MODULATION OF REASONING BIAS AND BRAIN ACTIVATION BY SEROTONIN TRANSPORTER GENOTYPE AND EMOTIONAL CONTENT

A Dissertation
submitted to the Faculty of the
Graduate School of Arts and Sciences
of Georgetown University
in partial fulfillment of the requirements for the
degree of
Doctor of Philosophy
in Psychology

By

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Washington, DC
August 27, 2010
MODULATION OF REASONING BIAS AND BRAIN ACTIVATION BY SEROTONIN TRANSPORTER GENOTYPE AND EMOTIONAL CONTENT

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ABSTRACT

Deductive reasoning is influenced by emotions and beliefs. It is unknown how factors relating to emotion and beliefs interact to affect logical reasoning. This dissertation explored the nature of emotion-belief interactions in relational reasoning using behavioral, genetic and neuroimaging techniques. In Study 1, reasoning behavior was influenced by beliefs such that participants were less accurate and slower to evaluate arguments in which the conclusion validity conflicted with beliefs, thereby replicating the belief bias effect. Moreover, belief-bias interacted with emotional content and serotonin transporter genotype; carriers of the short (S) allele of the serotonin transporter gene (5-HTTLPR) had increased emotional belief bias relative to long (L) carriers. Groups did not differ in non-emotional belief bias. In Study 2, I investigated the neural basis for this emotion-belief interaction using functional magnetic resonance imaging (fMRI). Healthy individuals with the S allele had decreased activation of right inferior frontal cortex (rIFC) and increased activity in ventromedial prefrontal cortex (vmPFC) when reasoning with emotional belief-logic conflict problems relative to L allele carriers. Anxiety was positively correlated with activation of vmPFC in emotional belief-logic conflict reasoning. These results have implications for depression and anxiety disorders, which are related to the 5-HTTLPR S allele, emotional reactivity, and deleterious beliefs.
ACKNOWLEDGEMENTS

This thesis would not have been possible without the generous support of so many people. First, I would like to thank my committee, Dr. Darlene Howard, Dr. Gerrod Parrott, and Dr. John Fossella for their encouragement and endless patience. I look forward to channeling your expertise in future discussions and debates about cognition, emotion, and genetics. Your comments and constructive criticism are extremely valuable to me and to the success of this thesis.

I would like to thank everyone at the Developmental Cognitive Neuroscience Lab, including Evan ‘Digital’ Gordon, Eric Murphy, Dr. Kelly Barnes, Devon Shook and Ericka Ruiz for their help and support, whether scientific or otherwise. I would also like to thank the many undergraduates with whom I have had the pleasure of working over the years. They have helped me with this research project and have helped me to develop my own skills as a mentor: Nick Parrott, Noah Schoenholtz, Adam Evans, Chris Tsang, Jane Dewire and Andrew Malzberg, with a special thank you to “Team Reason”, Stephanie Bean and Lindsay Anderson.

I would like to thank the Psychology Department for the opportunity to teach and assist in teaching many undergraduate courses and also for financial support. Many faculty and staff members of the department contributed to my education in unique ways; thank you. Dr. Vinod Goel, my former mentor, has been (and still is) a very influential force, shaping my research interests and sharpening my mind, and I am very grateful to him. I would also like to thank Dr. Joseph Devaney and his research team at Children’s National Medical Center for genetic analyses.

Important sources of financial support included a Doctoral Research Award from the Canadian Institutes of Health Research and a research grant from the Center for Brain Basis of Cognition.

I would like to thank my friends and colleagues who have also provided support along the way including Dr. Alexis Lauricella, Sarah Parsons, Jessie Simon, Dr. Sakura Minami, Dr. Jennifer Romano, Dr. Ilana Bennett, Dr. Amy Lowenstein, and Dr. Samantha Harvell. A special thank you to Dr. Vedran Lovic, who helped me through my undergraduate degree, fostering my interest in neuroscience and encouraging me to pursue a career as a research professor. Another special note of thanks to Dr. Oshin Vartanian who walked me through my first fMRI steps and imaging studies, put up with my endless questions about fMRI and logical reasoning, and for being a great friend and colleague.

Finally, and most importantly, I would like to thank my advisor Dr. Chandan Vaidya who has allowed me to explore this fascinating field of cognitive neuroscience from many different angles. Whether discussing developmental, clinical, genetic, cognitive, emotional, behavioral or neuroimaging aspects of neuroscience, she has given me guidance and encouraged me to explore the brain in different ways. She managed to provide the perfect balance of freedom and guidance. Her support, patience, and caring nature provided stability, despite my many ups and downs. My amazing mentor has truly been there for me whenever I needed her. She has made me a better researcher, writer, and teacher, and I cannot thank her enough.
I would like to dedicate this work to my family. They have been extremely supportive throughout this journey and they are always there for me.

My brother, Martin, has such incredible values and strengths that I try to emulate in my life as much as possible, making me a better teacher, researcher, and person as a whole.

My grandfather, George Dall, has been an invaluable source of wisdom. I love him dearly.

However, I hold my parents primarily responsible for daring to embark on this journey. My father, Peter, dissuaded me from law school because “this brain stuff is so cool”. He was right. His logical mind and love for argumentation has given me ample opportunity to practice defending my ideas; his sense of humor gave much needed comic relief. I am glad the apple did not fall far from the tree and I will forever feel honored to call myself ‘PhD’ – Peter’s honorary Daughter. My mother, Glenys, inspired me to become an educator and guided me into the field of education, which led to my interest in developmental disorders (ADHD, in particular), which in turn led to an interest in cognitive neuroscience. Her support came in so many forms, including nightly telephone de-briefings and an emergency visit to DC to provide sustenance and much needed giggles. I want to thank you both from the bottom of my heart.

With love,

MELANIE LOUISE STOLLSTORFF
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CHAPTER I: INTRODUCTION

Reasoning and decision-making in the real world depend on a complex interaction among many factors that can enhance or diminish our chances of success and survival. Under perfect conditions, most healthy individuals will demonstrate the highly coveted quality of rationality, an ability that is considered by some to be uniquely human (Goel & Dolan, 2003b). However, logical reasoning is not consistent across reasoning situations or across individuals. Many factors influence reasoning, including semantic content and beliefs (Evans, Barston, & Pollard, 1983) and emotionality of content or mood (Blanchette & Richards, 2004; Oaksford, Morris, Grainger, & Williams, 1996). Thus, reasoning accuracy depends on the content of the reasoning problem and how that interacts with beliefs and emotions of the individual. I have chosen to investigate the interaction between logic, beliefs and emotion in deductive reasoning by manipulating the congruency of beliefs with logical validity (belief-logic conflict) and the saliency of beliefs using emotional content (emotional versus non-emotional) and by investigating one factor that relates to individual differences in emotional reactivity (serotonin transporter genotype).

Deductive Reasoning

Our ability and sometimes inability to reason logically has fascinated great minds throughout history; Aristotle, Descartes and Piaget, to name but a few. Their ideas have permeated modern culture and ideology: Aristotle has given us the syllogism and *philosophy of logic*; Descartes insisted that “animal passions” oppose rationality (Wheelright & Fuss, 1963); and with Piaget came a theory of cognitive development in
which the final stage, *formal operations*, depends on the emergence of logical reasoning (Piaget, 1962). Not only is rationality considered an important ability in and of itself, it also relates to success in various aspects of contemporary society, including social intelligence and academic achievement.

**Reasoning Terms & Definitions.** Deductive reasoning is the process by which a conclusion is inferred or evaluated from a set of premises. A formal argument consists of premises followed by a conclusion. The **premises** contain information about particulars from which a logical conclusion may follow. A deductive argument must provide conclusive grounds for its conclusion; if it does so it is **valid**, if it does not it is **invalid**.

Deduction is the type of reasoning that is governed by the rules of formal logic. One example of such a rule is the principle of necessity. This rule states that a conclusion can only be valid if it holds true under every possible representation of the premises.

**Indeterminate** arguments do not demonstrate necessity. For example, the premises “A > B” and “A > C” do not provide enough information to determine the relationship between B and C, as there are 3 possibilities: B > C, B < C, or B = C. Any conclusion based on these premises would be invalid, as it would not **necessarily** be true. **Determinate** arguments provide the necessary information in the premises upon which to base a definitive conclusion.

There are different classes of deductive arguments used to probe reasoning ability, and although I will focus on relational (“transitive”) arguments that were used in the following experiments, I will describe the two other classes of deductive reasoning arguments briefly. **Categorical syllogisms** deal with membership to categories and have qualifiers such as “all”, “some”, or “none” (e.g. “All men are mortal; Socrates is a man;
Therefore, Socrates is mortal”). **Conditional** reasoning problems involve causal “if-then” statements, such as, “If one is at a bar, then one must be at least 21 years old; Linda is at a bar; Therefore, she must be at least 21 years old.” The widely used Wason Selection Task is a form of conditional reasoning (Wason, 1968, 1969). **Relational** reasoning problems involve transitive properties (e.g., bigger/smaller, or higher/lower) that connect the terms in the premises and conclusion. Relational reasoning problems can be explicitly spatial (e.g., “Canada is north of Mexico” or “Mountains are higher than valleys”) or not explicitly spatial (e.g., “Andrea is funnier than Monica”). They can be linear (e.g. A > B > C > D > E) or non-linear (e.g., A is to the left of B; B is in front of C; D is behind C; E is to the right of D; Therefore, B is in front of D). They can vary in the number of terms, or relational items to compare (e.g., 3 terms: A > B > C; 5 terms: A through E). **Inversion** of the relation between sentences in the argument can also vary; an argument without inversion is consistent throughout (e.g., A > B; B > C; A > C), whereas an argument with inverted relations requires one to interpret a change in the directionality (e.g., A > B; B < C; A < C). Inversion also relates to logical form/structure, which involves the order of the terms within the argument. There are many possible valid forms for linear relational arguments with 3 terms, for example, “A > B; A < C; B < C” or “A > B; B > C; C < A” (Evans, 1989). The following studies (described in Chapters II and III) utilize three-term linear relational arguments that vary in the logical properties of validity, determinacy, inversion, and structure/form.

When content is added (meaningful terms rather than abstract placeholders), the argument becomes concrete (e.g., “Trees are taller than grass”) rather than abstract (e.g. “X > Y”). It is important to remember that an argument is valid or invalid because of its
logical form and not due to its semantic content. Thus, deductive reasoning is concerned only with the logical structure of the argument and the information given within the premises; any outside information or knowledge is irrelevant. There is a large body of literature and empirical research to explain why certain types of errors in logic occur and what this can tell us about the way we reason in general, but most theories fail to fully explain certain patterns of human reasoning error and thus have not been agreed upon [e.g., Mental Models theory (Johnson-Laird, 2001); Mental Logic theory (Evans, Clibbens, & Rood, 1995)]. A recent and rapidly growing field uses neuroscientific methods to test cognitive theories of reasoning and has provided much insight into how we reason.

The Reasoning Brain. Research into the neural bases of deduction has begun to elucidate the various structures and networks of the brain involved in different types of reasoning. There have been several methods utilized thus far in the study of reasoning and the brain, including neuropsychological studies of brain-damaged patients, functional activation studies [event-related potentials (ERP), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), functional near-infrared spectroscopy (fNIRS)] and more recently, “temporary lesion” studies that use repetitive transcranial magnetic stimulation (rTMS) to temporarily disrupt an area of the brain. Studies of patients with focal brain lesions have found that impairments in certain types of deductive reasoning result from damage to specific neural structures. Results have implicated the left hemisphere (especially left prefrontal cortex) to be necessary for deductive reasoning (Goel, Shuren, Sheesley, & Grafman, 2004; Langdon & Warrington, 2000). Functional neuroimaging studies of healthy participants have identified
dissociable neural networks for different types of reasoning. For example, reasoning with abstract, content-free problems (versus reasoning with meaningful content) relies on a frontal-parietal-striatal network, whereas reasoning with belief-laden arguments (the reverse comparison: content versus no-content) relies on a frontal-temporal network (Goel, 2007; Goel, Buchel, Frith, & Dolan, 2000).

Belief Bias

Deductive reasoning can be tested using abstract, content-free arguments such as, “X is greater than Y; Y is greater than Z; Therefore, X is greater than Z”. Judging the validity of this abstract argument probes pure logical reasoning ability. However, it is not often that we encounter arguments in this pure, abstract form in everyday life. By adding meaningful content to the argument, we emulate real-life reasoning conditions much more closely. The content of an argument can affect one’s ability to reason logically. Content in accordance with one’s beliefs can help whereas conflicting content can hinder one’s ability to reason. The term ‘belief’ refers to anything a person believes to be true, whether it is an empirical fact (e.g., Germany is north of Italy), or an opinion (e.g., Germans are happier than Italians). The belief bias effect can be defined as the tendency to accept the conclusion of an argument if one finds it believable and reject the conclusion if one finds it unbelievable, irrespective of the logical validity of the argument (Evans, 1989; Evans et al., 1983; Oakhill, Johnson-Laird, & Garnham, 1989).

Belief bias involves two key factors: beliefs and logical validity. When the two are congruent (believable, valid or unbelievable, invalid conclusions), participants are faster and more likely to make a response in accordance with logic [relative to belief-
neutral and incongruent arguments; (Evans et al., 1983). Thus, when evaluating a belief-
logic congruent argument, beliefs are “facilitory” because they help reasoning
performance (Goel & Dolan, 2003a). When logic and beliefs are incongruent (“belief-
logic conflict”; believable, invalid or unbelievable, valid conclusions), participants are
slower and less likely to make a response in accordance with logic [relative to belief-
neutral and congruent arguments; (Evans et al., 1983)]. For example, consider the
following argument: “Canada is north of USA; Mexico is north of Canada; Therefore,
Mexico is north of USA”. This argument is logically valid, however, the conclusion is
unbelievable, thereby creating a conflict between logic and belief. Thus, when evaluating
belief-logic incongruent arguments, beliefs are “inhibitory” because they hinder
reasoning performance (Goel & Dolan, 2003a).

The difference in reasoning performance (accuracy or reaction time) between
incongruent and congruent trials is a good indicator of belief bias; that is, the extent to
which the decision is based on logical reasoning rather than beliefs. An accurate
response for an incongruent trial indicates that the participant has evaluated the
conclusion based on logical validity and has avoided the tempting, prepotent response in
accordance with beliefs. An accurate decision for a congruent trial could be based on
logic or beliefs, as the two do not conflict. Thus, we cannot be certain as to what the
participant had based his or her decision on, since both logic and beliefs could have led
him or her to the correct answer. When all of the logical aspects of the reasoning task are
equated across incongruent and congruent reasoning conditions, any significant
difference in performance between the two can be attributed to beliefs, since this is the
only factor that is different across conditions.
Belief bias is consistently found to be a significant source of error in deductive reasoning tasks, including categorical syllogistic (Evans et al., 1983), conditional (Byrne & Tasso, 1999) and relational (Roberts & Sykes, 2003) reasoning. The belief bias effect is increased by many factors, such as time pressure (Tsujii & Watanabe, 2010), additional cognitive demands [dual-task paradigm; (Tsujii & Watanabe, 2009)], development/ageing [both younger children (Handley, Capon, Beveridge, Dennis, & Evans, 2004) and older adults (Tsujii, Okada, & Watanabe, 2010) have increased belief bias (De Neys & Van Gelder, 2009)]. Even in healthy, educated, intelligent adults who are explicitly instructed to base their decision on logic rather than beliefs, the belief bias effect is still found (Stollstorff, Vartanian, & Goel, submitted). In short, we tend to be biased by our beliefs. What causes this effect? Why are we so tempted to go with beliefs rather than logic?

The Inhibition Hypothesis. In this account of belief bias, increased errors for incongruent reasoning problems are not caused by poor logical reasoning per se, rather by poor inhibitory control (De Neys & Franssens, 2009; Handley et al., 2004; Houde, 1997; Moutier, Plagne-Cayeux, Melot, & Houde, 2006; Stollstorff et al., submitted). When judging the validity of a conclusion, the participant must inhibit his or her prior knowledge to focus on the logic. Thus, belief-logic conflict requires decontextualization – a separation between previous knowledge and the information held in working memory – and therefore inhibition, to complete the task. A comparison of these reasoning tasks with classic inhibition tasks such as the famous Stroop task (Stroop, 1935) reveals that the tasks both test the same phenomenon – the ability to suppress one cognitive process in favor of another. In the Stroop task, participants are instructed to say the color of each
word as fast as they can. When the words are congruent with the color in which they are printed (e.g., “blue” is printed in the color blue), participants do not find this task too difficult (they tend to accurately name the color and their response is relatively fast). However, when the words are incongruent with the color in which they are printed, (e.g., “yellow” is printed in the color red), participant are slower and less accurate in their response. They have difficulty suppressing the automatic process of reading (the prepotent response) in favor of the less automatic process of color naming. Conclusion evaluation tasks with belief-laden content share this inhibitory control component with the Stroop task and other classic inhibitory control tasks. In the belief-logic conflict condition, participants must inhibit their beliefs that are activated upon reading the conclusion (prepotent, automatic), to respond instead on the basis of logical validity (less automatic). They must suppress one cognitive process (memory retrieval) in favor of another cognitive process (logical reasoning).

While the inhibitory control account is widely accepted (De Neys & Franssens, 2009; De Neys & Van Gelder, 2009; De Neys, Vartanian, & Goel, 2008; Handley et al., 2004; Houde et al., 2000; Luo et al., 2008; Moutier et al., 2006; Prado & Noveck, 2007; Tsujii & Watanabe, 2010), the evidence from behavioral and brain studies is not entirely convincing. The best attempt to link belief bias and inhibitory control behaviorally, in my opinion, is from a study of belief bias in children. Handley et al. (2004) investigated the relation between inhibitory control, working memory and belief-logic conflict in children. Whether reasoning with conditional or relational deductive arguments, children demonstrated significant belief bias. Working memory ability (but not inhibition) predicted reasoning performance in belief-neutral conditions. Critically, for belief-laden
conditions, working memory and inhibitory control ability (as measured by the Stop Signal inhibition task) predicted belief bias. Thus, inhibitory control was related specifically to reasoning with beliefs. This is a well-controlled study that links inhibition to belief bias in children; however, it is only one study. Given the interest in belief bias research and the popularity of the inhibition account, it is surprising that this has not been reported in adults. “Inhibition training” resulted in less belief bias in children and adults (Houde et al., 2000; Moutier et al., 2006), however, upon close inspection of the methods, the so-called inhibition training involved emotional/motivational factors and logical training and was therefore not well-controlled.

Brain evidence is also not completely convincing. The argument rests on the assumption that since the belief bias effect (incongruent versus congruent) in reasoning is similar to classic inhibition tasks (also contrasting incongruent versus congruent information), and since inhibition and belief bias both depend on the right inferior prefrontal cortex (rIFC), the underlying cognitive mechanism of belief bias is a lack of inhibitory control. While there is ample evidence that both inhibition (Aron, Robbins, & Poldrack, 2004) and belief bias suppression (Goel & Dolan, 2003a; Tsujii, Masuda, Akiyama, & Watanabe, 2010) rely on rIFC, this does not necessarily mean that belief bias suppression is the same process as inhibition. While behavioral and brain evidence is consistent with the inhibition hypothesis, further research is necessary before the account should be fully accepted.
Emotion

The idea that emotion opposes logic (“reason versus passion”), dates back to ancient times of Aristotle and other great philosophers and is still widely accepted today. There is, however, surprisingly little empirical data to support this commonly held belief. In fact, recent studies in cognitive neuroscience have provided evidence to suggest that emotional factors facilitate the reasoning process through the ventromedial prefrontal cortex (vmPFC). Patients with damage to vmPFC often have blunted or abnormal emotional responses (Stuss et al., 1986). They also seem to have difficulties in real-world decision-making (Anderson, Bechara, Damasio, Tranel, & Damasio, 2000; Bechara, Tranel, & Damasio, 2000). So perhaps emotion helps, or is even necessary for, successful reasoning. Evidence from the “Gambling Task” (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Tranel, & Anderson, 1998), which led to the highly influential “somatic marker hypothesis” (Damasio, 1996), has convinced many of the idea that emotion, processed by vmPFC and amygdala is beneficial for decision-making (Bechara, Damasio, & Damasio, 2000). This idea has gained popularity (at least within the field of cognitive neuroscience), perhaps prematurely. The gambling task relies on uncertain probabilities and outcomes that result in a varying amount of reward or punishment. While many real-world scenarios are functionally equivalent to this task, many are not. The inductive reasoning ability tapped by the gambling task is not representative of reasoning in general as it does not involve deductive reasoning.

Emotion in deductive reasoning. The limited amount of empirical research on the effect of emotion on deductive reasoning has painted a different picture – one more in line with the “old fashioned” view of logic and emotion in opposition. Both affective
content (words in the reasoning problem) and affective state (“mood”) reduce logical reasoning performance (Blanchette, 2006; Blanchette & Richards, 2004; Lefford, 1946; Oaksford et al., 1996). Reasoning performance was lower for emotionally-evoking statements, such as “War times are prosperous times, and prosperity is highly desirable, therefore, wars are much to be desired” (Lefford, 1946) or anxiety-related words “If there is danger, then one feels nervous” (Blanchette & Richards, 2004), relative to emotionally-neutral statements and words, such as “All whales live in water and all fish live in water, therefore, all fish must be whales” or “If one eats a sandwich, then he is eating cheese”. Furthermore, temporarily evoking negative or positive mood also reduces reasoning performance. Participants who were shown emotionally-evoking pictures prior to reasoning made more errors in a conditional reasoning task (Wason selection task) than a control group who were shown emotionally-neutral pictures (Oaksford et al., 1996). Furthermore, anxiety, related to negative mood, also influences reasoning. Patients with specific phobias and non-clinical participants with high social anxiety had increased belief bias in deductive reasoning (de Jong, Haenen, Schmidt, & Mayer, 1998; de Jong, Mayer, & van den Hout, 1997; Vroling & de Jong, 2009). Thus, emotion (content and mood) can hinder the reasoning process. We do not know why emotional content or mood/anxiety increases reasoning errors and we do not know how emotional factors interact with beliefs. Emotional factors (for example, anxiety) relate to individual differences in deductive reasoning performance, and individual differences in anxiety are attributable, in part, to genetic polymorphisms. Thus, it is possible that genetics contribute to reasoning errors through individual differences in emotional reactivity. We explore a gene that has been linked to anxiety and other aspects of emotional reactivity.
(the serotonin transporter gene) to further our understanding of deductive reasoning and errors caused by emotionality and beliefs.

**Serotonin Transporter Gene**

Serotonin (5-hydroxytryptamine; 5-HT), a monoamine neurotransmitter synthesized in the raphe nucleus (brain stem), is released throughout the entire brain. There are 7 classes of serotonin receptors comprised of 14 receptor subtypes (Barnes & Sharp, 1999). For example, the 5-HT1<sub>A</sub> autoreceptor inhibits serotonin function through negative feedback whereas the 5-HT2<sub>A</sub> receptor increases serotonergic action (although it is possible that the receptor subtypes have different effects in certain regions of the brain). The serotonin story is not a simple one, but it is certainly an important one as it relates to many aspects of human behavior and well-being.

The serotonin transporter protein (5-HTT), located on the pre-synaptic terminal, is the main mechanism for termination of 5-HT action. It “recycles” 5-HT back to the pre-synaptic neuron, thereby clearing it from the synapse and terminating its action. Selective serotonin reuptake inhibitors (SSRIs), a common treatment for depression and anxiety disorder, block 5-HTT. In the short term, this leads to increased 5-HT in the synapse. However, it is thought that the mechanism for the therapeutic effects of SSRIs, which takes approximately 6 weeks to occur, involves a complex interaction between multiple excitatory and inhibitory 5-HT receptors that alters receptor density and the tonic and phasic release of serotonin (Huezo-Diaz et al., 2009).

A polymorphism in the 5-HTTLPR (serotonin transporter long promoter region) of the serotonin transporter gene (SLC6A4) influences 5-HTT mRNA transcription. The
short “S” allele is linked to lower expression of serotonin transporter mRNA relative to the long “L” allele (Hu et al., 2006). Further, the L allele contains an A to G single nucleotide polymorphism (SNP rs25531) that influences transcriptional efficiency, rendering the $L_G$ allele functionally similar to the S allele (Hu et al., 2006). There is some evidence to suggest that 5-HTTLPR genotype influences functional expression of 5-HTT in the human brain, with the low expressing S variant relating to less 5-HTT expression relative to the high expressing $L_A$ allele, but null and contradictory findings indicate that the story is complex and not yet fully understood (Willeit & Praschak-Rieder, 2010).

5-HTTLPR genotype influences emotional reactivity. Findings of studies comparing S carriers (SS alone or with $S_L_G$) with homozygous L carriers (e.g., LL or $L_A L_A$) suggest that the S allele is associated with higher emotional reactivity. First, genetic association studies suggest that the S allele contributes to risk for affective psychiatric disorders as it is overtransmitted in those patients (Caspi et al., 2003). Second, healthy carriers of the S allele scored higher on measures of depressive and anxiety-related behaviors (Gonda et al., 2009; Lesch et al., 1996; Lonsdorf et al., 2009). They also showed a stronger bias towards emotional content (e.g., angry faces) in an emotional dot probe task (Beevers, Wells, Ellis, & McGeary, 2009; Perez-Edgar et al., 2010) and showed increased interference from negative stimuli (e.g., threat words or angry faces) in Stroop-like tasks (Koizumi et al., 2010). Third, numerous functional neuroimaging studies show that the amygdala, a critical brain region underlying emotional behavior, is more responsive to negative stimuli in healthy S carriers [see meta-analysis (Munafo, Brown, & Hariri, 2008)]. Together, these findings indicate that S (and $L_G$) carriers differ in emotional reactivity from L carriers (and $L_A$ alone). No study
has examined whether these allelic differences influence emotional processing in the context of logical reasoning.

**Research Goals & Rationale**

When rationality is of the utmost importance, such as in a court of law, one must rely on a set of logical rules and ignore prior held beliefs and emotions to avoid irrational or prejudiced decisions. While there is considerable research on cognitive biases in reasoning and some research on the effect of emotion on reasoning (Blanchette & Richards, 2004), little is known about how individual differences in emotional reactivity might enhance or diminish cognitive biases to influence the deductive reasoning process. In Study 1, we investigated the effect of emotional content on bias in logical reasoning and how this is modulated by a polymorphism for the serotonin transporter genotype (5-HTTLPR) that is known to influence emotional reactivity. Study 2 investigates the brain basis for this effect using fMRI. Both studies use a relational reasoning task as a measure of reasoning ability. The decision to choose relational reasoning was based on the fact that it is relatively neglected in the deductive reasoning literature (most behavioral studies have used categorical or conditional reasoning tasks) and it is considered somewhat easier than other deductive reasoning tasks making it a suitable choice for testing across the lifespan in future studies.
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CHAPTER II: RATIONALITY AND EMOTIONALITY: SEROTONIN TRANSPORTER GENOTYPE INFLUENCES REASONING BIAS

Abstract
Reasoning often occurs under emotionally charged, opinion-laden circumstances. The belief-bias effect indexes the extent to which reasoning is based upon beliefs rather than logical structure. We hypothesized that emotional content will increase this effect, particularly for individuals with higher emotional reactivity. The serotonin transporter genotype is associated with emotional reactivity such that it is higher in carriers of the S than L allele. Thus, we expected belief bias to be higher in SS/SL\(_G\) than in L\(_A\)L\(_A\) carriers for relational reasoning problems with emotional, but not non-emotional, content. Indeed, SS/SL\(_G\) carriers were less accurate selectively for evaluating relational reasoning emotional problems with belief-logic conflict relative to L\(_A\)L\(_A\) carriers. Further, genotype accounted for the association between trait anxiety and emotional belief bias. Thus, deductive reasoning, an important ability associated with academic achievement and socio-emotional intelligence, is sensitive to differences in emotionality rooted in serotonin neurotransmitter function.
Introduction

Humans are not perfectly rational. We display biases leading to errors in reasoning and decision-making (Birch & Bloom, 2007; Tversky & Kahneman, 1974). One common type of bias in deductive reasoning is when one accepts or rejects a conclusion based on one’s knowledge about the world (hereafter termed beliefs) rather than logical validity (Evans, Barston, & Pollard, 1983). In relational reasoning tasks, one must evaluate whether a conclusion follows logically from the premises, regardless of the believability of the content. For example, given the premises, “Cars are bigger than motorcycles” and “Motorcycles are bigger than airplanes”, the conclusion “Cars are bigger than airplanes” is logically valid but unbelievable, as cars are not bigger than airplanes in the real world. Participants tend to be slower or less accurate in accepting unbelievable conclusions as valid; similarly, participants are also slower or inaccurate in accepting believable conclusions that are logically invalid (Roberts & Sykes, 2003). Thus, accepting conclusions that are incongruent with our beliefs interferes with logical reasoning. Conversely, when the validity and belief of the conclusion are congruent (valid, believable or invalid, unbelievable), participants are faster or more accurate in evaluating the conclusion. Reduced performance for incongruent than congruent conclusions, termed the belief bias effect, indexes how much our beliefs interfere with reasoning and has been demonstrated using categorical syllogisms and conditional and relational reasoning problems (Byrne & Tasso, 1999; Goel & Dolan, 2003a; Roberts & Sykes, 2003).

In addition to our beliefs, emotion also influences deductive reasoning. Two lines of evidence indicate that manipulation of emotional processing hinders the reasoning
process. First, affective state (preexisting or induced) reduces logical reasoning performance. Patients with anxiety disorders made more errors on a conditional reasoning task (Wason Selection Task) than healthy controls when reasoning with anxiety-provoking stimuli (de Jong, Haenen, Schmidt, & Mayer, 1998; de Jong, Mayer, & van den Hout, 1997). In healthy participants, experimentally inducing negative or positive mood resulted in more errors on the Wason Selection Task relative to those without mood manipulation (Oaksford, Morris, Grainger, & Williams, 1996). Second, affective content (preexisting or conditioned) reduces reasoning performance relative to neutral content. Given logically identical reasoning problems, participants made more errors when problems comprised emotionally charged statements (e.g. “If there is danger, then one feels nervous”) than neutral statements (e.g. “If one is in a library, then one sees books”) for conditional (Blanchette, 2006; Blanchette & Richards, 2004) and categorical (Lefford, 1946) reasoning problems. Blanchette and Richards (2004) controlled for qualitative differences between emotional and neutral words by conditioning neutral words to acquire emotional valence via association with negative or positive emotional pictures and comparing them to neutral words associated with emotionally neutral pictures. Participants made more reasoning errors for problems with emotionally-conditioned words (more for negative than positive) relative to the neutral-conditioned words (also replicated by Blanchette, 2006). Thus, neutral content with experimentally induced emotional valence also reduced deductive reasoning performance. Together, these findings indicate that emotional states and content influence logical reasoning.

If emotional processing influences logical reasoning, then individual differences in emotional reactivity ought to influence reasoning performance. One source of
individual differences in emotional reactivity is a polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) that results in short (S) and long (L) variants. The S allele is linked to lower expression of serotonin transporter mRNA (Hu et al., 2006). Further, the L allele contains an A to G single nucleotide polymorphism (SNP rs25531) that influences transcriptional efficiency, rendering the L_G allele functionally similar to the S allele (Hu et al., 2006). Findings of studies comparing S carriers (SS alone or with SL_G) with homozygous L carriers (e.g., LL or L_A L_A) suggest that the S allele is associated with higher emotional reactivity. First, genetic association studies suggest that the S allele contributes to risk for affective psychiatric disorders as it is overtransmitted in those patients (Caspi et al., 2003). Second, healthy carriers of the S allele scored higher on measures of depressive and anxiety-related behaviors (Gonda et al., 2009; Lesch et al., 1996; Lonsdorf et al., 2009). They also showed a stronger bias towards emotional content (e.g., angry faces) in an emotional dot probe task (Beevers, Wells, Ellis, & McGeeary, 2009; Perez-Edgar et al., 2010) and showed increased interference from negative stimuli (e.g., threat words or angry faces) in Stroop-like tasks (Koizumi et al., 2010). Third, numerous functional neuroimaging studies show that the amygdala, a critical brain region underlying emotional behavior, is more responsive to negative stimuli in healthy S carriers [see meta-analysis (Munafo, Brown, & Hariri, 2008)]. Together, these findings indicate that S (and L_G) carriers differ in emotional reactivity from L carriers (and L_A alone). No study has examined whether these allelic differences influence emotional processing in the context of logical reasoning.

We investigated the effect of 5-HTTLPR genotype on belief bias in relational reasoning problems with and without emotional content. In light of evidence indicating
functional similarity between the S and L\textsubscript{G} alleles (Hu et al., 2006), we included L\textsubscript{G} carriers in the S group as done in past work (Armbruster et al., 2009). Other heterozygous carriers (SL\textsubscript{A}, L\textsubscript{A}L\textsubscript{G}) were excluded in order to maximize observed allelic differences (Roiser et al., 2009). We predicted that carriers of the 5-HTTLPR S or L\textsubscript{G} alleles (SS, SL\textsubscript{G}, L\textsubscript{G}L\textsubscript{G}) would demonstrate increased belief bias relative to homozygous carriers of the L\textsubscript{A} allele (L\textsubscript{A}L\textsubscript{A}) during reasoning with emotional, but not non-emotional, content. This prediction is based upon past findings of increased sensitivity to negative affective stimuli in S (and L\textsubscript{G}) carriers, which ought to make suppression of beliefs with emotional content more difficult relative to L\textsubscript{A}L\textsubscript{A} carriers. Furthermore, in light of past findings relating the S allele to increased anxiety, we measured this trait using the State-Trait Anxiety Inventory for Adults [STAI; (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983)] in order to determine whether belief bias in reasoning with emotional material relates to trait anxiety, one characteristic of emotional behavior in healthy adults.

**Method**

**Participants**

Participants were 169 undergraduate students (65 male) from Georgetown University, aged 18 to 22 years who were recruited from psychology classes and campus advertisements and received course credit or $10 for participation. They were primarily of European descent and were native English speakers or were fluent by 10 years of age. Participants had never received a psychiatric diagnosis and had no exposure to antidepressant or anxiolytic medications, based on self-report. Consent was acquired in accordance with the procedures set by the Georgetown University Institutional Review Board. Participants provided a saliva sample that was analyzed for the polymorphism in
the serotonin transporter-linked promoter region (5-HTTLPR) and the rs25531 SNP in the serotonin transporter gene (SLC6A4). After excluding LA$S$ and LA$LG$ genotypes our final sample included two groups, LA$LA$ and SS/SL$G$. The LA$LA$ group (N = 41; 44% Male; Age: M = 19.4, SD = 1.2) did not differ from the SS/SL$G$ group (N = 34; 41% Male; Age: M = 19.1, SD = 1.1) in age ($p > .4$) or gender ($p > .8$). The SS/SL$G$ group was composed of SS (n = 22) and SL$G$ (n = 12) carriers. No participants in this sample had the rare LG$LG$ genotype.

Genotyping

Saliva samples (Orgene, Ottawa, Canada) were analyzed for the 5-HTTLPR genotype using a two-step process. First, the long (L) and short (S) variants were determined. The repeat polymorphism in the promoter region of the 5-HTT gene was genotyped by PCR as previously described (Lesch et al., 1996) using the following primers at concentrations of 10 µM; Forward: 5'-GGCGTTGCCGCTCTGAATGC -3'
Reverse: 5'-GAGGGACTGAGCTG-GACAACCAC-3'. PCR was performed using the AccuPrime™ GC-Rich DNA polymerase system (Invitrogen) with the following PCR program: 95°C for 10 min, followed by 35 cycles of 95°C for 30 sec, 65°C for 30 sec, and 72°C for 1 min. A final extension time of 72°C for 10 min was performed after the 35 cycles were complete. The PCR products were then run out on a 2% agarose gel stained with ethidium bromide. The amplification yielded distinct bands at 484 bp (S allele = 14 copies of repeat) and 528 bp (L allele = 16 copies of repeat), which were distinguished by a 100 bp DNA ladder run on the same gel. Second, the LA and LG variants were determined for the rs25531 single nucleotide polymorphism (SNP), present only on the long allele. Genotyping for rs25531 was performed by digesting the PCR
products generated from the 5-HTTLPR PCR reactions with the restriction enzyme MspI (New England BioLabs). Specifically, 10 µL restriction digestion reactions were performed by combining 8 µL of the 5-HTTLPR PCR product, 1 µL of 10X NEBuffer 4, and 1 µL of MspI (concentration = 100,000 U/mL) and incubating the reactions for 2 hr at 37°C followed by heat inactivation of the enzyme at 80°C for 20 min. The substitution of the G for A in the SNP produces an additional MspI recognition site (CCGG) on the long allele of the 5-HTTLPR PCR product. Genotypes were determined by running the digested PCR products out on a 2% agarose gel stained with ethidium bromide. Samples with 2 copies of the A allele for rs25531 showed a band at 340 bp (as well as bands at 127 and 62 bp due to multiple MspI recognition sites on the 5-HTTLPR PCR product), while samples with 2 copies of the G allele for rs25531 had additional digestion of the 340 bp product, yielding bands at 166 and 174 bp (as well as bands at 127 and 62 bp). Samples that were heterozygous for rs25531 showed a combination of these 2 band patterns.

**Stimulus materials**

Stimuli consisted of 96 three-term relational reasoning problems (e.g., A>B, B>C, therefore A>C) that varied by emotion and congruency (see Table 1). Words for the reasoning problems were selected from the Affective Norms for English Words database [ANEW; (Bradley & Lang, 1999)] which provides ratings for arousal and valence on a 1-10 point scale. Emotional words were selected based on high arousal (> 3.5; Mean: 5.9) and extreme valence (< 4 = negative, 84.7%, > 7 = positive valence, 15.3%). Non-emotional words were selected based on low arousal (< 5.5; Mean: 4.2) and neutral valence (4-7; neither positive nor negative). Thus, emotional problems contained
primarily negative and highly arousing words whereas non-emotional problems contained
words that were neither positive nor negative and low in arousal.

Problems also varied on belief-logic congruency. For congruent problems, the
validity of the conclusion was in accordance with semantic beliefs (valid, believable and
invalid, unbelievable). For incongruent problems, the validity of the conclusion was in
conflict with semantic beliefs (valid, unbelievable and invalid, believable). A total of 96
logical reasoning problems were included (see Appendix 1) that varied by Emotional
content (emotional, non-emotional) and Congruency (congruent, incongruent), creating 4
conditions, each consisting of 24 problems: (1) Emotional Congruent, (2) Emotional
Incongruent, (3) Non-emotional Congruent, and (4) Non-emotional Incongruent. The 4
conditions were equated for conclusion believability (12 believable, 12 unbelievable),
validity (12 valid, 12 invalid), determinacy (18 determinate, 6 indeterminate), and content
type (13 non-living, 6 living, 5 abstract).

Table 1. Experimental conditions and example stimuli.

<table>
<thead>
<tr>
<th>Trial Type</th>
<th>Emotional</th>
<th>Non-emotional</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cockroaches are smaller than snakes.</td>
<td>Adults are younger than children.</td>
</tr>
<tr>
<td></td>
<td>Cockroaches are bigger than maggots.</td>
<td>Adults are older than infants.</td>
</tr>
<tr>
<td></td>
<td>So, snakes are bigger than maggots?</td>
<td>So, children are older than infants?</td>
</tr>
<tr>
<td></td>
<td>(Valid, Believable)</td>
<td>(Valid, Believable)</td>
</tr>
<tr>
<td>Congruent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incongruent</td>
<td>Tobacco is more poisonous than venom.</td>
<td>Trees are taller than flowers.</td>
</tr>
<tr>
<td></td>
<td>Tobacco is less poisonous than mucus.</td>
<td>Trees are shorter than grass.</td>
</tr>
<tr>
<td></td>
<td>So, venom is less poisonous than mucus?</td>
<td>So, flowers are shorter than grass?</td>
</tr>
<tr>
<td></td>
<td>(Valid, Unbelievable)</td>
<td>(Valid, Unbelievable)</td>
</tr>
</tbody>
</table>
**Procedure**

Participants underwent training for the reasoning task, followed by the experimental task, and then completed a belief questionnaire and the STAI-T.

*Training.* The experimenter described the task and explained what constitutes a logical conclusion. Participants were then instructed to determine if the third sentence (the conclusion) followed logically from the first two sentences (the premises) by basing the decision on logical form and not on the factual truth or falsity of the conclusion. Participants completed 14 practice problems on paper with unlimited time and were asked to re-think the problem if they made errors; participants then explained and corrected the error, ensuring that the task was fully understood.

*Reasoning Task.* Reasoning problems were presented on a computer screen in pre-determined random order that was held constant across participants. Participants were instructed to press the “F” key if a problem was ‘logical’ and the “J” key if it was ‘not logical’, and to respond as quickly as possible once they knew the answer. Premise 1 appeared on the screen for 3 seconds, followed by Premise 2 below it for 3 seconds, and then the conclusion below it, after which all three remained on the screen for 6 s. Participants could respond at any point after the conclusion appeared; the next problem appeared immediately after participants’ response or after 6 s if no response was made. No feedback was provided.

*Belief Questionnaire.* The questionnaire measured whether the participant’s beliefs were in accordance with those of the experimenters. It consisted of 48 conclusions (half believable, half unbelievable) that were selected randomly, including 12
problems from each of the four experimental conditions. Participants were asked to mark each conclusion as “True,” “False,” or “I Don’t Know,” based on their own knowledge.

**Trait Anxiety.** Participants completed the STAI, a self-report measure of state and trait anxiety. Twenty statements, rated on a scale of 1 (almost never) to 4 (almost always) about trait anxiety were scored and used in further analysis; an additional 20 statements about state anxiety were not included in further analysis as we were interested in the influence of a stable rather than situational characteristic of emotionality.

**Results**

**Belief Questionnaire**

For each participant, each response was coded based upon the match with the experimenter as agree (true or false by both), disagree (true or false mismatch between the two), or uncertain (“don’t know” response). For each participant, mean percentage of “agree” responses were calculated separately for each of the four experimental conditions and compared by genotype with separate independent samples t-tests. Since average disagreement (2.4%) and uncertainty (4.5%) across conditions was extremely low, genotype groups were compared with independent samples t-tests, regardless of condition. Mean agreement did not differ by genotype for any condition: emotional congruent (L\_A L\_A: M = 94.1%, SD = 7.2; SS/SL\_G: M = 92.1%, SD = 8.6; \( p > .2 \)), emotional incongruent (L\_A L\_A: M = 92.9%, SD = 6.7; SS/SL\_G: M = 92.8%, SD = 5.0; \( p > .9 \)), non-emotional congruent (L\_A L\_A: M = 94.3%, SD = 6.9; SS/SL\_G: M = 93.0%, SD = 6.4; \( p > .3 \)), non-emotional incongruent (L\_A L\_A: M = 92.9%, SD = 6.3; SS/SL\_G: M = 91.4%, SD = 7.3; \( p > .3 \)). Scores did not differ by genotype for disagreement (L\_A L\_A: M =
2.4%, SD = 1.6; SS/SL_G: M = 2.6%, SD = 1.8; p > .5) or uncertainty (L_AL_A: M = 4.2%, SD = 2.8; SS/SL_G: M = 4.8%, SD = 2.9; p > .3)

Reasoning Task
A response was scored as correct if it was consistent with the logical validity of the problem. A response was scored as incorrect if it was not consistent with logical validity or if there was no response within 6 s (‘timed-out’; M = 7% of problems). For each participant, mean accuracy (% correct) and mean reaction time for correct responses (in msec) was computed for congruent and incongruent problems with and without emotional content (see Table 2). For accuracy and reaction time data separately, a mixed ANOVA was computed with genotype (SS/SL_G vs. L_AL_A) as a between-subject factor and Congruency (congruent vs. incongruent) and Emotion (emotional vs. non-emotional content) as within-subjects factors.
Table 2. Mean anxiety (SD in parenthesis), accuracy and reaction time for relational reasoning problems with emotional and non-emotional content in SS/SL\(_G\) and L\(_A\)L\(_A\) carriers.

<table>
<thead>
<tr>
<th></th>
<th>Short (SS/SL(_G))</th>
<th>Long (L(_A)L(_A))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 34</td>
<td>N = 41</td>
</tr>
<tr>
<td>Trait Anxiety</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50.06 (10.31)</td>
<td>46.46 (7.56)</td>
</tr>
<tr>
<td>Accuracy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>85.57% (10.31)</td>
<td>85.88% (10.19)</td>
</tr>
<tr>
<td>Incongruent</td>
<td>73.93% (14.01)</td>
<td>80.74% (10.82)</td>
</tr>
<tr>
<td>Non-Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>85.06% (11.54)</td>
<td>88.27% (8.19)</td>
</tr>
<tr>
<td>Incongruent</td>
<td>77.94% (12.59)</td>
<td>80.67% (10.75)</td>
</tr>
<tr>
<td>Reaction Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>2482 msec (718)</td>
<td>2411 msec (572)</td>
</tr>
<tr>
<td>Incongruent</td>
<td>2850 msec (584)</td>
<td>2700 msec (468)</td>
</tr>
<tr>
<td>Non-Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>2586 msec (546)</td>
<td>2447 msec (528)</td>
</tr>
<tr>
<td>Incongruent</td>
<td>2785 msec (588)</td>
<td>2676 msec (521)</td>
</tr>
</tbody>
</table>

*Reasoning Accuracy.* There was a main effect of congruency \(F(1, 73) = 65.99, p < .001, \eta^2 = .47\] indicating a significant belief-bias effect as participants were more accurate for belief-logic congruent (M = 86.19%, SD = 8.77) than incongruent (M = 78.32%, SD = 10.83) problems. While no other main effects or two-way interactions reached significance \(p > .10\), the genotype X congruency X emotion interaction was significant \(F(1, 73) = 6.28, p = .014, \eta^2 = .08\]. Planned comparisons testing for group differences indicated that accuracy was lower in SS/SL\(_G\) (M = 73.93%, SD = 14.01) relative to L\(_A\)L\(_A\) (M = 80.74%, SD = 10.82) participants, only for problems in the emotional incongruent condition \(t(73) = 2.37, p = .020\]; the genotype groups did not differ in any other condition \(p > .20\). Further, planned comparisons were conducted to
test whether each genotype group exhibited belief bias (congruent > incongruent) for both emotional and non-emotional conditions. The SS/SL\(_G\) group showed significant belief bias for emotional \([t(33) = 6.31, p < .001]\), and non-emotional \([t(33) = 3.71, p = .001]\), conditions. The L\(_A\)L\(_A\) group also showed significant belief bias for emotional \([t(40) = 3.240, p < .001]\) and non-emotional \([t(40) = 5.30, p = .002]\), conditions.

In light of the 3-way interaction above, we also examined whether the amount of the belief bias effect, defined as the difference between accuracy for Congruent and Incongruent problems, differed by genotype and emotion (see Figure 1). A genotype X emotion ANOVA revealed an interaction \([F(1, 73) = 6.28, p = .014, \eta^2 = .08]\), such that SS/SL\(_G\) carriers \((M = 11.64\%, \text{SD} = 10.75)\) had higher belief bias relative to L\(_A\)L\(_A\) carriers \((M = 5.14\%, \text{SD} = 10.16)\) for emotional problems \((t(73) = 2.68, p = .009)\). Amount of belief bias did not differ between genotype groups for non-emotional problems \((\text{SS/SL}_G: M = 7.12\%, \text{SD} = 11.19; \text{L}_A\text{L}_A: M = 7.60\%, \text{SD} = 9.18; p > .8)\). Further, SS/SL\(_G\) carriers had higher belief bias for emotional \((M = 11.64\%, \text{SD} = 10.75)\) relative to non-emotional \((M = 7.12\%, \text{SD} = 11.19)\) problems \([t(33) = 2.234, p = .032]\); belief bias in L\(_A\)/L\(_A\) carriers did not differ by emotional content \((p > .2)\). There was no main effect of Emotional content or genotype \((ps > .1)\).
Figure 1. Mean belief bias (% correct congruent – incongruent) for relational reasoning problems with emotional and non-emotional content in SS/SLG and LA carriers (*p < .05).

Reasoning Reaction Time. There was a main effect of congruency \[ F(1, 73) = 64.86, p < .001, \eta^2 = .47 \], such that participants were faster to evaluate conclusions of congruent (M = 2477 msec, SD = 555) than incongruent (M = 2747 msec, SD = 505) problems. Thus, participants’ response latencies exhibited a belief bias effect. No other main effects or interactions reached significance (ps > .1, see Table 2).

Trait Anxiety. An independent-samples t-test comparing mean trait anxiety standard scores normed for college students from the STAI-T revealed that anxiety scores were higher in SS/SLG (M = 50.06, SD = 8.07) than LA (M = 46.46, SD = 7.56) participants \[ t(73) = 1.99, p = .050 \]. In light of higher anxiety in the SS/SLG group, we examined whether the magnitude of belief bias was associated with anxiety separately for emotional and non-emotional conditions. Trait anxiety scores correlated with the amount of belief bias for problems with emotional (r = .24, p = .040) but not non-emotional (r =
.03, $p = .789$) content (see Figure 2). Thus, individuals with higher trait anxiety were more biased towards their beliefs during reasoning with emotional content alone.

![Image of Figure 2: Correlation between Trait Anxiety and Emotional Belief Bias for $L_A L_A$ and $SS/SL_G$ carriers.]

**Figure 2.** Correlation between Trait Anxiety and Emotional Belief Bias for $L_A L_A$ and $SS/SL_G$ carriers.

**OLS Linear Regression.** In light of the association between anxiety and emotional belief bias and higher anxiety in $SS/SL_G$ carriers, we regressed emotional belief bias on 5-HTTLPR genotype and anxiety to determine the role of genotype in the relationship between anxiety and emotional belief bias. First, we ran a simple regression model in which we entered anxiety as the sole independent variable. The estimated association between anxiety and emotional belief bias was .32 with an associated standard error ($se$) of .15 ($p = .04$; standardized $\beta = .24$, replicating the bivariate correlation). Next, we added genotype to the model. Adding genotype reduced the association between anxiety and emotional belief bias to non-significance ($p > .1$). This
reduction suggests that the positive association between anxiety and emotional belief bias is explained by the covariance between both behavioral variables (anxiety and emotional belief bias) and genotype. Moreover, genotype was significantly associated with emotional belief bias even with anxiety held constant ($b = 5.61$, $se = 2.46$, $p = .02$). The unstandardized coefficient of 5.61 indicates that the SS/SL$_G$ group scored 5.61 percentage points higher on emotional belief bias than the LALA group, even with anxiety held constant. With both genotype and anxiety included, the model accounted for 12% of emotional belief bias variance.

**Discussion**

We found that a polymorphism of the serotonin transporter genotype influenced belief bias in deductive reasoning, selectively with emotional content. Overall, participants made more errors and were slower in evaluating conclusions of relational reasoning problems in which beliefs and logical structure were in conflict relative to congruent. Thus, participants exhibited a significant belief bias effect, indicating that beliefs interfered with deductive reasoning. Most importantly, the amount of belief bias differed by 5-HTTLPR genotype, depending upon the emotional content of the problems. Belief bias was higher in carriers of the S/L$_G$ alleles relative to the L$_A$ allele for problems with highly arousing and emotionally valenced content but not for those with less arousing and less emotional content. Further, while trait anxiety, one property of emotional reactivity, was higher in S/L$_G$ than L$_A$ carriers and correlated positively with belief bias for emotional problems, the 5-HTTLPR genotype accounted for the relationship between anxiety and emotional belief bias.
Reasoning with meaningful content involves inhibiting one’s semantic knowledge in order to process the logical structure (De Neys & Franssens, 2009; De Neys & Van Gelder, 2009; De Neys, Vartanian, & Goel, 2008; Handley, Capon, Beveridge, Dennis, & Evans, 2004; Houde et al., 2000; Luo et al., 2008; Prado & Noveck, 2007). Behaviorally, suppression of one’s beliefs is effortful as reflected in failures or slower speed of reasoning for problems where beliefs and logic conflict. Indeed, our participants exhibited significant belief bias regardless of the emotionality of semantic content. Evidence in support of an inhibitory process during deductive reasoning comes from the following findings: First, inhibitory control abilities appear to be associated with amount of belief bias. Children with higher inhibitory control (as measured by the stop signal response inhibition task) had lower belief bias in conditional and relational reasoning tasks (Handley et al., 2004). Second, functional brain imaging studies have shown a brain region known to support inhibitory control, namely, right inferior prefrontal cortex [rIFC; (Aron, Robbins, & Poldrack, 2004)] was consistently activated during belief bias suppression [e.g., incongruent versus congruent problems (Goel, Buchel, Frith, & Dolan, 2000); logical versus belief-based responses for incongruent problems (Goel & Dolan, 2003a)], and increased activity of this region but not its left-hemisphere homologue was associated with less belief bias (Tsujii & Watanabe, 2010). Causal evidence indicating that right IFC is involved in the suppression of belief bias comes from the application of transcranial magnetic stimulation during categorical reasoning with congruent and incongruent problems. Disruption of neural activity in the right, but not left, IFC reduced accuracy for incongruent, but not congruent, syllogisms, thereby increasing belief bias relative to a control group (Tsujii, Masuda, Akiyama, & Watanabe, 2010). Together,
these findings suggest that successful logical reasoning requires the inhibition of interference from semantic knowledge.

Our findings suggest that inhibiting emotionally valenced semantic knowledge was selectively effortful for carriers of the 5-HTTLPR short allele. Relative to \(L_A L_A\) carriers, \(S S / S L_G\) carriers had reduced accuracy for incongruent but not congruent problems with emotionally arousing words, yielding a larger belief bias effect. Overall reasoning abilities were similar in the two groups as their accuracy did not differ on either incongruent or congruent problems without emotional content. Thus, greater interference from beliefs in \(S\) carriers was specific to reasoning with emotional material.

Our study did not manipulate the nature of emotional valence, an important factor in light of past findings of the 5-HTTLPR polymorphism. Specifically, while \(S / L_G\) carriers are more responsive to negative emotional stimuli, there is some evidence to suggest that \(L / L_A\) carriers are biased towards positive emotional stimuli. Studies using the emotional dot-probe task, which measures attentional biases toward or away from negative or happy faces relative to neutral faces, found that \(S / L_G\) carriers had higher attentional bias towards negative faces than did \(L / L_A\) carriers and that \(L / L_A\) carriers had higher attentional bias towards happy faces than did \(S / L_G\) carriers, with heterozygotes somewhere in between [relatively low bias towards either positive or negative valence; (Beevers et al., 2009; Fox, Ridgewell, & Ashwin, 2009; Perez-Edgar et al., 2010)]. Emotional content in the present study was comprised primarily of negatively valenced words, with only a few highly arousing positive words that were often intermixed within the predominantly negative logic problem. Thus, it is not possible to examine our results by valence. However, if \(L / L_A\) carriers are more sensitive to positive emotional stimuli,
they ought to show more belief bias selectively for problems with positively valenced content. This prediction could be tested in future work. Furthermore, the interaction between emotional valence and 5-HTTLPR genotype could elucidate past findings of a detrimental effect of emotional content on deductive reasoning. Performance on both negative and positive valence conditions was reduced relative to non-emotional content (Blanchette, 2006; Blanchette & Richards, 2004). It is possible that positive emotional content was detrimental selectively for L_AL_A carriers (due to their tendency for attentional bias towards positive stimuli), and negative emotional content was detrimental selectively for S/L_G carriers (due to their tendency for attentional bias towards negative stimuli). This prediction can be tested in the future and could add to our understanding of the nature of emotion-reason interactions.

In the present study, enhanced belief bias from emotional content in S carriers who are known to be more emotionally reactive may result from two sources: Parallel to findings from emotional Stroop-like tasks [e.g. color-word and face-word, (Koizumi et al., 2010)], S carriers’ increased attention to negative emotional content could have increased inhibitory demands making its suppression more difficult than that of non-emotional information. Another possibility is that the emotional content, which was primarily negative, could have temporarily evoked a negative mood state. Indeed, past findings indicate that S carriers have a higher propensity for negative mood (Gonda et al., 2009; Lesch et al., 1996). Thus, negative emotional material may draw more attention and induce a negative affective state, two factors known to impede reasoning (Blanchette & Richards, 2004; Oaksford et al., 1996), thereby, reducing reasoning accuracy for
emotional problems with belief-logic conflict, only in participants with higher emotional reactivity.

Trait anxiety, one property of emotional reactivity, was higher in SS/SLSG than LALS carriers, consistent with previous reports (Lesch et al., 1996; Lonsdorf et al., 2009). Past studies using the emotional Stroop task found greater interference from threat-related words in patients with anxiety disorder (Becker, Rinck, Margraf, & Roth, 2001) as well as healthy participants with high trait anxiety (Dresler, Meriau, Heekeren, & van der Meer, 2009). Further, belief bias during reasoning with social-anxiety provoking statements was higher in healthy participants with higher levels of social anxiety (Vroling & de Jong, 2009). Similarly, belief bias for emotional problems was higher in participants with higher trait anxiety in the present study. However, multiple regression analysis revealed that 5-HTTLPR genotype accounted for the relationship between anxiety and emotional belief bias. Thus, a more anxious temperament due to the 5-HTTLPR genotype reduced inhibitory control during reasoning selectively with emotional material.

It is important to consider additional factors, however, as genotype and anxiety explained only 12% of variance in emotional belief bias. While many factors may influence emotional reactivity, a few known candidates include: (1) a polymorphism in the brain-derived neurotrophic factor (BDNF) gene, which is known to interact with serotonin to influence neurogenesis, synaptic plasticity and emotional reactivity (Martinowich & Lu, 2008); (2) dopaminergic genetic polymorphisms that influence both emotional regulation and inhibitory control such as COMT Val158Met (Bishop, Cohen, Fossella, Casey, & Farah, 2006; Lonsdorf et al., 2009); (3) environmental stressors, such
as traumatic life events, which can interact with 5-HTTLPR to influence anxiety (Armbruster et al., 2009) and susceptibility to affective disorders (Bukh et al., 2009). The extent to which these factors together with the 5-HTTLPR or alone influence susceptibility to higher belief bias in reasoning with emotional information can be investigated in future work.

The present genotypic differences may be manifested via differences in involvement of brain regions important for emotional regulation, reasoning and memory retrieval. Specifically, the hippocampus, a medial temporal lobe region, is important for retrieval of semantic knowledge (Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006), relational reasoning (Goel, Makale, & Grafman, 2004; Vartanian, Goel, Tierney, Huey, & Grafman, 2009) and emotional processing [emotional regulation (Lane et al., 1997) and emotional learning (Buchel, Dolan, Armony, & Friston, 1999; Phillips & LeDoux, 1992)]. 5-HTTLPR influences hippocampal structure (Frodl et al., 2010) and function (Gallinat et al., 2005), possibly through its interaction with BDNF (Martinowich & Lu, 2008). Interestingly, hippocampal activity is also related to trait anxiety (Gallinat et al., 2005). The amygdala and the ventromedial prefrontal cortex are also involved in emotional processing, memory and reasoning (Davidson, 2002; Goel & Dolan, 2003b) and functional activation of these regions are influenced by 5-HTTLPR as well (Roiser et al., 2009).

Another mechanism could be through differences in connectivity between these regions. During emotional reasoning, 5-HTTLPR genotype influenced prefrontal-amygdala connectivity (Roiser et al., 2009). Specifically, S/S carriers were more likely to make irrational decisions in accordance with the “framing bias” (i.e., whether the risk
was described in terms of potential loss or gain) relative to $L_A L_A$ carriers in an economic decision-making task. S/S carriers had increased amygdala activity when they made decisions in accord with the framing bias relative to when they avoided the bias. Furthermore, $L_A L_A$ carriers had higher amygdala-prefrontal cortex coupling when they successfully avoided the bias, a pattern that was not detected in S/S carriers (Roiser et al., 2009). Thus, while further research is necessary to elucidate the neural mechanism for increased emotional belief bias in $S/L_G$ carriers, evidence suggests that dysfunction in the hippocampus, amygdala and prefrontal cortex and reduced connectivity between these regions in S carriers could underlie this effect.

The ability to make rational decisions relates to success in various aspects of contemporary society. Superior deductive reasoning ability predicts higher academic achievement. Specifically, children showing less belief biased reasoning errors had higher math and reading performance (Handley et al., 2004). Furthermore, relational reasoning is also important for social functioning (Maclean, Merritt, & Brannon, 2008; Paz, Bond, Kamil, & Balda, 2004). For example, if Johnny knows that his older sibling Pat is stronger than him based on previous experience, and that Mark, the new kid in school, is stronger than Pat, the ability to infer that Mark is therefore stronger than Johnny without having to directly test this hypothesis can be highly beneficial. Interestingly, 5-HTTLPR genotype relates to a variety of social functions, including establishment of social dominance and aggression in animals that live in social groups (Neumann, Veenema, & Beiderbeck, 2010). In humans, stereotypes and prejudiced beliefs can be difficult to suppress, even in healthy educated adults, despite the fact that their expression can evoke anger and retaliation from others. The present findings show
that genotypic differences in the functioning of the serotonin transporter may leave some individuals more vulnerable to the influence of emotion and its deleterious effects on reasoning, an important ability for academic and social success.
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dementia selectively impairs transitive reasoning about familiar spatial

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CHAPTER III: SEROTONIN TRANSPORTER GENOTYPE INFLUENCES
BRAIN ACTIVATION DURING BELIEF BIAS SUPPRESSION IN REASONING

Abstract

Emotions interact with beliefs during deductive reasoning. One common source of error in reasoning is belief bias. The belief bias effect is associated with reduced activation of the right inferior frontal cortex (rIFC) and increased activation of ventromedial prefrontal cortex (vmPFC). The belief bias effect can be enhanced by emotional content, particularly for individuals with increased emotional reactivity due to a polymorphism of the serotonin transporter gene (5-HTTLPR). Carriers of the short (S) allele, but not the long (L) allele, tend to have increased attention to negative emotional stimuli and this is manifested in increased belief bias for emotional, relative to non-emotional, conditions. To understand the functional neuroanatomy of this effect, we used functional magnetic resonance imaging (fMRI) to investigate rIFC and vmPFC activation in carriers of the S allele versus homozygous carriers of the long allele (LAL) during emotional and non-emotional reasoning with and without belief-logic conflict. Relative to LAL carriers, S carriers had decreased activation of rIFC and increased activation of vmPFC while evaluating arguments with belief-logic conflict and emotional content. Furthermore, vmPFC activity increased as a function of emotional reactivity (as measured by anxiety self-report) during emotional belief-incongruent reasoning. Thus, emotional content is associated with a shift from lateral (rIFC) to medial (vmPFC) regions of prefrontal cortex and with increased susceptibility to reasoning bias in S carriers of the 5-HTTLPR.
Introduction

Reasoning decisions often must be made against a backdrop of strongly held opinions and beliefs. Meaningful content can either help or hinder deductive reasoning depending on whether it is in line with what one believes to be true. When evaluating the validity of an argument, participants tend to be less accurate when logic and beliefs conflict. Specifically, “belief-logic conflict” occurs when the logical conclusion is different from what one believes to be true regarding their knowledge of the world (valid, unbelievable or invalid, believable) – termed “incongruent”. When beliefs and logic are congruent (valid, believable or invalid, unbelievable), participants tend to respond faster and more accurately relative to incongruent reasoning problems - this is the belief bias effect (Evans et al., 1983). The belief bias effect has been demonstrated consistently in categorical syllogistic reasoning (Goel & Dolan, 2003a) as well as conditional (Byrne & Tasso, 1999) and relational reasoning (Roberts & Sykes, 2003). Furthermore, the most important decisions in life must often be made under emotional circumstances. Both emotional content and mood were found to be detrimental to deductive reasoning, resulting in more logical errors in emotional than non-emotional conditions (Blanchette, 2006; Blanchette & Richards, 2004; Lefford, 1946; Oaksford et al., 1996). While the effect of beliefs on logical reasoning has been well-established, the effect of emotion on reasoning is still in its infancy. Emotionality and belief-logic conflict were confounded in past studies. Belief bias studies do not control for emotionality of beliefs; conversely, emotional reasoning studies do not control for belief-logic conflict, even though both types of studies often involve both factors to some extent (emotional statements in belief bias studies; belief-logic conflict in emotional studies).
Recent behavioral (Vroling & de Jong, 2009) and behavioral-genetic (Study 1) research has begun to elucidate the interaction between emotion and beliefs in deductive reasoning. Vroling and de Jong (2009) found that individuals with higher social anxiety had increased belief bias for social anxiety statements in a relational reasoning task. Individual differences in emotional reactivity, such as anxiety and related affective disorders, are attributable in part to a polymorphism in the serotonin transporter gene [5-HTTLPR; (Hu et al., 2006; Lesch et al., 1996)]. The 5-HTTLPR ‘short’ (S) allele is related to increased emotional reactivity; carriers of the S allele [relative to carriers of the ‘long’ (L) allele] demonstrated increased attentional bias towards negative stimuli (Beevers et al., 2009; Koizumi et al., 2010; Perez-Edgar et al., 2010), increased anxiety and anxiety-related behaviors (Armbruster et al., 2009; Gonda et al., 2009; Lesch et al., 1996; Lonsdorf et al., 2009), and have increased risk for affective disorders (Caspi et al., 2003). In Study 2, we found that participants with higher anxiety also had increased belief bias for arguments with emotional content, but that this relationship was accounted for by 5-HTTLPR genotype. Specifically, while evaluating arguments containing belief-logic incongruency, participants had reduced accuracy and slower reaction time relative to arguments with belief-logic congruency, replicating the belief bias effect (Roberts & Sykes, 2003). Trait anxiety [as measured by the State-Trait Anxiety Inventory, STAI; (Spielberger et al., 1983)], was positively correlated with belief-bias, but only in problems containing (primarily negative) emotional content, thereby linking one aspect of emotionality to belief-based reasoning errors. Most notably, this relationship was accounted for by 5-HTTLPR. Carriers of the short (S) allele, who reported higher trait anxiety relative to carriers of the long (L) allele, had increased belief bias while
evaluating arguments with emotional content relative to non-emotional content. Belief bias was unaffected by emotional content in carriers of the long (L_A) allele. Thus, the confluence of several factors related to emotionality (5-HTTLPR genotype, anxiety, and affective semantic content) interacted with beliefs to influence deductive reasoning. Increased sensitivity to (negative) emotional stimuli and higher anxiety, both linked to the 5-HTTLPR S allele, can increase the likelihood of irrational decisions. The neural basis for this effect is unknown.

The brain bases of belief-bias and emotional reasoning have only been examined in independent studies. While these studies did not directly test the neural basis of belief-emotion interactions, both emotional and belief-bias studies highlight the involvement of two distinct, yet interconnected, regions within the prefrontal cortex (PFC). Belief-logic incongruency (valid, unbelievable or invalid, believable conclusions) is associated with activation of the right lateral prefrontal lobe; specifically, the right inferior frontal cortex (rIFC). Studies utilizing functional imaging techniques such as fMRI (Goel et al., 2000; Goel & Dolan, 2003a; Stollstorff, Vartanian, & Goel, submitted), near-infrared spectroscopy [fNIRS; (Tsujii & Watanabe, 2009, 2010)] and event-related potentials [ERP; (Luo et al., 2008)] as well as temporary functional brain disruption [repetitive transcranial magnetic stimulation, rTMS; (Tsujii et al., 2010)] have provided overwhelming evidence that rIFC is involved in and is necessary for dealing with belief-logic conflict in reasoning. Furthermore, incorrect responses for reasoning trials containing belief-logic incongruency, in which participants based their decisions on beliefs rather than logical validity, were associated with activation of vmPFC relative to correct responses in the same condition [when participants overcame belief-logic conflict;
Emotionality of content in this study (Goel & Dolan, 2003a) was not controlled. Emotional words such as reptiles, poison, frogs and cholesterol were included alongside emotionally neutral words such as elephants, grocers, hair, and mushrooms. It is possible that incorrect responses for particular incongruent problems resulted from emotional content in those problems; “correct” logical decisions interpreted as belief bias suppression could have resulted from less emotional content in those problems, as we know that emotion is also a factor in deductive reasoning. Thus, the effects of beliefs and emotion cannot be disentangled in this particular study.

Reasoning with emotional versus non-emotional content revealed a reciprocal activation pattern between left lateral PFC and vmPFC (Goel & Dolan, 2003b). In a categorical (“syllogistic”) reasoning task, participants evaluating arguments with emotionally charged statements (e.g. “All murderous people are criminals; All Nazis were murderous; Some Nazis are criminals”) demonstrated increased bilateral vmPFC and decreased left lateral PFC activation relative to logically identical arguments containing non-emotional statements (e.g. “Some Canadians are not children; All Canadians are people; Some people are not children”). The reverse comparison (non-emotional > emotional) revealed increased activation in left PFC (inferior/middle frontal gyrus) and relative deactivation of vmPFC. Thus, during belief-based reasoning, vmPFC and left lateral PFC regions responded in the opposite direction, the former being engaged by emotional content, and the latter engaged by non-emotional content. While the emotional and non-emotional conditions were equated on belief-logic congruency, any interaction between belief-logic conflict and emotion (in behavioral performance or brain activation) was not reported.
The purpose of the present study was to investigate the role of rIFC and vmPFC in the interaction between emotion and belief-logic conflict, and whether these regions differ by 5-HTTLPR. We measured activation of these regions using fMRI in healthy carriers of the S allele (‘S/L’) and homozygous L_A carriers (‘L_AL_A’) during a relational reasoning task that varied in emotional content and belief-logic congruency. Neutral problems, free of beliefs and emotional content, and non-reasoning baseline trials were also included in order to investigate the specificity of potential 5-HTTLPR genotypic differences during relational reasoning with and without meaningful and emotional content. We predicted that differences in brain activation by 5-HTTLPR will only be present during emotional reasoning problems with belief-logic conflict. This prediction is based on results from Study 1 in which S carriers had increased belief bias for emotional content and groups did not differ for non-emotional reasoning. Furthermore, we expected genotype differences in regions that are known to support successful belief bias suppression (rIFC) and unsuccessful belief bias suppression [vmPFC; (Goel & Dolan, 2003a)]. We tested the specificity of 5-HTTLPR effects on brain activation related to emotion and belief bias by also investigating genotype effects during belief-neutral reasoning problems that were identical in logical form to the belief-laden problems. If 5-HTTLPR differences in rIFC and vmPFC activation are specific to our conditions of interest (belief-based emotional reasoning), groups should not differ in activation of these regions during neutral reasoning.
Method

Participants

Participants were 30 undergraduate students (13 male) from Georgetown University (recruited from the larger group in Study 1), aged 18 to 22 years and received $60 for participation. They were primarily of European descent (27 White, 90%; 1 Hispanic, 1 Black, 1 Asian), primarily right-handed (29 RH, 1 LH) and were native English speakers or were fluent by age 3 years. Participants had never received a psychiatric diagnosis and had no exposure to psychotropic medication (such as antidepressants or anxiolytics), based on self-report. Consent was acquired in accordance with the procedures set by the Georgetown University Institutional Review Board. Participants provided a saliva sample which was analyzed for the polymorphism in the serotonin transporter-linked promoter region (5-HTTLPR) in the serotonin transporter gene (SLC6A4). Given that the single nucleotide polymorphism (SNP) rs25531 in the coding region of the 5-HTTLPR long allele (A → G) influences its functional expression, rendering it functionally more similar to the short allele (Hu et al., 2006), we grouped carriers of the L allele with S carriers. Our final sample included two groups: (1) “L_ALA” (homozygous for long 5-HTTLPR allele and homozygous for the A rs25531 SNP); (2) “S/L” (homozygous for the short 5-HTTLPR allele, SS, or heterozygous carriers of at least one S allele, SL_G or SL_A). The L_ALA group (N = 15; 7 Male; 14 RH; Age: M = 19.70, SD = 1.39) did not differ from the S/L group (N = 15; 6 Male; 15 RH; Age: M = 19.67, SD = 1.23) in age (p > .8), gender (p > .7), handedness (p > .3) or ethnicity (p > .3). The S/L group was composed of SS (n = 5), SL_G (n = 1) and SL_A (n = 9) carriers.
Genotyping

Saliva samples (Orgene, Ottawa, Canada) were analyzed for the 5-HTTLPR genotype using a two-step process. First, the long (L) and short (S) variants were determined. The repeat polymorphism in the promoter region of the 5-HTT gene was genotyped by PCR as previously described (Lesch et al., 1996) using the following primers at concentrations of 10 µM; Forward: 5’-GGCGTTGCGCTCTGAATGC-3’; Reverse: 5’-GAGGGACTGAGCTG-GACAACCAC-3’. PCR was performed using the AccuPrime™ GC-Rich DNA polymerase system (Invitrogen) with the following PCR program: 95°C for 10 min, followed by 35 cycles of 95°C for 30 sec, 65°C for 30 sec, and 72°C for 1 min. A final extension time of 72°C for 10 min was performed after the 35 cycles were complete. The PCR products were then run out on a 2% agarose gel stained with ethidium bromide. The amplification yielded distinct bands at 484 bp (S allele = 14 copies of repeat) and 528 bp (L allele = 16 copies of repeat), which were distinguished by a 100 bp DNA ladder run on the same gel. Second, the L\textsubscript{A} and L\textsubscript{G} variants were determined for the rs25531 single nucleotide polymorphism (SNP), present only on the long allele. Genotyping for rs25531 was performed by digesting the PCR products generated from the 5-HTTLPR PCR reactions with the restriction enzyme MspI (New England BioLabs). Specifically, 10 µL restriction digestion reactions were performed by combining 8 µL of the 5-HTTLPR PCR product, 1 µL of 10X NEBuffer 4, and 1 µL of MspI (concentration = 100,000 U/mL) and incubating the reactions for 2 hr at 37°C followed by heat inactivation of the enzyme at 80°C for 20 min. The substitution of the G for A in the SNP produces an additional MspI recognition site (CCGG) on the long allele of the 5-HTTLPR PCR product. Genotypes were determined by running the
digested PCR products out on a 2% agarose gel stained with ethidium bromide. Samples with 2 copies of the A allele for rs25531 showed a band at 340 bp (as well as bands at 127 and 62 bp due to multiple MspI recognition sites on the 5-HTTLPR PCR product), while samples with 2 copies of the G allele for rs25531 had additional digestion of the 340 bp product, yielding bands at 166 and 174 bp (as well as bands at 127 and 62 bp). Samples that were heterozygous for rs25531 showed a combination of these 2 band patterns.

**Stimulus materials**

Stimuli consisted of 110 three-term transitive arguments (e.g., A>B, B>C; A>C; “relational reasoning trials”) and 50 baseline control trials (e.g., A>B, B>C; Y>Z). Belief-laden reasoning trials (containing meaningful statements about which participants were likely to have knowledge/opinions) varied by emotion (emotional, non-emotional) and belief-logic congruency (congruent, incongruent). Belief-neutral reasoning trials were comprised of sentences about which the participants would have no beliefs. Baseline trials were comprised of 2 related premises followed by an unrelated conclusion and contained either emotional, non-emotional or belief-neutral statements. Thus, 8 conditions, described below, were created including belief-laden reasoning trials (emotional congruent, emotional incongruent, non-emotional congruent, non-emotional incongruent), belief-neutral reasoning, and 3 baseline conditions (emotional, non-emotional, neutral; see Table 1, Appendix 2).
Table 1. Experimental conditions and example stimuli.

<table>
<thead>
<tr>
<th>Trial Type</th>
<th>Reasoning</th>
<th>Baseline</th>
</tr>
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| Emotional    | **Congruent – 22 trials**
Hugs are better than fights.
Fights are better than rape.
Hugs are better than rape?
*(Example: valid, believable)*

**Incongruent – 22 trials**
Maggots are heavier than shotguns.
Shotguns are heavier than corpses.
Maggots are lighter than corpses?
*(Example: invalid, believable)*
|                                                        | 20 trials
Blood is thicker than urine.
Vomit is thicker than blood.
Volcanoes are smaller than hospitals? |
| Non-Emotional| **Congruent – 22 trials**
Pencils are sharper than whistles.
Needles are sharper than pencils.
Needles are sharper than whistles?
*(Example: valid, believable)*

**Incongruent – 22 trials**
Baskets are harder than doors.
Baskets are softer than beds.
Doors are softer than beds?
*(Example: valid, unbelievable)*
|                                                        | 20 trials
Umbrellas are taller than statues.
Lighthouses are shorter than statues.
Winter is warmer than summer? |
| Neutral      | **22 trials**
Lines are less fun than slits.
Edges are less fun than slits.
Lines are less fun than edges?
*(Example: invalid, no beliefs)*
|                                                        | 10 trials
Goopers are slower than Lessels.
Hops are slower than goopers.
Lindsay is shorter than Martin? |
|              | **Total** 110 50 |

Words for the belief-laden trials were selected from the Affective Norms for English Words database [ANEW; (Bradley & Lang, 1999)] which provides ratings for arousal and valence on a 1-10 point scale. Emotional words were selected based on high arousal (> 3.5; Mean: 5.8) and extreme valence (< 4 = negative, 75.2%, > 6 = positive valence, 24.8%). Non-emotional words were selected based on low arousal (< 5.5;
Mean: 4.1) and neutral valence (4-7; neither positive nor negative). Thus, emotional trials contained words that were primarily negative and highly arousing whereas non-emotional problems contained words that were neither positive nor negative in valence and low in arousal.

Belief-laden trials also varied on belief-logic congruency. For congruent trials, the validity of the conclusion was in accordance with beliefs (valid, believable and invalid, unbelievable). For incongruent trials, the validity of the conclusion was in conflict with beliefs (valid, unbelievable and invalid, believable). A total of 88 belief-laden reasoning trials were included that varied by Emotional content (emotional, non-emotional) and Congruency (congruent, incongruent), creating 4 conditions, each consisting of 22 problems: (1) Emotional Congruent, (2) Emotional Incongruent, (3) Non-emotional Congruent, and (4) Non-emotional Incongruent. The 4 conditions were equated for logical structure/form, conclusion believability (11 believable, 11 unbelievable), validity (11 valid, 11 invalid), determinacy (17 determinate, 5 indeterminate), inversion (13 inverted, such that the transitive connector switched between sentences, 9 non-inverted, such that the transitive connector was consistent, e.g. “John is shorter than Martin; Martin is shorter than Peter; John is shorter than Peter”), and content type (13 non-living, 5 living, 4 abstract).

The neutral reasoning condition was comprised of 22 trials that contained words (33.3%, e.g., “silver”) and non-words (66.7%, e.g., “haps”) incorporated into sentences that would not evoke beliefs. Words that had meaning did not relate to each other in a meaningful way, as their transitive connection created a belief-neutral sentence (e.g., “corners are brighter than levels”).
As in several previous deductive reasoning studies (Goel et al., 2000; Goel, Stollstorff, Nakic, Knutson, & Grafman, 2009), baseline trials were created by pairing a conclusion from one trial with the 2 premises from another trial in the same reasoning condition, such that the 2 related premises appeared (e.g., “Trees are taller than grass; Grass is taller than flowers”) followed by an unrelated conclusion (e.g., “Bricks are heavier than feathers”). Thus, upon reading the unrelated conclusion, the participant could disengage from the deductive reasoning task and press a button corresponding with “no” (same button for “not logical”). Baseline trials controlled for processes required by the reasoning trial that were of no interest (e.g., reading and motor response); these trials were identical to reasoning trials with the exception of not requiring a judgment based on deductive reasoning. Three baseline conditions were created: emotional baseline (20 trials; half from emotional congruent reasoning trials, half from incongruent), non-emotional baseline (20 trials; half from non-emotional congruent trials, half from incongruent) and neutral baseline (10 trials; from neutral reasoning trials).

Baseline trials were used to generate the general relational reasoning effect (across participants, to ensure activations were comparable to previous reasoning studies) and to generate the neutral reasoning effect to compare genotype groups on reasoning without beliefs. Baseline and neutral reasoning trials were not needed for the key comparisons of interest.

Procedure

Participants were recruited in two sessions: Session 1 occurred 10 months prior to scanning (18 participants); Session 2 occurred at least 2 months prior to scanning (3
months on average; 12 participants). During their initial visit to the laboratory, participants completed the State-Trait Anxiety Inventory [STAI; (Spielberger et al., 1983)] and provided a saliva sample for subsequent genotyping. Participants returned for fMRI scanning (the 2 genotype groups did not differ by initial recruitment session, $p > .1$). On the day of scanning, they first underwent training for the reasoning task, followed by the experimental task while undergoing fMRI scanning, an anatomical scan, and then completed a post-scan belief questionnaire.

**STAI Anxiety.** Participants completed the STAI, a self-report measure of state and trait anxiety that included 20 statements, rated on a scale of 1 (not at all) to 4 (very much so), about the participant’s immediate state of anxiety and 20 statements, on a scale of 1 (almost never) to 4 (almost always), about trait anxiety.

**Training.** Prior to scanning, the experimenter described the task and explained what constitutes a logical conclusion. Participants were then instructed to determine if the third sentence (the conclusion) followed logically from the first two sentences (the premises) by basing the decision on logical form and *not* on the truth or falsity of the conclusion (i.e., not based on their beliefs). Participants completed 14 practice problems on paper with unlimited time and were asked to re-think the problem if they made errors; participants then explained and corrected the error, ensuring that the task was fully understood.

**Reasoning Task.** Stimuli were presented in an event-related design (see Figure 1). Each trial began with a fixation cross which remained on the screen for 0.5 s. Fixation cleared, and each sentence of the reasoning problem appeared at 3 second intervals and remained on the screen throughout the remainder of the trial. Thus, after fixation cleared,
premise 1 appeared towards the top of the screen, followed by premise 2 below it 3 s later, followed by the conclusion below that 3 s later. Participants then had 7.5 s to respond by pressing a button box (with the right hand). The trials ended at 15s. The task was to determine whether the third sentence, the conclusion, followed logically and necessarily from the premises. Responses were made by pressing one of two buttons on a button box, corresponding with either ‘logical’ (button 1) or ‘not logical’ (button 2) using their right hand and two response fingers (index and middle). No feedback was provided.

Figure 1. Event-related stimuli presentation for a single trial.

Belief Questionnaire. The questionnaire measured whether the participant’s beliefs were in accordance with those of the experimenters. It was comprised of 50 conclusions that were selected randomly from problems in each of the 5 reasoning
conditions: 10 Emotional Congruent, 10 Emotional Incongruent, 10 Non-Emotional Congruent, 10 Non-Emotional Incongruent, 10 Neutral. Half of the belief-laden statements selected were true/believable and half were false/unbelievable, while belief-neutral statements were neither true nor false (uncertain). Participants were asked to rate each conclusion as “True,” “False,” or “Don’t Know,” based on their own knowledge.

**Imaging procedure**

The event-related trials were divided into 3 runs in a pseudo-random order (same for each participant), ensuring that conditions were equally divided across runs. Imaging data were acquired using a 3T Siemens magnet (Siemens Magnetom Trio, Erlangen, Germany). Head movement was minimized by foam padding that held the subject’s head in the coil firmly and comfortably. Participants viewed the stimuli via a mirror mounted on the coil that reflected the images that were projected onto a screen (209 x 279 cm) at the back of the bore of the magnet approximately 950 mm from the mirror. Stimuli were generated in E-prime (Version 2.0, Psychology Software Tools Inc., 2010) and viewed via a magnet-compatible projector.

Fifty axial slices (3.0 x 3.0 x 2.5 mm with .5 mm gap) were positioned to be parallel to the base of orbitofrontal cortex and covering the whole brain (TR = 3000 ms, TE = 30 ms, 192 x 192 mm FOV, 90° flip angle). A total of 812 volume images were acquired over 3 runs (Run 1: 274 volumes, 13:42 min, 54 trials; Runs 2 & 3: 269 volumes, 13:27 min, 53 trials each) using a T2*-sensitive gradient EPI sequence. After functional imaging, a high resolution sagittal T$_1$-weighted structural scan was acquired using a 3D MPRAGE sequence with the following parameters: TR = 2300 ms, TE = 2.94
ms, TI = 900 ms, 256 x 256 mm FOV, 160-mm slab with 1-mm-thick slices, 256 x 256 x 160 matrix (effective resolution of 1.0 mm$^3$), and a 90° flip angle.

**fMRI Processing & Data Analysis**

Images were analyzed in SPM5 (www.fil.ion.ucl.ac.uk/spm). The first 4 volumes of each run were discarded to allow for T1 equilibration effects, leaving 270 volumes for Run 1 and 265 volumes for each of Runs 2 and 3. Images were corrected for slice acquisition timing and were then corrected for translational and rotational motion by realigning to the first image of the run. All subjects demonstrated less than 2 mm of translational motion in any one direction and less than 2° of rotation around any one axis in each run. Images were coregistered with the high-resolution structural images of the participant. The structural images were segmented into separate gray and white matter images, and the gray matter image was normalized into standard MNI space by comparison with a template gray matter image. The normalization parameters used were then applied to the functional images to bring them into MNI space. All images were smoothed using a Gaussian kernel with full-width at half-maximum (FWHM) of 8mm.

The event of interest was neural activation after presentation of the conclusion, corresponding to the conclusion evaluation component of the task. The BOLD signal corresponding to this event was modeled using a canonical hemodynamic response function at the halfway point between the presentation of the third sentence and motor response [calculated for each individual trial for each participant; (Goel et al., 2009)]. Other events (sentences 1 and 2 onset and motor response) were also entered into the design matrix and were modeled as an event of no interest (using a canonical hemodynamic response function). Condition effects at each voxel were estimated using
the general linear model and regionally specific effects compared using linear contrasts. Each contrast produced a statistical parametric map of the $t$-statistic at each voxel, which was transformed to a normal $Z$-distribution (Friston, et al., 1995).

For each participant, activation maps for four contrasts were generated: (1) reasoning $>$ baseline (to determine activation associated with relational reasoning, regardless of content); (2) neutral reasoning $>$ neutral baseline (to determine activation associated with relational reasoning without beliefs); (3) emotional incongruent $>$ emotional congruent (to determine activation associated with emotional belief-logic conflict); (4) non-emotional incongruent $>$ non-emotional congruent (to determine activation associated with non-emotional belief-logic conflict).

At the group level, 4 analyses were conducted. As we had a priori hypotheses about activation for two regions, rIFC and vmPFC (Goel et al., 2000; Goel & Dolan, 2003a, 2003b; Tsujii et al., 2010), we used a voxel-level intensity threshold of $p < .001$ uncorrected, $k > 10$ extent threshold to identify activation in these two regions. To identify activation in the rest of the brain, a more conservative voxel-level intensity threshold was used, $p < .05$ corrected for multiple comparisons (using False Discovery Rate; FDR), $k > 10$. First, a one-sample $t$-test was conducted to determine regions that were involved in relational reasoning (reason $>$ baseline contrast), regardless of genotype or content. The purpose of this analysis was to relate our results to previous studies of relational reasoning. Second, a two-sample $t$-test was conducted to examine regions that differed by genotype groups ($L_A L_A$, $S/L$) in the neutral reasoning condition (neutral reasoning $>$ neutral baseline contrast). The purpose of this analysis was to test whether activation was comparable across genotype groups for relational reasoning without
beliefs. Third, a one-sample t-test was conducted to determine regions involved in relational reasoning with neutral content only (neutral reasoning > neutral baseline contrast). The purpose of this analysis was to compare neutral reasoning to our overall effect of relational reasoning, and to link these findings with previous studies of neutral reasoning. Fourth, a mixed ANOVA was conducted (our key analysis of interest), with genotype (LAL, S/L) as a between-subjects factor and emotion (emotional, non-emotional) as a within-subject factor.

Contrast estimates were extracted from activated clusters showing a genotype X emotion interaction using MARSBAR (Brett, Anton, Valabregue, & J.-B., 2002) and examined for genotype and emotional content differences with t-tests. Further, to examine the relationship between our regions of interest, the contrast estimates were entered into a mixed ANOVA with genotype (LAL, S/L) as a between subjects factor and emotion (emotional, non-emotional) and prefrontal region (rIFC, vmPFC) as within subjects factors. Correlations were conducted to examine the relationship between activation of vmPFC, rIFC and anxiety. All reported coordinates are converted from MNI to Talairach space using the algorithm mni2tal (http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach).

Results

Belief Questionnaire

For each participant, each response was coded based upon the match with the experimenter as agree (true, false, or uncertain by both) or disagree (mismatch between the two). Statements from the neutral condition were uncertain; thus, a “Don’t know” response for belief-neutral statements was coded as ‘agree’. For each participant, mean
percentage of agreement was calculated separately for each of the five reasoning conditions and compared by genotype using a mixed ANOVA with condition (5 levels) as a within-subject factor and genotype (LAL, SS/SLG) as a between-subject factor (see Table 2). Mean agreement did not differ by genotype (p > .8). There was a main effect of condition [F(4, 112) = 5.91, p < .001], such that participants, regardless of genotype, had higher agreement for the neutral condition than each of the 4 belief-laden conditions (ps < .05). There was no genotype X condition interaction (p > .7), indicating that belief agreement scores for LAL and SS/SLG groups did not differ across conditions.

Table 2. Mean belief agreement on post-scan belief questionnaire (%), SD in parentheses) by reasoning condition and genotype.

<table>
<thead>
<tr>
<th>Reasoning Condition</th>
<th>LAL</th>
<th>SS/SLG</th>
<th>Condition Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional Congruent</td>
<td>94.7 (6.4)</td>
<td>94.0 (7.4)</td>
<td>94.3 (6.8)</td>
</tr>
<tr>
<td>Emotional Incongruent</td>
<td>94.0 (6.3)</td>
<td>93.3 (9.0)</td>
<td>93.7 (7.6)</td>
</tr>
<tr>
<td>Non-Emotional Congruent</td>
<td>96.7 (4.9)</td>
<td>96.0 (8.3)</td>
<td>96.3 (6.7)</td>
</tr>
<tr>
<td>Non-Emotional Incongruent</td>
<td>92.7 (7.0)</td>
<td>95.3 (6.4)</td>
<td>94.0 (6.7)</td>
</tr>
<tr>
<td>Neutral</td>
<td>99.3 (2.6)</td>
<td>100 (0)</td>
<td>99.7 (1.8)</td>
</tr>
<tr>
<td>Group Average</td>
<td>95.5 (2.8)</td>
<td>95.7 (4.8)</td>
<td>95.6 (3.8)</td>
</tr>
</tbody>
</table>

Reasoning Task

For reasoning trials, a response was scored as correct if it was consistent with the logical validity of the problem and incorrect if it was not consistent with logical validity or the participant did not respond within the 7.5 s (timed out). For baseline trials, a “no” response (button 2) was scored as correct; no response (timed out) or a Button 1 press was considered incorrect. Only 2.5% of trials were “timed out”. For each participant,
mean accuracy (% correct) and mean reaction time for correct responses (in msec) was computed for the five reasoning conditions and three baseline conditions separately. In addition, mean accuracy and mean reaction time for each participant was computed for belief-laden conditions (regardless of emotion or congruency (for analysis #2, see below)). Three analyses were conducted (for accuracy and reaction time data separately) that map onto the fMRI analyses described earlier: (1) To examine reasoning versus baseline conditions (including belief-laden and belief-neutral conditions), a mixed ANOVA was computed with genotype (L_A L_A, S/L) as a between-subject factor and Task (reason, baseline) and Content (belief-laden, belief-neutral) as within-subjects factors (“5-HTTLPR x Task x Content”). (2) To examine group differences in the neutral content conditions, we conducted a mixed ANOVA with genotype (L_A L_A, S/L) as a between-subjects factor and task (reason, baseline) as a within-subjects factor. (3) To examine the belief bias effect by emotion and genotype, we restricted the analysis to belief-laden reasoning conditions. A mixed ANOVA was computed with genotype (L_A L_A, S/L) as a between-subject factor and Emotion (emotional, non-emotional) and Congruency (congruent, incongruent) and as within-subjects factors (“5-HTTLPR x Emotion x Congruency”). Accuracy and reaction time data are presented in Table 3.
Table 3. Mean accuracy (SD in parenthesis) and Reaction Time (in msec) for relational reasoning and baseline trials in S/L and L<sub>A</sub>L<sub>A</sub> carriers.

<table>
<thead>
<tr>
<th></th>
<th>Long (L&lt;sub&gt;A&lt;/sub&gt;L&lt;sub&gt;A&lt;/sub&gt;) N = 15</th>
<th>Short (S/L) N = 15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Congruent</strong></td>
<td>92.12% (7.77)</td>
<td>89.39% (9.51)</td>
</tr>
<tr>
<td><strong>Incongruent</strong></td>
<td>89.39% (9.36)</td>
<td>90.00% (12.17)</td>
</tr>
<tr>
<td>Non-Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Congruent</strong></td>
<td>93.94% (10.40)</td>
<td>90.30% (10.29)</td>
</tr>
<tr>
<td><strong>Incongruent</strong></td>
<td>87.58% (10.37)</td>
<td>85.15% (10.37)</td>
</tr>
<tr>
<td>Neutral</td>
<td>86.67% (9.64)</td>
<td>82.73% (13.33)</td>
</tr>
<tr>
<td>Emotional Baseline</td>
<td>98.67% (2.97)</td>
<td>98.67% (5.16)</td>
</tr>
<tr>
<td>Non-Emotional Baseline</td>
<td>99.00% (2.80)</td>
<td>99.67% (1.29)</td>
</tr>
<tr>
<td>Neutral Baseline</td>
<td>100.00% (0.00)</td>
<td>98.00% (5.61)</td>
</tr>
<tr>
<td><strong>Reaction Time</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Congruent</strong></td>
<td>2796 msec (816)</td>
<td>2422 msec (790)</td>
</tr>
<tr>
<td><strong>Incongruent</strong></td>
<td>2831 msec (820)</td>
<td>2525 msec (921)</td>
</tr>
<tr>
<td>Non-Emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Congruent</strong></td>
<td>2730 msec (595)</td>
<td>2565 msec (1075)</td>
</tr>
<tr>
<td><strong>Incongruent</strong></td>
<td>2850 msec (783)</td>
<td>2680 msec (1116)</td>
</tr>
<tr>
<td>Neutral</td>
<td>2983 msec (866)</td>
<td>2580 msec (855)</td>
</tr>
<tr>
<td>Emotional Baseline</td>
<td>1574 msec (405)</td>
<td>1336 msec (435)</td>
</tr>
<tr>
<td>Non-Emotional Baseline</td>
<td>1522 msec (388)</td>
<td>1201 msec (389)</td>
</tr>
<tr>
<td>Neutral Baseline</td>
<td>1643 msec (515)</td>
<td>1343 msec (395)</td>
</tr>
</tbody>
</table>

Reasoning & Baseline Accuracy (5-HTTLPR x Task x Content). A main effect of task [F(1, 28) = 65.06, p < .001] indicated that participants were more accurate for baseline trials (M = 99.00%, SD = 2.99) than reasoning trials (M = 88.72%, SD = 8.89). A main effect of content [F(1, 28) = 14.81, p = .001] indicated that participants were more accurate for belief-laden (M = 94.37%, SD = 5.41) than belief-neutral trials (M =
91.85%, SD = 7.08). A task x content interaction was found [F(1, 28) = 18.16, p < .001], such that accuracy was higher [t(29) = 4.48, p < .001] for belief-laden (M = 89.73%, SD = 8.53) than belief-neutral (M = 84.70%, SD = 11.62) reasoning trials, but did not differ (p > .9) for baseline trials (Belief-laden: M = 99.00%, SD = 2.91; Belief-neutral: M = 99.00%, SD = 4.03). Most importantly, there was no main effect of genotype (p > .3), and genotype did not interact with any factor (p > .1).

**Reasoning & Baseline Reaction Time (5-HTTLPR x Task x Content).** A main effect of task [F(1, 28) = 98.20, p < .001] indicated that responses were faster for baseline (M = 1451, SD = 73) than reasoning trials (M = 2728, SD = 151). A main effect of content approached significance [F(1, 28) = 4.03, p = .054], such that participants responded marginally faster for belief-laden (M = 2042, SD = 555) than belief-neutral (M = 2137, SD = 592) trials. Similar to accuracy, reaction time did not differ by genotype (p > .1), and genotype did not interact with any factor (p > .3).

**Neutral Reasoning Accuracy (5-HTTLPR x Task).** A main effect of task [F(1, 28) = 59.26, p < .001] indicated that participants were less accurate in the neutral reasoning (M = 84.70%, SD = 11.60) than neutral baseline (M = 99.00%, SD = 4.02) conditions. There was no main effect of genotype or genotype x task interaction (ps > .2).

**Neutral Reasoning Reaction Time (5-HTTLPR x Task).** A main effect of task [F(1, 28) = 85.15, p < .001] indicated that participants were slower in the neutral reasoning (M = 2781, SD = 870) than neutral baseline (M = 1493, SD = 476) condition. There was no main effect of genotype or genotype x task interaction (ps > .1).
Belief-Laden Reasoning Accuracy (5-HTTLPR x Emotion x Congruency). A main effect of congruency [F(1,27) = 13.695, p = .001] indicated a significant belief-bias effect as participants were more accurate for congruent (M = 91.44%, SD = 8.20) than incongruent problems (M = 88.03%, SD = 9.55). There was an emotion X congruency interaction [F(1,27) = 4.497, p = .043], such that participants were more accurate for emotional (M = 89.70%, SD = 10.67) than non-emotional (M = 86.36%, SD = 10.27) incongruent problems (t(29) = 2.12, p = .042). Accuracy did not differ by emotion for congruent problems (Emotional: M = 90.76%, SD = 8.65; Non-Emotional: M = 92.12%, SD = 10.33; p > .4). Further, non-emotional problems had higher accuracy for congruent (M = 92.12%, SD = 10.33) relative to incongruent (M = 86.36%, SD = 10.27) problems [t(29) = 4.08, p < .001]; accuracy for emotional trials did not differ by congruency (p > .4). There was no main effect of Emotional content or genotype (ps > .1) and genotype did not interact significantly with any factor (ps > .2).

Belief-Laden Reasoning Reaction Time (5-HTTLPR x Emotion x Congruency). A main effect of congruency approached significance [F(1,27) = 3.558, p = .070], such that participants showed a trend for faster evaluation of congruent (M = 2628 msec, SD = 790) than incongruent (M = 2721 msec, SD = 887) conclusions, indicating a marginal belief bias effect. There were no main effects of emotion or genotype (ps > .3) or interactions (ps > .1).

Anxiety

Two independent samples t-tests were computed comparing genotype groups on mean anxiety standard scores normed for college students from the STAI (separately for state and trait anxiety). A significant group difference for state anxiety [t(28) = 2.92, p =
.007] indicated that SS/SLG carriers (M = 48.5, SD = 3.7) had higher state anxiety than LAL carriers (M = 42.6, SD = 6.9). Groups did not differ in trait anxiety [SS/SLG: M = 51.4, SD = 10.86; LAL: M = 47.1, SD = 8.7, p > .2] and therefore, it was not included in fMRI analysis.

fMRI Results

Reasoning versus Baseline. A one-sample t-test for the relational reasoning contrast (all reasoning trials > all baseline trials) revealed activation in bilateral frontal regions [left inferior prefrontal gyrus, Brodmann Area (BA) 45, left medial frontal gyrus (BA 6), and bilateral motor/pre-motor cortex (BA 4/6)], bilateral parietal regions [medial superior parietal cortex (BA 5), bilateral intraparietal sulcus (BA 7/40)] and right ventral striatum [nucleus accumbens/globus pallidus/caudate nucleus; (see Figure 2; Table 4)]. We report regions that survived voxel-level FDR correction at p < .01, as most clusters were indistinguishable at the more lenient p <.05 threshold.
Table 4. Regions more active during reasoning (reasoning > baseline).

<table>
<thead>
<tr>
<th></th>
<th>BA</th>
<th>Voxels</th>
<th>Voxel Coordinates</th>
<th>Z-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frontal Cortex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left inferior prefrontal gyrus</td>
<td>45</td>
<td>86</td>
<td>x -48 Y 22 z 22</td>
<td>4.15</td>
</tr>
<tr>
<td>Left medial frontal gyrus</td>
<td>6</td>
<td>149</td>
<td>x -2 Y 4 z 54</td>
<td>4.19</td>
</tr>
<tr>
<td>Left motor/pre-motor cortex</td>
<td>4/6</td>
<td>1342</td>
<td>x -32 Y 0 z 58</td>
<td>5.13</td>
</tr>
<tr>
<td>Right motor/pre-motor cortex</td>
<td>4</td>
<td>509</td>
<td>x 34 Y -6 z 46</td>
<td>4.36</td>
</tr>
<tr>
<td><strong>Parietal Cortex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial superior parietal cortex</td>
<td>5</td>
<td>101</td>
<td>x -26 Y 58</td>
<td>4.35</td>
</tr>
<tr>
<td>Left intraparietal sulcus</td>
<td>7</td>
<td>1086</td>
<td>x -20 Y -60 z 58</td>
<td>5.10</td>
</tr>
<tr>
<td>Right intraparietal sulcus</td>
<td>40</td>
<td>122</td>
<td>x -40 Y 44</td>
<td>4.10</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>580</td>
<td>x -66 Y 58</td>
<td>5.78</td>
</tr>
<tr>
<td><strong>Sub-cortical regions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right ventral striatum (nucleus accumbens, globus pallidus, caudate nucleus)</td>
<td>n/a</td>
<td>88</td>
<td>x 8 Y 12 z -2</td>
<td>4.38</td>
</tr>
</tbody>
</table>

*Note: FDR-corrected p < .01.*
Figure 2. Relational reasoning (all reasoning trials > baseline trials).
Neutral Reasoning. A two-sample t-test was conducted to examine regions that differed by genotype groups (L_AL_A, S/L) in the neutral reasoning condition (neutral reasoning > neutral baseline contrast). No significant regions differed by genotype for neutral reasoning. A one-sample t-test revealed areas active for neutral reasoning, regardless of genotype. This activation pattern was very similar to the overall reasoning contrast (which included belief-laden trials). They included left inferior prefrontal cortex (BA 9/44; x, y, z = -32, 22, 28; Z = 4.52; k = 56), bilateral motor/pre-motor cortex (BA 4/6; Right: x, y, z = 28, -2, 52; Z = 4.53; k = 259; Left: x, y, z = -30, -2, 50; Z = 4.30; k = 248), bilateral intraparietal sulci (BA 40; Right: x, y, z = 34, -50, 48; Z = 3.64; k = 13; Left: x, y, z = -24, -46, 42; Z = 4.20; k = 46), and bilateral intraparietal sulci extending into precuneus [BA 7; Right: x, y, z = 20, -58, 60; Z = 4.06; k = 231; Left: x, y, z = -20, -58, 60; Z = 4.44; k = 324; (see Figure 3)].
Figure 3. Neutral reasoning (neutral reason > neutral baseline).

5-HTTLPR x Emotion Interaction. A genotype x emotion interaction (for the belief-logic contrast) was observed in right inferior frontal cortex [rIFC; BA 44/45 (x, y, z = 58, 18, 32; Z = 3.48; k = 11)] and left ventromedial prefrontal cortex [vmPFC; BA 10/11/32 (x, y, z = -18, 34, -6; Z = 3.51; k = 10)]. Comparison of contrast estimates from rIFC showed that activation was lower in S/L carriers relative to L_A L_A carriers for emotional [t(28) = 3.84, p = .001] but not non-emotional (p > .2) belief-logic conflict conditions. Comparison of contrast estimates from vmPFC showed that activation was
higher in S/L carriers relative to LₐLₐ carriers for emotional \[t(28) = 3.71, p = .001\] but not non-emotional \((p > .1)\) belief-logic conflict conditions (see Figure 4). Furthermore, LₐLₐ carriers had increased activation of rIFC in emotional relative to non-emotional conflict conditions \[t(14) = 3.68, p = .002\] and had decreased activation of vmPFC in emotional relative to non-emotional conflict conditions \[t(14) = 2.87, p = .012\]. S/L carriers had decreased activation of rIFC in emotional relative to non-emotional conflict conditions \[t(14) = 2.92, p = .011\]. Activation of vmPFC in S/L carriers did not differ by emotional content \((p > .1)\).
Figure 4. Regions showing an interaction between Emotion and 5-HTTLPR during reasoning trials with belief-logic conflict (incongruent > congruent). Graphs show mean contrast estimates (± standard error) in the activated cluster by genotype and emotional content (* p < .05).
Given that both of our *a priori* regions of interest, rIFC and vmPFC, were activated in the genotype x emotion ANOVA, contrast estimates were analyzed with mixed 3-way ANOVA with genotype ($L_A L_A$, $S/L$) as a between-subject factor and emotion (emotional, non-emotional) and prefrontal region of interest (rIFC, vmPFC) as within-subject factor in order to compare these regions directly. A 3-way interaction was found [$F(1, 28) = 32.89, p < .001$; see Figure 5]. Independent samples t-tests comparing groups for each condition for each brain region revealed significant differences for emotional reasoning conditions, such that $L_A L_A$ carriers had increased activation of rIFC [$t(28) = 3.84, p = .001$], but decreased activation of vmPFC [$t(28) = 3.71, p = .001$], relative to $S/L$ carriers. Groups did not differ during non-emotional reasoning in rIFC ($p > .2$) or vmPFC ($p > .1$) activation.
Figure 5. A 3-way interaction between 5-HTTLPR (L_{A}L_{A}, S/L), Emotion (emotional, non-emotional) and Prefrontal Region (rIFC, vmPFC). (Extracted from 5-HTTLPR x Emotion ANOVA, \( p < .001 \) uncorrected, \( k > 10 \)). Graphs of mean contrast estimates (± standard error) in the activated cluster (for belief bias contrast: incongruent > congruent) by genotype and brain region, separately for emotional and non-emotional content (* \( p < .05 \)).

Correlations. During emotional reasoning, belief-logic conflict activation of rIFC was negatively correlated with that of vmPFC (\( r = -.39, N = 30, p = .033 \)); that is, participants who tended to have higher activation of rIFC tended to have lower activation
of vmPFC during emotional belief-logic conflict trials (see Table 5). These regions were not correlated during non-emotional belief-logic conflict trials ($p > .6$).

Table 5. Bivariate correlations between activation in rIFC and vmPFC (during emotional and non-emotional belief-logic conflict) and state anxiety.

<table>
<thead>
<tr>
<th></th>
<th>rIFC Emotional</th>
<th>vmPFC Emotional</th>
<th>rIFC Non-Emotional</th>
<th>vmPFC Non-Emotional</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>rIFC (Emotional)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>vmPFC (Emotional)</td>
<td>-.390*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rIFC (Non-emotional)</td>
<td>.220</td>
<td>-.121</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vmPFC (Non-emotional)</td>
<td>.220</td>
<td>-.241</td>
<td>.079</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>State Anxiety</td>
<td>-.228</td>
<td>.470**</td>
<td>-.228</td>
<td>-.261</td>
<td>1</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01

State anxiety was positively correlated with vmPFC activation during emotional ($r = .47$, $N = 30$, $p = .009$), but not non-emotional belief-logic conflict ($p > .1$), indicating that participants that with higher anxiety tended to have increased activation of vmPFC during emotional reasoning with conflict. However, when controlling for genotype in a partial correlation analysis, this relationship was not significant ($p > .1$). Thus, 5-HTTLPR genotype accounted for the relationship between anxiety and vmPFC activity during emotional belief-incongruent reasoning.

**Discussion**

We found that a polymorphism of the serotonin transporter gene (5-HTTLPR) was related to individual differences in deductive reasoning, selectively with emotional content. Specifically, emotionality (emotional content and 5-HTTLPR) modulated activity in rIFC and vmPFC in opposite directions during belief-incongruent relational
reasoning. S/L carriers had decreased rIFC activation and increased vmPFC activation relative to L_AL_A carriers. Furthermore, estimates for the emotional belief bias contrast (emotional content trials: belief incongruent > belief congruent) showed a negative correlation between rIFC and vmPFC; higher rIFC activation was related to lower vmPFC activation. Furthermore, increased vmPFC activity in the emotional belief bias condition was related to higher anxiety, however, this relationship was accounted for by 5-HTTLPR.

In contrast to Study 1, behavioral results in the present study did not reveal an interaction between genotype and content. Several factors could account for this discrepancy. First, the “S” group in Study 1 was comprised of carriers of the functionally equivalent S and L_G alleles only, whereas in the present study, heterozygous carriers of the L_A allele (i.e., SL_A carriers, n = 9) were included in the “S” group. Past studies have found SL_A carriers to be intermediate (SS/S_L_G > SL_A > L_A L_A) in terms of serotonin mRNA transcription (Hu et al., 2006) and behavior (Perez-Edgar et al., 2010). Thus, the present study had increased allelic heterogeneity in the “S” group that was not present in Study 1. Second, smaller sample size in the present study could have reduced power to detect the interaction. A third factor is that reasoning problems differed in the proportion of negatively valenced emotional content; the present study had less negative content (75%) than Study 1 (85%). Future studies should increase sample size, exclude heterozygous SL_A carriers from the “S” group, and investigate genotypic differences in reasoning with positive versus negatively valenced content.

A second difference with Study 1 is that 5-HTTLPR group differences in trait anxiety were not detected (instead, groups differed on state anxiety scores). This
behavioral difference also could have been due to allelic heterogeneity in the S/L group (which included heterozygous L\textsubscript{A} carriers). Trait anxiety scores in the present study for the SL\textsubscript{A} subgroup (n = 9) were in between that of SS/SL\textsubscript{G} (n = 6) and L\textsubscript{A}L\textsubscript{A} (SS/SL\textsubscript{G} > SL\textsubscript{A} > L\textsubscript{A}L\textsubscript{A}), although this did not reach statistical significance possibly due to small sample size. Thus, grouping SL\textsubscript{A} with SS/SL\textsubscript{G} carriers reduced the “S” group mean trait anxiety scores (towards the mean for L\textsubscript{A}L\textsubscript{A} carriers), resulting in non-significant group differences for trait anxiety. State anxiety, however, was similar for the two S/L subgroups (SS/SL\textsubscript{G} = SL\textsubscript{A} > L\textsubscript{A}L\textsubscript{A}) and we were therefore able to detect differences in state anxiety. This could reflect real differences between 5-HTTLPR effects on trait versus state anxiety or could be attributable to small sample size and therefore insufficient power to detect statistical differences between all three subgroups on state and trait anxiety scores.

The network of regions activated during reasoning, regardless of content or genotype, was consistent with that found in previous functional imaging studies of healthy adult participants. A frontal-striatal-parietal system has consistently been found during relational reasoning tasks (Acuna, Eliassen, Donoghue, & Sanes, 2002; Fangmeier, Knauff, Ruff, & Sloutsky, 2006; Goel & Dolan, 2001; Goel et al., 2004; Heckers, Zalesak, Weiss, Ditman, & Titone, 2004; Knauff, Fangmeier, Ruff, & Johnson-Laird, 2003). Consistent with the present findings of prefrontal activation, previous studies of relational reasoning (using linguistic or non-linguistic stimuli) found activation in bilateral premotor cortex (BA 6) and left lateralized activation of more anterior regions, including dorsolateral and middle frontal gyrus (BA 8, 9, 45, 46). Striatal and bilateral parietal regions (BA 7 and 40) were also consistently activated during relational
reasoning. Other regions often found during relational reasoning tasks included medial temporal regions [including hippocampus; (Goel et al., 2004; Heckers et al., 2004; Knauff et al., 2003)] and occipital cortex (Goel & Dolan, 2001; Goel et al., 2004), but involvement of these regions seems to be dependent on the type of stimuli used in the task (e.g., arguments involving familiar spatial environments) and is thought to reflect the extent to which participants are accessing semantic knowledge (Goel, 2007). Thus, regional activation in the present study during relational reasoning (regardless of content) and also neutral reasoning were consistent with previous research. It is important to note that there were no genotype differences during neutral reasoning and therefore 5-HTTLPR effects in our key comparison of interest are not attributable to baseline reasoning differences in the brain between S and L carriers. Rather, 5-HTTLPR effects in this task were likely to be related to factors of emotional content and belief-logic congruency.

Our key comparison of interest revealed that rIFC and vmPFC activation was reciprocal during emotional reasoning with belief conflict, regardless of genotype. When rIFC activation was high, vmPFC activation tended to be low; if rIFC was less active, vmPFC was more active. During emotional belief-logic conflict, the direction of response depended on 5-HTTLPR genotype: LA LA carriers had high rIFC activity and low vmPFC activity, while S/L carriers had the reverse pattern (low rIFC activity and high vmPFC activity). Our interpretation of these results rests on the premise that emotional information increases saliency of beliefs, thereby making them more difficult to inhibit (De Neys & Franssens, 2009; Moutier, Plagne-Cayeux, Melot, & Houde, 2006), similar to findings from the emotional stroop task (Becker et al., 2001; Dresler et al.,
2009). In Study 1, LAL carriers were able to overcome this increased saliency and therefore belief bias was unaffected by emotional content. S carriers, on the other hand, were unable to suppress the increased saliency of beliefs due to emotional content, resulting in increased emotional belief bias. The present study elucidates the neural mechanism for this effect. In emotional belief-incongruent reasoning, “bottom up” emotional reactivity would have theoretically increased saliency of beliefs, requiring more “top down” inhibitory control from rIFC. The LA group showed the optimal brain response: an increase in rIFC recruitment to suppress the response to emotional content and vmPFC involvement. While the S/L group was able to appropriately recruit rIFC during non-emotional reasoning in response to belief-logic conflict, their response to the conflict when content was emotional was a different story: low rIFC and high vmPFC activation. Thus, S/L carriers, who tend to be more sensitive to negative emotional content, demonstrated an alternative pattern of prefrontal recruitment during reasoning. In this group, the emotional nature of the reasoning problem activated a more medial prefrontal region (vmPFC), known to be involved in affective processing, rather than rIFC, known to resolve belief-logic conflict. Affective neural circuitry is perhaps unsuited for logical reasoning. The present study cannot determine whether the origin of S/L dysfunction during this task arises from rIFC, vmPFC, or communication between the two. Research on 5-HTTLPR effects on functional and structural connectivity between vmPFC and rIFC is needed to elucidate this reciprocal response between rIFC and vmPFC and to test our interpretation of these results. The present findings contribute to our understanding of emotion-belief interactions in deductive reasoning and provide a
basis upon which to guide future research aimed at elucidating the causal mechanism for rIFC-vmPFC dysfunction related to 5-HTTLPR genotype.

State anxiety scores were positively correlated with vmPFC activity during the emotional belief bias condition, linking an important aspect of emotional behavior to affective neural processing during deductive reasoning. The STAI was not administered on the day of fMRI scanning, and thus did not directly assess anxious state in participants at the time they completed the deductive reasoning task. However, since state anxiety scores reflect current levels of anxiety and are highly sensitive to change depending on environmental context, it is possible that individual differences in state anxiety levels evoked by the experience of participating in a psychological/genetic research study was more predictive of the participants’ anxious state at the time of scanning than trait anxiety because it reflects the tendency for increased anxiety to participating in research. Future studies should investigate this possibility. Nevertheless, when genotype was held constant, the relationship between anxiety and vmPFC was not significant. Thus, the anxiety-vmPFC correlation was attributable to the finding of higher vmPFC activity and state anxiety in S carriers relative to L_A L_A carries. Previous studies have not provided a clear picture regarding vmPFC involvement in anxiety-related behaviors (Haas, Omura, Constable, & Canli, 2007; Kim & Whalen, 2009). This could be attributable to the use of different measures of anxiety (STAI-T, STAI-S, neuroticism, harm avoidance) and vmPFC function (fMRI BOLD response, functional connectivity, structural connectivity), and various emotional tasks used to probe vmPFC activity (passive viewing of threatening stimuli, volitional control over emotional reactivity). Most importantly, previous studies did not control for 5-HTTLPR genotype. The present study adds to our
understanding of the relationship between anxiety and vmPFC function by highlighting the importance of 5-HTTLPR in this relationship and extending the findings to a different area of cognition-emotion (i.e., deductive reasoning).

Results of the present study could provide insight into depression and anxiety related disorders. The S allele confers risk for depression, generalized anxiety disorder and specific phobias (Caspi et al., 2003; Lesch et al., 1996; Lonsdorf et al., 2009). Treatment with selective serotonin reuptake inhibitors (SSRIs), a common treatment for anxiety and depression that targets the serotonin transporter protein, is less effective in carriers of the 5-HTTLPR S carriers relative to L carriers (Huezo-Diaz et al., 2009). This makes other treatment options even more critical for S allele carriers. Cognitive behavioral therapy, a common treatment for depression, anxiety and specific phobias, focuses on changing beliefs of the patient that are related to the disorder. For example, if a patient suffering from social phobia has a fear of public speaking because they believe that the audience will criticize them, a therapist provides instruction and guidance to help the patient change these negative cognitions. S allele carriers in the present study had less involvement of rIFC and instead recruited vmPFC during emotional belief-logic conflict reasoning. Thus, they are relying on a region of the brain that is involved with emotional processing, rather than belief-logic conflict resolution, which could lead to decisions based on highly salient emotional beliefs, rather than logical reasoning. Thus, anxiety-provoking or depressive thoughts could be more resistant to change using rational persuasion in S carriers. In fact, there is evidence to suggest that a fear-confirming negativity bias could contribute to the development of affective disorders (Williams et al., 2009). Participants in the present study did not have anxiety disorder,
however, previous research found that patients with specific phobias had increased belief bias in deductive reasoning for phobia-related arguments (de Jong et al., 1997). Future research should examine the contribution of genetic polymorphisms related to emotion-cognition interactions in clinical populations with depression and anxiety disorder, as this could lead to improved treatment for these affective disorders that involve cognitive biases and are linked to serotonin transporter genotype and prefrontal function.
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CHAPTER IV: GENERAL DISCUSSION

Results from these studies indicate that emotion and beliefs can interact to influence deductive reasoning performance and that this is related to individual differences in anxiety and 5-HTTLPR genotype, mediated by ventromedial and right inferior prefrontal cortex. Our research found that S allele carriers, who had higher anxiety relative to L_A L_A carriers, were less able to overcome emotionally-charged beliefs in favor of logic. Results from Study 2 indicate that this could be due to dysfunction within regions of the brain that support emotional and cognitive regulation (i.e., lateral and ventromedial regions of prefrontal cortex; rIFC and vmPFC). S allele carriers had less involvement of rIFC and instead recruited vmPFC during emotional belief-logic conflict reasoning. Thus, they recruited a region of the brain that is involved with emotional processing, rather than belief-logic conflict resolution, which could lead to decisions based on highly salient emotional beliefs, rather than logical reasoning. Participants were explicitly instructed during reasoning training that their prior knowledge/beliefs should be ignored and that only the logical structure of the argument should be considered. However, even healthy, intelligent adults could not completely overcome the conflict.

Conflict & Cognitive Control

While there is convincing evidence that the rIFC is involved in, and is necessary for, overcoming belief bias (Goel & Dolan, 2003; Tsujii, Masuda, Akiyama, & Watanabe, 2010), other sources of conflict in reasoning recruit rIFC as well. This has led to an alternative account of belief bias that could replace or modify the inhibition account. The right lateral PFC involvement could be understood in terms of conflict,
more generally. At least two other types of reasoning tasks have revealed significant right lateral PFC activation: indeterminate reasoning trials and “belief-content” conflict. Indeterminate reasoning relies on right lateral PFC (Goel & Dolan, 2004; Goel, Stollstorff, Nakic, Knutson, & Grafman, 2009). Indeterminate arguments have multiple conclusions. Given the premises, “David is taller than Beth” and “David is taller than Mary”, we cannot determine with certainty whether Beth is taller than Mary, Mary is taller than Beth, or perhaps they are equally as short. Thus, indeterminate problems require the consideration of multiple models in working memory in order to maintain this uncertainty. Similarly, in belief-logic incongruent arguments, there are multiple models to consider: one scenario that is true according to beliefs, and another conflicting scenario that is true according to logic. This could be considered another form of uncertainty, and therefore, one must resolve the conflict before making a decision; sometimes logic will win this battle, and sometimes beliefs prevail. In fact, it could be beneficial to maintain this uncertainty. In real-life reasoning situations, if we strongly disagree with a conclusion, but find it to be logically valid based on the premises, detecting and maintaining uncertainty could result in closer inspection and testing of the premises. Seeing things in black and white, right or wrong, may not always be beneficial; the ability to maintain ambiguity and consider multiple options can be valuable in many situations.

“Belief-content conflict” is something I have explored in previous work that also recruits rIFC and involves consideration of multiple options and has the element of conflict and uncertainty. Belief-logic conflict concerns the conclusion and involves the conflict between logical validity and whether one believes the conclusion or not. Belief-
content conflict, however, refers to the conflict between one’s beliefs and the content of a statement. An unbelievable sentence (premise or conclusion) in a reasoning problem creates a conflict between what we know to be true, and what we must temporarily accept as true for the purposes of constructing a mental representation of the problem. Belief-content conflict is characterized by a mismatch between beliefs and the content of an argument (including premises and the conclusion) and does not involve a conflict between beliefs and conclusion validity. Thus, an unbelievable sentence is the source of belief-content conflict. In a parametric analysis of neural response to varying numbers of unbelievable sentences in the argument, we found that rIFC was modulated by the amount of belief-content conflict in the argument; that is, the mere presence of counterfactual (or counter-opinion) statements was sufficient to engage the rIFC (Stollstorff, Vartanian, & Goel, submitted). Additionally, rIFC was activated independently of belief-logic conflict; even in arguments in which the conclusion of the argument was belief-logic congruent, rIFC was recruited when there were unbelievable sentences that had to be processed. When conflict is present in the reasoning problem (either belief-logic, belief-content), the same area of the brain is consistently activated.

The “conflict” hypothesis was proposed as a more unifying and parsimonious explanation than the inhibition hypothesis because it explains several cases of rIFC involvement. But is the “conflict” hypothesis actually inconsistent with the inhibition hypothesis? If we consider the concept of “cognitive control”, which is thought to be comprised of inhibition and working memory processes, cognitive control could be conceived as the mechanism for “dealing with conflict”. Perhaps if the inhibition hypothesis was modified to include cognitive control more generally (inhibition and
working memory), it would better account for other sources of reasoning error as well as belief-logic conflict.

**Gene-Gene Interactions**

There has been no research into the neurochemical basis of logical reasoning or belief bias prior to this thesis. However, we know that multiple neurotransmitters (controlled by multiple genes) contribute to complex cognitive functions. Given the inhibition, or “cognitive control” hypothesis of belief bias and the role of dopamine (DA) in cognitive control, it is likely that genetic differences in DA-regulating genes will contribute to individual differences in belief bias suppression and in neural activation supporting this critically important human cognitive ability. Working memory, also involved in logical reasoning more generally, is also regulated by DA and mediated by the PFC, and genetic variations affecting working memory should thus affect overall reasoning performance.

Nature provides us with a wonderful tool to test theories in the disciplines of psychology, philosophy, and neuroscience, to name a few. Scientific research has yielded a great foundation for understanding how certain neurotransmitter systems influence activity in certain regions of the brain. With the advances in genetics, we can test these mechanisms in the living, active, human being without the need to manipulate their biology. This is not to say that studies that use pharmacological methods, for example, are not useful – on the contrary. The combination of neuroimaging, genetic and pharmacological methods has yielded insight into healthy and disordered human thought and behavior (Bishop, Cohen, Fossella, Casey, & Farah, 2006; Fossella, Bishop, &
Casey, 2003; Green et al., 2008; Stollstorff et al., 2010; Stollstorff, Foss-Feig et al., submitted). There is a rapidly growing field of behavioral-genetic and imaging-genetic studies that have already begun to inform theories of cognition/emotion.

**Dopamine.** If cognitive control ability is the underlying process supporting belief bias suppression, then genetic factors affecting cognitive control should in turn relate to individual differences in the ability to suppress belief bias. DA is thought to be a critical neurotransmitter underlying cognitive control. Various genes affecting dopaminergic function in the brain have been linked to cognitive control and could also translate to individual differences in deductive reasoning, which relies on cognitive control.

**COMT.** Catechol-O-methyltransferase (COMT) is an enzyme that degrades catecholamines (including dopamine) in the synapse, thereby terminating the action of the neurotransmitter in the synapse. It is an important mechanism of dopamine deactivation, especially in the prefrontal cortex where the dopamine transporter (DAT) is less expressed. A single-nucleotide polymorphism (SNP) in the COMT gene, Val158Met, which substitutes methionine for valine, results in lower levels of COMT (which in turn leads to less DA breakdown). Individuals who inherit two copies of the met allele (met/met) have less COMT and therefore more DA functioning in the synapse compared to those inheriting two copies of the val allele (val/val), with heterozygotes (val/met) somewhere in between (Chen et al., 2004). There is research demonstrating functional consequences of the COMT gene on cognition and neural activation. Children and adult homozygous carriers of the met allele tend to have better performance on cognitive control and attentional tasks than homozygous carriers of the val allele (Blasi et al., 2005; Diamond, Briand, Fossella, & Gehlbach, 2004). Although the COMT enzyme
is present throughout the brain, it seems to have particular influence in the prefrontal cortex and is thought to be the primary mechanism of DA clearance from the synapse there. In fMRI studies in which cognitive performance is equal (e.g. N-back working memory task), val/val individuals tend to activate a more diffuse area of PFC compared to met/met or heterozygotes, and are therefore thought to have inefficient prefrontal recruitment (Bertolino et al., 2006; Blasi et al., 2005). It is interesting that while the met allele has been associated with superior cognitive control for non-emotional stimuli (Diamond et al., 2004) the same allele is also associated with reduced control for emotionally salient stimuli (Bishop et al., 2006).

*DAT.* The dopamine transporter protein (DAT) clears DA from the synapse and recycles it back up to the presynaptic terminal, thereby inactivating DA. Although DAT is distributed in many parts of the brain, including PFC, the striatum (caudate, putamen and globus pallidus) has a particularly high DAT density (Lewis et al., 2001). The DAT polymorphism (DAT1) results in individual differences in DAT density in the brain. The two most common variants are the 9- and 10-repeat alleles. The 10-repeat allele is associated with more DAT and therefore less DA action at the synapse. Individuals inheriting two copies of the 10-repeat allele (10/10) have higher DAT density, a higher prevalence of ADHD, and lower performance on cognitive control tasks (Cook et al., 1995; Cornish et al., 2005; Stollstorff et al., 2010; VanNess, Owens, & Kilts, 2005). Functional MRI studies have found effects of DAT1 on prefrontal activation during working memory tasks, with 10/10 individuals demonstrating less prefrontal activation (Bertolino et al., 2006). The 10/10 DAT1 genotype is also associated with impaired cognitive control and prefrontal-striatal-parietal function in children (Stollstorff et al.,
a network of regions that was also found to be active during relational reasoning (reasoning > baseline) in Study 2.

**DRD4.** The dopamine receptor D4 is considered part of the D2 dopamine receptor subfamily (D2, D3 and D4). In the brain, the receptor is expressed most abundantly in prefrontal cortex, hippocampus, amygdala and hypothalamus, and is sparse in the striatum (Oak, Oldenhof, & Van Tol, 2000). The gene has an exon 3 variable number of tandem repeats (VNTR) that ranges from 2- to 10-repeats. The 4-repeat and 7-repeat alleles are the most frequent in humans at 64% and 20% respectively (Oak et al., 2000). Relatively little is known about effects of the DRD4 polymorphism on receptor density and function. It is thought that the D4 4-repeat receptor has higher binding affinity and potency compared to 7-repeat D4 receptors (Oak et al., 2000). However, specific functional consequences in the brain by the DRD4 polymorphism are not well understood. The DRD4 7-repeat allele has been linked to ADHD and poor cognitive control (Congdon, Lesch, & Canli, 2008; Faraone & Khan, 2006). Little is known about the effect of DRD4 on brain activation during higher cognitive function tasks and this should be addressed in future research.

In terms of gene-gene interactions, COMT and DAT1 genes interact in healthy participants to influence stress reactivity and endocrine response to stress (with the COMT met allele and DAT1 10-repeat allele associated with increased emotional reactivity) (Anderson et al., 2010). Dopamine-regulating genes also influence susceptibility to affective disorders such as depression. Thus, dopamine genes could provide insight to deductive reasoning and emotional belief bias, as they clearly relate to individual differences in cognitive control and emotional regulation.
**BDNF.** A polymorphism in the brain-derived neurotrophic factor (BDNF) gene is known to interact with 5-HT to influence neurogenesis and synaptic plasticity (Martinowich & Lu, 2008). BDNF interacts with 5-HTTLPR and DAT1 (among other monoamine-regulating genes) to influence anxiety and depression related traits in healthy participants and increases susceptibility to affective disorder. Carriers of the BDNF met allele have higher emotional reactivity if they also carry the DAT1 10/10 genotype (Hunnerkopf, Strobel, Gutknecht, Brocke, & Lesch, 2007) or the 5-HTTLPR S allele (Martinowich & Lu, 2008). These findings could contribute to our understanding of individual differences in reasoning and could have implications for affective disorders.

**Natural selection?**

The theory of evolution seems to be at odds with the high frequency of “risk” alleles for serious neuropsychiatric disorders, such as the DAT1 10-repeat allele in ADHD or the 5-HTTLPR S allele in anxiety and depression. Why are these genes so frequent? Has natural selection led us astray? It is possible that while these alleles confer risk in certain aspects of functioning, they could have increased our chances of survival in the past. For example, the 10-repeat allele seems to increase behaviors related to ADHD such as hyperactivity and risky behavior. Perhaps this allele was beneficial for our ancestors who needed to take risks and explore new environments in search of food or new habitat. Perhaps Christopher Columbus was a carrier of the DAT1 10/10 genotype? It is possible that future carriers of this genotype will be the first to land on Mars. Another example is the very common 5-HTTLPR S allele. A negativity bias and increased sensitivity to negative stimuli including threat in S carriers seems to put them at
risk for anxiety and depression. Could this also have promoted survival? Detecting threat can be very important not only for one’s own survival, but to the survival of the entire social group. Someone needs to be on the lookout for predators and other dangerous threats. It is possible that the tendency for L_AL_A carriers to “accentuate the positive” in addition to the tendency for S carriers to resist “eliminating the negative” contribute to a successful society as a whole.

**Future Directions**

Attention deficit hyperactivity disorder (ADHD) is a developmental disorder in which cognitive control and emotional regulation (and supporting brain regions) are affected, possibly due to dysfunction in the monoamine neurotransmitter systems. Investigating belief bias in typical and atypical development as well as in adults could lead to a better understanding of the neural basis of belief bias and deductive reasoning more generally. Research into the neural bases of belief bias in reasoning is gaining momentum, however, there are many gaps yet to be filled. Research into populations with impaired inhibitory control, such as ADHD, could provide insight into the relationship between inhibitory control and belief bias. Functional imaging studies of ADHD have revealed abnormal activation in frontal regions (including lPFC, vmPFC), cingulate cortex and striatum, and more posterior regions including parietal cortex and precuneus (Bush et al., 2008; Castellanos et al., 2008; Silk et al., 2005; Stollstorff, Foss-Feig et al., submitted; Vaidya et al., 2005). Thus, regions of the brain affected in ADHD overlap to a large extent with brain regions involved in logical reasoning and belief bias.
suppression. Future studies of ADHD, dopamine-regulating genes and 5-HTTLPR could
provide insight into the nature of emotion-cognition interactions in deductive reasoning.

Conclusion

Although we might have the potential for logical reasoning, humans do not
always demonstrate this ability, as evidenced by errors in deductive reasoning tasks.
Some of these errors are predictable and can be accounted for by known factors, such as
belief bias. Some factors, such as emotion, that seem to predict patterns of reasoning
error are at earlier stages of investigation. Still other factors that contribute to error
variance are unknown. Environmental and genetic factors could help elucidate factors
that promote or inhibit logical reasoning.

To our knowledge, this is the first study to find that genes contribute to individual
differences in deductive reasoning. We found that 5-HTTLPR influenced emotion-
cognition interactions in the brain and behavior. This is one of many genes that
contribute to functional changes in 5-HT neurotransmission, which in turn is one of
several neurotransmitters known to contribute to brain function and behavior related to
emotional and cognitive control. It is fascinating that this small region of our DNA could
actually relate to our ability to make rational decisions in the real world and thereby
enhance or diminish our chances of survival. It is even more intriguing to consider the
combination of genes that are known to have similar effects on cognition and
emotionality. Future investigations of gene-gene interactions and their impact on
rationality and emotionality look promising.
References


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Appendix A: Stimuli from Chapter 1

Emotional Congruent Reasoning Problems

Virgins are less violent than terrorists.
Whores are less violent than virgins.
Terrorists are more violent than whores.

Toys are sharper than knives.
Toys are sharper than pillows.
Pillows are sharper than knives.

Abduction is worse than abortion.
Abortion is worse than divorce.
Abduction is worse than divorce.

Waterfalls are taller than beaches.
Mountains are taller than beaches.
Mountains are taller than beaches.

Vomit is thicker than blood.
Blood is thicker than urine.
Vomit is thicker than urine.

Bombs are louder than radios.
Bombs are louder than wasps.
Wasps are louder than radios.

Sharks are bigger than fish.
Sharks are bigger than mosquitoes.
Fish are smaller than mosquitoes.

Rifles are smaller than tanks.
Rocks are smaller than rifles.
Tanks are bigger than rocks.

Rats are bigger than cockroaches.
Cockroaches are bigger than mosquitoes.
Rats are smaller than mosquitoes.

Prison bars are safer than hospital beds.
Hospital beds are safer than land mines.
Prison bars are safer than land mines.

Deserters are less faithful than whores.
Whores are less faithful than virgins.
Virgins are more faithful than deserters.

Mutilation is more violent than crucifixion.
Crucifixion is more violent than electrocution.
Mutilation is more violent than electrocution.
Emotional Incongruent Reasoning Problems

Funerals are happier than birthdays.
Birthdays are happier than weddings.
Funerals are happier than weddings.

Vomit smells better than mildew.
Blood smells worse than mildew.
Vomit smells better than blood.

Lightbulbs are bigger than coffins.
Coffins are smaller than airplanes.
Lightbulbs are smaller than airplanes.

Corpses are lighter than shotguns.
Shotguns are lighter than cockroaches.
Cockroaches are heavier than corpses.

Drowning is more serious than cancer.
Burns are more serious than cancer.
Burns are less serious than drowning.

Murderers are nicer than rapists.
Rapists are nicer than priests.
Murderers are nicer than priests.

Bicycles are faster than cars.
Cars are faster than ambulances.
Bicycles are slower than ambulances.

The market is quieter than the jail.
The jail is quieter than the morgue.
The market is louder than the morgue.

Thieves are worse than assassins.
Killers are better than assassins.
Thieves are worse than killers.

Corks are sharper than bullets.
Bullets are sharper than daggers.
Daggers are sharper than corks.

Sudan is smaller than Iraq.
Russia is smaller than the Sudan.
Iraq is bigger than Russia.

Skijumps are shorter than rollercoasters.
Rollercoasters are taller than taxis.
Skijumps are taller than taxis.

Tobacco is more poisonous than venom.
Tobacco is less poisonous than mucus.
Venom is less poisonous than mucus.

Cockroaches are bigger than snakes.
Cockroaches are smaller than maggots.
Maggots are bigger than snakes.

Indonesia is more powerful than France.
France is more powerful than America.
America is more powerful than Indonesia.

A quarrel is more serious than a revolt.
A revolt is more serious than a war.
A quarrel is not as serious as a war.

Mosques are smaller than churches.
Mosques are bigger than cathedrals.
Churches are bigger than cathedrals.

Wounds are more devastating than an ulcer.
Paralysis is less devastating than an ulcer.
Wounds are more devastating than paralysis.

Alcohol is more harmful than narcotics.
Alcohol is less harmful than pasta.
Narcotics are less harmful than pasta.

Rape is better than fights.
Fights are better than hugs.
Hugs are better than rape.

Tasers are less harmful than pepper spray.
Pepper spray is more harmful than rulers.
Tasers are more harmful than rulers.

Madmen are crazier than robbers.
Madmen are crazier than scholars.
Robbers are crazier than scholars.

Embarrassment is worse than distress.
Depression is better than distress.
Embarrassment is worse than depression.

Cash is better than trophies.
Cash is better than utility bills.
Trophies are better than utility bills.
Non-Emotional Congruent Reasoning Problems

Cottages are smaller than houses.
Houses are smaller than palaces.
Cottages are bigger than palaces.

Coins are smaller than barrels.
Barrels are smaller than cars.
Coins are smaller than cars.

Lions are lighter than dogs.
Lions are lighter than frogs.
Dogs are lighter than frogs.

An iron is heavier than a fork.
A fork is heavier than a hairpin.
A hairpin is heavier than an iron.

Windows are smaller than houses.
Houses are smaller than skyscrapers.
Windows are smaller than skyscrapers.

Towers are taller than clocks.
Clocks are taller than lightbulbs.
Towers are taller than lightbulbs.

Runners are faster than gymnasts.
Gymnasts are faster than wrestlers.
Wrestlers are faster than runners.

Yachts are bigger than sailboats.
Sailboats are bigger than bathtubs.
Bathtubs are bigger than yachts.

Poland is east of Germany.
Germany is east of France.
Poland is east of France.

Puddles are bigger than lakes.
Oceans are smaller than puddles.
Lakes are bigger than oceans.

Keys are smaller than eggs.
Eggs are smaller than lamps.
Keys are smaller than lamps.

A cold is less serious than the measles.
Malaria is less serious than the measles.
A cold is more serious than malaria.

Doctors are smarter than dancers.
Janitors are less smart than dancers.
Doctors are smarter than janitors.

Violinists are noisier than chins.
Chins are noisier than plants.
Violinists are quieter than plants.

Boredom is less pleasing than comfort.
Fatigue is more pleasing than boredom.
Fatigue is more pleasing than comfort.

The neck is higher than the stomach.
The leg is lower than the stomach.
The neck is higher than the leg.

Artists are more creative than chefs.
Doctors are less creative than chefs.
Artists are more creative than doctors.

Sailboats are bigger than cars.
Violins are smaller than cars.
Violins are smaller than sailboats.

Hairdryers are smaller than lanterns.
Stoves are larger than hairdryers.
Lanterns are larger than stoves.

Kerosene is more toxic than perfume.
Milk is less toxic than perfume.
Milk is less toxic than kerosene.

True is more vague than false.
False is less vague than undetermined.
Undetermined is less vague than true.

Improvement is better than obedience.
Wastefulness is worse than obedience.
Wastefulness is worse than improvement.

Kettles are heavier than dustpans.
Dustpans are heavier than forks.
Kettles are lighter than forks.

A cabinet is louder than a banner.
A banner is quieter than a trumpet.
A cabinet is louder than a trumpet.
Non-Emotional Incongruent Reasoning Problems

Bees are larger than butterflies.
Butterflies are larger than birds.
Bees are larger than birds.

Trees are taller than flowers.
Trees are taller than grass.
Flowers are taller than grass.

Arms are shorter than hands.
Hands are shorter than fingers.
Arms are shorter than fingers.

Cities are smaller than towns.
 Towns are smaller than villages.
Cities are smaller than villages.

Snakes are faster than rabbits.
Pigs are faster than snakes.
Rabbits are faster than pigs.

Pencils are heavier than books.
Books are heavier than tables.
Pencils are lighter than tables.

Lighthouses are shorter than statues.
Statues are shorter than umbrellas.
Lighthouses are shorter than umbrellas.

Pizza is more healthy than pancakes.
Pancakes are more healthy than salad.
Pizza is less healthy than salad.

Summer is colder than autumn.
Winter is less cold than autumn.
Summer is colder than winter.

Tables are longer than streets.
Streets are longer than highways.
Tables are shorter than highways.

Doors are softer than baskets.
Beds are harder than baskets.
Doors are softer than beds.

Adults are older than children.
Adults are older than infants.
Children are older than infants.

Taxis are larger than buses.
Trucks are smaller than buses.
Trucks are smaller than taxis.

Needles are sharper than pencils.
Needles are sharper than whistles.
Pencils are sharper than whistles.

Years are shorter than weeks.
Days are longer than weeks.
Days are longer than years.

Doves are larger than lambs.
Lambs are larger than lions.
Doves are smaller than lions.

Jockeys are larger than soccer players.
Sumo wrestlers are smaller than soccer players.
Sumo wrestlers are smaller than jockeys.

Eggs are more fragile than glass.
Metal is less fragile than eggs.
Glass is more fragile than metal.

Horses are smaller than owls.
Owls are smaller than rabbits.
Rabbits are larger than horses.

Hamburgers are less tasty than pizza.
Pizza is less tasty than hay.
Hay is more tasty than hamburgers.

Computers are bigger than scissors.
Computers are bigger than coins.
Scissors are bigger than coins.

Yellow is darker than green.
Green is darker than black.
Yellow is brighter than black.

History is longer than a month.
History is longer than a moment.
A moment is shorter than a month.

The bowl is flatter than the chair.
The chair is flatter than the thermometer.
The bowl is flatter than the thermometer.
Appendix B: Stimuli from Chapter 2

*Emotional Congruent Reasoning Problems*

<table>
<thead>
<tr>
<th>Emotionally Congruent Reasoning Problems</th>
<th>Emotionally Congruent Reasoning Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hugs are better than fights.</td>
<td>Rollercoasters are shorter than skijumps.</td>
</tr>
<tr>
<td>Fights are better than rape.</td>
<td>Rollercoasters are taller than taxis.</td>
</tr>
<tr>
<td>Hugs are better than rape.</td>
<td>Taxis are taller than skijumps.</td>
</tr>
<tr>
<td>Whores are less violent than terrorists.</td>
<td>Drowning is more serious than ridicule.</td>
</tr>
<tr>
<td>Whores are more violent than virgins.</td>
<td>Cancer is more serious than drowning.</td>
</tr>
<tr>
<td>Terrorists are more violent than virgins.</td>
<td>Cancer is less serious than ridicule.</td>
</tr>
<tr>
<td>Ambulances are faster than cars.</td>
<td>Thunder is louder than tornadoes.</td>
</tr>
<tr>
<td>Bullets are faster than ambulances.</td>
<td>Thunder is louder than snow.</td>
</tr>
<tr>
<td>Cars are slower than bullets.</td>
<td>Snow is louder than lightning.</td>
</tr>
<tr>
<td>Mountains are higher than waterfalls.</td>
<td>Killers are worse than assassins.</td>
</tr>
<tr>
<td>Waterfalls are higher than beaches.</td>
<td>Thieves are better than assassins.</td>
</tr>
<tr>
<td>Mountains are higher than beaches.</td>
<td>Thieves are worse than killers.</td>
</tr>
<tr>
<td>The market is louder than the jail.</td>
<td>Cash is better than trophies.</td>
</tr>
<tr>
<td>The morgue is quieter than the jail.</td>
<td>Cash is better than slime.</td>
</tr>
<tr>
<td>The market is louder than the morgue.</td>
<td>Trophies are worse than slime.</td>
</tr>
<tr>
<td>Abortion is worse than sex.</td>
<td>Alcohol is more harmful than pasta.</td>
</tr>
<tr>
<td>Abduction is worse than abortion.</td>
<td>Alcohol is more harmful than narcotics.</td>
</tr>
<tr>
<td>Sex is better than abduction.</td>
<td>Narcotics are less harmful than pasta.</td>
</tr>
<tr>
<td>Guillotines are sharper than corks.</td>
<td>Electrocution is more violent than mutilation.</td>
</tr>
<tr>
<td>Guillotines less sharp than daggers.</td>
<td>Mutilation is less violent than intercourse.</td>
</tr>
<tr>
<td>Corks are less sharp than daggers.</td>
<td>Electrocution is less violent than intercourse.</td>
</tr>
<tr>
<td>Guns are smaller than rifles.</td>
<td>Germs are worse than aches.</td>
</tr>
<tr>
<td>Tanks are bigger than rifles.</td>
<td>Tumors are better than germs.</td>
</tr>
<tr>
<td>Guns are smaller than tanks.</td>
<td>Aches are worse than tumors.</td>
</tr>
<tr>
<td>Osama Bin Laden is more evil than Fidel Castro.</td>
<td>Scalpels are holier than crucifixes.</td>
</tr>
<tr>
<td>Fidel Castro is more evil than Barrack Obama.</td>
<td>Bibles are holier than crucifixes.</td>
</tr>
<tr>
<td>Osama Bin Laden is more evil than Barrack Obama.</td>
<td>Scalpels are holier than bibles.</td>
</tr>
<tr>
<td>Blood is thicker than urine.</td>
<td>Puppies are bigger than rats.</td>
</tr>
<tr>
<td>Vomit is thicker than blood.</td>
<td>Rats are bigger than lice.</td>
</tr>
<tr>
<td>Vomit is thicker than urine.</td>
<td>Lice are smaller than puppies.</td>
</tr>
<tr>
<td>Hospitals are smaller than prisons.</td>
<td>Fish are bigger than sharks.</td>
</tr>
<tr>
<td>Prisons are smaller than volcanoes.</td>
<td>Sharks are bigger than mosquitoes.</td>
</tr>
<tr>
<td>Volcanoes are smaller than hospitals.</td>
<td>Mosquitoes are bigger than fish.</td>
</tr>
</tbody>
</table>
Emotional Incongruent Reasoning Problems

Funerals are happier than birthdays.
Birthdays are happier than weddings.
Funerals are happier than weddings.

Killers are less erotic than hostages.
Killers are more erotic than strippers.
Hostages are more erotic than strippers.

Coffins are bigger than airplanes.
Kittens are bigger than coffins.
Airplanes are smaller than kittens.

Maggots are heavier than shotguns.
Shotguns are heavier than corpses.
Maggots are heavier than corpses.

Iraq is bigger than Afghanistan.
Russia is smaller than Afghanistan.
Iraq is bigger than Russia.

Distress is worse than depression.
Embarrassment is worse than distress.
Depression is better than embarrassment.

Tobacco is more poisonous than venom.
Tobacco is less poisonous than mucus.
Venom is less poisonous than mucus.

Snakes are smaller than cockroaches.
Maggots are bigger than cockroaches.
Snakes are smaller than maggots.

Murderers are nicer than rapists.
Rapists are nicer than priests.
Murderers are nicer than priests.

Wounds are nastier than paralysis.
An ulcer is nastier than wounds.
An ulcer is nastier than paralysis.

Palestine is more powerful than Israel.
Israel is more powerful than America.
America is more powerful than Palestine.

Nicotine is less addictive than chocolate.
Nicotine is more addictive than heroin.
Heroin is more addictive than chocolate.

Scorpions are bigger than sharks.
Termites are bigger than scorpions.
Termites are smaller than sharks.

Interest is more severe than infatuation.
Infatuation is more severe than obsession.
Obsession is more severe than interest.

Fish are smaller than sharks.
Mosquitoes are bigger than sharks.
Mosquitoes are smaller than fish.

Pistols are less safe than crutches.
Pistols are less safe than grenades.
Crutches are more safe than grenades.

Toys are sharper than knives.
Toys are sharper than pillows.
Pillows are less sharp than knives.

Wasps are louder than bombs.
Bombs are quieter than screams.
Wasps are quieter than screams.

The Pope is holier than Jesus.
Hitler is not as holy as the Pope.
Jesus is holier than Hitler.

Fireworks are brighter than parades.
Presentations are brighter than parades.
Fireworks are brighter than presentations.

Quarrels are more serious than revolts.
Revolts are more serious than war.
War is less serious than quarrels.

Vaginas are more masculine than nipples.
Nipples are more masculine than penises.
Penises are more masculine than vaginas.
Non-Emotional Congruent Reasoning Problems

A month is longer than history.
History is longer than a moment.
A month is longer than a moment.

Gymnasts are slower than runners.
Gymnasts are faster than wrestlers.
Runners are faster than wrestlers.

Cars are bigger than violins.
Sailboats are bigger than cars.
Violins are smaller than sailboats.

Tables are heavier than books.
Books are heavier than pencils.
Tables are heavier than pencils.

Skyscrapers are bigger than houses.
Windows are smaller than houses.
Skyscrapers are bigger than windows.

Obedience is worse than improvement.
Wastefulness is worse than obedience.
Improvement is better than wastefulness.

Pancakes are more healthy than pizza.
Pancakes are less healthy than salad.
Pizza is less healthy than salad.

Coins are smaller than barrels.
Cars are bigger than barrels.
Coins are smaller than cars.

Adam Sandler is funnier than Morgan Freeman.
Morgan Freeman is funnier than Tom Cruise.
Adam Sandler is funnier than Tom Cruise.

Computers are bigger than coins.
Scissors are bigger than computers.
Scissors are bigger than coins.

Yellow is brighter than green.
Green is brighter than black.
Black is brighter than yellow.

Eggs are smaller than lamps.
Eggs are bigger than keys.
Keys are bigger than lamps.

Ignorance is better than failure.
Happiness is better than ignorance.
Happiness is worse than contempt.

Trees are taller than flowers.
Flowers are taller than grass.
Grass is taller than trees.

Owls are smaller than lambs.
Cows are bigger than lambs.
Cows are smaller than owls.

Needles are sharper than pencils.
Needles are sharper than whistles.
Pencils are less sharp than whistles.

The stomach is higher than the leg.
The stomach is higher than the neck.
The neck is lower than the leg.

Glass is more fragile than eggs.
Eggs are less fragile than metal.
Glass is less fragile than metal.

Infants are younger than adults.
Children are older than infants.
Adults are younger than children.

Tables are longer than streets.
Highways are longer than streets.
Tables are longer than highways.

Georgetown is north of Virginia.
Virginia is north of Florida.
Florida is south of Georgetown.

Canada is north of USA.
USA is north of Mexico.
Mexico is north of Canada.
### Non-Emotional Incongruent Reasoning Problems

<table>
<thead>
<tr>
<th>Days are longer than weeks.</th>
<th>Pizza is less tasty than hay.</th>
<th>Pizza is tastier than hamburgers.</th>
<th>Hamburgers are tastier than hay.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks are longer than years.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days are longer than years.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hands are shorter than fingers.</td>
<td>False is more vague than true.</td>
<td>Undetermined is more vague than false.</td>
<td>Undetermined is less vague than true.</td>
</tr>
<tr>
<td>Hands are longer than arms.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fingers are longer than arms.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Towns are bigger than cities.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Villages are bigger than towns.</td>
<td></td>
<td>Sailboats are bigger than yachts.</td>
<td></td>
</tr>
<tr>
<td>Cities are smaller than villages.</td>
<td></td>
<td>Yachts are bigger than bathtubs.</td>
<td></td>
</tr>
<tr>
<td>Florida is north of Maryland.</td>
<td></td>
<td>SUMO wrestlers are smaller than soccer players.</td>
<td></td>
</tr>
<tr>
<td>Maryland is north of Maine.</td>
<td></td>
<td>Jockeys are bigger than soccer players.</td>
<td></td>
</tr>
<tr>
<td>Florida is north of Maine.</td>
<td></td>
<td>Jockeys are smaller than SUMO wrestlers.</td>
<td></td>
</tr>
<tr>
<td>Umbrellas are taller than statues.</td>
<td></td>
<td>Cottages are smaller than houses.</td>
<td></td>
</tr>
<tr>
<td>Lighthouses are shorter than statues.</td>
<td></td>
<td>Palaces are smaller than houses.</td>
<td></td>
</tr>
<tr>
<td>Umbrellas are taller than lighthouses.</td>
<td></td>
<td>Cottages are smaller than palaces.</td>
<td></td>
</tr>
<tr>
<td>Autumn is colder than winter.</td>
<td></td>
<td>Horses are bigger than lions.</td>
<td></td>
</tr>
<tr>
<td>Summer is colder than autumn.</td>
<td></td>
<td>Horses are bigger than doves.</td>
<td></td>
</tr>
<tr>
<td>Winter is warmer than summer.</td>
<td></td>
<td>Doves are smaller than lions.</td>
<td></td>
</tr>
<tr>
<td>Baskets are harder than doors.</td>
<td></td>
<td>Fatigue is more pleasing than boredom.</td>
<td></td>
</tr>
<tr>
<td>Baskets are softer than beds.</td>
<td></td>
<td>Boredom is less pleasing than comfort.</td>
<td></td>
</tr>
<tr>
<td>Doors are softer than beds.</td>
<td></td>
<td>Fatigue is less pleasing than comfort.</td>
<td></td>
</tr>
<tr>
<td>Trucks are smaller than buses.</td>
<td></td>
<td>Chefs are less creative than doctors.</td>
<td></td>
</tr>
<tr>
<td>Taxis are larger than buses.</td>
<td></td>
<td>Artists are more creative than chefs.</td>
<td></td>
</tr>
<tr>
<td>Trucks are smaller than taxis.</td>
<td></td>
<td>Doctors are less creative than artists.</td>
<td></td>
</tr>
<tr>
<td>Bees are larger than butterflies.</td>
<td></td>
<td>Dogs are heavier than rabbits.</td>
<td></td>
</tr>
<tr>
<td>Butterflies are larger than birds.</td>
<td></td>
<td>Frogs are heavier than rabbits.</td>
<td></td>
</tr>
<tr>
<td>Bees are larger than birds.</td>
<td></td>
<td>Dogs are heavier than frogs.</td>
<td></td>
</tr>
<tr>
<td>A fork is heavier than an iron.</td>
<td></td>
<td>New York is west of Colorado.</td>
<td></td>
</tr>
<tr>
<td>A hairpin is heavier than a fork.</td>
<td></td>
<td>Colorado is west of California.</td>
<td></td>
</tr>
<tr>
<td>A hairpin is heavier than an iron.</td>
<td></td>
<td>California is east of New York.</td>
<td></td>
</tr>
<tr>
<td>Forks are heavier than dustpans.</td>
<td></td>
<td>Hairdryers are larger than lanterns.</td>
<td></td>
</tr>
<tr>
<td>Dustpans are heavier than kettles.</td>
<td></td>
<td>Lanterns are larger than stoves.</td>
<td></td>
</tr>
<tr>
<td>Kettles are heavier than forks.</td>
<td></td>
<td>Stoves are larger than hairdryers.</td>
<td></td>
</tr>
</tbody>
</table>
Neutral Reasoning Problems

Haps are funnier than wenkles.
Wenkles are funnier than routes.
Haps are funnier than routes.

Jark is north of Maralon.
Jark is south of Gleese.
Maralon is south of Gleese.

Lardon is more populated than Corland.
Faria is more populated than Lardon.
Corland is less populated than Faria.

Michael is happier than Stephanie.
Stephanie is happier than Martin.
Michael is happier than Martin.

Tarop is west of Rorland.
Salim is east of Rorland.
Tarop is west of Salim.

Goopers are slower than lessels.
Hops are slower than goopers.
Lessels are faster than hops.

Johnathan is taller than Lindsay.
Johnathan is shorter than Eric.
Lindsay is shorter than Eric.

Christopher is less advanced than Tom.
Daniela is more advanced than Tom.
Christopher is less advanced than Daniela.

Jeremy is smarter than Katherine.
Katherine is smarter than Nick.
Jeremy is smarter than Nick.

Levels are brighter than obelisks.
Corners are brighter than levels.
Corners are brighter than obelisks.

Narlows are sharper than cheltons.
Cheltons are sharper than sakas.
Sakas are sharper than narlows.

Smithland is colder than Torotown.
Smithland is warmer than Wellington.
Wellington is warmer than Torotown.

Green is more vague of silver.
Magenta is more vague of green.
Magenta is less vague of silver.

Squares are smaller than circles.
Circles are smaller than triangles.
Triangles are smaller than squares.

Farmour is better than Greenspur.
Capelton is worse than Greenspur.
Capelton is better than Farmour.

Lines are less fun than slits.
Edges are less fun than slits.
Lines are less fun than edges.

Darlows are higher than burtons.
Darlows are higher than fazams.
Fazams are lower than burtons.

Ramaloos are more expensive than nimors.
Nimors are less expensive than alfops.
Ramaloos are less expensive than alfops.

Crillats are less shiny than quillows.
Wafs are more shiny than crillats.
Quillows are less shiny than wafs.

Hanshals are larger than kropans.
Andars are larger than kropans.
Hanshals are larger than andars.

Cardon is more evasive than hull.
Hull is more evasive than prawl.
Prawl is less evasive than cardon.

Luppers are cuter than grors.
Grors are cuter than shups.
Shups are cuter than luppers.
**Emotional Baseline Problems**

- Whores are less violent than terrorists.
- Whores are more violent than virgins.
- Cars are slower than bullets.

- Mountains are higher than waterfalls.
- Waterfalls are higher than beaches.
- The market is louder than the morgue.

- Abortion is worse than sex.
- Abduction is worse than abortion.
- CORKS are less sharp than daggers.

- Guns are smaller than rifles.
- Tanks are bigger than rifles.
- Osama Bin Laden is more evil than Barrack Obama.

- Blood is thicker than urine.
- Vomit is thicker than blood.
- Volcanoes are smaller than hospitals.

- Rollercoasters are shorter than skijumps.
- Rollercoasters are taller than taxis.
- Cancer is less serious than ridicule.

- Lightning is louder than tornadoes.
- Tornadoes are louder than snow.
- Thieves are worse than killers.

- Cash is better than trophies.
- Cash is better than slime.
- Narcotics are less harmful than pasta.

- Electrocution is more violent than mutilation.
- Mutilation is less violent than intercourse.
- Aches are worse than tumors.

- Scapels are holier than crucifixes.
- Bibles are holier than crucifixes.
- Lice are smaller than puppies.

- Fish are bigger than sharks.
- Sharks are bigger than mosquitoes.
- Funerals are happier than weddings.

- Killers are less erotic than hostages.
- Killers are more erotic than strippers.
- Airplanes are smaller than kittens.

- Maggots are heavier than shotguns.
- Shotguns are heavier than corpses.
- Iraq is bigger than Russia.

- Distress is worse than depression.
- Embarrassment is worse than distress.
- Venom is less poisonous than mucus.

- Snakes are smaller than cockroaches.
- Maggots are bigger than cockroaches.
- Murderers are nicer than priests.

- Wounds are nastier than paralysis.
- An ulcer is nastier than wounds.
- America is more powerful than Palestine.

- Nicotine is less addictive than chocolate.
- Nicotine is more addictive than heroin.
- Termites are smaller than sharks.

- Interest is more severe than infatuation.
- Infatuation is more severe than obsession.
- Mosquitoes are smaller than fish.

- Pistols are less safe than crutches.
- Pistols are less safe than grenades.
- Pillows are less sharp than knives.

- Wasps are louder than bombs.
- Bombs are quieter than screams.
- Jesus is holier than Hitler.
**Non-Emotional Baseline Problems**

| Days are longer than weeks. | New York is west of Colorado. |
| Weeks are longer than years. | Colorado is west of California. |
| Fingers are longer than arms. | Stoves are larger than hairdryers. |

| Towns are bigger than cities. | A month is longer than history. |
| Villages are bigger than towns. | History is longer than a moment. |
| Florida is north of Maine. | Runners are faster than wrestlers. |

| Umbrellas are taller than statues. | Cars are bigger than violins. |
| Lighthouses are shorter than statues. | Sailboats are bigger than cars. |
| Winter is warmer than summer. | Tables are heavier than pencils. |

| Baskets are harder than doors. | Skyscrapers are bigger than houses. |
| Baskets are softer than beds. | Windows are smaller than houses. |
| Trucks are smaller than taxis. | Improvement is better than wastefulness. |

| Bees are larger than butterflies. | Pancakes are more healthy than pizza. |
| Butterflies are larger than birds. | Pancakes are less healthy than salad. |
| A hairpin is heavier than an iron. | Coins are smaller than cars. |

| Forks are heavier than dustpans. | Adam Sandler is funnier than Morgan Freeman. |
| Dustpans are heavier than kettles. | Morgan Freeman is funnier than Tom Cruise. |
| Hamburgers are tastier than hay. | Scissors are bigger than coins. |

| False is more vague than true. | Yellow is brighter than green. |
| Undetermined is more vague than false. | Green is brighter than black. |
| Yachts are bigger than bathtubs. | Keys are bigger than lamps. |

| Sumo wrestlers are smaller than soccer players. | Ignorance is better than failure. |
| Jockeys are bigger than soccer players. | Happiness is better than ignorance. |
| Cottages are smaller than palaces. | Grass is taller than trees. |

| Horses are bigger than lions. | Owls are smaller than lambs. |
| Horses are bigger than doves. | Cows are bigger than lambs. |
| Fatigue is less pleasing than comfort. | Pencils are less sharp than whistles. |

| Chefs are less creative than doctors. | The stomach is higher than the leg. |
| Artists are more creative than chefs. | The stomach is higher than the neck. |
| Dogs are heavier than frogs. | Glass is less fragile than metal. |
Neutral Baseline Problems

Haps are funnier than wenkles.
Wenkles are funnier than routes.
Maralon is south of Gleese.

Lardon is more populated than Corland.
Faria is more populated than Lardon.
Shups are cuter than luppers.

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Stephanie is happier than Martin.
Tarop is west of Salim.

Goopers are slower than lessels.
Hops are slower than goopers.
Lindsay is shorter than Eric.

Christopher is less advanced than Tom.
Daniela is more advanced than Tom.
Jeremy is smarter than Nick.

Levels are brighter than obelisks.
Corners are brighter than levels.
Sakas are sharper than narlows.

Smithland is colder than Torotown.
Smithland is warmer than Wellington.
Magenta is less vague of silver.

Squares are smaller than circles.
Circles are smaller than triangles.
Capelton is better than Farmour.

Lines are less fun than slits.
Edges are less fun than slits.
Fazams are lower than burtons.

Ramaloos are more expensive than nimors.
Nimors are less expensive than alfops.
Quillows are less shiny than wafs.