2 Genes of rationality

Building blocks for the neurobiology of reasoning

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Introduction

Genes are the building blocks for life; from infancy to senescence, our genes play a role in making us who we are. Our genetics interact with the environment to make us unique individuals, capable of creative and novel ideas, and at times, "creative logic". Do our genes predispose us to logical errors? Here I will present some initial evidence that they do. These initial studies might be thought of as the building blocks for the study of reasoning from a neurobiological/genetic perspective.

Generally speaking, healthy adults can reason logically, but tend to make errors in predictable ways (i.e., heuristic biases). Upon learning about human reasoning biases, I'm sure that many individuals think to themselves, "not me!" and can readily provide examples of others whose logic is considerably more error-prone. One classic example of a reasoning heuristic is the belief-bias effect, which is a tendency to solve a reasoning problem based on one's beliefs or prior semantic knowledge rather than logical structure (Evans et al., 1983); that is, to be swayed by beliefs rather than logic. It is known that certain external factors, such as time pressure (Tsujii and Watanabe, 2010) and emotional content (Blanchette and Richards, 2004), increase reasoning bias. Are some people more sensitive to these factors and therefore more prone to logical errors than others? Yes! Internal factors, that is, those arising from within the individual such as working memory and inhibitory control, can influence reasoning bias (Handley et al., 2004). Various cognitive neuroscience methods have begun to shed light on the neurobiology of reasoning over the last 15 years including many types of neuroimaging studies (Goel, 2007; Goel et al., 2000; Luo et al., 2008; Prado et al., 2011; Tsujii and Watanabe, 2009). In this chapter, I will describe findings from a new field of reasoning research: reasoning genetics. Recent research has identified genes to be another internal source of variance that influences deductive reasoning and more specifically, belief-bias (Stollstorff, Bean, et al., 2012). It seems that our genetic make-up influences our ability to reason logically and can account for significant variance in errors which was previously unexplained. This chapter will highlight evidence that reasoning ability is, in part, determined by our genes.

While there is considerable research on cognitive biases in reasoning and some research on the effect of emotion on reasoning (Blanchette and Richards, 2004),

little is known about how individual differences in emotional reactivity might enhance or diminish cognitive biases to influence the deductive reasoning process. I will describe a series of studies that investigate the effect of emotional content on bias in logical reasoning and how this behavior and its brain bases are modulated by a polymorphism for the serotonin transporter genotype (SERT) that is known to influence emotional reactivity. I will also explore how dopamine, known to influence cognitive control processes such as working memory and inhibition, can influence the neural bases of biased decision-making. I will conclude by briefly describing other neurobiological factors (neurotransmitters and genes that regulate them) that could help elucidate questions in the field of human reasoning.

Genes, brains and neurotransmitters

Our genetic code programs the building blocks for human thought. The essential neurobiological ingredients for reasoning, such as neurotransmitters, neurons and synapses, arise from our genes. Genes interact with the environment to produce individual differences in many aspects of human thought, feeling and behavior. These differences result, at least in part, from genetic polymorphisms. A genetic polymorphism arises from a mutation that occurred at some point in our evolutionary history that has been preserved and passed on through generations, especially if they promote survival. I will focus primarily on one common genetic polymorphism (the serotonin transporter gene: 5-HTTLPR or "SERT") and its effect on belief-bias in emotional reasoning.

What do genes have to do with reasoning? Genetics provide a natural model to investigate individual differences in reasoning ability without having to manipulate anything experimentally. In animal models, scientists can have more flexibility; for example, they can inject dopamine into the basal ganglia and test the animal's behavior. However, human experimental manipulation of neurotransmitters is not as straightforward or scientifically controlled; we can administer drugs to patients with pre-existing conditions and occasionally even to healthy individuals. However, with genetics, we have a ready-to-go model: genetic polymorphisms exist among healthy humans that have known functional consequences on neurotransmitter function, sometimes localized to specific brain regions. It is a great experimental model and a wonderful tool to test psychological theory.

Genetics 101: the basics and the methods

The human genome is incredibly complex and molecular geneticists practically have their own language. However, the good news is that for our purposes, genetics can be quite simple to understand and to utilize in psychological research studies. Let me walk you through the process to clarify the methods and introduce some important basic genetic concepts: first, we ask participants to "spit in a cup". They provide a saliva sample into a specially prepared (or purchased) collection kit. Other common methods include collecting buccal cheek cells from the inside of the mouth or from blood draws. The end result, regardless of method, is a

sample containing the DNA of the participant. Once the DNA is extracted from the saliva (or cheek cells or blood), they are genotyped for the specific polymorphisms of interest (or several of them).[1]

A polymorphism is a region in our genetic code that differs across individuals. A "functional" polymorphism is a part of our DNA strand with multiple forms that results in differential expression of the protein that it codes for, ultimately resulting in some type of individual difference in our biology, such as eye color. Typically, you might be interested in a single nucleotide polymorphism (SNP), which is a point in the strand of our DNA where one of those nucleotide pairs has been switched (e.g., from A to G). Popular/infamous examples of SNPs include: COMT (val-allele linked to schizophrenia (Egan et al., 2001)), or FTO (A-allele linked to obesity (Frayling et al., 2007)). Or you might be interested in a variable-number tandem repeat (VNTR) polymorphism, where a section or small chunk of the DNA strand is repeated a different number of times. Well-known examples of VNTRs include: APOE (E4-allele linked to Alzheimer's disease), DAT1 and DRD4 (10/10 DAT1 genotype and 7-repeat DRD4 alleles linked to ADHD (Cook et al., 1995; Rowe et al., 1998)), SERT (short allele linked to mood disorders (Caspi et al., 2003)).

Polymorphisms vary in their contribution to a particular behavior or disease. Some genes directly cause a disease; for example, if you inherit even one of the risk alleles (36-repeat allele or higher), you *will* develop Hungtington's disease. Individuals who inherit the non-risk allele (<36 repeats) will not inherit this disease (Walker, 2007). For other genes, for example, BRCA1, you are at a much higher risk for breast cancer (50–80 per cent more likely to develop breast cancer) if you carry the mutation (Domchek et al., 2010) and therefore other contributing factors (genetic and/or environmental) must be involved as well. And yet for others, inheriting the risk alleles increases your risk only slightly (for example, ~4 per cent for the DAT1 10/10 genotype and ADHD (Waldman et al., 1998)). That leaves huge room for other genes and known or yet-unknown environmental factors to contribute, either by additive or interactive effects. To some critics, these low gene-to-behavior effect sizes render single polymorphism genetic studies useless. The contribution of a single polymorphism to a psychiatric disorder can be low and replication studies sometimes fail. However, I believe this is true of all aspects of biological psychology. It is difficult to predict with scientific precision any phenomenon that is itself somewhat vague. Many psychiatric disorders have no reliable biomarkers or tests and diagnosis is arguably subjective, based on manuals with different criteria depending on which continent the clinician is from. Genetics in psychology and cognitive neuroscience is in its infancy. But this is why, in my opinion, it is that much more important to focus our research efforts on genetics to begin to untangle this complicated puzzle of genes and behavior. Once a polymorphism is identified as a possible contributor to psychological function or dysfunction, we can, and should, begin to elucidate the mechanism by which this gene has its effect through psychological and cognitive neuroscience methods. Ultimately, these genetic polymorphisms influence the neurotransmitters that fuel the brain, which in turn gives rise to reasoning and errors in logic.

While genetic differences amongst us are complicated and surely interact with the environment as we develop, we are beginning to elucidate the mechanisms that underlie human reasoning and natural tendencies towards specific heuristics and biases. Humans differ in their reaction to environmental triggers that lead to irrational decisions. The large body of reasoning literature in psychology describes the nature of these patterns in errors and has even begun to elucidate the cognitive bases for these irrational biases. Here, we begin to unravel the story one step further by using genetics and neurobiological evidence.

Belief-bias

The most interesting source of logical error, in my opinion, is the belief-bias heuristic. It interests me for two reasons. First, the most important arguments are often made in the context of strongly held beliefs. Real-world, everyday reasoning is typically based in a system of beliefs and knowledge and the more important a decision, often the more emotionally charged it is. Second, the effect is strong and has been replicated in many types of deductive reasoning (e.g., categorical syllogistic (Evans, et al., 1983); conditional (Byrne and Tasso, 1999) and relational (Roberts and Sykes, 2003)) in many populations (children and adults with and without psychiatric disorder (de Jong et al., 1997; Handley et al., 2004). The belief-bias effect has been well studied for decades from a psychological perspective and has generated many hypotheses and theories in the field of reasoning. To this day, it amazes me that highly intelligent university students, despite explicit instruction to ignore beliefs and respond based on logic alone, consistently fall prey to belief-bias. In my experience across several reasoning experiments (behavioral and fMRI), comparing performance on belief-congruent versus belief-incongruent trials consistently yields medium to large effect sizes (~0.4–0.5). In psychology, this is quite impressive! In sum, belief-bias (and more recently, emotion) have been my main research focus and the tools I use to study them are largely from cognitive neuroscience and neurobiology, functional magnetic resonance imaging (fMRI) and genetics.

The belief-bias effect is increased by many factors, such as time pressure (Tsujii and Watanabe, 2010); additional cognitive demands (dual-task paradigm (Tsujii and Watanabe, 2009)) and development/ageing (i.e., both younger children (Handley, et al., 2004) and older adults have increased belief-bias (De Neys and Van Gelder, 2009; Tsujii, Okada, and Watanabe, 2010)). 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, et al., 2012). 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 of belief bias

The inhibition hypothesis of belief-bias posits that increased errors for incongruent reasoning problems are not caused by poor logical reasoning per se, rather

by poor inhibitory control (De Neys and Franssens, 2009; Handley, et al., 2004; Houde et al., 2000; Moutier et al., 2006; Stollstorff, Vartanian, et al., 2012). 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), participants 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, more effortful). They must suppress one cognitive process, memory retrieval, in favor of another cognitive process, logical reasoning.

Not only does belief-bias share essential cognitive task features with traditional inhibition tasks, it also relies upon the same brain region: the right lateral prefrontal cortex (rlPFC). Many methods have now converged upon the same result: fMRI studies find rlPFC to be active during successful belief-bias suppression (Goel and Dolan, 2003a; Stollstorff, Vartanian, et al., 2012); and disrupting the function of this region using repetitive transcranial magnetic stimulation (rTMS) impairs reasoning for incongruent trials (Tsujii et al., 2010). The evidence is quite convincing that the right lateral PFC, known to be recruited for classic inhibition tasks (Aron et al., 2004), is involved in belief-bias suppression.

Emotion and reason

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 the vmPFC often have blunted or abnormal emotional responses and also seem to have difficulties in real-world decision-making (Anderson et al., 2006; Bechara et al., 2000;

Stuss et al., 1992). So perhaps emotion helps, or is even necessary for, successful 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 and 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 statements, such as "If there is danger, then one feels nervous" (Blanchette and 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 et al., 1998; de Jong, et al., 1997; Vroling and de Jong, 2009). Thus, emotion (content and mood) can hinder the reasoning process. In terms of brain mechanisms, emotional reasoning recruits the ventromedial prefrontal cortex (vmPFC) rather than the more lateral prefrontal cortex typically engaged during non-emotional reasoning (Goel and Dolan, 2003b).

Serotonin transporter gene and emotional reactivity

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 (Canli and Lesch, 2007). Serotonin (5-hydroxytryptamine; 5-HT), a neurotransmitter synthesized in the raphe nucleus (brain stem), is released throughout the entire brain. The serotonin transporter protein (5-HTT), located on the pre-synaptic terminal of the neuron, is the main mechanism for termination of 5-HT action. It clears serotonin back to the pre-synaptic neuron, removing it from the synapse and thereby terminating its action.[2] There is a region in the serotonin transporter gene (SLC6A4) where a polymorphism occurs and this region is referred to as "5-HTTLPR" (Serotonin Transporter Long Promoter Region, or "SERT"). SERT influences 5-HTT mRNA transcription, which results in different levels of the 5-HTT protein (Hu et al., 2006). Our genetic code is quite brilliantly redundant, often containing sections that repeat many times. The short "S" allele, which repeats only 14 times, is linked to lower expression of serotonin transporter mRNA relative to the long "L" allele, which repeats 16 times (Hu et al., 2006). Further, the L allele contains an A to G single nucleotide polymorphism (SNP rs25531) that influences transcriptional

efficiency, rendering the LG allele functionally similar to the S allele. Therefore, the SERT genetic polymorphism is actually "triallelic", meaning three alleles: S, LG, and LA. Since the LG allele is functionally equivalent to the S allele, we will simplify things and group the LG and S alleles together (S'), separate from the LA allele (L). We inherit two alleles, one from each parent, so an individual can be one of the following three genotypes: SS, SL, or LL.

SERT genotype influences emotional reactivity. Findings of studies comparing S carriers with homozygous L carriers (LL) 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 over transmitted 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 negative emotional content (e.g., angry faces) in an emotional dot probe task (Beevers et al., 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 (Munafo et al., 2008; von dem Hagen et al., 2011). Together, these findings indicate that Short carriers differ in emotional reactivity from Long carriers, suggesting a "negativity bias" or heightened sensitivity for negative emotion.

In addition, evidence now suggests a "positivity bias" for the Long (LL) genotype (Fox et al., 2009; Perez-Edgar, et al., 2010). For example, in an emotional dot probe paradigm, Long carriers are more attracted to happy faces; that is, they tend to pay more attention to positive emotion. Groups did not differ in reaction to neutral faces. Furthermore, Stroop-like interference effects in the prefrontal cortex and posterior processing areas are increased by positive emotional content (happy faces) for the carriers of the Long/Long genotype (Stollstorff et al., in press). In sum, the Short/Short individuals are more likely to detect fearful faces and other threats in the environment, whereas the Long/Long individuals are more likely to detect happy faces and positive environmental stimuli. The Long group "accentuates the positive" while the Short group seems to be primed to attend to threats and other negative emotional content.

What is the mechanism by which emotion interferes with logic? How does emotion interact with beliefs? If emotional reactivity reduces reasoning performance and a genetic polymorphism increases emotional reactivity, the genetic polymorphism ought to reduce reasoning performance. As I explained, 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. Consequently, in my studies I began by exploring 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.

Beliefs, emotions and serotonin

I used to believe in the tooth fairy. When my brother disputed this belief, I did everything in my power to dissuade him from his erroneous position including resorting to violence and a massive crying fit. Our strongest beliefs can be the most resistant to change and providing evidence that logically contradicts the belief can evoke a strong emotional reaction. Are individuals who have stronger emotional reactivity more biased by their beliefs?

Evidence from my research suggests that this is indeed the case. Healthy adults were genotyped for SERT status (S/S, S/L or L/L). We excluded heterozygotes (carriers of both the S and L alleles) and included two groups in our reasoning experiment: Short (S'/S' carriers) and Long (L/L carriers). Participants completed a logical reasoning task to measure belief-bias under two conditions: negative emotional content and emotionally neutral content. The participants' task was to determine whether the conclusion was logical or not logical, irrespective of their beliefs or knowledge about the truth or falsity of the conclusion. An example of an emotional problem: cockroaches are smaller than snakes; cockroaches are bigger than maggots; snakes are bigger than maggots. An example of a non-emotional problem: trees are taller than flowers; trees are shorter than grass; flowers are shorter than grass. Problems were either belief-logic congruent or belief-logic incongruent. A belief-bias index was calculated by the difference between performance for congruent and incongruent problems. Problems were logically identical across conditions; they only varied in the level of affective intensity (high or low negative affect) and in belief-logic congruency (congruent, incongruent).

As predicted, the Short group, associated with biased attention towards negative information, displayed higher belief-bias in the emotional condition relative to the Long group; groups did not differ in the non-emotional condition (Stollstorff, Bean, et al., 2012). Furthermore, the Short group reported higher trait anxiety (STAI) (Spielberger et al., 1983) relative to the Long group; evidence that individuals in the Short group did perceive themselves to have higher negative affect. Anxiety was positively correlated with the level of emotional (but not non-emotional) belief-bias (i.e., individuals with higher anxiety tended to have higher emotional belief-bias). Thus, one's genetic predisposition towards negative affect influences the ability to reason logically in an emotional context.

What is the neural mechanism by which the serotonin transporter polymorphism influences belief-bias? As described previously, a key region in reducing belief-bias susceptibility is the right lateral prefrontal cortex (rlPFC) (Goel and Dolan, 2003a; Stollstorff, Vartanian, et al., 2012; Tsujii, et al., 2010). To link the effect of SERT on emotional belief-bias to previous brain studies, I needed to ascertain whether this key brain region, the rlPFC, is modulated by SERT during emotional belief-bias suppression. Participants were recruited for an fMRI study similar to the behavioral-genetic study described above; that is, two groups (Short or Long carriers) solving reasoning problems with emotional or non-emotional content that were either belief-logic congruent or incongruent. Since evidence had developed indicating that SERT Long homozygotes (L/L) have increased

sensitivity to positive information, we included a positive emotional condition as well.

Neuroimaging results revealed a double dissociation in two key regions: the rlPFC and bilateral amygdala. Behavioral performance was quite high, likely due to a computer practice session prior to the experimental task, and groups did not differ in belief-bias performance accuracy or reaction time. However, differences were detected in the brain. The Short group required more activation of the rlPFC to overcome negative belief-bias, while the Long group required more activation of this region to overcome positive belief-bias. The same pattern of activity was found in the amygdala, and we interpret this as bottom-up reactivity to the positive and negative stimuli for Long and Short carriers, respectively. That is, the amygdala was more reactive to negative emotional content in Short carriers and more reactive to positive emotional content in Long carriers, requiring more top-down inhibitory control from rlPFC. Therefore, lower-level attentional bias towards or away from a specific emotional valence, caused by serotonin transporter genotype, can affect high-level thinking and reasoning via basic emotional and cognitive control brain regions (Stollstorff et al., in prep).

The studies I have discussed thus far involved healthy participants solving problems in a relatively emotionally neutral environment (i.e., no major threats, no major potential rewards). One might wonder what would happen if the emotional stakes were raised slightly? To begin to address this issue, we decided to set up an fMRI experiment similar to our behavioral-genetic study, in the sense that the context was more overwhelmingly negative. In this study, we contrasted negative and emotionally neutral problems only (excluding a positive valence condition), so that ~50 per cent of the material was negative. We targeted the negatively-biased Short group first, as this group is at risk for clinical disorder such as depression and anxiety (Caspi, et al., 2003). Our results showed that Short allele carriers had less involvement of the rIPFC and instead recruited the ventromedial prefrontal cortex (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. I propose that the negative context of the experiment caused a shift in the neural circuitry recruited by the Short carriers: from a "cool" logical lateral prefrontal network to a "hot" affective ventromedial network, perhaps more susceptible to emotionally biased reasoning. The idea is the following: for certain individuals (Short carriers), under higher demand (overwhelmingly negative context), the rlPFC "shuts down" and disengages, and the brain relies instead on an affective network more sensitive to heuristic biases and bottom-up emotional reactivity. Further research is necessary to test this hypothesis: (1) this study requires replication; (2) other manipulations of emotion could be made (for example, to test this in depressed patients or to evoke negative mood in healthy participants); and (3) the Long group should be tested under high positive demands to see if they, too, "break down" under high emotional demands and recruit affective brain networks rather than the cognitive right lateral prefrontal cortex.

Dopamine, inhibitory control and belief-bias

Just as the serotonin transporter gene influences emotional reactivity, which in turn leads to increased belief-bias, the dopamine transporter gene (DAT1) might also contribute to belief-bias by influencing inhibitory control. If inhibitory 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.

Dopamine is thought to be a critical neurotransmitter supporting inhibitory control in the prefrontal cortex (Goldman-Rakic et al., 1992; Murphy et al., 1996). Various functional genetic polymorphisms influence dopamine function in the brain and thereby influence cognitive control, for example, the dopamine transporter gene (DAT1). The dopamine transporter protein (DAT) clears dopamine from the synapse and recycles it back up to the presynaptic terminal, thereby inactivating dopamine. Although DAT is distributed in many parts of the brain, including the 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 dopamine 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 et al., 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., 2010), a network of regions also found to be active during relational reasoning (Goel, 2007; Stollstorff and Vaidya, in prep).

In a recent study, we found that healthy adult carriers of the 10/10 genotype had increased belief-bias relative to the 9/10 genotype. Furthermore, the 10/10 genotype group recruited the rlPFC to a lesser extent than did the 9/10 genotype group (Stollstorff and Vaidya, in prep). Thus, individuals inheriting the DAT1 10/10 genotype, which is associated with poor inhibitory control, have impaired ability to inhibit their beliefs in favor of logic. These data support the Inhibition Hypothesis of the belief-bias effect.

Preliminary data investigating the interaction between serotonin (SERT) and dopamine (DAT1) transporter genes on negatively valenced emotional belief-bias suppression indicate that carriers of *both* risk alleles (for negative emotional reactivity and poor inhibitory control: Short SERT and 10/10 DAT1, respectively) have significantly higher belief-bias (~17 per cent belief-bias score) relative to the other genotype groups (~6 per cent belief-bias score). Although this finding will need to be replicated in a large-scale study, it is as would be predicted, since these individuals are more sensitive to the distracting negative emotional content and have less inhibitory control to suppress it in favor of logic. It highlights

that gene x gene interaction could explain much more variance than a single gene alone.

Implications

Our work has important implications for studies of emotional reasoning. I have presented evidence that the serotonin transporter gene, known to influence attention towards or away from emotionally valenced information, can affect logical reasoning and the brain mechanisms that support this process. This is not to say that the (roughly) 20 per cent of us who carry this genotype cannot overcome our predisposition. However, we should be aware that certain environmental contexts or triggers might make it more difficult to reason logically for some individuals and could have the opposite effect for other individuals. For example, cognitive therapy for specific phobia that focuses on changing the patient's irrational fear of spiders might work better in a positive context for individuals who carry two copies of the SERT short allele, in light of their high sensitivity to negative context and resulting logic-resistant beliefs. But this same positive environment might have distracting and opposing effects for someone with the Long genotype. We can also see why some studies of the effect of emotion on reasoning might yield mixed results if valence and genotype are not taken into account.

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. Genetics could help elucidate underlying mechanisms that promote or inhibit logical reasoning.

The emerging work that I presented in this chapter indicated that SERT and DAT1 influenced emotion-cognition interactions in brain function and behavior. 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.

Notes

1 DNA extraction and genotyping are either processed "in house" (contact your nearest biology department), by a dedicated genetics laboratory in an academic research environment, or commercially.
2 For example, antidepressants, such as Prozac and Zoloft, work by blocking serotonin re-uptake by blocking the serotonin transporter (Huezo-Diaz et al., 2009).

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