

# Investigating the Role of Testosterone on Risk-Taking Behavior in Male Sprague Dawley Rats

**Menzi Mhlanga\***

Department of Neuroscience  
Lake Forest College  
Lake Forest, Illinois 60045

## Abstract

**Testosterone plays a critical role in the development of gender and gender specific traits. While the physiological functions of testosterone are well established, the hormone's influence on cognition is poorly understood. Evidence suggests that testosterone increases sensation seeking, dominance seeking, aggression, and mate-seeking behavior: behaviors that carry a component of risk. More recent findings suggest a strong association between testosterone and risky decision making in financial markets. However, the causal relationship between testosterone and risk-taking behavior has yet to be determined. In the present study, we used rats, subcutaneously injected with testosterone, to test the hypothesis that exogenous testosterone administration increases risk-taking behavior. We report finding a non-significant increase in risk-taking behavior following a three day testosterone administration period. Evaluation of individual subjects, however, suggests a role of testosterone on modulating risk-taking behavior. Further replications using testosterone assays are necessary to establish a clear role of testosterone on risk-taking behavior.**

## Introduction

The emerging field of neuroeconomics seeks to understand how organisms, such as ourselves, make decisions and which factors contribute to the decision making process (Zak, 2004; Zweig, 2007). Deciding what to wear for a party or what to eat at a restaurant requires the agent to weigh the potential risks and benefits of each possible outcome. Our brains constitute a fast decision making machine that must efficiently and quickly decide our fate in order to maximize our gains. From an evolutionary point of view, only those organisms best able to maximize their gains are fit to survive in an ever-dynamic environment (Watson & Platt, 2008). By combining the disciplines of neuroscience and economics, neuroeconomics provides a potentially powerful tool for understanding the biological correlates of decision-making and subsequent behavior. Many of our daily decisions are not only motivated by the potential benefits (rewards) associated with the outcome, but also by the potential risks of punishment and negative reinforcement (Brynes, Miller, & Schafer, 1999). Such an observation has led to the question, "what motivates risk-taking behavior?" While there is no clearly defined construct of risk-taking behavior, a broad classification of risk-taking behavior comprises two components that are generally consistent across all definitions of risk. First, there must be at least two choices from which the subject chooses from and secondly, there must be at least two outcomes, each of which carries an estimated probability of gain (reward) or loss (negative outcome).

A system of assessing risky decision-making, such as the one stated above is appealing because it encompasses a broad category of behaviors, which allows for easy identification and measurement of the construct. Therefore, any assessment of risk-taking behavior offers the opportunity for a more inclusive framework of interpretation and application of results.

Problems with such a broad based definition of risk-taking behavior arise when we attempt to *i)* quantify the consequence in order to establish the severity of the reward or the negative outcome, and *ii)* to establish the probability that each outcome will occur (Brynes, Miller, & Schafer, 1999). Driving a car (regardless of a driver's speed or alcohol influence) on a highway would be considered risk-taking behavior under a broad classification of risk behavior. However, from an assessment point of view, *only* driving at an extremely high speed or driving under the influence of alcohol may be considered risk-taking behavior.

Another complicated layer of risk-taking behavior assessment is related to the validity of the risk-taking construct. Is the individual perception of risk more relevant or, is risk assessment from a societal point of view adequate for defining what is risky decision-making and what is not? A competent professional motor racer may see no risk in driving at extremely high speeds, but society may view such behavior as being risky. The context in which the behavior is being defined also poses additional problems related to defining risk-taking. From a health perspective, severe negative outcomes (e.g. injury or illness) are seen as being risky, whereas economic perspectives may differ in the way in which risky behavior is defined.

The above issues relate to the construct validity of risk-taking behavior and, as a consequence, undermine the validity of the measures used to assess risk-taking behavior and the extent to which we can infer relevant conclusions from studies of risky decision-making. However, because of the broad domains of behavior classifiable under the risk-taking construct, it is plausible to use domain specific methods of assessment when investigating risk-taking behavior. Economic models of assessment have been popular amongst investigators because they make it possible to quantify the risks and rewards associated with specified outcomes in universal monetary terms.

Economic theories and games provide mathematical models for assessing risk-taking behavior in a financial context (Zak, 2004; Schultz, 2008). Frank Knight, the renowned economist of the early 20th century defined risk as the "uncertainty about which of several outcomes will occur, whereby the probability of each outcome is known" (Knight, 1921). In theory, our decision-making processing should be objective and rational when calculating the odds of loss and reward. In reality, however, our decision processing and subsequent behavior is far from rational. Lapses in rationality are often blamed upon our failure to regulate our emotions (Krueger, Grafman, & McCabe, 2008). For example, Wilson and Daly (2003) asked men to rate pictures of women (appealing or not appealing) and later offered the participants a choice between 1) a guaranteed small amount of money the following day or 2) a 75 percent chance of receiving an unspecified higher amount of money after a significantly longer delay. Men who had been exposed to the "appealing women" were more likely to discount future rewards for the safer reward (Wilson & Daly, 2003). This, and similar studies, have led to the belief that rational decisions can, and are, modulated by our emotional states.

\*This author wrote the paper as a senior thesis in biology under the direction of Dr. Shubhik DebBurman.

Testosterone constitutes a class of hormones that influence emotional processing. We, therefore, ask the question, is testosterone associated with risk-taking behavior? If so, what is the nature of the association?

Understanding the biological correlates of risk-taking behavior is essential. Risk-taking behavior is prevalent among adolescents and men of all ages, a phenomenon that carries significant implications for health and various other aspects of social engagement such as antisocial behavior and stereotypes (Eagly, 1995). Stereotypes of women being inferior to men in the workplace, because they are less likely to be aggressive or take risk, are still pervasive in society (Eagly, 1995). Therefore, an understanding of the biological and external correlates of risk-taking behavior is critical to the field of neuroeconomics. In the current study, we sought to investigate the role of testosterone on risk-taking behavior by using a rat model. In this paper, I will cover:

- 1) Testosterone's classical properties, routes of action, and the hormone's influence on the nervous system
- 2) Review the literature on risk-taking behavior from Neuroimaging studies, and financial markets
- 3) Discuss the objectives of the current study and procedures used to test our hypothesis
- 4) Report the findings of the current study and move into a discussion of the significance of the data.

#### *Testosterone Physiology and Classical Actions*

Vertebrate organisms display a great deal of sexual dimorphism in terms of their physical appearance and behavior (Becker, Breedlove, & Crews, 2001; Kalat, 2009). Undoubtedly, such variations are due to a combination of genetic, biological, neural, and environmental factors. Many of the biological substrates of sexual dimorphism are well established, including steroid hormones (e.g. androgens and estrogens) and gene expression patterns that extend beyond the X and Y chromosomes (Van Nas et al, 2009; Wu et al, 2009; Auyeung et al, 2008).

Testosterone is the principal androgenic hormone in males, a hormone being a class of chemicals secreted from one area of the body to produce a change in another region of the body. Testosterone secretion is largely regulated by the hypothalamus, via, the pituitary gland. Figure 1 illustrates the overall mechanism by which testosterone is released in the human body. The anterior region of the hypothalamus releases gonadotropin-releasing hormone (*GnRH*) into the bloodstream, whereupon it is absorbed by the pituitary gland, causing the release of luteinizing hormone (*LH*) and follicle-stimulating hormone (*FSH*) into the bloodstream. In males, LH orchestrates the biosynthesis and cleavage of cholesterol into testosterone, while FSH is critical for spermatogenesis. Many factors (both internal and external) have been shown to influence GnRH, and ultimately testosterone content levels in the bloodstream (Breedlove, 2010; Oyegbile & Marler, 2005; Zak et al, 2009). Cleaved from cholesterol, testosterone is largely produced by the Leydig cells of the testes. Indeed, more than 95% of circulating testosterone in males is produced in the testes whereas the remaining 5% is produced in the adrenal cortex of the adrenal gland. Females also produce testosterone in the ovaries and the cortex of the adrenal, albeit to a lesser extent than their male peers.

Classical models of testosterone function classify testosterone actions into two broad categories of action: *virilizing* effects and *anabolic* effects. Virilizing effects (androgenic) are those that promote and maintain the

development of male secondary characteristics such as growth of body hair and deepening of the voice during puberty. On the other hand, anabolic effects are those concerned with muscle growth, bone density and structure (Lin & Erinhoff, 1990).

The steroid nature of testosterone allows the hormone to easily penetrate every lipid membraned cell of the body. The hormone's ability to penetrate the cell nucleus allows for androgenic regulation of gene expression patterns, and subsequent protein synthesis. Testosterone easily diffuses into the cell to bind the intracellular androgen receptor (AR), also known as the Nuclear Receptor Subfamily 3, Group C, Member 4 (NR3C4). Androgen receptors are thought to be present in almost every tissue of mammalian organisms (Lin & Erinhoff, 1990), a belief that is consistent with the steroid hormones' ability to organize male physical characteristics in a vast majority of tissues. Van Nas and colleagues (2009) report finding extensive differential expression of genes in a gender specific manner under the influence of steroid hormones (van Nas et al, 2009).

Testosterone can also be metabolized into several steroid hormones (e.g. estradiol) in a tissue specific manner. Testosterone is converted into estradiol by the enzyme *aromatase* that, in males, is selectively expressed nervous tissue. Estradiol seems to play a role in the expression of transient effects of testosterone, such as copulation in vertebrate males (Breedlove, Watson, & Rosenzweig, 2010). Consequently, gonad steroid action is now classified as producing *organizing* and *activating* effects. The former refers to the hormone's ability to induce permanent male/female physical and behavioral characteristics during the early stages of development.

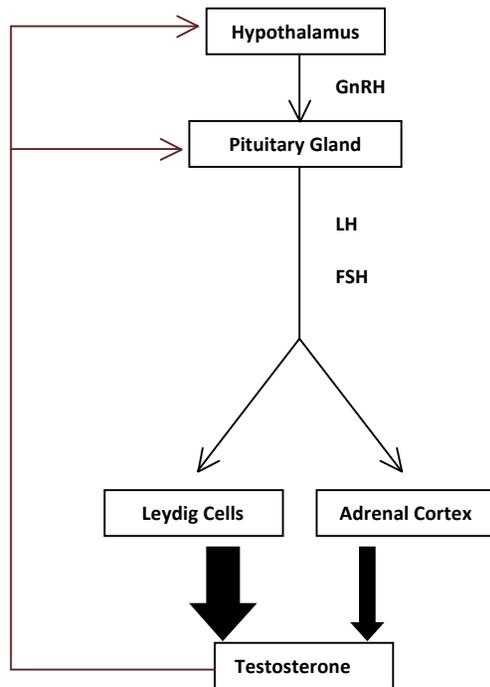
A relevant example of testosterone's *organizing* effect is the human finger length ratio. The length of the index finger (2nd finger) to the length of the ring finger (4th finger) has been shown to be a sexually dimorphic feature, whereby men exhibit a low 2D: 4D ratio (< 1) compared to women who possess a higher 2D: 4D ratio (>1) (Manning et al, 1998; Lutchmaya et al, 2003).

Activational effects of testosterone are those induced later in adult stage of development and are thought to be responsible for producing transient behaviors such as sexual arousal and copulation in males (Breedlove, 2010). Therefore, a distinguishing feature between a steroid's organizational and activational effects is that organizational features are established during critical periods of development (sensitive period), often occurring in the early gestational period or infancy. Activational effects, on the other hand, do not require any specific period and may manifest themselves at any stage in the organism's development.

Research has uncovered several mechanistic roles of steroid action in the cognitive processing of information. Steroid hormones, such as testosterone and estradiol, have been studied extensively in an effort to find the biological correlates of gender differences in behavior (Newman, Guinn Sellers, & Josephs, 2004). The following section will discuss several lines of evidence to illustrate various mechanisms by which testosterone acts on the nervous system at the organizing and activating level, and how such evidence may underlie behaviors such as aggression, status maintenance, and cognitive processing involved in risky decision making.

#### *Testosterone and the Brain*

Testosterone modulation of gender differences in physical traits (sexual dimorphisms) raises the question as to whether testosterone also influences cognitive processing of information and other higher order functions. Because neural processes underlie all forms of human behavior, it is



**Figure 1: Testosterone Secretion Axis:** The hypothalamus, through interacting with several cortical areas, secretes Gonadotropin Releasing Hormone (GnRH) into the bloodstream, whereupon it is absorbed by the Anterior Pituitary gland, causing the release of Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) into the blood stream. In the specialized Leydig Cells of the Testes, LH is used to initiate the cleavage of cholesterol to produce the steroid testosterone. Feedback mechanisms regulate the amount of GnRH and LH released into the bloodstream so as to inhibit testosterone production.

plausible to hypothesize that sexual dimorphisms within the nervous system, as a result of steroid hormone function, do in fact influence behavior in a gender-biased manner. Such knowledge suggests an indirect role of sex hormones, such as testosterone, in influencing behavior.

#### *Gender Dimorphisms in Brain Anatomy*

What are the sexually dimorphic regions of the vertebrate brain that are modulated by testosterone action? Studies done in rodents and birds have identified consistent male vs. female differences in brain anatomy. In rats and mice, the nucleus of the preoptic area of the hypothalamus, known as the sexually dimorphic nucleus of the preoptic area (SDN-POA), is >5 times larger in male rodents compared to female rodents (Breedlove, Watson, & Rosenzweig, 2010; Gorski et al, 1978). Dimorphisms within the preoptic area are mediated by the hormone testosterone. Male rats castrated at birth develop a smaller SDN-POA, whereas female rats treated routinely with the hormone testosterone develop a significantly larger SDN-POA (Gorski et al, 1978). These findings were the first to demonstrate a sex-hormone-mediated dimorphism in the central nervous system. Studies done using bird models have found similar masculinizing effects of androgens. Female zebra finches treated with testosterone after hatching sing much like male zebra finches. This was only observed when testosterone treatment was administered early in the developmental stage, suggesting that testosterone acts early in the critical period

to masculinize the nervous system (Breedlove, Watson, & Rosenzweig, 2010).

Do the dimorphisms found in other vertebrate organisms translate to the same observations in human? Dimorphisms within the human brain have been difficult to illustrate because they are very subtle and interpretations of such findings are often met with much more controversy than rationale (Breedlove et al, 2001). In a controversial study published by LeVay (1991), the researchers reported size differences in specific hypothalamic nuclei after a postmortem examination of brain tissue samples obtained from heterosexual women, men, and homosexual men (LeVay, 1991). His report found that the third interstitial nucleus of the hypothalamus (INAH-3) was >2 times larger in heterosexual men compared to heterosexual women. Interestingly, they also found the same INAH-3 nucleus to be significantly larger in heterosexual men when compared to homosexual men.

A more recent investigation of the INAH-3 area by Garcia-Falgueras and Swaab (Garcia-Falgueras & Swaab, 2008) extends LeVay's findings by reporting similar gender-biased size differences in the INAH-3 region. An analysis of post-mortem brain slices of heterosexual men and women (controls), male-to-female transsexuals, and female-to-male transsexual subjects revealed significantly larger INAH-3 sizes in heterosexual men vs. heterosexual women. Data from transsexuals showed that male-to-female nuclei sizes were comparable to those of heterosexual females, whereas female-to-male nuclei sizes were comparable to those of heterosexual males.

Whereas the evidence to define the function of the INAH-3 is yet to be uncovered, the anterior hypothalamus, in which the preoptic area is located, is known to regulate the release of GnRH, which promotes the release of LH in the pituitary gland (Bears, Connors, & Paradiso, 2001). Such findings suggest that steroid-hormone-induced brain physiology has the potential to influence cognitive appraisal of one's gender identity.

A recent publication by Goldstein et al (2001) reports finding significant dimorphic differences in cortical and sub-cortical brain regions which correlate highly to the distribution pattern of androgen receptors (Goldstein et al, 2001). Men reportedly have a larger frontomedial cortex, hypothalamus, and amygdala size (relative to cerebellum). Women were found to have larger cortices, relative to cerebellum, particularly in the frontal and medial paralimbic cortices. The finding that size differences in cortical and sub-cortical regions of the brain are more prominent in areas with a high population of androgen receptors suggests that these differences may be mediated by steroid hormones, such as testosterone and estradiol, early in the developmental stage (Perrin et al, 2008; Goldstein et al, 2001).

Findings of dimorphic size differences in brain areas do not, however, give us adequate information about the significance of the size with regards to the expression of specific behaviors.

#### *Testosterone and Synaptic Plasticity*

Molecular investigations of gonad hormones on behavior have explicitly demonstrated the activational role of steroid hormones in regulating plastic changes within the brain (Cooke & Wooley, 2005). In vitro exposure of hippocampal CA1 pyramidal neurons to estradiol causes a significant increase in dendritic spine density (Murphy & Segal, 1996). Moreover, dendritic spine gain is attenuated by NMDA receptor antagonists, but not by AMPA receptor antagonists, thus demonstrating an NMDA-mediated pathway by which estradiol exerts its impact on neuron physiology. Not surprisingly,  $Ca^{2+}$  signaling within postsynaptic membranes increases significantly in estradiol-treated neurons (Murphy

& Segal, 1996; Sarkar et al, 2008). A closer examination of synaptic activity indicates that estradiol increases glutamate binding to NMDA receptors, but not to AMPA receptors. This suggests that estradiol does not influence low-level, AMPA mediated, synaptic activity. Instead estradiol mediates synaptic signaling by increasing the synapse's sensitivity to NMDA mediated potentiation, thus suggesting a likely mechanism by which sex hormones induce transient activational effects within the central nervous system (Wooley et al, 1997).

Similar findings have been demonstrated consistently in vivo using animal models. In a study by Wooley and McEwen (1993), ovariectomized female rats showed rapid significant losses in dendritic spine density within the hippocampal CA1 area. The authors report that losses in dendritic spines were rapidly rescued by subsequent treatment with estradiol. Primate studies have replicated similar findings. Orchidectomized (castrated) male monkeys showed significant losses of dendritic spine density within the CA1 area of the hippocampus (Leranth et al, 2004). A more striking feature reported by the authors is the finding that intact males possess significantly lower spine densities when compared to intact or ovariectomized female monkeys, a finding that could likely be explained by differences in circulating levels of estradiol in males vs. females.

Fast-acting steroid-hormone-induced plasticity has been shown in other brain areas such as the amygdala (important for emotional processing), hypothalamus (important for regulating steroid hormone secretion, maintenance of sexual behaviors and identity), and the spinal nucleus of the bulbocavernosus (Cooke & Wooley, 2005).

Despite such findings of hormone-mediated changes in synaptic potentiation, plasticity, and overall brain physiology, we still know very little about the role of steroid induced plasticity to specific behaviors. However, they do provide us with a potential framework by which sex hormones induce changes in behavior and cognition. Cognitive studies in the field of learning and memory attribute changes in behavior to changes in synapse signaling and physiology (Purves et al, 2008). NMDA receptor-mediated pathways are associated with changes in potentiation, whereby the strength of signaling between two communicating neurons is increased, a process known as long-term potentiation (LTP). Plasticity changes and LTP have been reliably demonstrated throughout various brain areas and implicated in learning, memory, and performance ability (Purves et al, 2008; Bear, Connors, & Paradiso, 2001). Therefore, findings of steroid hormone influence on brain plasticity, suggest a potential route of influence on cognitive information processing such as decision-making and risk-taking behavior (Newman, Sellers, & Josephs, 2004).

#### *Brain Imaging Studies*

Classical economic models of risk-taking behavior have neglected the role of environmental, emotional, and biological variables when modeling economic behavior (Zweig, 2007; Zak, 2004; Sanfey et al, 2003). Neuroeconomics combines neuroscience tools and methods to study the internal factors associated with decision-making. Used in conjunction with economic game models, non-invasive neuroimaging technology, such as functional magnetic resonance imaging (fMRI,) provides a powerful tool for studying the underlying neural correlates of decision making (Weller et al, 2007; Xiao & Houser, 2005; Christopoulos et al, 2009; Kuhnen & Knutson, 2005; Watson & Platt, 2008; Mohr, Biele, Heekeren, 2010). Economic

game models, such as the Dictator Game or Ultimatum Game, have the advantage of being objective in quantifying the proportion of expected rewards and losses, thus making [them] a suitable model for assessing risk-taking behavior (Krueger, Grafman, & McCabe, 2008).

One model that is consistently used in risk-taking behavior analysis is the Ultimatum Game, first introduced by Guth and colleagues in 1982 (Guth, Schmittberger, & Schwarze, 1982). In this game, two players are given a sum of money to divide between themselves in a manner dictated by the proposer. The responder's decision, to accept or reject the proposer's offer, determines whether or not the money is given to the two players. Acceptance of an offer results in the distribution the money according to the proposer's offer and rejection of an offer results in a null trial (i.e. none of the players receive the money). Recent adaptations of the Ultimatum Game utilize computer software to assume the role of the proposer as a method of predetermining the probability of specific offers (Krueger, Grafman, McCabe, 2008).

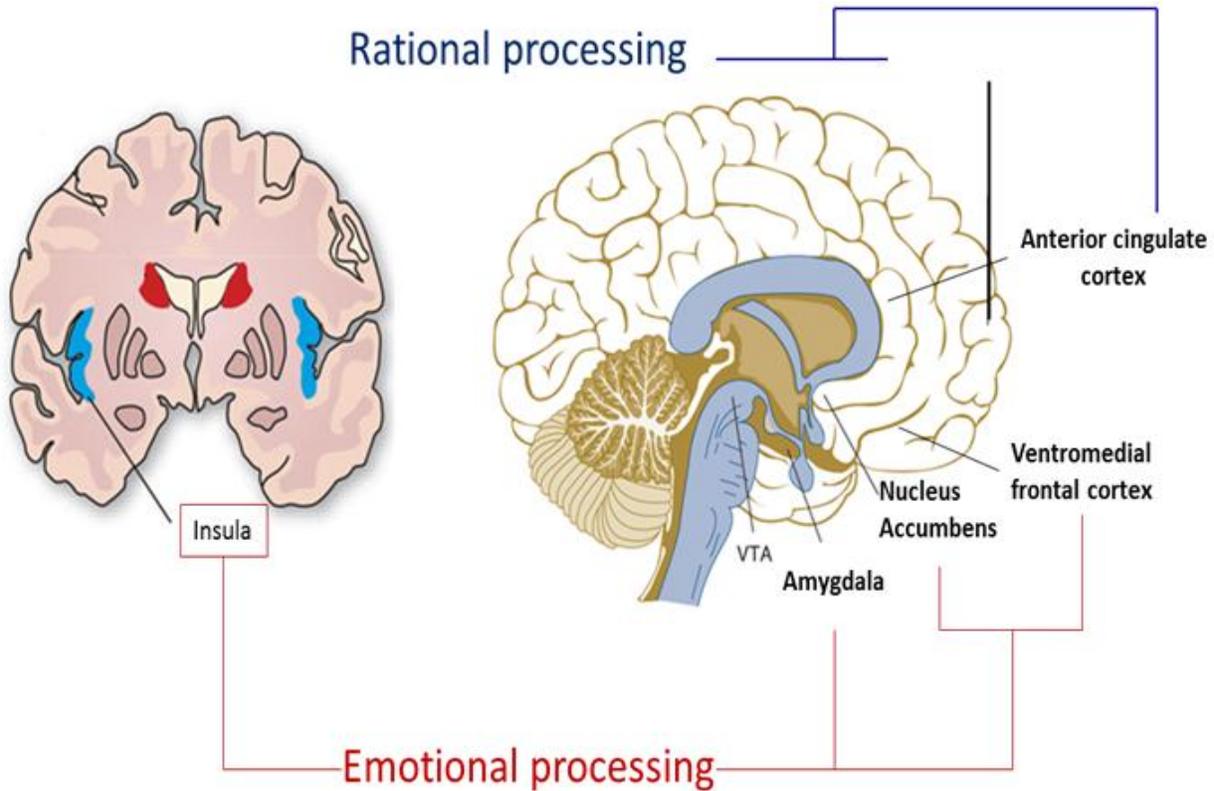
Sanfey and colleagues (2003) investigated the behavioral responses of the responder to fair vs. unfair offers in the Ultimatum Game while scanning their [responder] brains in an MRI scanner. Participants were made aware that they would be playing against another human subject (proposer) or against a computer. Fair offers were defined as a \$5:\$5 split of a \$10 amount and an unfair offer as a \$7:\$3, \$8:\$2, or \$9:\$1 offer. Their results indicate significant bilateral activation of the anterior insula, dorsolateral prefrontal cortex (DLPFC), and the anterior cingulate cortex (ACC) in response to unfair offers. Activation of the anterior insula was greatest when responding to unfair human offers and least prominent (although significant) when responding to computer generated offers. The insula is known to show significant activation during negative emotional states (Phan et al, 2002).

Activation in the anterior insula, ACC, and the DLPFC has been consistently associated with risk decision-making in other similar studies (Mohr, Biele, & Heekeren, 2010; Kuhnen & Knutson, 2005; Christopoulos et al, 2009). In a related study by Mohr, Biele, and Heekeren (2010) using a novel economic game, they report finding substantial activation of the anterior insula when participants were faced with potential losses.

The above findings illustrate the powerful influence that emotions have on risk-taking behavior in financial assessment models. This is further substantiated by the observation that participants in the Sanfey et al (2003) Ultimatum Game experiment were more likely to reject unfair offer made by a human proposer than a computer-generated offer.

Several other researchers have demonstrated similar findings that associate emotion centers in the brain with risk-taking behavior. Prominent among these are the amygdala, nucleus accumbens, and ventromedial prefrontal cortex (Weller et al, 2007; Kuhnen & Knutson, 2005; Martino, Camerer, & Adolphs, 2009). Amygdala impairment has been shown by Weller et al (2007) to attenuate economic decision making when considering potential gains, but not when considering potential losses (Weller et al, 2007).

What emotions, then, play a role in modulating risk-taking behavior in economic game models? In a similar version of the Ultimatum Game, Xiao and Houser (2005) asked responders to write a message to the proposer as they chose to accept or reject the proposer's offer (Xiao & Houser, 2005). By coding the message as expressing a negative, neutral, or positive emotion, the authors showed that when given the opportunity to express their emotions,



**Figure 2: Modeling the role of emotions on decision-making:** According to neuroeconomic models of decision-making, two competing processes occur when making decisions. Emotions, mediated by emotional centers in the brain compete with executive integrative processes of the frontal lobe, considered to be responsible for rational decision-making.

Responders in the ultimatum game are more willing to accept unfair offers; therefore, suggesting rejection of unfair offers (risks) in traditional Ultimatum models is an expression of emotional discontent.

Emotional regulation plays an important role in moderating our decisions when undertaking actions that are risky. Koenigs and Tranel (2007) assessed the choices of seven individuals with damage to the ventromedial prefrontal cortex (VMPC) in the Ultimatum game. Clinical assessment of patients with damage to the VMPC characterize their behavior as being slightly abusive, aggressive, and short-tempered, indicating defects in regulating negative emotions (Koenigs & Tranel, 2007). Their findings indicate that damage to the VMPC further exaggerates rejection of unfair offers compared to control subjects.

It is possible, therefore, to model decision making under risk as shown in Figure 2 (below). According to such a model, biological factors such as testosterone may mediate activation of emotion brain centers such as the amygdala and insula and, consequently, one's decision when faced with uncertain outcomes.

#### *Risk-Associated Behaviors: The role of gender*

Psychological literature provides a vast amount of data associating the male gender to health-associated risks such as driving under alcohol influence, smoking, occupational hazards, and risky sexual behavior with multiple partners and less contact with physicians (Sutton, Baum, & Johnston, 2005; Booth, Johnson, & Granger, 1999; Lin & Erinhoff, 1990). Various personality traits have been studied as potential causes of gender biases in risk-taking behavior. Here, I will review literature related to a personality trait

defined by its high affinity for risk: sensation-seeking behavior.

Sensation seeking is defined by Zuckerman (Zuckerman, 1994) as the personality trait in which an "individual seeks out novel, complex, and varied experiences and the willingness to seek out such experiences despite the risks associated with the experience". Zuckerman makes a clear distinction between sensation-seeking and risk-taking behavior. Sensation seekers engage in activities thought to stimulate their arousal and include a wide range of socially acceptable and unacceptable behaviors such as high-risk sports, reckless driving, excessive alcohol and drug abuse, promiscuous sexual activity, stimulating occupations, gambling, and binge drinking (Roberti, 2004). The degree to which risk is associated with such experiences varies from one activity to another; however, most sensation seekers pursue stimulating activities despite the risks associated with the behavior. A distinction between sensation seeking and risk-taking behavior, therefore, lies in the difference in probability of obtaining a reward. Sensation seekers obtain their reward (stimulation) regardless of whether the risk associated with the behavior manifests itself. That is, although risk is a possible outcome, it follows as a consequence of the behavior, not as an outcome by itself. Risk-taking behavior, as defined in the paper, is defined by the uncertainty of the outcome. Thus, risk-taking behavior results in obtaining either a positive reward or a negative outcome. However, there is a strong correlation between risk-taking behavior and sensation seeking (Roberti, 2004; Leland & Paulus, 2004), reinforced by the fact that, in sensation seeking and risk-taking, the prospect of a obtaining a positive reward outweighs the prospect of

punishment, regardless of the odds. Therefore, the same biological and social substrates may underlie both behaviors and this section will review some of the findings in the available literature.

The consistency of gender biases in sensation-seeking behaviors has led to investigations of the biological mechanisms responsible for high sensation seeking in men. A handful of researchers have studied gonad hormones and their correlation to the sensation seeking personality (Rosenblitt et al, 2000; Voracek, Tran, & Dressler, 2009; Campbell et al, 2010; Aluja & Garcia, 2004). Such studies have generally failed to produce a correlation between testosterone and sensation seeking. A closer analysis reveals potential methodological errors that may result in inaccurate findings. Rosenblitt et al (2000) sought to investigate the relationship between testosterone and sensation seeking in undergraduate college students. Participating subjects were administered the Zuckerman Sensation Seeking Scale (SSS-V) and also had their saliva samples collected for hormone assays. The authors report finding significantly higher scores for men compared to women on the sensation seeking scale, but fail to find a relationship between sensation seeking and testosterone levels (Rosenblitt et al, 2000). A major flaw in the methodology of this study is that the experimenters expected to find a correlation between a single sample of circulating testosterone and pervasive behavior. The experimenters assume that 1) testosterone levels are equal across all individuals and that 2) the level of testosterone remains stable across daily activities. Both assumptions are inaccurate. Testosterone levels are known to vary depending on various internal and external factors such as medication, contraceptive treatment, or social context and hierarchy (Sutton, Baum, & Johnston, 2005). Losing or winning a game (Oyegbile & Marler, 2005) or watching one's favorite candidate lose an election (Stanton et al, 2009) have also been demonstrated to cause significant variations in circulating testosterone levels. Therefore, one measure of testosterone is not a reliable measure of the hormone's potential activating effect. Still other studies have sought to find a relationship between markers of testosterone's prenatal exposure (e.g. 2D: 4D) and sensation seeking (Voracek, Tran, & Dressler, 2009- *meta-analysis*). Similarly, such studies have failed to produce any relationship between prenatal markers of testosterone exposure and sensation seeking. The authors attribute such findings as being consistent with the hypothesis that testosterone's *organizing* effects have little to do with adult transient behaviors.

Theories of sensation-seeking behavior attribute biases in the sensation-seeking phenotype to differences in cognitive appraisal of risks associated with certain behaviors. According to this perspective, high sensation seekers appraise 'high risks' as less threatening, whereas low sensation seekers appraise similar risks as more threatening (Roberti, 2004). In fact Hovarth and Zuckerman (1993) find that high scorers in the sensation seeking scale were less likely to self-report 'crime risk' and 'sports risk' as risky behaviors.

It is possible that testosterone acts as a mediator by influencing one's appraisal of a risky situation (e.g. challenging another male for a mate). Thus, not only does testosterone increase one's physical fitness, it may also increase one's "cognitive fitness." Such a hypothesis is appealing in light of the literature suggesting that testosterone decreases male sensitivity to punishment consequences in social confrontations (Boissy & Bouissou, 1994). Van Honk and colleagues (2004) report finding decreased sensitivity to punishment in the IOWA gambling game after subjects were treated with testosterone (Van

Honk et al, 2004). In this task, participants are asked to draw a card from one of four decks for 100 consecutive trials. Two decks are known to be highly disadvantageous and the other two are considered modest. The disadvantageous decks provide extremely high rewards but very infrequently and these rewards often come after significant losses, which occur frequently. The modest decks offer modest rewards at a frequent rate and are accompanied by modest low frequency losses. Women treated with a single shot of testosterone were more likely to choose the disadvantageous decks compared to the control group (Van Honk et al, 2004). The findings of this study suggest that testosterone may in fact shift sensitivity to punishment or otherwise inhibit disinhibition when making a risky decision. This is compliant with a neural model of risk-taking, whereby disinhibition of emotions can, and does, lead to irrational risk-taking behavior.

#### *Testosterone in the Financial Market*

Gender differences in risk aversion have led to several investigations that have sought to examine the relation between sex hormones and career preferences (Purifoy & Kopmans, 1974; Sapienza, Zingales, & Maestriperi, 2009). Purifoy and Koopmans collected blood samples from fifty-five women for hormone assays, which they then correlated to professional occupational categories (such as managerial positions, students, and technical workers) and non-professional occupations (housewives, clerical occupations). Their findings demonstrated high testosterone levels among women engaged in professional occupations whereas low levels of testosterone were typical of housewives and clerical workers. Similar results were reported by Sapienza and colleagues (2009), who found that high circulating levels of testosterone and low 2D:4D are highly predictive of risky career choices (Sapienza, Zingales, & Maestriperi, 2009). Such findings undermine the role of external factors that contribute to career preferences (Joel & Tarrasch, 2010).

Positive associations of testosterone and aggression, criminal behavior, alcohol and drug abuse, promiscuous sexual activity, sensation seeking, and dominance-seeking behavior have led to the hypothesis that testosterone directly influences risk-taking behavior. Few studies have examined the role of testosterone in financial risk-taking behavior tasks and, although inconsistent, overall results indicate a positive association between testosterone and risk-taking behavior. Inconsistencies in findings may be due to the varied approach several studies have taken in examining the relationship between testosterone and risk-taking behavior, some using prenatal markers of testosterone exposure, and others circulating measures of the hormone.

Studies that have focused on prenatal exposure to testosterone have generally found a positive relationship between the 2D:4D and risk-taking behavior (Coates, Gurnell, & Rustichini, 2009; Strenstrom et al, 2010), though findings to the contrary have also been reported (Apicella et al, 2008). Real life, male financial traders in a London trading floor were assessed for prenatal exposure to testosterone by Coates, Gurnell, and Rustichini (2009) who report finding a significant negative correlation between trader's 2D:4D digit ratios and the magnitude of profits and losses made by each trader. That is, the lower the digit ratio (indicative of high prenatal testosterone exposure) the higher the profits and losses made during the trader's career. Similar findings are reported by Strenstrom and colleagues (2010). Using a risk-taking survey (Weber, 2002), they report a significant negative correlation between 2D:4D ratios and risk-taking behavior in financial, recreational, and social, but not health and ethical contexts (Strenstrom et al, 2010). These findings were applicable to men, but not women, which limits the

interpretations that can be drawn from such studies. The gender correlation between 2D:4D ratio and risk-taking behavior may in fact be a redundant replication of the correlation between gender and risk-taking behavior since 2D:4D is a marker of testosterone's *organizing* effect. Indeed, a true correlation between 2D:4D and risk-taking behavior would be observable in women with high vs. low digit ratios.

Studies that have examined circulating levels of testosterone and risk-taking behavior have also produced inconsistent data, some finding significant correlations (Coates & Herbert, 2007; Burnham, 2007; Apicella et al, 2008; Sapienza, Zingales, & Maestripieri, 2009) and others finding no correlation (Zethraeus et al, 2008; Stanton et al, 2011). Recruiting and following the income progress of real life financial traders during their working hours, Coates and Herbert (2007) report finding a positive relationship between morning (11:00 am) and afternoon (4:00 pm) testosterone levels and daily profits and losses. That is, on days when traders possessed above average levels of testosterone, they were more likely to make very significant profits or very significant losses. The authors also report that above average morning levels of testosterone are predictive of daily profits and losses, which suggests that testosterone may in fact cause increased risk-taking behavior. Similar findings have been replicated in controlled laboratory settings whereby elevated levels of circulating testosterone have been positively correlated with risk-taking in economic games such as the Ultimatum game (Apicella et al, 2008; Burnham, 2007; Van Honk et al, 2004). In a double blind, placebo-controlled study, women administered testosterone were less risk-averse than a placebo control group in the IOWA gambling task (Van Honk et al, 2004).

I propose several ways in which testosterone increases risk-taking behavior in a broad spectrum of behaviors. Testosterone's association to aggression and sexual reproductive behavior suggest that the hormone is responsible for mediating emotions such as anger and pleasurable experiences. Testosterone may act on the emotional-neural circuitry and brain centers associated with the expression of emotion such as the amygdala, ventral striatum, nucleus accumbens, and anterior insular cortex (Coates, Gurnell, & Sarnyai, 2010). Several lines of evidence lend support to this hypothesis. Firstly, responders in the Ultimatum game are less likely to risk rejecting unfair offers when playing a computer than when pitted against another human (Sanfey et al, 2003). Secondly, male proposers in the Ultimatum game are more likely to initiate unfair offers when pitted against another male than they do when playing with a female confederate (Saad & Gill, 2001). Testosterone has been shown to increase rapidly in human and non-human vertebrate organisms immediately after brief encounters with the opposite sex (Roney, Mahler, & Maestripieri, 2003; Roney, Lukaszewski, & Simmons, 2007), suggesting a role of testosterone in regulating emotional encounters.

Two key, recently published studies provide further evidence for testosterone-mediated emotional activation that impairs rational decision-making. Winning fights has been shown to selectively enhance sensitivity to the androgen receptor, specifically in the nucleus accumbens and the ventral tegmental area (Fuxjager et al, 2010). Moreover, the authors report finding significant associations between androgen receptor sensitivity and the ability to win subsequent fights. These data suggest that testosterone directly enhances the ability to succeed in aggressive encounters by inducing changes in the dopamine mediated reward circuitry (Fuxjager et al, 2010). In another study, Hermans et al (2010) report finding enhanced activation of the ventral striatum, an area consistently

implicated in reward anticipation (Christopoulos et al, 2009), following testosterone administration in financial risk task (Hermans et al, 2010). Both studies suggest that a possible interaction between dopamine pathways and testosterone may exist, which would further implicate testosterone's role in reward acquisition, and consequently, risk-taking behavior.

Concurrently, testosterone may also mediate cognitive appraisal of risk behavior, thus decreasing the level of risk aversion in an individual. Such a hypothesis has yet to find support, as limited research has been done to investigate testosterone's direct impact on cognition.

Evidence associating testosterone and risk-taking behavior has so far been correlational and a further investigation of the causal nature of the relationship is necessary for practical applications and interpretation of results. Therefore, a clearer understanding of testosterone's influence on risk-taking behavior is necessary to allow for the appropriate interpretation of results and conclusions.

#### *Gap in Knowledge*

The correlation between circulating levels of testosterone and risk-taking behavior in a financial paradigm could indicate that:

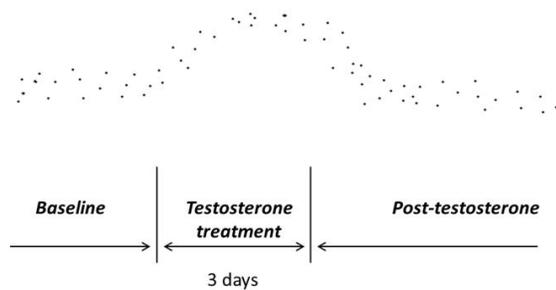
- 1) Risk-Taking behavior enhances the biological mechanisms responsible for testosterone release in the testes, thus causing more testosterone to circulate in the blood. Such an effect could be of evolutionary importance whereby testosterone levels are increased to prepare the individual for competitive behavior as evidenced by the winner effect (Coates, Gurnell, & Sarnyai, 2010).
- 2) Another possible explanation for the correlation between testosterone and risk-taking behavior is that testosterone may in fact cause the increase in risk-taking behavior. From this perspective, testosterone modulates the level of risk-taking behavior.

To determine the causal nature of this relationship, I conducted an experiment using a rat model. Knowledge about the causal nature of the relationship between testosterone and risk-taking behavior will allow future studies to infer accurate conclusions from the association. Knowing the causal nature of the correlation will also allow for better interpretation of results into other domains of behavior. By knowing the significance of testosterone in modulating risk-taking behavior, we also gain more insight into the underlying biological correlates of decision-making in general.

#### *Current Study*

The goal of my experiment was to investigate the causal relationship between risk-taking behavior and testosterone content. I used a rodent model to assess risk-taking behavior in a risky decision-making choice task using a two-choice discrimination box. The aims of the study were to:

1. Establish a baseline performance level for all test animals in a two-choice discrimination box before, during, and after testosterone treatment.
2. Assess the performance of each individual test animal before, during, and after testosterone treatment.
3. Determine whether any significant change in risk-taking behavior would result from hormone treatment.



**Figure 3: Hypothesis**

I hypothesize that artificially raising circulating testosterone levels will result in an increase in risk-taking behavior. Moreover, I expect short-lived effects evidenced by a decrease in risk-taking behavior post-testosterone treatment.

#### *Hypothesis*

In the current study, I sought to investigate the hypothesis that *increasing levels of testosterone increases risk-taking behavior*.

#### **Methods**

##### *Subjects*

Male Sprague Dawley rats ( $n=3$ ; Charles River Laboratories; weighing 350-420g during the study period) were individually housed in a 12 hour light/dark cycle with free access to water and food, except during the testing period. During the testing period, rats were maintained at 80% of their free-feeding weight. All procedures were approved by the Lake Forest College Institutional College Animal Care and Use Committee (IACUC).

##### *Apparatus*

Testing was conducted in a two-choice discrimination box of our own design (Figure 4). The box consists of a long placement chamber in which rats are placed in the beginning of each trial. At the opposite end of the placement chamber are two identical swing doors to the left and right, each leading to a food delivery chamber. Food rewards were placed in Petri dishes located at the end of each delivery chamber. Each swing door is hinged so as to prevent any exit opportunity once the test animal has made a choice about which door to enter. Partitioning the delivery chambers is a wire mesh to evenly distribute food smell across both chambers so as to limit any potential behavioral bias due to the smell of food.

#### **Behavioral Procedures**

##### *Shaping*

Shaping began by widely opening either one of the two doors (keeping the other closed) while training each test animal to enter the open delivery chamber for a food reward (Cheerio). Upon completing 60 consecutive trials, each trial lasting no longer than 30 seconds, the order of the doors was reversed and training began as described above. After completing the first portion of the training, both doors were gradually closed until each door was completely shut while still maintaining food delivery training.

Thereafter, each test animal was trained to enter either through the right side door or left side door (counterbalanced across the group) to obtain the “better” large food reward (LFR) for a period of 60 consecutive trials (other door blocked). For the following 60 trials, the door leading to the LFR was blocked and each test animal trained

to enter the opposite door for a small food reward (food pellets chopped into sizably small pieces). This procedure was conducted at the start of the experiment and was not repeated at any other time.

##### *Baseline Risk Analysis Task*

During the shaping procedure, the location (left or right) of each food reward was kept constant for each test animal. Therefore if test animal A was conditioned to enter the right side door for the LFR and left side door for the SFR, this position was kept constant for the entire duration of the experimental procedure.

Test sessions in this phase of the study were carried out in 4 blocks, each block consisting of a 120 trials at a specified probability of obtaining the LFR. For each trial, the rat was placed in the placement chamber and allowed to make a choice between one of the two doors to obtain a food reward. In each block, the probability of the LFR being present was systematically decreased from 100-50-25-15 % respectively. Therefore, block 1, consisting 120 trials, was carried out at 100% probability of obtaining the LFR. In subsequent blocks, the probability of obtaining the LFR systematically decreased from the initial 100 to 50-25-15% in that sequence. The number of entries each test animal made into the LFR delivery chamber versus the SFR delivery chamber was noted for every block.

##### *Testosterone Risk Analysis Task*

During this phase of the experiment, all rats were treated with 1% testosterone in 1, 2-dimethoxyethane solution via subcutaneous injection into the lower back region. Testing in the two-choice discrimination box resumed at 15% probability, as this was the probability with considerable variance during the baseline risk analysis phase. Parameters in this phase were identical to the baseline risk analysis phase, except that the probability was maintained at 15%. The number of entries into the LFR door and the SFR door were recorded.

##### *Post-Testosterone Risk Analysis*

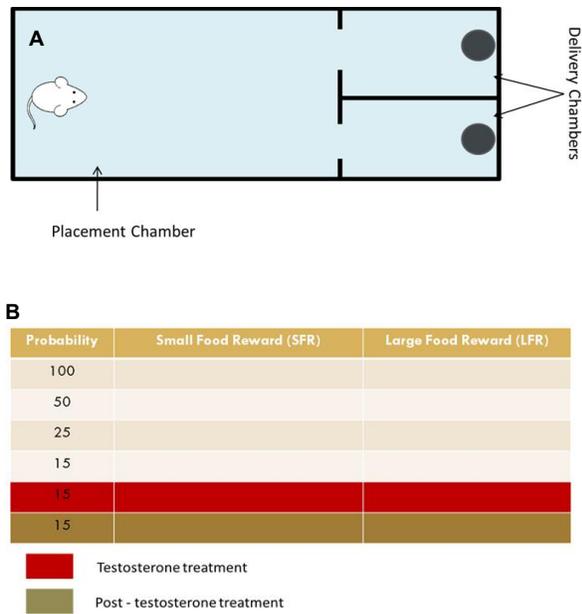
Seven days after being treated with testosterone, each test animal was again assessed for risk-taking behavior in the same two-choice discrimination box using the same procedure described above (*Baseline Risk Analysis Task*). However, just as in the *Testosterone Risk Analysis Task* phase, test animals were run at 15% of obtaining the LFR.

##### *Testosterone Administration*

Testosterone solution was obtained as 1% testosterone in 1, 2-dimethoxyethane in 1.0 mL vials obtained from Sigma Aldrich. Testosterone injections were administered every morning at 11:00 am. Each rat was administered 0.4 mL of testosterone via a subcutaneous injection into the lower back region for three consecutive days before testing resumed. Testosterone is a hazardous substance. Care in handling and disposal of vials was exercised at all times.

##### *Data Analysis*

All statistical analysis was run on PASW Statistics 18. Data were coded to note the number of entries each test animal made into the LFR delivery chamber and SFR delivery chambers per 120 trials in each experimental condition. The influence of testosterone and risky decision-making was assessed using a paired t-test analysis, which compared the means of LFR choices made during the pre-testosterone, during testosterone, and post-testosterone phases when the probability was set at 15%. In all cases,  $p$  significance was considered at a  $p$  value of  $< 0.05$ .



**Figure 4: Risk-Taking Assessment and Apparatus:**

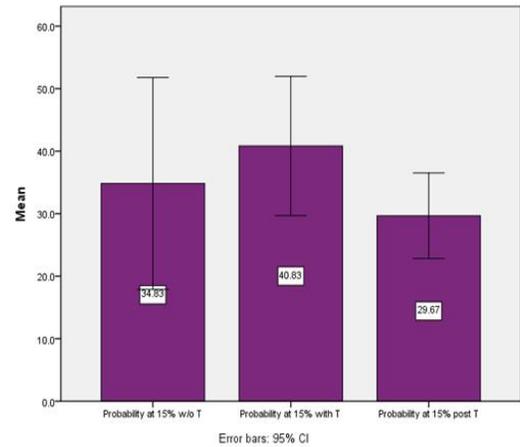
A) Illustrates the two-choice discrimination apparatus used to measure risk-taking behavior in test animals. For each trial, the test animal was placed in the placement chamber and allowed to approach the delivery chambers where it would pick either of the two doors for a SFR or a LFR. Swing doors (not shown) ensure that the presence of each food reward is obscured and does not allow exiting after a rat had picked a chamber. B) We count the number of entries into the SFR entrance and the LFR entrance as we decreased the probability for each test animal receiving the LFR.

**Results**

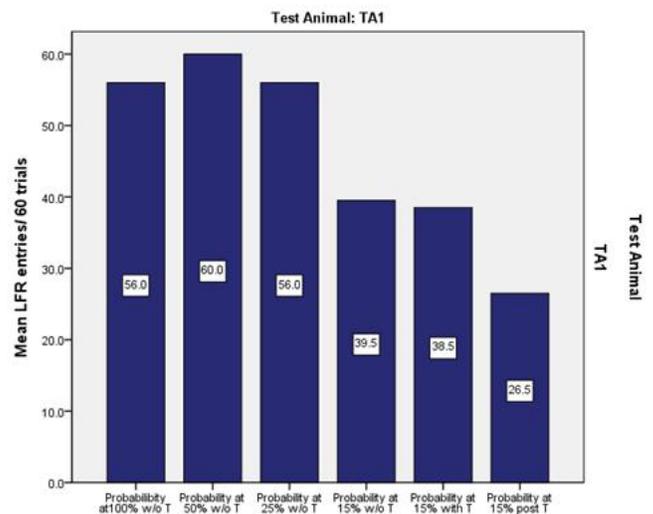
We predicted that the number of entries into the LFR chamber during the testosterone treatment phase (M= 40.83, SD= 4.48) would be higher than the number of entries during the pre-testosterone phase (M= 34.83, SD= 6.825) and the post-testosterone phase (M= 29.67, SD= 2.75) across all three-test animals. To test whether the apparent increase in LFR entries during the testosterone phase was significant, we ran a student's t-test to compare the mean number of entries during each phase. We found that the number of entries into the LFR chamber during testosterone treatment were not statistically different from those made during the pre-testosterone trials ( $p = .238$ ) (see Figure 5A). Another t-test comparing the mean LFR entries for testosterone and post-testosterone phases revealed a significant decrease in risk-taking behavior post-testosterone treatment ( $p = .046$ ).

I then assessed the data for each individual test animal to determine whether any significant changes in risk-taking behavior would be apparent. Because the statistical analysis required for comparing single subject data for a *Reversal Time-Series Design* is beyond the scope of my knowledge, and that of experts I consulted during the course of this investigation, I resorted to graphically illustrating the performance of each test animal using a bar graph (see Figure 5b-d). Observation of the graphs indicates that test animal two (TA2) and three (TA3) showed a slight increase in risk-taking behavior, whereas test animal one (TA1) showed no difference in risky behavior before and during testosterone phases.

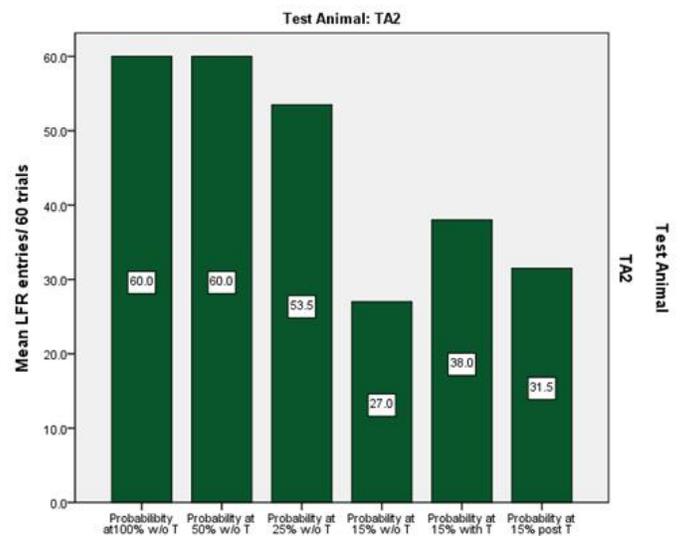
**A**



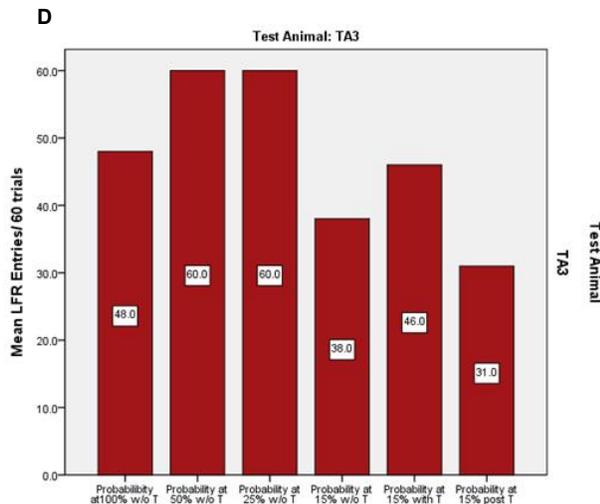
**B**



**C**



**Figure 5: Overall and Individual Performance Graphs**



a) Mean risky choices (LFR choices) made before, during, and after testosterone treatment. b-d) Individual illustration of LFR choices for each test-animal from for entire duration of the study.

## Discussion

Recent findings in neuroeconomics highlight the importance of hormonal action on decision-making behavior. To the best of our knowledge, the evidence supporting the relationship between steroid hormones and risk decision-making has, thus far, been correlational. It is necessary, therefore, to elucidate the cause and effect nature of the relationship between steroids and risky decision-making. Understanding the relevant biological substrates of risk-taking behavior is essential for a theoretical understanding of how we process information in order to make decisions. The implications of such findings are potentially beneficial to research on decision-making, especially in financial markets where decisions are constantly made under high levels of ambiguity.

In the current study, I used a rat model to investigate the causal nature of the relationship between testosterone and risk-taking behavior. The aim of the study was to determine whether increasing levels of testosterone can result in an increase in risky decision making. I tested the hypothesis that exogenous treatment with testosterone would increase risk-taking behavior.

We found a 10% increase in overall risky decision choices after three days of successive treatment with testosterone across all test subjects. Statistically, the observed increase in risk behavior was not significant. A case by case analysis revealed significant increments in risk-taking behavior in two out of the three rats used for this experiment. The results of this study suggest a role of testosterone's activating effects on risky decision-making.

### Overall Non-Significant Increase in Risk-Taking Behavior

The finding that overall risky decision making increased (but not significantly) by 10% suggests that testosterone does have some level of influence on risk-taking behavior. We attribute this ambiguity to the major limitations of the study. Exogenous treatment with testosterone requires that baseline levels of circulating testosterone be established in order to determine the appropriate amounts of hormone to administer. Limited resources restricted our ability to assay for circulating levels of plasma testosterone in order to establish an appropriate, biologically relevant, concentration of testosterone to administer to each test animal. We relied heavily on previous literature estimates of testosterone circulation content in a variety of rodent species (Lee et al, 1975; Cefalu et al, 1986; Bartke et al, 1973). A complication

with this method is that testosterone estimates have been assessed in a variety of rat species, which do not directly translate to our specific Sprague Dawley strain.

To overcome this limitation, we used estimated supra levels of testosterone (0.4ml of 1% testosterone in 1, 2-dimethoxyethane) to be administered to each test animal. Approximated high concentrations were extrapolated from previous research using rats of comparable gender, age, and weight (Rezek & Whalen, 1978; Shemisa et al, 2006; Aloisi et al, 2004). The improvised nature of the study limits our confidence in the validity of our estimated supra concentrations of testosterone. Two possible outcomes arise from this procedure:

- 1) Exogenous testosterone administration indeed increased the level of circulating testosterone to the desired supra level. In this scenario, the biological relevance to every day risk-taking behavior is diminished as normal fluctuations in testosterone content rarely exceed extremely high concentration thresholds. Moreover, there is evidence to suggest that exceedingly high (and exceedingly low) concentrations of testosterone result in risk ambiguity (Stanton et al, 2011). In a task assessing economic preferences, Stanton et al (2011) report finding a U-shaped association between testosterone and risk preferences. Individuals with significantly lower or higher levels of testosterone were found to be risk-neutral whereas individuals with modest levels of testosterone were highly risk-averse. Although the same study does not support the role of testosterone in economic risk preferences, it does provide evidence of a differential effect of testosterone depending on the level of circulation.
- 2) Another possible outcome is that the 'estimated' concentration of administered testosterone produced differential effects in each test subject based on pre-existing levels of circulating testosterone. High variations in pre-existing testosterone levels amongst all three subjects raises the possibility that those rats with already high baseline levels of testosterone were not affected by the administered testosterone. Likewise, those subjects with modest or low baseline levels were significantly affected by the exogenous testosterone. This view is supported by the high variation seen in the collected data. It is possible that TA1 was not affected by testosterone administration because of an already high baseline concentration. The significant differences in risk preference by TA2 and 3 could likely be a result of modest-low baseline concentrations which were affected by exogenous testosterone administration.

Both of the above outcomes are highly plausible in light of the inadequate resources necessary to make a complete assessment of the results. Therefore, as a prospective future study, we propose conducting a detailed assay of circulating testosterone concentration before and after testosterone treatment to validate the parameters of the study.

### Significance of the Data

Based on the overall and individual data, we speculate that the slight increase in risk preference during testosterone treatment was in fact due to the testosterone treatment. This view is supported by the observation that post-testosterone performance was significantly lower for all three test subjects. A qualitative analysis of the data is important and relevant to realistic observations in a financial context. A major difference between the two-choice discrimination box

assessment of risk and a similar assessment in financial risk/reward behavior in humans rests on the measure of risk. In humans, risk behavior is assessed via the magnitude of the risk/reward outcome. In the current study, the quality of the LFR (Cheerio) was constant. Here, risk was assessed by the number of times each subject made risky choices rather than the magnitude of the loss or gain in food.

To further illustrate this point, I will briefly compare the method used in this study and that used by Coates and Herbert (2007). As described previously, the financial performance of seventeen financial traders in a London trading floor was followed for a period of eight consecutive days while maintaining daily measures of morning and afternoon salivary testosterone. As reported, the results of the study found that on days when financial traders had higher than average levels of testosterone, they were more likely to make significantly higher profits of losses. The conclusions of this study are based on the *magnitude or size* of profits and losses rather than the *number of times* the traders made profits and losses.

Although subtle, this difference in assessment makes a considerable difference in the way in which we can interpret the data from this experiment. This point also illustrates a potential improvement for the two-choice discrimination box whereby the magnitude (size) of the better food reward can be manipulated to better conform to human forms of risky decision assessment.

#### *Mechanism of Action*

As suggested earlier, emotion plays a significant role in modulating decision-making. Evidence for emotional influence on irrational decision making are supported by brain imaging studies, which have shown consistent activation in emotion associated areas of the brain such as the amygdala and insula (Krueger, Grafman, & McCabe, 2008). Anger is the emotion most associated with the hormone testosterone (Simpson, 2001). Thus, it is plausible to envision a mechanism of modulation whereby testosterone increases anger emotions, which in turn would decrease rational decision-making. This hypothetical model of risk behavior is appealing because it supports an

#### References

- Alexander GM, Packard MG, & Hines M. (1994). Testosterone has rewarding affective properties in male rats: implications for the biological basis of sexual motivation. *Behavioral Neuroscience*. 108(2), 424-8.
- Aloisi AM, Ceccarelli I, Fiorenzani P, De Padova AM, & Massafra C. (2004). Testosterone affects formalin-induced responses differently in male and female rats. *Neuroscience Letters*. 361(1-3), 262-4.
- Aluja A, & Garcia LF. (2005). Sensation seeking, sexual curiosity and testosterone in inmates. *Neuropsychobiology*. 51(1), 28-33.
- Anderson K, Bones B, Robinson B, Hass C, Lee H, Ford K, Roberts TA, & Jacobs B. (2009). The morphology of supragranular pyramidal neurons in the human insular cortex: a quantitative Golgi study. *Cerebral Cortex* (New York, N.Y. : 1991). 19(9), 2131-44.
- Apicella C. L., Dreber A., Campbell B. Gray P., Hoffman M., Little A.C. (2008). Testosterone and financial risk preferences. *Evolution and Human Behavior* 29:384-390.

evolutionary role of testosterone in priming an individual for risk when faced with a potentially ambiguous threat or opportunities for mating (Lopez, Hay, & Conklin, 2009; Roney, Lukaszewski, & Simmons, 2007).

Priming effects of transient testosterone increments are likely to induce irrational decision making at the unconscious level of thought processing. Emotions are largely affected by the external agents and perceived loci of control. The finding by Sanfey et al (2003) reporting exceedingly high emotional activation (and increased risk taking) when participants interacted with a human player (vs. computer program) suggests that emotional influence on risk behavior is limited by the context of the behavior. Further evidence to support this is provided by (Saad & Gill, 2001), who found that men were more likely to make unfair offers towards other men than to women. Therefore, the role of emotion our two-choice discrimination box may be downplayed by the inanimate nature of the experimental set-up and the perceived lack of control over the situation.

#### Conclusion

In conclusion, the present study demonstrates potential transient (activating) effects of testosterone administration on risk-taking behavior. However, the lack of sufficient knowledge about the pre-existing levels of testosterone limits the extent to which the present data can be interpreted. We suggest a more refined replication of the study, whereby testosterone is assayed throughout the duration of the study.

*Note: Eukaryon is published by students at Lake Forest College, who are solely responsible for its content. The views expressed in Eukaryon do not necessarily reflect those of the College. Articles published within Eukaryon should not be cited in bibliographies. Material contained herein should be treated as personal communication and should be cited as such only with the consent of the author.*

- Archer J. (2006). Testosterone and human aggression: an evaluation of the challenge hypothesis. *Neuroscience and Biobehavioral Reviews*. 30(3), 319-45.
- Arregger AL, Contreras LN, Tumilasci OR, Aquilano DR, & Cardoso EM. (2007). Salivary testosterone: a reliable approach to the diagnosis of male hypogonadism. *Clinical Endocrinology*. 67(5), 656-62.
- Auyeung B, Baron-Cohen S, Ashwin E, Knickmeyer R, Taylor K, Hackett G, & Hines M. (2009). Fetal testosterone predicts sexually differentiated childhood behavior in girls and in boys. *Psychological Science : a Journal of the American Psychological Society / APS*. 20(2), 144-8.
- Baron D, Montfort J, Houlgatte R, Fostier A, & Guiguen Y. (2007). Androgen-induced masculinization in rainbow trout results in a marked dysregulation of early gonadal gene expression profiles. *BMC Genomics*. 8, 357.
- Bartke A, Steele RE, Musto N, & Caldwell BV. (1973). Fluctuations in plasma testosterone levels in adult male rats and mice. *Endocrinology*. 92(4), 1223-8.

- Bear M.F., Connors B.W., Paradiso M. A. (2001). *Neuroscience: Exploring the Brain*, (2nd Ed). Pennsylvania: Lippincott Williams & Wilkins.
- Becker, J.B., Breedlove, S.M., Crews, D., & McCarthy, M.M. (2002). *Behavioral Endocrinology* (2nd Ed.). Cambridge, MA: MIT Press.
- Blanco C, Ibanez A, Blanco-Jerez CR, Baca-Garcia E, & Saiz-Ruiz J. (2001). Plasma testosterone and pathological gambling. *Psychiatry Research*. 105(1-2), 117-21.
- Booth A, Johnson DR, & Granger DA. (1999). Testosterone and men's health. *Journal of Behavioral Medicine*. 22(1), 1-19.
- Bos PA, Terburg D, & van Honk J. (2010). Testosterone decreases trust in socially naive humans. *Proceedings of the National Academy of Sciences of the United States of America*. 107(22), 9991-5.
- Breedlove M.S., Watson N.V., Rosenzweig M.R. (2010). *Biological Psychology: An Introduction to Behavioral, Cognitive, and Clinical Neuroscience* (6th Ed). Massachusetts: Sinauer Associates.
- Burn, C. C. (2008). What is it like to be a rat? Rat sensory perception and its implications for experimental design and rat welfare. *Applied Animal Behaviour Science*, 112, 1-32.
- Burnham TC. (2007). High-testosterone men reject low ultimatum game offers. *Proceedings. Biological Sciences / The Royal Society*. 274(1623), 2327-30.
- Byrnes, J. P., & Miller, D. C. (1999). Gender differences in risk taking: A meta-analysis. *Psychological Bulletin*, 125(3), 367.
- Campbell BC, Dreber A, Apicella CL, Eisenberg DT, Gray PB, Little AC, Garcia JR, Zamore RS, & Lum JK. (2010). Testosterone exposure, dopaminergic reward, and sensation-seeking in young men. *Physiology & Behavior*. 99(4), 451-6.
- Carney D, Mason M. Decision making and testosterone: When the ends justify the means. *Journal of Experimental Social Psychology* [serial online]. July 2010;46(4):668-671. Available from: Academic Search Premier, Ipswich, MA. Accessed April 11, 2011.
- Carney, D. R., & Mason, M. F. (2010). Decision making and testosterone: When the ends justify the means. *Journal of Experimental Social Psychology*, 46(4), 668-671. doi:10.1016/j.jesp.2010.02.003
- Cefalu WT, Pardridge WM, Chaudhuri G, & Judd HL. (1986). Serum bioavailability and tissue metabolism of testosterone and estradiol in rat salivary gland. *The Journal of Clinical Endocrinology and Metabolism*. 63(1), 20-8.
- Chen JR, Yan YT, Wang TJ, Chen LJ, Wang YJ, & Tseng GF. (2009). Gonadal hormones modulate the dendritic spine densities of primary cortical pyramidal neurons in adult female rat. *Cerebral Cortex* (New York, N.Y. : 1991). 19(11), 2719-27.
- Choleris E, Clipperton-Allen AE, Phan A, & Kavaliers M. (2009). Neuroendocrinology of social information processing in rats and mice. *Frontiers in Neuroendocrinology*. 30(4), 442-59.
- Christopoulos GI, Tobler PN, Bossaerts P, Dolan RJ, & Schultz W. (2009). Neural correlates of value, risk, and risk aversion contributing to decision making under risk. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 29(40), 12574-83.
- Coates JM, & Herbert J. (2008). Endogenous steroids and financial risk taking on a London trading floor. *Proceedings of the National Academy of Sciences of the United States of America*. 105(16), 6167-72.
- Coates JM, & Page L. (2009). A note on trader Sharpe Ratios. *PLoS One*. 4(11), e8036.
- Coates JM, Gurnell M, & Rustichini A. (2009). Second-to-fourth digit ratio predicts success among high-frequency financial traders. *Proceedings of the National Academy of Sciences of the United States of America*. 106(2), 623-8.
- Coates JM, Gurnell M, & Sarnyai Z. (2010). From molecule to market: steroid hormones and financial risk-taking. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 365(1538), 331-43.
- Crawley J., Gerfen C., McKay M., Sibley D., Skolnick P. (1999). *Current Protocols in Neuroscience*. vol.1, Supplement 8.
- Dabbs JM Jr, & Hargrove MF. (1997). Age, testosterone, and behavior among female prison inmates. *Psychosomatic Medicine*. 59(5), 477-80.
- Eagly, A. H. (1995). The science and politics of comparing women and men. *American Psychologist*, 50(3), 145.
- Eisenegger C, Naef M, Snozzi R, Heinrichs M, & Fehr E. (2010). Prejudice and truth about the effect of testosterone on human bargaining behaviour. *Nature*. 463(7279), 356-9.
- Fuxjager MJ, Forbes-Lorman RM, Coss DJ, Auger CJ, Auger AP, & Marler CA. (2010). Winning territorial disputes selectively enhances androgen sensitivity in neural pathways related to motivation and social aggression. *Proceedings of the National Academy of Sciences of the United States of America*. 107(27), 12393-8.
- Garcia-Falgueras A, & Swaab DF. (2008). A sex difference in the hypothalamic uncinate nucleus: relationship to gender identity. *Brain : a Journal of Neurology*. 131(Pt), 3132-46.
- Garling T., Kirchler E., Lewis A., Van Raaij F. (2009). Psychology, Financial Decision Making and Financial Crises. *Psychological Science in the Public Interest*, 10(1) 1-47.
- Glickman SE, Coscia EM, Frank LG, Licht P, Weldele ML, & Drea CM. (1998). Androgens and masculinization of genitalia in the spotted hyaena (*Crocuta crocuta*). 3. Effects of juvenile gonadectomy. *Journal of Reproduction and Fertility*. 113(1), 129-35.
- Goldstein JM, Seidman LJ, Horton NJ, Makris N, Kennedy DN, Caviness VS Jr, Faraone SV, & Tsuang MT. (2001). Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. *Cerebral Cortex* (New York, N.Y. : 1991). 11(6), 490-7.
- Granger DA, Schwartz EB, Booth A, & Arentz M. (1999). Salivary testosterone determination in studies of child health and development. *Hormones and Behavior*. 35(1), 18-27.

Hermans EJ, Bos PA, Ossewaarde L, Ramsey NF, Fernandez G, & van Honk J. (2010). Effects of exogenous testosterone on the ventral striatal BOLD response during reward anticipation in healthy women. *NeuroImage*. 52(1), 277-83.

Jentsch JD, Woods JA, Groman SM, & Seu E. (2010). Behavioral characteristics and neural mechanisms mediating performance in a rodent version of the Balloon Analog Risk Task. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*. 35(8), 1797-806.

Kempenaers B, Peters A, & Foerster K. (2008). Sources of individual variation in plasma testosterone levels. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 363(1497), 1711-23.

Knight, F. H. (1921). *Risk, Uncertainty, and Profit*. *Library of Economics and Liberty*. Retrieved April 11, 2011 from the World Wide Web: <http://www.econlib.org/library/Knight/knRUP.html>.

Koenigs M, & Tranel D. (2007). Irrational economic decision-making after ventromedial prefrontal damage: evidence from the Ultimatum Game. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 27(4), 951-6.

Korenchevsky V., Dennison M., and Hall K. (1937). The effects of testosterone and testosterone propionate on adult male rats (compared with those on female rats). *Biochemistry Journal*, 31(8), 1434-7.

Krueger F, Grafman J, & McCabe K. (2008). Neural correlates of economic game playing. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 363(1511), 3859-74.

Kuhnen CM, & Knutson B. (2005). The neural basis of financial risk taking. *Neuron*. 47(5), 763-70.

Laviola G, Macri S, Morley-Fletcher S, & Adriani W. (2003). Risk-taking behavior in adolescent mice: psychobiological determinants and early epigenetic influence. *Neuroscience and Biobehavioral Reviews*. 27(1-2), 19-31.

Lee VW, de Kretser DM, Hudson B, & Wang C. (1975). Variations in serum FSH, LH and testosterone levels in male rats from birth to sexual maturity. *Journal of Reproduction and Fertility*. 42(1), 121-6.

Leland, D. S. & Paulus, M. P. (2005). Increased risk-taking decision-making but not altered response to punishment in stimulant-using young adults. *Drug Alcohol Dependence*. 78, 83-90.

Leranth C, Prange-Kiel J, Frick KM, & Horvath TL. (2004). Low CA1 spine synapse density is further reduced by castration in male non-human primates. *Cerebral Cortex* (New York, N.Y. : 1991). 14(5), 503-10.

Leranth, C., Petnehazy, O., & MacLusky, N. J. (2003). Gonadal Hormones Affect Spine Synaptic Density in the CA1 Hippocampal Subfield of Male Rats. *Journal of Neuroscience*, 23(5), 1588.

Lewis JG. (2006). Steroid analysis in saliva: an overview. *The Clinical Biochemist. Reviews / Australian Association of Clinical Biochemists*. 27(3), 139-46.

Lin G.C., Erinhoff L. (1990). Anabolic Steroid Abuse. *Research Monograph*, 102.

Logan F.A. (1965). Decision Making by Rats: Delay Versus Amount of Reward. *Journal of Comparative and Physiological Psychology*. 59, 1-12.

Lopez H. H., Hay A. C., & Conklin P. H. (2009). Attractive men induce testosterone and cortisol release in women. *Hormones and Behavior*. 56(1), 84-92.

Lutchmaya S, Baron-Cohen S, Raggatt P, Knickmeyer R, & Manning JT. (2004). 2nd to 4th digit ratios, fetal testosterone and estradiol. *Early Human Development*. 77(1-2), 23-8.

Manning JT, Scutt D, Wilson J, & Lewis-Jones DI. (1998). The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. *Human Reproduction* (Oxford, England). 13(11), 3000-4.

Miller DC, & Byrnes JP. (1997). The role of contextual and personal factors in children's risk taking. *Developmental Psychology*. 33(5), 814-23.

Miller DC, & Byrnes JP. (1997). The role of contextual and personal factors in children's risk taking. *Developmental Psychology*. 33(5), 814-23.

Mohr PN, Biele G, & Heekeren HR. (2010). Neural processing of risk. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 30(19), 6613-9.

Murphy DD, & Segal M. (1996). Regulation of dendritic spine density in cultured rat hippocampal neurons by steroid hormones. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 16(13), 4059-68.

Newman, M. L., Sellers, J., & Josephs, R. A. (2005). Testosterone, cognition, and social status. *Hormones & Behavior*, 47(2), 205-211. doi:10.1016/j.yhbeh.2004.09.008.

Oyegbile TO, & Marler CA. (2005). Winning fights elevates testosterone levels in California mice and enhances future ability to win fights. *Hormones and Behavior*. 48(3), 259-67.

Packard MG, Cornell AH, & Alexander GM. (1997). Rewarding affective properties of intra-nucleus accumbens injections of testosterone. *Behavioral Neuroscience*. 111(1), 219-24.

Perrin JS, Herve PY, Leonard G, Perron M, Pike GB, Pitiot A, Richer L, Veillette S, Pausova Z, & Paus T. (2008). Growth of white matter in the adolescent brain: role of testosterone and androgen receptor. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 28(38), 9519-24.

Powell, M., Ansic D.(1998). Gender Differences in Risk Behavior in Financial Decision-Making: An Experimental Analysis. Working Paper, University of Leeds, United Kingdom.

Purifoy FE, & Koopmans LH. (1979). Androstenedione, testosterone, and free testosterone concentration in women of various occupations. *Social Biology*. 26(3), 179-88.

- Purves D., Augustine G.J., Fitzpatrick D., Katz L., LaMantia A., McNamara J., and Williams M.S. (2001). *Neuroscience*. (2nd Ed). Massachusetts: Sinauer Associates.
- Rangel, A., Camerer, C., Montague, P.R. (2008). A framework for studying the neurobiology of value-based decision making. *Nature Reviews Neuroscience* 9, 545–556.
- Raznahan A, Lee Y, Stidd R, Long R, Greenstein D, Clasen L, Addington A, Gogtay N, Rapoport JL, & Giedd JN. (2010). Longitudinally mapping the influence of sex and androgen signaling on the dynamics of human cortical maturation in adolescence. *Proceedings of the National Academy of Sciences of the United States of America*. 107(39), 16988-93.
- Rezek DL, & Whalen RE. (1978). Testosterone metabolism in male rat brain during maturation. *Biology of Reproduction*. 18(5), 886-91.
- Roberti, J. W. (2004). A review of behavioral and biological correlates of sensation seeking. *Journal of Research in Personality*, 38(3), 256. doi:10.1016/S0092-6566(03)00067-9.
- Roney JR, Lukaszewski AW, & Simmons ZL. (2007). Rapid endocrine responses of young men to social interactions with young women. *Hormones and Behavior*. 52(3), 326-33.
- Rosenblitt JC, Soler H, Johnson SE, & Quadagno DM. (2001). Sensation seeking and hormones in men and women: exploring the link. *Hormones and Behavior*. 40(3), 396-402.
- Rosenbloom T. (2003). Risk Evaluation and Risky Behavior of high and low Sensation Seekers. *Social Behavior and Personality*, 31(4), 375-386.
- Saad, G., & Gill, T. (2001). Sex differences in the ultimatum game: An evolutionary psychology perspective. *Journal of Bioeconomics*, 3, 171–193.
- Sanfey AG, Rilling JK, Aronson JA, Nystrom LE, & Cohen JD. (2003). The neural basis of economic decision-making in the Ultimatum Game. *Science* (New York, N.Y.). 300(5626), 1755-8.
- Sapienza, P., Zingales, L., & Maestripiet, D. (2009). Gender differences in financial risk aversion and career choices are affected by testosterone. *Proceedings of the National Academy of Sciences of the United States of America*, 106(36), 15268-15273. doi:10.1073/pnas.0907352106.
- Sarkar SN, Huang RQ, Logan SM, Yi KD, Dillon GH, & Simpkins JW. (2008). Estrogens directly potentiate neuronal L-type Ca<sup>2+</sup> channels. *Proceedings of the National Academy of Sciences of the United States of America*. 105(39), 15148-53.
- Schultz W. (2008). Introduction. Neuroeconomics: the promise and the profit. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 363(1511), 3767-9.
- Schwerdtfeger A, Heims R, & Heer J. (2010). Digit ratio (2D:4D) is associated with traffic violations for male frequent car drivers. *Accident; Analysis and Prevention*. 42(1), 269-74.
- Shemisa K, Kunnathur V, Liu B, Salvaterra TJ, & Dluzen DE. (2006). Testosterone modulation of striatal dopamine output in orchidectomized mice. *Synapse* (New York, N.Y.). 60(5), 347-53.
- Simon NW, Gilbert RJ, Mayse JD, Bizon JL, & Setlow B. (2009). Balancing risk and reward: a rat model of risky decision making. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*. 34(10), 2208-17.
- Simpson, K. (2001). The role of testosterone in aggression. *McGill Journal of Medicine*, 32–40.
- Slovic P, Finucane ML, Peters E, & MacGregor DG. (2004). Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality. *Risk Analysis : an Official Publication of the Society for Risk Analysis*. 24(2), 311-22.
- Slovic P. (1964). Assessment of Risk Taking Behavior. *Psychological Bulletin*. 61, 220-33.
- Smejkalova T, & Woolley CS. (2010). Estradiol acutely potentiates hippocampal excitatory synaptic transmission through a presynaptic mechanism. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 30(48), 16137-48.
- Stanton SJ, Mullette-Gillman OA, McLaurin RE, Kuhn CM, Labar KS, Platt ML, Huettel SA. (2011). Low- and High-Testosterone Individuals Exhibit Decreased Aversion to Economic Risk. *Psychological Science* [Epub ahead of time].
- Stanton, S. J., Liening, S. H., & Schultheiss, O. C. (2011). Testosterone is positively associated with risk taking in the Iowa Gambling Task. *Hormones & Behavior*, 59(2), 252-256. doi:10.1016/j.yhbeh.2010.12.003.
- Stanton, Steven J., Jacinta C. Beehner, Ekjyhot K. Saini, Cynthia M. Kuhn, and Kevin S. LaBar. 2009. "Dominance, Politics, and Physiology: Voters' Testosterone Changes on the Night of the 2008 United States Presidential Election." *PLoS One* 4(10):e7543.
- Steffensmeier, D., & Allan, E. (1996). GENDER AND CRIME: Toward a Gendered Theory of Female Offending. *Annual Review of Sociology*, 22(1), 459.
- Stone C.P. (1938). Activation of impotent male rats by injections of testosterone propionate. *Journal of computational Psychology*. 26: 445-150.
- Strenstrom E., Saad G., Nepomuceno M., & Mendenhall Z. (2010). Testosterone and domain-specific risk: Digit ratios (2D:4D and rel2) as predictors of recreational, financial, and social risk-taking behaviors. *Personality and Individual Differences* [Article in Press].
- Turner, C., & McClure, R. (2003). Age and gender differences in risk-taking behaviour as an explanation for high incidence of motor vehicle crashes as a driver in young males. *Injury Control & Safety Promotion*, 10(3), 123.
- Van Honk J, Schutter DJ, Hermans EJ, Putman P, Tuiten A, & Koppeschaar H. (2004). Testosterone shifts the balance between sensitivity for punishment and reward in healthy young women. *Psychoneuroendocrinology*. 29(7), 937-43.
- Van Honk, J., Schutter, D. J., Bos, P. A., Kruijt, A., Lentjes, E. G., & Baron-Cohen, S. (2011). Testosterone

administration impairs cognitive empathy in women depending on second-to-fourth digit ratio. *Proceedings of the National Academy of Sciences of the United States of America*, 108(8), 3448-3452. doi:10.1073/pnas.10118911108.

Van Nas A, Guhathakurta D, Wang SS, Yehya N, Horvath S, Zhang B, Ingram-Drake L, Chaudhuri G, Schadt EE, Drake TA, Arnold AP, & Lusis AJ. (2009). Elucidating the role of gonadal hormones in sexually dimorphic gene coexpression networks. *Endocrinology*. 150(3), 1235-49.

Vermeersch H, T'Sjoen G, Kaufman JM, & Vincke J. (2008). Estradiol, testosterone, differential association and aggressive and non-aggressive risk-taking in adolescent girls. *Psychoneuroendocrinology*. 33(7), 897-908.

Vermeersch H, T'Sjoen G, Kaufman JM, & Vincke J. (2008). The role of testosterone in aggressive and non-aggressive risk-taking in adolescent boys. *Hormones and Behavior*. 53(3), 463-71.

Voracek M., Tran U.S., and Dressler S.G. (2010). Digit ratio (2D:4D) and sensation seeking: New data and meta-analysis, *Personality and Individual Differences* 48,72-77.

Walker WH. (2010). Non-classical actions of testosterone and spermatogenesis. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 365(1546), 1557-69.

Watson KK, & Platt ML. (2008). Neuroethology of reward and decision making. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 363(1511), 3825-35.

Weller JA, Levin IP, Shiv B, & Bechara A. (2007). Neural correlates of adaptive decision making for risky gains and losses. *Psychological Science : a Journal of the American Psychological Society / APS*. 18(11), 958-64.

Wilson M, & Daly M. (2004). Do pretty women inspire men to discount the future? *Proceedings. Biological Sciences / The Royal Society*. 271, S177-9.

Wood RI. (2004). Reinforcing aspects of androgens. *Physiology & Behavior*. 83(2), 279-89.

Woolley CS, & McEwen BS. (1994). Estradiol regulates hippocampal dendritic spine density via an N-methyl-D-aspartate receptor-dependent mechanism. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 14(12), 7680-7.

Woolley CS, Weiland NG, McEwen BS, & Schwartzkroin PA. (1997). Estradiol increases the sensitivity of hippocampal CA1 pyramidal cells to NMDA receptor-mediated synaptic input: correlation with dendritic spine density. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 17(5), 1848-59.

Wu MV, Manoli DS, Fraser EJ, Coats JK, Tollkuhn J, Honda S, Harada N, & Shah NM. (2009). Estrogen masculinizes neural pathways and sex-specific behaviors. *Cell*. 139(1), 61-72.

Xiao E, & Houser D. (2005). Emotion expression in human punishment behavior. *Proceedings of the National Academy of Sciences of the United States of America*. 102(20), 7398-401.

Zak PJ. (2004). Neuroeconomics. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*. 359(1451), 1737-48.

Zethraeus, N., Kocoska-Maras, L., Elligsen, T., von Schoultz, B., Hirschberg, A., & Johannesson, M. (2009). A randomized trial of the effect of estrogen and testosterone on economic behavior. *Proceedings of the National Academy of Sciences of the United States of America*, 106(16), 6535-6538.

Zweig J. (2007). *Your Money & Your Brain: How the New Science of Neuroeconomics Can Help Make You Rich*. NY: Simon & Schuster.