive measure of executive function, the COMT genotype with the Val allele was associated with poorer performance on the task (Egan et al., as cited by Savitz, Solms & Ramesar, 2005). While this evidence does support our hypothesis, it is important to note that the Wisconsin Card Sorting Test was designed as a measure to assess cognitive flexibility and not executive

functioning. That notwithstanding, the results do suggest that this specific polymorphism may hinder executive functioning which, as stated earlier, contains working memory and fluid intelligence. There is also evidence that the COMT polymorphism may extend influence over semantic and episodic memory (Frias et al., as cited by Savitz, Solms & Ramesar, 2005). While this study is examining working memory which is a type of executive functioning, the prospect of episodic and semantic memory being influenced by this polymorphism lends credence to the large amount of DA that is being influenced by this polymorphism. If the COMT polymorphism does in fact exert influence over different types of complex memory functions than the idea that fluid intelligence is modulated by COMT is also possible.

There has been a large amount of studies that have examined this genetic polymorphism and its association with scores on the Wisconsin Card Sorting Test but as stated before the task is not the most effective and valid measure for studying working memory. In a study done by Cirulli, Kasperaviciute, Attix, Need, Ge, Gibson, & Goldstein (2010), there was a failure to find common variants that explain differences in common traits through genome wide association studies. The tests given for this study was the Digit Symbol substitution of the Weschsler Adult Intelligence Scale-III and the Stroop Color-Word test. The issues with the measures used are that they are not studies that focus in on the primary function of these genetic polymorphisms. With the knowledge that cognition is based on a multitude of genes, methodology must be used to get an accurate read on a gene's role involving a specific cognitive process.

The most recent research in his area is marred with inconsistencies. In a study done by Bruder, Keilp, Xu, Sikhman, Schori, and Gorman (2005) using a Word Serial

Position test, an N-back test, a Letter-Number Sequencing test, and a Spatial Delayed Response Test yielded no significant difference between genotypes except for the performance on the Letter-Number Sequencing test. It is also important to note that the difference among genotypes was only found when analysis was repeated for only Caucasian subjects (Bruder et al., 2005). In an fMRI study Bertolino, Blasi, Latorre, Rubino, Rampino, Sinibaldi, Caforio, Petruzzella, Pizzuti, Scarabino, Nardini, Weinberger, and Dallapiccola (2006) found that COMT genotypes were independently related to BOLD activation in the working memory cortical network during an N-Back task. Results from a visuospatial working memory task done in an fMRI demonstrated an age x genotype interaction where the MET allele emerged as a benefit for the task after 10 years of age (Dumontheil, Roggeman, Ziermans, Peyard-Janvid, Matsson, Kere, and Klingberg, 2011). Goldberg, Egan, Gscheidle, Coppola, Weicket, Kolachana, Goldman, and Weinberger (2003) found a significant effect between Val/Val individuals having the lowest N-Back performance and Met/Met individuals having the highest performance using a population of schizophrenic patients, their healthy siblings, and controls. In another study using the N-Back test, the polymorphisms were not associated with any significant differences (Wardle, Wit, Penton-Voak, Lewis, and Munafo, 2013). What does this mean? This means that there are inconsistencies in the latest research within the field which our research aims to help alleviate.

Another area of research that we hope to illuminate is the relationship between working memory and fluid intelligence. As stated earlier, working memory training has been associated with increase memory in fluid intelligence (Jaeggi et al., 2008). However, as a potential baseline participants who do not meet our screening criteria will

still have their working memory and fluid intelligence measured as a potential to see if increased working memory is already associated with increased fluid intelligence. This hypothesis could potentially illuminate reasoning why there has been an issue with replication, if a participant has a biologically pre-determined working memory capacity that is below average, it may not be possible to increase fluid intelligence through training due to the overlap in neural networks and the inability to tune dopaminergic systems as well due to the lower levels of dopamine (Klingberg, 2010; Schlagenhauf et al., 2013).

With the evidence presented earlier in this paper it is plausible to assume that the hypothesis stated will yield significant results. Current empirical knowledge points toward COMT having a large enough influence on DA in the PFC, which is known to affect learning, working memory, and fluid intelligence therefore we can assume that our hypothesis will illuminate gaps in the area of knowledge involving genetics and executive functioning. Part of the inconsistencies within the field could be in part due to the measures being used to capture a participant's working memory capacity. The tests mentioned including the N-Back test may not be accurate enough at capturing the full dimension of working memory and part of the reason that fMRI activation may be picking up results versus cognitive testing could be due to the testing being inadequate but the BOLD activation is enough to display results.

Implications

If a relationship between COMT, working memory capacity, and fluid intelligence is supported by evidence through this study there are several implications. Evidence suggests that training people to improve their working memory resulted in

improvements in a measure of fluid intelligence (Jaeggi, Buschkuehl, Jonides & Perrig, 2008). Many other investigators have found working memory measures to be a useful indicator of how well people will complete complex tasks (Ilkowska & Engle, 2010). With this evidence a potential identifier involving COMT and working memory can be implemented which can be manipulated through training. Another implication involves advancing knowledge in the growing field of psychology combined with genetics. This knowledge of a potential relationship would also help alleviate some of the inconsistences involving working memory training and fluid intelligence increases. There has been conflicting evidence about whether or not working memory training can improve fluid intelligence and this study could potentially explain some of that relationship.

Method

Design

This experiment was a quasi-experimental between-subjects design. Participants were administered a familial history questionnaire involving any knowledge of dopamine related disorders (Parkinson's, Schizophrenia, ADHD, drug abuse) that they knew of. Participants were also asked if they are/or have ever taken stimulants that are used in the treatment of ADD/ADHD and/or Atypical anti-psychotics used for the treatment of psychological disorders.

Measures

For the familial history questionnaire, participants were asked to fill out their age, gender and were then faced with 4 questions with the options for 3 answers. The questions consisted of asking if the participant has knowledge of any of the following; 1)

Do you have any knowledge of anyone in your extended family being diagnosed with Parkinson's? 2) Do you have any knowledge of anyone in your extended family being diagnosed with Schizophrenia? 3) Do you have any knowledge of anyone in your extended family being diagnosed with ADHD? 4) Do you have any knowledge of anyone in your family suffering from drug abuse? 5) Are you currently taking stimulants for the treatment of ADD/ADHD? 6) Are you currently taking atypical antipsychotics for the treatment of mental health disorders? The answers to the 6 of these questions will be; No, Maybe, Yes. The reasoning behind these questions is to attempt to have explanations for potential confounds in the genotyping. With the knowledge of the role of dopamine dysfunction in these 6 items I can potentially limit confounding results. I am also looking to get as a homogenous a sample as possible for our genotyping. If a participant answers yes to one of these questions they will still complete the working memory capacity battery and the fluid intelligence test as they can still be of use to one of our hypotheses.

For DNA genotyping we used an Oragene: DISCOVER DNA collection kits. These were chosen due to the non-invasive collection (saliva) and the room temperature stability of the kits once they have been used. These kits were sent out all together to an Oragene supported analysis lab where the COMT polymorphism was identified. I chose Oragene kits due to the amount of genetic data yielded from such a small sample, combined with their non-invasive method, and their year-long stability at room temperature (http://www.dnagenotek.com/ROW/index.html).

For working memory capacity measurement a series of 4 tests in Matlab using the Psychophysics toolbox were selected. These tasks were created by Stephan Lewandowsky and included; a working memory updating task (WMU), an operation-

span task (OS), a sentence span task (SS), and a spatial short-term memory task (SSTM). The WMU task requires participants to store series of digits in their memory then mentally update those digits based on arithmetic operations presented to them and finally recall the updated digits (Lewandowsky, 2011). The OS task has arithmetic operations that must be graded on their correctness (Lewandowsky, 2011). The SS task was similar to the OS task except in will be sentences that must be judged on correctness versus arithmetic operations (Lewandowsky, 2011). The SSTM involved memorization of the location of circles that are located in a 10 x 10 grid (Lewandowsky, 2011). None of the tasks were timed as they relied on the participant to answer in order to move forward. These tasks were chosen because of their ability to look at different facets of working memory capacity.

For our measure of fluid intelligence, participants were given a Ravens Progressive Matrix as this is the standard in the field for a fluid intelligence measure. These were filled out by hand and scored by hand.

Procedure

The experiment took place in one session. Participants were college undergraduate students completing the experiment in fulfillment of course credit of an introductory to psychology course requirement, undergraduate participants completing the experiment for 10 dollars compensation, and college graduate students completing the experiment for 10 dollars compensation. College students are being chosen due to ease of access. The distribution of the COMT allele's have a near even frequency among European descent (Palmatier, Kang, & Kidd, 1999) which will make finding the right sample size relatively simple amongst a small college campus.

Participants entered the lab and were given a 1 page questionnaire regarding any knowledge of familial cases of dopamine disorders (Parkinson's, Schizophrenia, ADHD, drug addiction). After filling out the questionnaire participants then gave a saliva sample to a lab assistant. Post saliva sampling participants then completed the 4 working memory tasks. After completing the working memory tasks the participants then completed a Ravens Progressive Matrix. After the matrix task, the experiment was complete and participants were debriefed on the nature of the experiment. Genotyping on the saliva samples were done by the Oragene lab and were mailed back to me.

Participants were given a written consent form prior to participating in the experiment. Participants were also given a hand out explaining the goal of the experiment and why these measures were used to accomplish our research goal.

Results

Statistical measures run to analyze the data included a correlation between the working memory battery scores and the fluid intelligence scores and ANOVA between the polymorphism's and their respective working memory scores and fluid intelligence scores in order to analyze if there is a significant difference between the means. Table 1 displays the means on each of the batteries.

Table 1

Mean Scores on Working Memory Capacity Measures and Fluid Intelligence Measure

Measure	Mean Score
Memory Updating (MU)	0.443
Operating Span (OS)	0.561
Sentence Span (SS)	0.551
Spatial Short Term Memory (SSTM)	0.809
Fluid Intelligence (Ravens Matrix)	0.523

The Fluid Intelligence measures were scored by adding up the amount of correct answers on the Ravens Matrix and putting that into a percentage form so that they were in the same format as the WMC answers. In order to analyze our hypothesis regarding the relationship between WMC and Fluid Intelligence we ran a Pearson's correlation between each test in the WMC battery and the Ravens Matrix. This hypothesis had an n of 36. Each test in the WMC battery was correlated significantly with the measure of fluid intelligence (see Table 2).

Table 2

Correlation Between Working Memory Capacity Measure and Fluid Intelligence

Measure	r with Fluid Intelligence
Memory Updating (MU)	.467*
Operating Span (OS)	.407*
Sentence Span (SS)	.478*
Spatial Short Term Memory (SSTM)	.315*

*=p<.05

Therefore we rejected our null hypothesis and accept our alternative hypothesis.

For our participant's genotype, the polymorphism broke it down into the following numbers, 13 A/G, 6 A/A, and 9 G/G. In order to analyze our hypothesis regarding the COMT polymorphisms, WMC, and fluid intelligence we conducted a one factor ANOVA comparing the WMC battery and fluid intelligence scores with their genotype as a category. This hypothesis had an n of 28. There was not a significant effect for the COMT genotype on MU at the $p<.05$ level for the three conditions [$F(2,25)=0.148$, $p=0.862$]. There was not a significant effect for the COMT genotype on OS at the $p<.05$ level for the three conditions [$F(2,25)=1.100$, $p=.348$]. There was not a significant effect for the COMT genotype on SS at the $p<.05$ level for the three conditions [$F(2,25)=0.371$, $p=0.694$)]. There was not a significant effect for the COMT genotype on SSTM at the $p<.05$ level [$F(2,25)=0.371$, $p=0.694$)]. There was also no significant effect for the COMT genotype on Fluid Intelligence at the $p<.05$ level

[F(2,25)=.975, p=0.391)]. Table 3 shows the means of the measures as a function of their respective genotype.

Table 3

Means of Working Memory and Fluid Intelligence Measures as a Function of Genotype

Measure	Mean (A/A)	Mean (A/G)	Mean (G/G)
Memory Updating (MU)	.49	.44	.42
Operating Span (OS)	.67	.52	.60
Sentence Span (SS)	.81	.83	.81
Spatial Short Term Memory (SSTM)	.81	.83	.81
Fluid Intelligence (Ravens Matrix)	.63	.50	.52

Therefore we fail to reject the null and reject the alternative hypothesis involving COMT polymorphisms, WMC, and fluid intelligence. However, while we did not find statistical significance, the means were all in the expected direction for our ANOVA.

Discussion

The findings in this paper further support the evidence that humans working memory capacity and fluid intelligence are related. This result adds to the literature involving the relationship between working memory and fluid intelligence. Future studies involving WMC and fluid intelligence could use more in depth measures of fluid intelligence in order to more adequately explain the relationship between these two facets of executive functioning. It is important to note that as with any correlational data, the results do not equate causation. While we failed to find support for our COMT hypothesis

there are potential limitations which may explain the lack of significant findings. One potential limitation is stated well by Savitz, Solms, & Ramesar, (2006) many genes most likely contribute a small amount to the complex trait of cognition. It is plausible that COMT does not contribute enough to the role of cognition which will negate any potential for statistically significant results. While empirical evidence does point towards COMT being responsible for a large portion of dopamine in the frontal lobe and having a large role in reinforcement learning as opposed to other genes, it is still important to state the potential issues with such a study. With that being said, the data here does follow the trend hypothesized involving the direction of the mean scores on the WMC battery and the Ravens Matrix in regards to the COMT polymorphisms.

The human body is a system of regulation which poses obstacles for a study such as this one. With the human body being a system of regulation, having one gene be responsible for such a large amount of two executive functions could be viewed as an evolutionary disadvantage. If your system could be thrown off by one polymorphism then normal functioning would be in danger. Along these same lines I did not have any other measures of genes related to COMT which creates the issue of not being able to hypothesize if COMT is being used as a method of regulating another gene responsible involved in any of the catecholamines. While COMT could be being used as a way to regulate for neurotransmitter issues with the catcholamines a potential issue with not having any other genetic information is that even if the COMT VAL allele is not present another gene could be producing less dopamine as a form of regulation thereby negating any effects of COMT on working memory or fluid intelligence. With this type of study the knowledge of the inverted U-shape regarding dopamine functioning is important to

keep in mind because that level of dopamine is going to sought after by the body in order to maximize functioning which presents a multitude of confounding variables that I did not have the time or money to account for. However with that knowledge in mind it makes the findings presented here and the trends present in the data very promising for future research regarding COMT's involvement with working memory capacity and fluid intelligence.

Another limitation is the potential confounding presence of underlying dopamine disorders. With the role of dopamine in this study being well documented and supported by evidence, the potential role of dopamine disorders, whether known or unknown, in participants may skew results or interfere with what the normal functioning of the polymorphism being studied is. Another limitation is something brought up by Cools & D'Esposito (2011) stating that the initial dopamine levels can potentially influence how effective dopamine is on cognitive functioning. Since we do not have prior dopamine measures we cannot tell if the polymorphism is helping or harming the participant.

The role of COMT in the catecholamines may also provide evidence for its existence. As stated before, the body will attempt to regulate any dysfunction in neurotransmitters in order to assure proper functioning. With COMT controlling such a large amount of enzymatic degradation any minor genetic change within the catecholamines could cause COMT to form this polymorphism without any noticeable changes in functioning since it is a functional polymorphism. This could explain the evolutionary reason for COMT existing, COMT could have continued to exist for so long in humans because it is used as a potential "safety valve" when genes malfunction due to its functional polymorphism controlling so much activity within the catecholamine group

of neurotransmitters. This may also help explain why understanding and studying this gene is more difficult than previously hypothesized.

Finally, the sample size used in this study was an issue. Due to the time constraints we could not increase our sample size high enough to potentially alleviate error. This is important because of the multiple factors stated earlier, so the larger the sample size is, the more likely I would be able to detect such a small difference. Using a power analysis the sample size needed to notice detect a difference would be 130 participants, which makes these findings with this sample size that more interesting. Future studies involving COMT could involve these two executive functions being compared through the use of neuroimaging instead of cognitive tests which could potentially highlight the significant differences between COMT polymorphisms that are too sensitive for typical cognitive tests via the use of neural activation instead of scores.

Appendix

Family History Questionnaire

Name:

Gender: **M** **F**

Please answer the following questions to the best of your knowledge by circling your response. Your responses will be kept confidential.

1) Do you have any knowledge of anyone in your extended family being diagnosed with Parkinson's? **Yes** **Maybe** **No**

2) Do you have any knowledge of anyone in your extended family being diagnosed with Schizophrenia? **Yes** **Maybe** **No**

3) Do you have any knowledge of anyone in your extended family being diagnosed with ADHD?

Yes **Maybe** **No**

4) Do you have any knowledge of anyone in your extended family being suffering from drug abuse? **Yes** **Maybe** **No**

5) Are you currently taking stimulants for the treatment of ADD/ADHD?

Yes **Maybe** **No**

6) Are you currently taking atypical antipsychotics for the treatment of mental health disorders?

Yes **Maybe** **No**

Initial Instructions

This study investigates the relationship between specific genes and cognitive processes. In order to do so we will need to do a few things. First, we need to ask you some questions about your family history. Second, we need to take a sample of your saliva in order to get your genetic information. Finally, we will be administering a series of computerized tests to measure a specific cognitive process. During this time if you feel uncomfortable at all please let us know. You will not be required to continue the experiment if you do not wish to and any of your data and/or information will be destroyed at your request. We thank you for your participation and for helping us better understand how biological processes influence psychology. For any information and/or to ask any questions please contact Douglas N. Zacher at douglasnzacher@gmail.com. Thank you.

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