Studies in Neuroscience, Psychology and Behavioral Economics

Martin Reuter
Christian Montag *Editors*

Neuroeconomics

Springer

Chapter 3
Hormones and Economic Decisions

Amos Nadler and Paul J. Zak

Abstract Hormones are chemical messengers released into the body that change the probability of behavior. Because hormones are both measurable and manipulable they lend themselves to experimental methodology that can establish causal relationships. Neuroeconomics studies have shown hormones' influence on decision-making using quantifiable treatment and outcome variables in economic and social contexts. This chapter provides background and methodology for hormonal research in neuroeconomics and reviews significant studies on how oxytocin, testosterone, arginine vasopressin, dopamine, serotonin, and stress hormones impact decisions, and how research can be used to improve decisions and the business of life.

3.1 Introduction

The traditional approach to economic research employs a set of simplifying assumptions on human behavior from which to describe and predict choices. These assumptions provide a rigid framework for analyzing decision-making and facilitate models that generate predictions that can be empirically tested. For the second half of the twentieth century, theoretical modeling of people as 'rational agents' was economics' state-of-the-art methodology. However, as much as simplifying assumptions make questions analytically tractable, they also obviate the richness in behavior from the very element under analysis: human beings (Vercoe and Zak 2010).

A. Nadler
Ivey Business School, Western University, 1255 Western Road, London, ON N6G 0N1, Canada
e-mail: anadler@ivey.ca

P.J. Zak (✉)
Claremont Graduate University, 150 E 10th St, Claremont, CA 91711, USA
e-mail: paul@neuroeconomicstudies.org; paul.zak@cgu.edu

M. Reuter and C. Montag (eds.), *Neuroeconomics*, Studies in Neuroscience, Psychology and Behavioral Economics, DOI 10.1007/978-3-642-35923-1_3

Neoclassical economic models of decision-making involve rational and predictable economic agents who have specific and well-defined utility functions based on ordered, transitive preferences. Yet observation of actual people shows the opposite—rapid, heuristic-driven decisions, and decades of psychological and neuroscientific studies show that memories, cues, primes, and emotions affect decisions (Camerer et al. 2005). Fortunately, economics has continued to evolve by producing richer and more accurate models of human behavior, with more realistic assumptions, greater conformability with empirical data, and deviations from rationality. Models have advanced and new tools have been (cautiously) adopted, such as functional magnetic resonance imaging (fMRI), neurophysiology, genetics, and direct manipulation of hormones. While ignored until recently, hormones have been shown to initiate and mediate changes in the central and peripheral nervous systems and affect economic decisions (Zak 2013; Kandasamy et al. 2014; Camerer et al. 2005).

Economists have traditionally been constrained by the type of data at their disposal and relied on archival (i.e., secondary) data to generate findings. In contrast, the natural sciences produce models largely based on primary data from which causal relationships are identified—data informs the model, not the other way around. Instead of the formation of a multitude of models bearing similar explanatory power, this inductive method offers what Francis Bacon called a "selective process of elimination among a number of alternative possibilities" (1895, III, p. 340). The experimental approach to studying economic behavior produces primary data from which to draw conclusions. In particular, hormonal and physiologic research offers a robust inductive method to study biological influence on economic decision-making and produce neurally informed models of human behavior (Zak 2010). Most importantly, direct manipulation of hormones and physiologic states has begun to identify biological mechanisms motivating specific behaviors.

Over the course of evolution mammals developed two integrated communication systems—one faster, and one slower—to respond to changing environments and regulate homeostasis (i.e., physiologic stability). The nervous system communicates rapidly through neurotransmitters and neuromodulators while the hormonal system uses molecular messengers which cause both temporary and permanent changes in the body . In essence, hormones are chemical messengers that change the probability of a behavior or biological function and are the focus of this chapter.

Hormones have long been known to influence physiologic states, physical development, and genetic transcription in humans and animals yet recent developments show hormones impact cognition, mood, and, most recently, economic decision-making. Neuropeptides, such as oxytocin and arginine vasopressin, and steroid hormones, such as testosterone and estradiol, play a central role in humans in a variety of behavioral and social domains (McCall and Singer 2012). Economics' founding father, Adam Smith, connected emotions and morality to prosperity; Thorstein Veblen stated that economics should be thought of as a field

of biology and that only social science shaped by biology could be considered 'scientific' (Hodgeson 1998). Alfred Marshall, one of the exponents of mathematical rigor within economics, wrote that, "the Mecca of the economist lies in economic biology rather than in economic dynamics" (1890). By putting human beings back at the center of economic analysis, neuroeconomics returns economics to its roots.

3.2 Hormones Defined

Hormones are chemical messengers that circulate in biofluids (e.g., blood) to regulate physiologic activity and maintain homeostasis (the ability to maintain and regulate internal physical equilibrium regardless of external changes) by acting on targets organs. Hormone production is regulated by the brain and mostly produced by organs in the periphery of the body, such as the kidneys, pancreas, and gonads (although some hormones and their precursors are made in the brain itself). Most hormones have receptors in the brain that allow them directly affect neural activity.

For example, in men, testosterone (T) is produced primarily by the Leydig cells in the testes in response to hormonal signaling from the brain (Midzaka et al. 2009). T is synthesized from cholesterol and released into the bloodstream. Further, it crosses the blood-brain barrier in small quantities due to high lipid solubility, modulating neural activity in the brain that changes, for instance, the threshold for aggression (Schwartz and Pohl 1992). T is also made by women, though at 5–10 % the levels in men, and has similar effects (Carré et al. 2010). For those interested in the assessment of hormones and related methodological issues we recommend Chap. 24, "Hormones" by Robert Miller and Clemens Kirschbaum in this book.

3.3 Mechanisms of Action

Once produced and attached to cell receptors, hormones initiate changes in the body at two levels: genomic[1] and non-genomic (also called classical and nonclassical, respectively). Genomic action occurs when a hormone attaches to a target cell receptor and initiates genetic transcription; this occurs on a time scale of hours to years (Falkenstein et al. 2000). For example, testosterone influences transcription of genes by interacting with receptors on the outside of the cell, initiating muscle growth and secondary sexual characteristics in males (Beato 1996). Non-genomic action, on the other hand, occurs by changing characteristics of cells themselves,

[1]Hormones differ in their endogenous release patterns and active half-lives (Santen and Bardin 1973). Genetic factors mediate receptor availability and molecular metabolism, meaning that no two people are precisely the same in the way they respond to the same hormone; this aspect can be measured in some studies (Crabbe et al. 2007).

and acts much more rapidly, on the scale of seconds to minutes (Lösel et al. 2003; McEwen 1991; Falkenstein et al. 2000). Evidence of this has been demonstrated experimentally with T, whereby infusion reduces anxiety in many animals, including humans (van Honk et al. 2005; Frye and Seliga 2001).

Studying hormonal influences on decision-making requires a comprehensive, multi-pronged approach. The 'basal model' proposed by Mazur and Booth (1998), uses endogenous ('within the body'), or basal levels as predictors of behavior, whereby participants' unaltered hormone levels are measured and used as explanatory variables. This model assumes that measurements over time represent short-term fluctuations near characteristic levels. For example, Sapienza et al. (2009) study basal levels among MBA students to predict risk aversion and career choice.

An approach better suited to identifying causation, is the exogenous ('outside the body') manipulation method, whereby participants are given a specific amount of a drug to increase their levels of a hormone (or block the action of a hormone or neurotransmitter on receptors). This methodology tests 'activational' properties of a hormone, provides a clear treatment that can be compared to placebo, and lends itself to rigorous manipulation verification through biofluid assay. For example, Kandasamy et al. (2013) test the influence of cortisol (a stress hormone) on risk preferences by increasing participants' stress hormone levels through hydrocortisone dosing and measuring changes in risk preferences over time.

A related method is through precursor manipulation, which can enhance or impair availability of the specified molecule. For example, a study tested the effects of dopamine (abbreviated 'DA') inhibition by administering participants naltrexone (a DA receptor blocker) in an asset trading experiment to test how impaired DA will affect behavior and market bubbles (Efremidze and Zak, in press). Also, modulation of chemical precursors are also used in experiments, such as tryptophan depletion or enhancement (Crockett and Fehr 2013).

Another approach evaluates changes in levels as predictors of behavior. This can be applied to both endogenous and exogenous contexts, where instead of using basal levels, percent change or absolute change from baseline is used as an explanatory variable. Apicella et al. (2014) test the influence of changes in T on willingness to compete and find a positive relationship.

In addition to explaining behavior, changes in hormones are used to measure physiologic response *to* an event, such as competition, winning, and losing (Booth et al. 1989). Understanding the process fully—the hormonal response to an event and the subsequent change in behavior motivated by a change in hormones—clarifies the hormonal role in dynamic human decision-making.

Findings are generally not as strong for basal levels relative to exogenous methods (Schipper 2015; Apicella et al. 2008; Cueva et al. 2015). Also, matching endogenous range with exogenous amounts can be challenging due to difficulties in measurement of endogenous amounts and clear understanding of receptor sensitivity and regulation under various conditions.

Experimentally manipulating a single hormone can produce changes in behavior, yet behavior is jointly driven by downstream interactions between hormones,

neurotransmitters (chemical messengers in the brain), neural activity, and physiologic tone. Thus, conclusions drawn from pharmacologic manipulations are conditional on basal physiologic states and interactions with other biological factors (Zak 2004, 2005, 2011; Breedlove et al. 2007, p. 123). As a result, a thorough assay of basal physiology is necessary, which can also be assessed using electroencephalograms (EEGs), electrocardiograms (ECGs), and galvanic skin response (GSR). Unfortunately, neurotransmitters are difficult to measure directly without invasive and risky approaches (such as lumbar punctures to harvest spinal fluid) and are therefore typically indirectly assessed in human studies through, for example, urine collection to measure breakdown products.

A convergent approach is necessary to fully understand how hormones affect human decision-making. The first step is to assess basal physiologic state. Step two measures endogenous hormonal response to stimuli. The final step establishes causation by exogenously administering or inhibiting a hormone and measuring changes in behavior. This comprehensive approach is necessary because all physiologic systems are noisy and this approach helps avoid false-positive results. In this way, endogenous effects are demonstrated as well as causal relationships established. This method is summarized in Fig. 3.1.

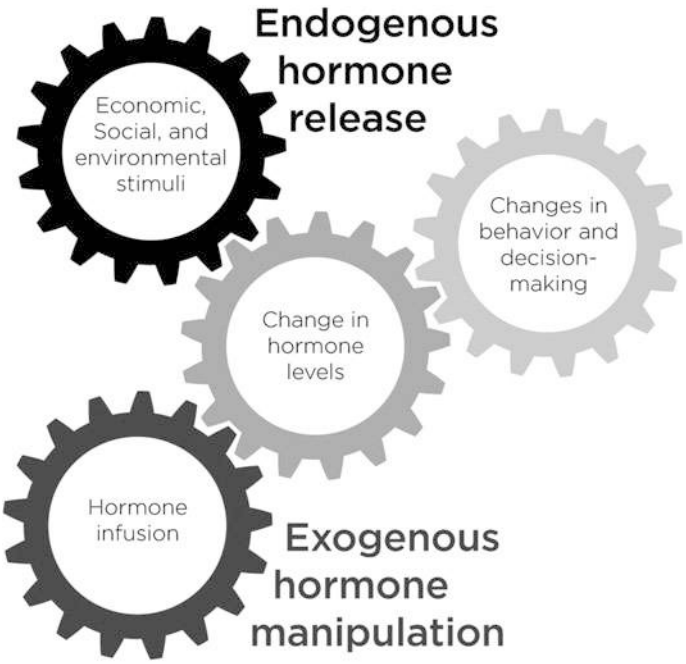

Fig. 3.1 A complete assessment of the role of hormones on decisions requires showing that (1) the endogenous hormones affect a particular behavior, and (2) that manipulating the hormone changes the behavior

3.4 Laboratory Experiments

Despite the abundance and history of hormone research in medicine and biology, the literature on hormones and economic decision-making is in early stages (Zak 2004). Hormonal neuroeconomics experiments were pioneered after animal research suggested related hormonal roles in human behavior. Findings have been both mixed and consistent in terms of convergence and replicability—some studies show contradicting results and non-replicability for the same hormones, while other hormones show corroborating patterns. In addition to testing for behavioral effect, hormone research requires understanding the precise pathways, half-lives, inhibiting and promoting qualities, and effect on other hormones, all of which are an ongoing scientific endeavor. Among the multitude of hormones produced in the human body, a subset is studied most closely and the majority of behavioral research has focused on oxytocin, testosterone, estrogen, glucocorticoids (stress hormones), arginine vasopressin, serotonin, and dopamine.

Tasks commonly used in neuroeconomics research include the trust game (TG) that measures trust and reciprocity, the ultimatum game (UG) that measures generosity or selfishness and theory of mind, the dictator game (DG) that measures unilateral altruism, and double auctions of assets (DAA) where participants trade an asset of known value. The TG, UG, and DG measure by the amount of money people choose to share with others under various experimental situations. The participant who makes the first decision is called Decision Maker 1 (DM1), and the person receiving the transfer or responding is called Decision Maker 2 (DM2). DAA experiments allow participants to buy and sell financial assets in simplified dynamic markets which simulate trading in financial markets by allowing one to make real-time decisions that respond to prices determined by the traders themselves (Smith et al. 1988). For a detailed overview on economic games we recommend reading of Chap. 2 “Games in Experimental Economics” by Claudia Civai and Daniel R. Hawes in this book.

3.5 Specific Hormones

3.5.1 Oxytocin

Oxytocin (abbreviated ‘OT’) is a hormone named for its role in mammalian reproduction (oxytocin means *quick birth* in Greek). In 1909, the English pharmacologist and neurophysiologist Sir Henry Hallett Dale showed it causes uterine contractions and isolated it, earning him the Nobel Prize in Physiology or Medicine in 1936. Produced by the hypothalamus and secreted by the posterior pituitary gland, OT is one of the few hormones that are directly synthesized in the brain and released in the brain, peripheral circulation, and various organs including gastrointestinal tract and heart (Zak 2011; Kiss and Mikkelsen 2011).

Starting in the late 1970s animal research showed OT release was associated with positive social behaviors and a groundbreaking study showed OT injection initiated maternal behavior in rats toward biologically unrelated offspring (Pederson and Prange 1979; Gimpl and Fahrenholz 2001). Convergent evidence pointed toward likely analogous influences on human behavior, leading to incorporation in economic decision tasks that provide active, measurable, and meaningful measures of greed, prosociality, trust, and profit maximization. By measuring and manipulating hormones in these tasks, an understanding the role of OT in human social behaviors has begun to emerge.

The first neuroeconomics study measuring and endogenously manipulating OT in relation to economic decisions is by Zak et al. (2004) who show that the receipt of trust signal is associated with higher peripheral OT. This study indicates intentional trust in the TG was associated with higher OT levels as measured in blood compared to individuals who received the same amount of money determined by random draw. Further, the level of OT predicted the amount of money that was reciprocated to the person who had shown trust. An analysis that extended the sample size using the same protocol corroborated the findings (Zak et al. 2005a).

A subsequent study was designed to causally connect OT to trusting behaviors by manipulating intranasal administration. In a double-blind protocol, 24 International Units (IU) of synthetic OT or an equal quantity of placebo were administered to participants who made decisions in four rounds of the TG with random rematching with other participants each round (Kosfeld et al. 2005). Those who received OT exhibited more than double the trust (as measured by monetary transfers) compared to those who received the placebo. Decisions in control tasks, such as choices among lotteries, as well as assessments of cognitive function were unchanged between conditions. It is important to point out that OT infusion did not increase allocations of money when the return on investment was determined by chance, showing that administration affected only social decision-making.

In similar studies, Baumgartner et al. (2008) found that the OT group did not send more money to DM2, although they did send more money after being given feedback about others' monetary transfers. Klackl et al. (2012) and Ebert et al. (2013) find that OT infusion did not increase trust in the TG and the latter propose OT acts as a modulator of social interaction rather than a prosocial neuropeptide. Yao et al. (2014) show no main effect of OT trust restoration, yet the design and objectives differ markedly, making the study incomparable to Kosfeld et al. (2005). In a study of basal OT (i.e., without exogenous manipulation) Christensen et al. (2014) test whether endogenous OT affects trust in an iterated DG and found no association between repeated sampling and trusting decisions.

Subsequent research found that 40 IU of intranasal OT increased generosity in the UG, complementing findings regarding its effects on the TG (Zak et al. 2007). In this study, OT did not affect decisions in unilateral DG. The authors included the DG as a control task because it does not require an understanding of another's intentions to make a decision. This finding shows the importance of context and structure to hormonal neuromodulation. A study by Mikolajczak (2010) showed that OT does not affect people indiscriminately—participants in the OT condition

made larger monetary transfers but only to others who had trustworthy characteristics. This suggests that multiple brain systems are involved in decisions and OT interacts with neural inputs that influence choice, and extensive work shows OT plays an influential role in proximal and distal prosocial behaviors.

Endogenous OT release was stimulated using a video featuring a child with terminal brain cancer and a change in OT correlated with the subjective experience of empathy for the characters in the video (after controlling for distress) (Barraza and Zak 2009). High levels of empathic concern predicted larger donations to the charity that produced the video. This study identified a psychological mechanism behind the effect of OT on behavior, and connected its findings to large literatures in psychology and moral philosophy regarding the role of empathy in prosocial behaviors (see Zak 2011). The causal effect of OT on distal prosocial behaviors was demonstrated by Barraza et al. (2011) who show a causal yet conditional effect of OT of increased donations to known charities among those who donated. Other studies show exogenous OT increases gaze to the eyes (Guastella et al. 2010), enhances social memory (Guastella et al. 2010), as well as improving emotional recognition among youth with autism (Guastella et al. 2010).

The mechanism by which hormones are released throughout the body and, most importantly, pass the blood-brain-barrier and reach the brain, is central to this area of research (McEwan 2004). Carson et al. (2015) show that plasma OT concentrations significantly and positively predict cerebrospinal fluid (CSF) OT concentrations while Kagerbauer et al. (2013) show no correlation. In a small study, Striepens et al. (2013) tested the effects of exogenous OT on CSF and plasma and show differential time-courses following administration: plasma concentrations peaked 15 min after administration and CSF levels were significantly higher 75 min later with no significant correlation between the two biofluids. Relatedly, OT half-life is between 3 and 4.5 min (Rydén and Sjöholm 1969). Given the broad distribution of OT receptors throughout the body it is likely that release between brain and other organs is related but not necessarily coupled. The mechanism by which exogenous administration increases physiologic levels is still under investigation with several feasible explanations.

Further studies have brought closer attention to measurement methodology in hormone research. The extraction method long used in biomedical research was eschewed in the early 2000s, which complicates clear interpretation of data from those studies. Extraction is the process of removing distinct physical products prior to assay extraction by separation of OT from its biological matrix (e.g., saliva). This facilitates avoiding measuring compounds resembling the substance of interest as unextracted samples contain molecules similar to OT and can drastically distort its measurement—extracted and unextracted OT measurements differ by orders of magnitude. McCullough et al. (2014) discuss the evolution of measurement standards and the incommensurate results stemming from lack of standardization and distortions in measurement caused by measuring unextracted samples. Christensen et al. (2014) test differential sensitivity between ELISA (enzyme-linked immunosorbent assays) and RIA (radioimmunoassay) to extraction as part of

their experimental paper and, although both methods show significant sensitivity, the former has higher sensitivity to extraction.

The path of oxytocin research is exciting and exemplifies the importance of assessing if, why, and how endocrinological mechanisms impact decisions. In addition to understanding the basic biology underlying OT release, half-life, and physiologic distribution, researchers need reliable behavior paradigms for testing the effects of OT on decision-making. As with any type of biological research, OT studies require adaptation and inclusion of new technology and a movement toward standardization to advance research to fully understand its function.

3.5.2 Testosterone

Testosterone (abbreviated 'T') is a gonadal hormone present in both sexes, with a receptor for it in every cell in the body. T varies seasonally as well as daily, producing a diurnal cycle that peaks in the early morning and declines throughout the day (Brambilla et al. 2009). Gonadal hormones can be both slow and fast acting, causing both long- and short-term effects. Long-term effects are caused by passive diffusion into cells where they bind to steroid-receptor complex, then DNA, and change gene transcription; fast action is caused by direct action on neurons with corresponding receptor cells. T affects not only the path of neuroanatomic and physiologic development (organizational effects) in mammals but also behavior throughout the lifespan (Thilers et al. 2006). Men's T levels peak around age 20 and decrease with age.

T has been extensively studied in medicine in relation to physical development, puberty, fertility, and pathology. It has been shown to affect mood, aggression, sexuality, and more recently, financial behavior (Nadler et al. 2016; Cueva et al. 2015). In addition to affecting—and being affected by—aggressive behavior, gonadal hormones are related to competition, spatial tasks, memory, certain sensation seeking scales, and risk preferences (Cherek et al. 1996; Roberti 2004; Apicella et al. 2008; Sapienza et al. 2009; Goudriaan et al. 2010).

3.5.3 Basic Biology of Testosterone

Steroid hormones are synthesized from precursors in the smooth endoplasmic reticulum, processed further in the mitochondria, and returned to the smooth endoplasmic reticulum for completion. Both steroid and steroid-like hormones are not stored in vesicles and simply diffuse out of cells after synthesis at a rate governed by production. Leydig cells produce T in response to hormonal signaling from the pituitary gonadotropin luteinizing hormone (LH) (Midzaka et al. 2009; Haider 2004; Mendis-Handagam 1997). Adult Leydig cell production depends on the pulsatile secretion of LH into peripheral circulation by the pituitary gland (Ellis

et al. 1983). T (which is produced in the ovaries in women) is a precursor to estrogen, and estrogen is a metabolite of T (the testes produce some estrogen). Despite the stereotype, T is not an exclusively male hormone, as estrogen is not exclusively female, and their proportions vary by gender and (wildly) by species.

3.5.4 Types of Testosterone

There are three types of T frequently analyzed in medical and behavioral literature: total T, Free T, and DHT (androstenedione is discussed primarily in medical literature[2]). T circulates in the body primarily bound (98 %) to serum proteins, mostly sex hormone-binding globulin (SHBG) and albumin; only 1–2 % of serum T is not protein-bound (Dunn et al. 1981). Due to the fact that SHBG binds T with high affinity and the off time of T bound to SHBG is remarkably slow, SHBG-bound T is considered unavailable for dissociation to act onto target tissues via classical androgen receptor mechanisms (Pardridge et al. 1979). Albumin-bound T is low-affinity and dissociation is rapid (Manni et al. 1985). Consequently, both albumin-bound T and free T are considered available for androgen action, and are called 'bioavailable' or 'non-SHBG-bound' T (Matsumoto and Bremner 1984).

3.5.5 Total T

Serum T, also known as Total T (TT), plays an important role in the clinical evaluation of numerous common endocrine disorders, such as hypogonadism, and delayed or precocious puberty in males, as well as a variety of conditions in females. Routine assays began approximately 40 years ago and required chromatographic separation. Today, assays are more precise, specific, require less blood, and nonradioactive methods (Stanczyk and Clarke 2010; Matsumoto and Bremner 1984).

3.5.6 Free T

Forty-four percent of circulating T is bound to sex hormone-binding globulin (SHBG), 50 % to albumin, and 3–5 % to cortisol binding globulin, leaving about

[2]Androstenedione (A), also known as 'Andro', is a steroid hormone produced in the gonads and adrenal glands in men and women. Androstenedione an intermediate step in the biochemical pathway that produces T and estrone and estradiol. This hormone was at the center of controversy of baseball players and androgen use in the 1990s. Leder et al. find that sufficiently high doses (300 mg) oral A increase serum T and estradiol in some healthy men, supporting the rationale of the ban issued by the World Anti-Doping Agency (2000).

2–3 % T free (FT). Bioavailable T is the free circulating in addition to the albumin-bound portion. Salivary T represents the portion of plasma T that diffuses passively across salivary glands (Arregger et al. 2007). It is from this small percent of total T that FT can be aromatized via 5-alpha reductase to dihydrotestosterone.

3.5.7 Dihydrotestosterone

Dihydrotestosterone (DHT) is converted from T through the action of 5-alpha reductase in peripheral tissue. Both T and A are precursors of DHT (Ito and Horton 1971). As mentioned above, of total T, there is but a small amount of free T available for conversion. As discussed earlier, androgens act at transcriptional levels of gene expression via classical androgenic processes by passively diffusing through cell membranes and 'locking' into their respective receptors. Yet evidence has accumulated that some steroids may also alter neuronal excitability through interactions with specific neurotransmitter receptors at the scale of milliseconds to seconds (Rupprecht and Holsboer 1999). DHT binds faster (Hemat 2004) and remains in the cell longer (Grino et al. 1990) than TT due to higher receptor affinity, thereby likely to have more significant behavioral effects.

3.5.8 T in Behavioral Experiments

Behavioral studies involving T include basal levels, changes in endogenous levels, and exogenous administration. Burnham (2007) found that DM2 males with higher T rejected low offers more than their lower T counterparts in the UG. Endogenous variations in T have been shown to increase patience for monetary rewards for non-impulsive participants, while reducing discount rates for impulsive participants, showing an inverted-U-shape (Takahashi et al. 2006). Higher T males were also more likely to make utilitarian decisions in 'trolley car' problems (lives sacrificed to save other lives) compared to lower T males (Carney and Mason 2010).

Apicella et al. (2014) find that participants who showed an increase in T were more willing to compete. These findings may suggest 'hormonal typology' among individuals, making behavior partly explainable by baseline levels and reactivity to particular hormones. Zak et al. (2005b) showed that men had a rise in DHT when distrusted by receiving small amounts of money as DM2 in the TG. High DHT levels were associated with little or no reciprocation, and partially explain the gender gap in reciprocity in the TG in which women reciprocate more money on average than men.

The challenge with relying on endogenous levels or changes is that hormone release is noisy and subject to interindividual heterogeneity, thereby yielding unreliable control and identification. Using extensively studied exogenous treatments helps solve these problems as their pharmacokinetics and associated risks

have been extensively studied in medical research (Swerdloff et al. 2000).[3] For example, typical starting dosage is 50 mg of T (and often increased to 100 mg), providing researchers with a basis for administering quantities with a predictable effect on circulating levels. Providing insight about immediate changes of exogenous T, Eisenegger et al. (2013) test the effects of T (and estradiol) administration in young men and demonstrate a rapid rise with a peak in serum T reached at 3 hours post-administration. Tuiten et al. (2000) show sublingual T caused sharp rise in serum T within 15 min (with a return to baseline after 90 min) and lagged increases in genital arousal in women. In another pharmacokinetics study of females, van Rooij et al. (2011) show sublingual T showed dose-dependence and peak levels reached in 15 min and return to baseline within 2.5 h. Yet despite vast medical literature on androgens, behavioral studies with exogenous T are limited.

Zak et al. (2009) manipulated T pharmacologically in male participants playing the UG. In this within-subject s study, participants received 10 g of Androgel® (1 % testosterone gel) on one visit and a placebo gel on another. Blood samples were obtained before and after substance administration to quantify the rise in T as well as to assess parametric effects of T on behavior. The authors showed that T decreased DM1 offers as well as increased the minimum acceptable offers by DM2 s. Both these effects scaled positively with three measures of T (T, free T, DHT). This finding is consistent with a known physiologic mechanism in which high levels of T inhibit the release of OT (Insel et al. 1993). A similar paper with females only by Eisenegger et al. (2010) purported to show the opposite effect. In the study, 0.5 mg of sublingual T or placebo was administered to women in a between-subjects study, absent an assessment of the rise in T (baseline T was measured). The authors found no main effect of T on UG offers or rejections when compared to placebo, yet found that T increased UG offers if one controls for the substance participants believed they received (Eisenegger et al. 2010, online supplementary material).

Additional manipulation studies include Bos et al. (2010), who tested the relationship between T and distrust among women in a placebo-controlled within-subject design and found that T reduced ratings of trustworthiness when viewing pictures of men's faces. Boksem et al. (2013) study the effects of exogenous on trust and reciprocity and show it inhibits trust and promotes reciprocity. Hermans et al. and Goetz et al.'s fMRI studies show that T increases neural reactivity to threat. Wibral et al. (2012) study lying and find that T reduces it relative to placebo. The role of T in asset trading behavior was assessed using a DAA paradigm (Nadler et al. under review) who found the sessions with high T traders resulted in larger asset bubbles compared to placebo sessions due to higher T participants bidding higher prices. Cueva et al. (2015) show that participants who

[3]Due to the rise of easily obtainable drugs and associated advertising to remedy "low testosterone syndrome" or "andropause", a large and growing proportion of men is currently using Androgel® (and similar generics), and many inject even higher doses (Baillargeon et al. 2013; Handelsman 2013). In fact, the proliferation of these drugs among financial professionals allows our experiment to mimic the "testosterone shock" in real-world asset markets such as the NYSE.

received exogenous testosterone had a higher willingness to invest in high-variance stocks. Nave et al. (under review) show exogenous T reduced men's ability to inhibit instinctive and incorrect responses in the Cognitive Reflection Task while having no impact on mathematical skills, task engagement, or motivation in a large (n = 243) sample of young men. This result, supported by previous evidence of T increasing impulsivity, suggests T 'nudges' decision-making toward rapid and intuitive processing.

A related mechanism for these findings is that T correlates with willingness to engage in competition and decrease risk aversion via allosteric modulation of $GABA_A$ receptors (Reddy and Jian 2010; Carré and McCormick 2008). In addition, dopamine, which is associated with risk-taking, positively co-varies with T and may contribute to the sensation seeking aspect of financial trading though further work is needed to identify T's effect on risk per se (Szczypka et al. 1998).

3.5.9 2D-4D Ratio

The ratio of second to fourth finger (2D:4D) has been (inconsistently) shown to negatively correlate with prenatal T exposure and that men have a lower 2D:4D ratio than women (Manning et al. 2004, 1998). Apicella et al. (2008) found that 2D:4D does not significantly correlate with economic risk-taking and Apicella et al. (2015) show males displaying *higher* ratios than women among Hadza tribe members. Contrarily, Sapienza et al. (2009) reported that 2D:4D ratio and salivary T negatively correlated with risk aversion and that high T individuals chose higher risk professions (finance, broadly defined). Coates (2012) found that 2D:4D ratio predicted high-frequency traders' long-term profitability as well as duration of employment in the profession. Brañas-Garza and Rustichini (2011) find that lower 2D:4D ratios are associated with greater risk-taking and higher abstract reasoning scores among females (188 participants, 72 female).

3.5.10 Arginine Vasopressin

Arginine vasopressin (abbreviated AVP') is a hormone synthesized in the hypothalamus and stored in vesicles in the posterior pituitary. One of its primary functions is water regulation in the body and has been shown to have behavioral influences. Despite being molecularly similar to OT and lends itself to the same endogenous and exogenous approaches to being studied, AVP has different behavioral influences. Whereas OT facilitates bonding and trust, AVP is associated with reactive aggression, stress-responses, and mate- and nest- guarding (Bester-Meredith et al. 2005; Young and Wang 2004; Young et al. 1999). Coccaro et al. (1998) show that AVP is positively associated with aggressive behavior for men with personality disorders. AVP administration increases physical arousal,

biasing individuals to respond aggressively to neutral stimuli (Shalev et al. 2011; Ebstein et al. 2009; Thompson et al. 2004). In regard to social perception, Uzefovsky et al. (2012) show AvP administration leads to significant decrease in men's recognition of others' emotional states, while Kenyon et al. (2013) showed no significant effect of AVP in the same task.

Rilling et al. (2011) found that AVP increased reciprocation after cooperation with human partners as well as functional connectivity between the amygdala and the anterior insula. Israel et al. (2012) found no influence of AVP on cooperative behavior in a public goods game. Similarly, blood levels of AVP were unrelated to distrust in the TG (Zak unpublished data). In addition, an AVP infusion study produced no differences when compared to a placebo for a variety of economic decisions (Zak 2011). Determining how AVP affects economic decisions will require additional studies.

3.5.11 Dopamine

Dopamine (abbreviated 'DA') is a neurotransmitter (a chemical released by nerve cells to communicate with other nerve cells) with a central role in human functioning considered the 'gas pedal' to pursuing reward. Cell bodies of DA neurons are mostly in the midbrain and release DA with nerve impulses (Moore and Bloom 1978). The DA system broadly encodes abstract information about reward. The majority of midbrain dopamine neurons respond in unison to unpredicted rewards, with remaining neurons unresponsive to stimuli (Tobler et al. 2005).

The DA system encodes value and provides a signal of 'pure reward' vis-à-vis its expectation. Put differently, it responds not to absolute rewards, but to their reward relative to its expectation—the difference between them is known as reward prediction error (RPE). Delivery of unexpected rewards increases phasic midbrain activity while its absence decreases it (Schultz 2004). Together, the DA system forms a reinforcement learning system that guides behavior and attention toward optimal reward guided by experience and predictions of unknowns (For a comprehensive review see Schultz 1998). Based on an this extensive literature of animal studies, neuroeconomics research has successfully shown DA's role in predicting and responding to monetary reward (Preuschoff et al. 2007).

Pharmacological studies include increasing DA as well as blocking its receptors and precursors. Menon et al. (2007) tested differential effects on BOLD responses and found amphetamine treatment—which increases DA—caused larger BOLD reward prediction errors in the midbrain. Efremidze and Zak (in press) test effects on learning by blocking DA receptors with naltrexone in a DAA experiment and find interrupted reinforcement learning and larger and longer lasting price bubbles. This result is consistent with Pessiglione et al. (2006) who show that participants given L-DOPA (DA-promoting drug) performed better than those who received haloperidol (drug that binds to DA receptors as an agonist but induces the opposite response). Sevy et al. (2006) showed that tyrosine (a DA precursor) depletion

impaired performance of the Iowa Gambling Task by increasing the weight to temporally proximal outcomes. Thematically similar, Scarná et al. (2005) demonstrate that participants underweighted magnitude of bad outcomes when given the same branch chain amino acid (BCAA) mixture.

Despite the multitudes of studies on this neurotransmitter, Rogers (2011) summarizes the complicating factors associated with interpreting DA studies, which include; (i) uncertainty about the pre versus postsynaptic actions; (ii) lack of specificity of medications between receptor subtypes (pharmacological studies are hamstrung by limited specifity of agents administrable to humans); and (iii) uncertainty about interaction of effects with participants' 'baseline' abilities. Also, ensuring experimental double-blind treatment is difficult given the sometimes nauseating effects of tryptophan depleting BCAA liquid given to participants (Crockett and Fehr 2013).

As mentioned earlier, biological systems are interconnected, and specific molecules can promote as well as inhibit other molecules, as illustrated by DA and serotonin; Daw et al. (2002) provide a summary of their opponency, and Cools et al. (2011) discuss their complementarity.

3.5.12 Serotonin

In 1948 Maurice Rapport, Arda Green, and Irvine Page at the Cleveland Clinic discovered a vasoconstrictor substance in blood serum affecting vascular tone and named it serotonin (Abbreviated '5-HT' due to its chemical formula). About 90 % of it is in the gastrointestinal tract where it regulates intestinal movements and the rest is synthesized in serotonogenic neurons where it regulates mood, appetite, and sleep and plays important roles in cognition and learning (Berger et al. 2009).

Experiments testing 5-HT on decisions suggests it affects risk-taking with probabilistic outcomes, time discounting, impulsivity, and cooperation. In a study of the effects of increasing 5-HT, Murphy et al. (2009) find a significant three-way interaction between treatment, size of possible gains, and size of possible losses, and suggest 5-HT modulates non-normative decision-making under uncertainty. Doya (2002) proposes that 5-HT controls the time scale of reward prediction in a theoretical model of integrated neuromodulatory learning, which is experimentally supported by Crockett et al. (2010) who deplete 5-HT's amino acid precursor (tryptophan) and find increased impulsive choice in a discounting task. They also find it jointly increased impulsive choice and altruistic punishment (i.e., rejecting an unfair albeit nonzero offer), suggesting that 5-HT modulates self control and impulsivity. In the same experiment, Crockett et al. (2008) show the 5-HT depletion protocol increased rejection rates among unfair offers. Wood et al. (2006) find that 5-HT depletion caused significant reduction in cooperation in the PD on day 1 of a cross-over, within-subject study.

3.5.13 Stress Hormones

The body responds to physical and psychological demands by releasing hormones, and virtually all people can attest to their focusing and motivating effects in the urgency of a deadline or exigency of a crisis. Stress hormones prepare the body to engage in challenging tasks by focusing attention, increasing cardiovascular tone, energy availability, and suppressing the immune system (Born et al. 1990; Axelrod and Reisine 1984). Stress hormones have long been known to affect physiology and new research shows their impact on economic and social decision-making.

Mammalian physiology has complex and specific responses to the multitude of threats and scenarios organisms are likely to face. Specific stress hormones are released as follows: Adrenocorticotropic hormone (ACTH) from the anterior pituitary, glucocorticoids (GCs) from the adrenal cortex, epinephrine from the adrenal medulla, and norepinephrine from sympathetic nerves. Instead of a one-size-fits-all stress response, the body has an evolved 'set' of hormonal responses ranging from fast release and brief influence to slower release with effects of longer duration. The neural path, known as the sympathetic adrenomudullary system, acts immediately upon exposure to stress, and releases adrenaline (epinephrine) and noradrenaline (norepinepherine) from the adrenal medulla (Elmadjian et al. 1957). The sympathetic nervous system reacts by temporarily increasing heart rate, blood pressure, and perspiration, then returning them to baseline within approximately 10 min (Het et al. 2009). The slower system involves reactions along the hypothalamic-pituitary axis (HPA), starting with the release of corticotrophin-releasing hormone, which stimulates release of hormones from the adrenal cortex and precipitating changes in physiologic state that last 10–60 min and sometimes longer (Sapolsky et al. 2010).

Stress hormones have also recently been shown to affect decision-making and risk preferences. A study using the Iowa Gambling Task (IGT) showed that men with elevated levels of cortisol, a long-acting stress hormone, performed more poorly while women show an inverse relationship, performing best with slightly elevated levels (van den Bos 2009). Putman et al. (2009) showed that elevating stress hormones pharmacologically increased risky decision-making involving potentially large rewards as well as risk-seeking choices when probability of loss was high. A related study using the Balloon Analogue Risk Task (BART) showed that under high levels of stress, men tended to increase risk-taking while women reduced it (Lighthall 2012). Kandasamy et al. (2013) also show that chronically high stress hormones increase risk aversion, though acute elevation of stress hormones does not.

Stress hormones have been shown to play a role in discounting future gains, with men showing a negative relationship between discounting and stress hormones, and women showing a positive relationship (Takahashi 2010). Moral reasoning, too, has been shown to be sensitive to stress, with higher stress correlating with less utilitarian choices among hypothetical personal moral dilemmas such as making a life-or-death decisions (Youssef et al. 2012).

ACTH in particular has been shown to be a neurochemical signal that sustains and increases visual attention (Born et al. 1990). Testing this in a consumer neuroscience paradigm, Lin et al. (2013) show that attending to a public service announcement (PSA) causes significantly higher ACTH release in both men and women. The authors posit that ACTH sustains attention to the PSA and is requisite for preparing action in market decisions.

Together, these results suggest stress hormones are instrumental to species perpetuation by focusing attention on salient and relevant information and new evidence shows tilting decisions toward outcomes more likely to ensure survival. Further, these finding are in line with the proposition that stress hormones have an inverted-U effect on cognition, affect and behavior—deficient and excessive amounts of stress hinder cognition while intermediate levels improve it (McEwan and Sapolsky 1995). Future work will likely explore the interaction between stress and other hormones to better understand their mutual influences on economic decisions.

3.5.14 Female-Specific Hormonal Influences

Sex differences exist in the brain, both in morphology and function (Cahill 2006). For example, receptor affinity for glucocorticoids is half as great in females than males, which has implications for the direction and magnitude of their influence between genders (Madeira and Lieberman 1995). Several studies show sex differences in the serotonin system as well as the analgesic effect of opioid peptides (Nishizawa 1997; reviewed in Craft 2003). The prefrontal cortex, responsible for executive function, has sex hormone receptors including the highest concentration of estrogen receptors in the brain (Bixo et al. 1995). For a review of differences in gender due to sex hormones see Collaer and Hines (1995).

In addition to differences in neuroanatomy and function, hormonal variations drive behavioral differences between men and women in decision-making. Buser (2012) finds that women show less trust in the TG than men in menstrual and premenstrual phases, but have similar trust to men in the middle stages of their cycles. As mentioned above, Zak et al. (2004) showed that women in the luteal phase of their menstrual cycle were less trustworthy in the TG than either men or women in the follicular phase. Women's satisfaction with life varies over the menstrual cycle through the interaction of estradiol, progesterone, and OT (Grosberg et al. in review).

Senior et al. (2007) found that women allocate more resources to dominant-looking men during the follicular phase of their cycles, and allocate less to non-dominant men during the luteal phase, suggesting a hormonal role for resource allocation as a sexual signal. Miller et al. (2007) found that women working in gentleman's clubs earned more money during fertile phases of their cycle. Zethraeus et al.'s (2009) randomized study of postmenopausal women found no effect of T or estrogen in a modified DG, UG, TG, and risk aversion. Further work is needed in ascertaining the hormonal role in gender differences in development as well as activational properties of specific hormones.

3.6 Field Studies

Lab work builds the basic science underlying neurobehavioral influences on decision-making and is the right place to start. However, we cannot faithfully assume that people's behavior in the lab will perfectly represent behavior outside the lab; thus the field is next frontier that offers radical improvement in ecological validity. Fieldwork requires running studies outside tightly controlled environments as well as learning how to interpret the surviving influences of biological vectors in complex scenarios. Translating data from lab experiments is an integral aspect of science and thus further work is needed to bring theory and reality into greater congruence and be able to improve practice (See Harrison and List (2004) for a thorough exposition of economic field experiments). However, the significant challenge of adapting field experiments to lab studies is ethical feasibility of pharmacologic manipulation. For example, one could not use the same double-blind T protocol used by Nadler et al. on actual traders at a trading firm without introducing substantial risk to the individual traders, employer, and the market.

In one of the few field studies involving hormones and economic behavior, Coates and Herbert (2007) studied the relationship between T, stress hormones, and trading performance in professional stock traders. They found that higher morning T was associated with higher average returns (relative to recent trading performance), and that cortisol increased with market volatility. The T finding is consistent with greater risk-taking producing larger returns (following the security market line), while the cortisol finding matches the neurophysiologic measurements of foreign exchange traders in Lo and Repin (2002). Lo and Repin's experiment tested reactivity of securities traders by their quantifiable physiologic responses driven by cognitive-emotional interactions during live trading and found heterogeneity in responses based on trading experience.

Zak (2012) reports that a variety of rituals, such as soldiers marching, rugby teams' pre-match warm up, and a war dance by indigenous peoples in Papua New Guinea are associated with increases in both OT and T. In these studies, OT was associated with a sense of group affiliation, while changes in T appeared to rise due to potential competition, consistent with the challenge hypothesis of T (Wingfield et al. 1990). This indicates that such rituals facilitate in-group bonding in response to out-group aggression, demonstrating the interactive effect of hormones on behavior.

More fieldwork is needed to assess the influence of hormones on decision-making as it occurs in complex environments, and especially to translate laboratory findings into problem-solving applications and intelligently inform policy.

3.7 Summary, Conclusions, and Future Directions

Hormones do much more than regulate homeostasis and initiate physiologic and developmental changes. From moderating trust in strangers, to affecting how much people pay for financial assets, to shifting risk tolerance, hormones play an important role in our economic and social lives.

However, modeling hormonal influences on behavior is complicated. Many hormones assert influence in nonlinear ways, often displaying inverted-U relationships between the quantity of a hormone and behavior (Zak 2010). Further, hormones are released in pulses, can respond rapidly to environmental stimuli, and vary dramatically over time meaning that hormonally based models will be complicated (Santern and Bardin 1973). Finally, hormones vary in their timeframe of effect and are influenced by and interact with agonist and antagonist hormones (Breedlove et al. 2007, p. 123; Jackson et al. 1997) further complicating model building. For example, despite clear results in the asset trading paradigm, T has been shown to act as an allosteric modulator of $GABA_A$ receptors as well as positively correlating with DA, which complicates simplistic modeling of its influence through a simple, single channel. Another important question is whether specific hormones affect high-level cognition, or whether they modulate lower level processes and manifest as experimental shift variables (e.g., T increases risk-taking; OT increasing trust). For these reasons we caution that adopting a mechanistic perspective linking hormones to decisions that does not consider holistic neural activity is likely to produce inaccurate predictions.

Neuroeconomics studies of hormonal influences on decisions follow the approach in the biological sciences where convergent evidence corroborates hypotheses using a variety of methods. When studying hormones and decision-making, we believe it is critical to use the three-stage process outlined above: establish baselines, measure endogenous hormone changes, and assess the impact of pharmacologic manipulation on specific, measurable behavior. Further, hormones can be radio-tagged to show how they affect neural activity using PET, and genetic assays can reveal relationships between different alleles and hormone function, methods that are covered elsewhere in this book.

An application of hormonal effects on behavior is in the design of institutions. Institutions can mitigate risk, off-load cognition for difficult decisions, and provide external resources. Well-functioning institutions can reduce stress, increase OT, and optimize performance and satisfaction. However, one of the significant risks of this research is simplistic interpretation and direct application to complex situations without careful translation. For example, one of the most common questions we get regarding the T and asset trading experiment is, “If testosterone causes men to trade irrationally, and if women have less testosterone than men, why don’t you just have women trade along with the men?” There is scientific (and anecdotal) evidence why this ‘solution’ is unlikely to effectively reduce risk-taking among men, and actually more likely to increase it (see Ronay and von Hippel 2010).

Nobel Prize winner Ronald Coase stated that, "the degree to which economics is isolated from the ordinary business of life is extraordinary and unfortunate" (2012). Neuroeconomics provides positive and normative improvements to the business of life by identifying the mechanisms underlying economic decisions. By judiciously applying its methods to extant problems, neuroeconomics can improve institutions, individual happiness and performance, and society.

References

Arregger LNC, Alejandro L, Tumilasci OR, Aquilano DR, Cardoso EML (2007) Salivary testosterone: a reliable approach to the diagnosis of male hypogonadism. Clinic Endocrinol 67:656–662

Apicella C, Dreber A, Campbell B, Hoffman M, Little A (2008) Testosterone and financial risk preferences. Evol Hum Behav 29:384–390

Apicella C, Dreber A, Mollerstrom J (2014) Salivary testosterone change following monetary wins and losses predicts future financial risk-taking. Psychoneuroendocrinology 39:58–64

Apicella CL, Tobolsky VA, Marlowe FW, Miller KW (2015) Hadza hunter-gatherer men do not have more masculine digit ratios (2D:4D). Am J Phys Anthropol 159: 223–32

Axelrod J, Reisine T (1984) Stress hormones: their interaction and regulation. Science 224:452–459

Bacon F, Selby FG (1895). The advancement of learning (Macmillan)

Baillargeon J, Urban R, Ottenbacher KK, Goodwin J (2013) Trends in androgen prescribing in the United States, 2001 to 2011. JAMA Intern Med 173(15):1465–1466

Barraza J, Zak P (2009) Empathy toward strangers triggers oxytocin release and subsequent generosity. Ann NY Acad Sci 1167:182–189

Barraza J, McCullough M, Zak PJ (2011) Oxytocin infusion increases charitable donations regardless of monetary resources. Horm Behav 60:148–151

Baumgartner T, Heinrichs M, Vonlanthen A, Fischbacher U, Fehr E (2008) Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. Neuron 58(4):639–650

Beato M, Chavez S, Truss M (1996) Transcriptional regulation by steroid hormones. Steroids 61 (4):240–251

Berg J, Dickhaut J, McCabe K (1994) Trust, reciprocity, and social history. Games Econ Behav 10:122–142

Berger M, Gray J, Roth B (2009) The expanded biology of serotonin. Annu Rev Med 60:355–366

Bester-Meredith JM (2005) Manipulations of vasopressin alter aggression differently across testing conditions in monogamous and non-monogamous peromyscus mice. Aggressive Behav 31:189–199

Bixo M, Backstrom T, Winblad B, Andersson A (1995) Estradiol and testosterone in specific regions of the human female brain in different endocrine states. J Steroid Biochem Mol Biol 55:297–303

Boksem MA et al. (2013) Testosterone inhibits trust but promotes reciprocity. Psychol Sci:0956797613495063

Booth A, Shelley G, Mazur A, Tharp G, Kittok R (1989) Testosterone, and winning and losing in human competition. Horm Behav 23:556–571

Born J, Bathelt B, Pietrowsky R, Pauschinger P, Fehm H (1990) The influence of display characteristics on visual exploratory search behavior. J Consum Res 101:34–38

Bos P, Terburg D, van Honk J (2010) Testosterone decreases trust in socially naïve humans. PNAS 107(22):9991–9995

Brambilla D, Matsumoto A, Araujo A, McCinlay J (2009) The effect of diurnal variation on clinical measurement of serum testosterone and other sex hormone levels in men. J Clin Endocrinol Metab 94(2):907–913

Brañas-Garza P, Rustichini A (2011) Organizing effects of testosterone and economic behavior: not just risk taking. PlosOne 6(12):e29842

Breedlove M, Rosenweig M, Watson N (2007) Biological psychology. Sinauer, Sunderland, MA, USA

Burham T (2007) High-testosterone men reject low ultimatum game offers. Proc R Soc B 274 (1623):2327–2330

Buser T (2012) Digit ratios, the menstrual cycle and social preferences. Games Econ Behav 76:457–470

Cahill L (2006) Why sex matters for neuroscience. Nat Rev Neurosci 7(6):1–8

Camerer C, Loewenstein G, Prelec D (2005) Neuroeconomics: how neuroscience can inform economics. J Econ Lit 43(1):9–64

Carney DR, Mason MF (2010) Decision making and testosterone: when the ends justify the means. J Exper Social Psychol 46(4):668–671

Carré J, McCormick C (2008) Aggressive behavior and change in salivary testosterone concentrations predict willingness to engage in a competitive task. Horm Behav 54:403–409

Carré J, Gilchrist J, Morrissey M, McCormick C (2010) Motivational and situational factors and the relationship between testosterone dynamics and human aggression during competition. Biol Psychol 84:346–353

Carson D et al. (2015) Cerebrospinal fluid and plasma oxytocin concentrations are positively correlated and negatively predict anxiety in children. Mol Psychiat 20(9):1085–1090

Cherek DR, Schnapp W, Moeller FG, Dougherty DM (1996) Laboratory measures of aggressive responding in male parolees with violent and nonviolent histories. Aggressive Behav 22(1):27–36

Christensen J, Shiyanov P, Estrepp J, Schlager J (2014) Lack of association between human plasma oxytocin and interpersonal trust in a prisoner's dilemma paradigm. PLoS ONE 9(12): e116172

Coase R, Wang N (2012) Saving economics from the economists. Harvard Bus Rev 90(12):12–36

Coates J (2012) The hour between dog and wolf: risk-taking, gut feelings and the biology of boom and bust. HarperCollins, London, UK

Coates J, Herbert J (2007) Endogenous steroids and financial risk taking on a london trading floor. PNAS 105(16):6167–6172

Coccaro E, Kavoussi RH, Cooper T, Ferris C (1998) Erebrospinal fluid vasopressin levels: correlates with aggression and serotonin function in personality-disordered subjects. Arch Gen Psychiatry 55:708–714

Collaer M, Hines M (1995) Human behavioral sex differences: a role for gonadal hormones during early development? Psychol Bull 118(1):55–107

Cools R, Nakamura K, Daw N (2011) Serotonin and dopamine: unifying affective, activational, and decision functions. Neuropsychopharmacology 36:98–113

Crabbe P, Bogaert V, De Bacquer D, Zmierczak H, Kaufman J (2007) Part of the interindividual variation in serum testosterone levels in healthy men reflects differences in androgen sensitivity and feedback set point: contribution of the androgen receptor polyglutamine tract polymorphism. J Clin Endocrinol Metab 92(9):3604–3610

Craft R (2003) Sex differences in opioid analgesia: from mouse to man. Clin J Pain 19:175–186

Crockett M, Fehr E (2013) Social brains on drugs: tools for neuromodulation in social neuroscience. SCAN 1(5):nst113

Crockett M, Clark L, Tabibnia G, Lieberman M, Robbins T (2009) Serotonin modulates behavioral reactions to unfairness. Science 320(27):1739

Crockett M, Clark L, Tabibnia G, Lieberman M, Robbins T (2010) Impulsive choice and altruistic punishment are correlated and increase in tandem with serotonin depletion. Emotion 10 (6):855–862

Cueva C, Roberts RE, Spencer T, Rani N, Tempest M, Tobler PN, Herbert J, Rustichini A (2015) Cortisol and testosterone increase financial risk taking and may destabilize markets. Sci Rep 5:11206

Daw N, Kakade S, Dayan P (2002) Influential exposition of opponency between dopamine and serotonin in terms of coding average reward and punishment rates, and prediction errors. Neural Netw 15:603–616

Doya K (2002) Metalearning and neuromodulation. Neural Networks 15(4):495–506

Dunn J, Nisula B, Rodbard D (1981) Transport of steroid hormones: binding of 21 endogenous steroids to both testosterone-binding globulin and corticosteroid-binding globulin in human plasma. J Clin Endocrinol Metab 53(1):58–68

Ebert A et al. (2013) Modulation of interpersonal trust in borderline personality disorder by intranasal oxytocin and childhood trauma. Soc Neurosci 8(4):305–313

Ebstein R, Israel S, Lerer E, Uzefovsky F, Shalev S, Gritsenko I et al (2009) Arginine vasopressin and oxytocin modulate human social behavior. Ann NY Acad Sci 1167:87–102

Efremidze L, Sarraf G, Miotto, K, Zak, PJ (in press) The Neural Inhibition of Learning Increases Asset Market Bubbles: Experimental Evidence. Journal of Behavioral Finance.

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(21):356–361

Eisenegger C, von Eckardstein A, Fehr E, von Eckardstein S (2013) Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. Psychoneuroendocrinology 38:171–178

Ellis G, Desjardins C, Fraser H (1983) Control of pulsatile LH release in male rats. Neuroendocrinol 37(3):177–183

Elmadjian F, Hope JM, Lamson ET (1957) Excretion of epinephrine and norepinephrine in various emotional states. J Clin Endocrinol Metab 17(5):608–620

Falkenstein E, Tillmann H-C, Michael C, Martin F, Martin W (2000) Multiple actions of steroid hormones—a focus on rapid, nongenomic effects. Pharmacol Rev 52:513–555

Frye C, Seliga A (2001) Testosterone increases analgesia, anxiolysis, and cognitive performance of male rats. Cogn Affect Behav Neurosci 1(4):371–381

Gimpl G, Fahrenholz F (2001) The oxytocin receptor system: structure, function, and regulation. Physiol Rev 81(2):629–683

Grino B, Griffin J, Wilson J (1990) Testosterone at High Concentrations Interacts with the Human Androgen Receptor Similarly to Dihydrotestosterone*. Endocrinology 126:1165–1172

Grosberg D, Merlin R, Zak P (n.d.) What makes women happy: oxytocin release correlates with life satisfaction (in review)

Goudriaan AE et al. (2010) The influence of high-normal testosterone levels on risk-taking in healthy males in a 1-week letrozole administration study. Psychoneuroendocrinol 35(9):1416–1421

Guastella AJ et al. (2010) Intranasal Oxytocin Improves Emotion Recognition for Youth with Autism Spectrum Disorders. Biol Psychiat 67(7):692–694

Haider SG (2004) Cell biology of Leydig cells in the testis. Int Rev Cytol 233:181–241

Harrison G, List J (2004) Field experiments. J Econ Lit 1009–1055

Hemat RAS (2004) Principles Of Orthomolecularism

Het S, Rohleder N, Schoofs D, Kirschbaum C, Wolf O (2009) Neuroendocrine and psychometric evaluation of a placebo version of the trier social stress test. Psychoneuroendocrinology 34:1075–1086

Hodgeson G (1998) On the evolution of Thornstein Veblen's evolutionary economics. Camb J Econ 22:415–431

Holdcraft RW, Braun RE (2004) Hormonal regulation of spermatogenesis. Inter J Androl 27 (6):335–342

Insel T, Young L, Witt D, Crews D (1993) Gonadal-steroids have paradoxical effects on brain oxytocin receptors. J Neuroendocrinol 5:619–628

Israel S, Weisel O, Ebstein R, Bornstein G (2012) Oxytocin, but not vasopressin, increases both parochial and universal altruism. Psychoneuroendocrinology 37:1341–1344

Ito T, Horton R (1971) The source of plasma dihydrotestosterone in man. J Clinic Invest 50 (8):1621
Jackson T, Richer J, Bain D, Takimoto G, Tung L, Horwitz K (1997) The partial agonist activity of antagonist-occupied steroid receptors is controlled by a novel hinge domain-binding coactivator L7/SPA and the corepressors N-CoR or SMRT. Mol Endocrinol 11(6):693–705
Kagerbauer SM et al. (2013) Plasma oxytocin and vasopressin do not predict neuropeptide concentrations in human cerebrospinal fluid. J Neuroendocrinol 25(7):668–673
Kandasamy N, Hardy B, Coates J (2013) Cortisol shifts financial risk preferences. PNAS
Kandasamy N et al. (2014) Cortisol shifts financial risk preferences. Proc Natl Acad Sci U S A 111 (9):3608–3613
Kenyon A, Alvares G, Hickie I, Guastella A (2013) The effects of acute arginine vasopressin administration on social cognition in healthy males. J Horm
Kiss A, Mikkelsen J (2011) Oxytocin-anatomy and functional assignments: a minireview. Endocr Regul 39(3):97–105
Klackl J, Pfundmair M, Agroskin D, Jonas E (2013) Who is to blame? Oxytocin promotes nonpersonalistic attributions in response to a trust betrayal. Biol Psychol 92(2):387–394
Kosfeld M, Heinrichs M, Zak P, Fischbacher U, Fehr E (2005) Oxytocin increases trust in humans. Nature 435(2):673–676
Lighthall N, Sakaki M, Vasunilashorn S, Nga L, Somayajula S, Chen E et al (2012) Gender differences in reward-related decision processing under stress. SCAN 476–484
Lin P-Y, Grewal NS, Morin C, Johnson WD, Zak PJ (2013) Oxytocin increases the influence of public service advertisements. PloS one 8(2):e56934
Lo W, Repin D (2002) The psychophysiology of real-time financial risk processing. J Cogn Neurosci 14(3):323–339
Losel R, Wehling M (2003) Nongenomic actions of hormones. Nature 4:46–56
Madeira M, Lieberman A (1995) Sexual dimorphism in the mammalian limbic system. Prog Neurobiol 45:275–333
Manni A, Pardridge W, Cefalu W, Nisula B, Bardin C, Santner S et al (1985) Bioavailability of albumin-bound testosterone. J Clin Endocrinol Metab 61(4):705
Manning J, Scutt D, Wilson J, Lewis-Jones D (1998) The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone lutenizing hormone and oestrogen. Hum Reprod 13(11):3000–3004
Manning J, Stewart A, Bundred P, Trivers R (2004) Sex and ethnic differences in 2nd to 4th digit ratio of children. Early Hum Dev 80(2):161–168
Marshall A (1890) Principles of economics. Prometheus
Matsumoto AM, Bremner WJ (1984) Modulation of pulsatile gonadotropin secretion by testosterone in man*. J Clinic Endocrinol Metabol 58(4):609–614
Mazur A, Booth A (1998) Testosterone and dominance in men. Behav Brain Sci 21:353–397
McCall C, Singer T (2012) The animal and human neuroendocrinology of social cognition, motivation and behavior. Nat Neurosci 15(5):681–688
McCullough M, Churchland P, Mendez A (2013) Problems with measuring peripheral oxytocin: Can the data on oxytocin and human behavior be trusted? 37:1485–1492
McEwen B (1991) Genomic and non-genomic effects of steroïds on neuronal activity. Trends Pharmacol Sci 12:141–147
McEwan B (2004) Brain-fluid barriers: relevance for theoretical controversies regarding vasopressin and oxytocin memory research. Adv Pharmacol 50:531–592
McEwan B, Sapolsky R (1995) Stress and cognitive function. Curr Opin Neurobiol 5(2):205–216
Mendis-Handagama S (1997) Luteinizing hormone on Leydig cell structure and function. Histol Histopathol 12(3):869–882
Menon M, Jensen J, Vitcu I, Graff-Guerrero A, Crawley A, Smith M (2007) Temporal difference modeling of the blood-oxygen level dependent response during aversive conditioning in humans: effects of dopaminergic modulation. Biol Psychiatry 62:765–772
Midzaka A, Chena H, Papadopoulos V, Zirkina B (2009) Leydig cell aging and the mechanisms of reduced testosterone synthesis. Mol Cell Endocrinol 23:23–31

Mikolajczak M, Gross J, Lane A, Corneille O, de Timary P, Luminet O (2010) Oxytocin makes people trusting. Not Gullible. Psychol Sci 21(8):1072–1074
Miller G, Tybur J, Jordan B (2007) Ovulatory cycle effects on tip earnings by lap dancers: economic evidence for human estrus? Evol Hum Behav 28:375–381
Moore R, Bloom F (1976) Central catecholamine neuron system: anatomy and physiology of the dopamine system. Ann Rev Neurosci 1:129–169
Murphy SE et al. (2009) The role of serotonin in nonnormative risky choice: the effects of tryptophan supplements on the "reflection effect" in healthy adult volunteers. J Cognitive Neurosci 21(9):1709–1719
Nadler A, Jiao P, Johnson C, Alexander V, Zak P (2016) The bull of Wall street: experimental analysis of testosterone and asset trading, under review
Nishizawa S et al (1997) Differences between males and females in rates of serotonin synthesis in human brain. Proc Natl Acad Sci 5308–5313
Pardridge W, Moeller T, Mietus L, Oldendorf W (1980) Blood-brain barrier transport and brain sequestration of steroid hormones. Am J Physiol Endocrinol Metab E96–E102
Pederson C, Prange JA (1979) Induction of maternal behavior in virgin rats after intracerebroventricular administration of oxytocin. PNAS 76(12):6661–6665
Pessiglione M, Seymour B, Flandin G, Dolan R, Frith D (2006) Dopaminedependent prediction errors underpin reward-seeking behaviour in humans. Nature 442:1042–1045
Preuschoff K, Bossaerts P, Quartz S (2006) Neural differentiation of expected reward and risk in human subcortical structures. Neuron 381–390
Putman P, Antypa N, Crysovergi P, van der Does J, Does W (2009) Exogenous cortisol acutely influences motivated decision making in healthy young men. Psychopharmacology 298:257–263
Rapport M, Green A, Page I (1948) Serum vasoconstrictor (serotonin) IV. Isolation and characterization. J Biol Chem 176(3):1243–1251
Reddy DS, Jian K (2010) The testosterone-derived neurosteroid androstanediol is a positive allosteric modulator of GABAA receptors. J Pharmacol Exper Therapeut 334(3):1031–1041
Rilling JK et al. (2012) Effects of intranasal oxytocin and vasopressin on cooperative behavior and associated brain activity in men. Psychoneuroendocrinol 37(4):447–461
Roberti JW (2004) A review of behavioral and biological correlates of sensation seeking. J Res Pers 38(3):256–279
Rogers RD (2011) The roles of dopamine and serotonin in decision making: evidence from pharmacological experiments in humans. Neuropsychopharmacol 36(1):114–132
Ronay R, von Hippel W (2010) The presence of an attractive woman elevates testosterone and physical risk taking in young men. Soc Psychol Pers Sci 1(57):57–64
Rupprecht R, Holsboer F (1999) Neuroactive steroids: mechanisms of action and neuropsychopharmacological perspectives. Trends Neurosci 22(9):410–416
Rydén G, Sjöholm I (1969) Half-life of oxytocin in blood of pregnant and non-pregnant women. Acta Endocrinol 61(3):425–431
Santen R, Bardin C (1973) Episodic analysis, clinical interpretation, physiologic mechanisms. J Clin Invest 52:2617–2628
Santern R, Bardin C (1973) Episodic luteinizing hormone secretion in man. J Clin Investig 52:2617–2628
Sapienza P, Zingales L, Maestripieri D (2009) Gender differences in financial risk aversion and career choices are affected by testosterone. PNAS 106(36):15268–15273
Sapolsky R, Romero M, Munck A (2010) How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev 2(1):55–89
Scarná A, McTavish S, Cowen P, Goodwin G, Rogers R (2005) The effects of a branched chain amino acid mixture supplemented with tryptophan on biochemical indices of neurotransmitter function and decision-making. Psychopharmacology 179:761–768
Schipper BC (2015) Sex Hormones and Competitive Bidding. Manage Sci 61:249–266
Schultz W (1998) Predictive reward signal of dopamine neurons. J Neurophysiol 25(1):236–245

Schultz W (2004) Neural coding of basic reward terms of animal learning theory, game theory, microeconomics and behavioural ecology. Curr Opin Neurobiol 14:139–147
Schwarz S, Pohl P (1992) Steroid hormones and steroid hormone binding globulins in cerebrospinal fluid studied in individuals with intact and with disturbed blood-cerebrospinal fluid barrier. Neuroendocrinology 55(2):174–182
Senior C, Lau A, Butler MJ (2007) The effects of the menstrual cycle on social decision making. Int J Psychophysiol 63(2):186–191
Sevy S, Hassoun Y, Bechara A, Yechiam E, Napolitano B, Burdick K et al (2006) Emotion-based decision-making in healthy subjects: short-term effects of reducing dopamine levels. Psychopharmacology 188:228–235
Shalev II (2011) Vasopressin needs an audience: neuropeptide elicited stress responses are contingent upon perceived social evaluative threats. Horm Behav 60:121–127
Smith V, Suchanek G, Williams A (1988) Bubbles, crashes, and endogenous expectations in experimental spot asset markets. Econometrica 56(6):1119–1151
Stanczyk F, Clarke N (2010) Advantages and challenges of mass spectrometry assays for steroid hormones. J Steroid Biochem Mol Biol 121:491–495
Striepens N et al. (2013) Elevated cerebrospinal fluid and blood concentrations of oxytocin following its intranasal administration in humans. Sci Rep 3:3440
Swerdloff R, Wang C, Cunningham G, Dobs A, Iranmanesh A, Matsumoto A et al (2000) Long-term pharmacokinetics of transdermal testosterone gel in hypogonadal men. J Clin Endocrinol Metab 85(12):4500–4510
Szczypka M, Zhou Q, Palmiter R (1998) Dopamine-stimulated sexual behavior is testosterone dependent in mice. Behav Neurosci 112(5):1229–1235
Takahashi T, Shinada M (2010) Stress hormones predict hyperbolic time-discount rates six months later in adults. Neuro Endocrinol Lett 31(5):616–721
Takahashi T, Sakaguchi K, Oki M, Homma S, Hasegawa T (2006) Testosterone levels and discounting delayed monetary gains and losses in male humans. Neuro Endocrinol Lett 27 (4):439–444
The Concise Encyclopedia of Economics (n.d.) Retrieved 27 Jan 2013, from Library of Economics and Liberty: http://www.econlib.org/library/Enc/bios/Marshall.html
Thilers PP, Macdonald SW, Herlitz A (2006) The association between endogenous free testosterone and cognitive performance: a population-based study in 35 to 90 year-old men and women. Psychoneuroendocrinology 31(5):565–576
Thompson R, Gupta S, Miller K, Mills S, Orr S (2004) The effects of vasopressin on human facial responses related to social communication. Psychoendocrinology 29:35–48
Tobler P, Fiorillio C, Schultz W (2005) Adaptive coding of reward value by dopamine neurons. Science 307(5715):1642–1645
Tuiten A, van Honk J, Koppeschaar H, Bernaards C, Thijssen J, Verbaten R (2000) Time course of effects of testosterone administration on sexual arousal in women. Arch Gen Psychiatry 57:149–153
Uzefovsky F, Shalev I, Israel S, Knafo A, Ebstein R (2012) Vasopressin selectively impairs emotion recognition in men. Psychoneuroendocrinology 37:570–576
van den Bos R, Harteveld M, Stoop H (2009) Stress and decision-making in humans: performance is related to cortisol reactivity, albeit differently in men and women. Psychoneuroendocrinology 34:1449–1458
van Honk J, Peper JS, Schutter DJ (2005) Testosterone reduces unconscious fear but not consciously experienced anxiety: implications for the disorders of fear and anxiety. Biol Psychiatry 58:218–225
van Rooij K et al. (2012) Pharmacokinetics of three doses of sublingual testosterone in healthy premenopausal women. Psychoneuroendocrinol 37(6):773–781
Vercoe M, Zak P (2010) Inductive modeling using causal studies in neuroeconomics: brains on drugs. J Econ Method 2:123–137
Wibral M, Dohmen T, Klingmüller D, Weber B, Falk A (2012) Testosterone administration reduces lying in men. PloS one 7(10):e46774

Wingfield JC, Hegner RE, Dufty AM, Ball GF (1990) The challenge hypothesis: theoretical implications for patterns of testosterone secretion, mating systems, and breeding strategies. Am Nat 829–846

Wood R, Rilling J, Sanfey A, Bhagwager Z, Rogers R (2006) Effects of tryptophan depletion on the performance of an iterated prisoner's dilemma game in healthy adults. Neuropsychopharmacology 31:1075–1084

Yao S, Zhao W (2014) Oxytocin makes females, but not males, less forgiving following betrayal of trust. Int J Neuropsychopharmacol 17:1785–1792

Young L, Wang Z (2004) The neurobiology of pair bonding. Nat Neurosci 7:1048–1054

Young L, Nilsen R, Waymire G, MacGregor G, Insel T (1999) Increased affiliative response to vasopressin in mice expressing the V1a receptor from a monogamous vole. Nature 400:766–768

Youssef F, Dookeeram K (2012) Stress alters personal moral decision making. Psychoneuroendocrinology 37:491–498

Zak P, Matzner W, Matzner W (2004) The neurobiology of trust. Ann NY Acad Sci 1032:224–227

Zak P, Borja K, Matzner W, Kurtzban R (2005a) The neuroeconomics of distrust: sex differences in behavior and physiology. Am Econ Rev Papers Proc 95(2):360–363

Zak PJ, Stanton AA, Ahmadi S (2007) Oxytocin increases generosity in humans. PloS one 2(11): e1128

Zak P (2011) Moral markets. J Econ Behav Organ 77(2):212–233

Zak P (2012) The moral molecule: the source of love and prosperity. Penguin New York

Zak P (2005) Trust: a temporary human attachment facilitated by oxytocin. Behav Brain Sci 28 (3):368–369

Zak P, Kurtzban R, Matzner W (2005b) Oxytocin is associated with human trustworthiness. Horm Behav 48:522–527

Zak P, Kurzban R, Ahmad S, Swerdloff S, Park J (2009) Testosterone administration decreases generosity in the ultimatum game. PLOSone

Zethraeus N et al. (2009) A randomized trial of the effect of estrogen and testosterone on economic behavior. Proc Natl Acad Sci U S A 106(16):6535–6538