

Endocrine State is the Physical Manifestation of Subjective Beliefs^{†‡}

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Abstract

Over the past two decades, economists have begun to incorporate evidence from neuroscience into applied economic research. While some progress has been made, the wider economics profession has yet to embrace the new field of “neuroeconomics.” I argue here that a broad reconciliation of emerging evidence from neuroscience with conventional economic decision theory can be achieved by emphasizing the critical role of neuroendocrine signaling molecules and their receptors. Many of these molecules are amenable to measurement and manipulation in laboratory settings, and most have—when viewed in light of their natural history—a parsimonious interpretation as representing what economists refer to as subjective beliefs.

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1 Introduction

“A major conceptual shift in neuroscience has been wrought by the realization that brain function is modulated by numerous chemicals in addition to classical neurotransmitters. Many of these informational substances are neuropeptides...Their number presently exceeds 50 and most, if not all, alter behaviour and mood states...”

Pert et al. (1985, p820s)

“...endocrine systems were designed to mediate allocation decisions.”

Grebe and Gangestad (2019, p320)

We economists have long prided ourselves on practicing a value-neutral behavioral science, studying human agents who are presumed to know what is best for themselves when making choices in the marketplace. With our axiomatic approach to behavior comes the benefit of never needing to ask what our subjects are thinking; we need merely look for patterns in the data, while testing and refining our theories accordingly.

But what if we *could* read our subjects’ minds?

In recent years, a good deal of effort has been invested in incorporating biomedical technologies (e.g., fMRI brain imaging) into the theory and practice of empirical microeconomics (Camerer et al., 2005; Camerer, 2013; Smith et al., 2014). In principle, if we could get inside our subjects’ heads—if we could, in effect, read their minds—then we might just be able to build a better economic science: one that has at its disposal a more richly detailed and realistic model of human behavior. And while a better positive (descriptive) model of behavior alone would be of great value, it seems likely (to me) that this deeper knowledge of human nature—if achieved—will also speak to nagging questions about the normative implications of human imperfection, for individuals and for markets and for society.

By the standards of the natural sciences, collaborations between economists and neuroscientists have in many instances been wildly successful, as evidenced by a growing number of publications in the world’s most prestigious science journals (Sanfey et al. 2003; Kosfeld et al. 2005; Hsu et al. 2005; Hare et al. 2009, and see this special issue’s papers, e.g., Giannelis et al. 2023; Schipper 2023). But despite these successes—or perhaps because of them—the economics profession at large has not been kind to the field of neuroeconomics, with numerous published critiques expressing overt skepticism (Harrison, 2008; Gul and Pesendorfer, 2008; Bernheim, 2009; Gul and Pesendorfer, 2009; Stanton, 2009; Conlisk, 2011; Nave et al., 2015; Konovalov and Krajbich, 2019).¹ In this paper, I want to suggest that it is not yet time to give up. In particular, I argue that neuroeconomists, by

¹It bears mentioning that in the history of science, those who push the frontiers of knowledge

emphasizing the use of fMRI imaging technology, have mostly been looking in the wrong place. The physical locus of human decision-making, if there is one, surely lies in neuroendocrine signaling molecules.^{2,3}

As the opening quotations above suggest, neuroscientists have known for some time now that the spatial dynamics of blood flow detected by fMRI scanners are only a small part of the story when it comes to the complex biological soup that governs human physiology and behavior. Information is transferred within our neural networks both by electrical impulse (this occurs within individual neurons, the specialized cells that comprise the “wiring” of the nervous system) and by the release, detection, and reuptake of the dozens of specialized molecules neuroscientists refer to as “informational substances” (Schmitt, 1984; Pert et al., 1985; Holmgren and Jensen, 2001).⁴ This latter (extracellular) process facilitates information transfer in the brain both locally (i.e., in the synapses between neurons) and more generally across greater distances, via the body’s system of endocrine hormones.

While fMRI datasets are surely impressive in size and technological achievement, they suffer from a severe limitation in that they measure only the four dimensions of space-time. This is unfortunate because, for instance, activity in a particular brain region has very different implications for behavior when it coincides with a flood of serotonin than it does when instead (or in addition) the same region of the brain is flooded with dopamine or cortisol or oxytocin.⁵ When these molecules are interpreted in light of what is known about their functions in natural history, it becomes apparent that their presence or absence is best interpreted as representing what economists refer to as “information state” or “subjective beliefs” (Smith, 2002; Smith and Tasnádi, 2007; Lee and Smith, 2008; Smith, 2009; Roney, 2016). Moreover, while these molecules cannot (yet) be easily measured with real time imaging technologies, many can be readily measured in blood or saliva, and can be manipulated experimentally by behavioral or pharmaceutical interventions

in ways that challenge the status quo are frequently met with stubborn resistance (Kuhn, 1970). Such resistance is natural and likely often grounded in valid methodological critiques, as new fields typically lack a solid base of methodological consensus.

²To be clear, this claim admittedly stretches the conventional meaning of the phrase “physical locus.” I do not mean to imply that activity *in the human brain* is not of central significance to behavioral science. Rather, as explained below, I would argue that today’s conventional fMRI studies omit the most important dimensions of neural activity (specifically, the n -dimensional mix of signalling molecules at a particular locus in space-time).

³A glossary of selected terms from neuroendocrinology is provided in Table 1.

⁴Indeed, the high dimensionality and spatial ubiquity of neurotransmitters, neuromodulators, and their receptors has led some neuroscientists to suggest that rather than viewing the brain as a metaphorical computer, it is better thought of as “a bag of hormones” (Pert, 1997).

⁵For example, Montoya et al. (2012) review evidence that serotonin appears to block impulsive aggression, but only in the presence of high testosterone and low cortisol.

(Drewnowski et al., 1995; Geddes, 2010; Zilioli and Watson, 2012; Smyth et al., 2013).⁶

This paper proceeds as follows: Section 2 briefly describes the essential properties of ligand-receptor systems, Section 3 explains how and why endocrine state can be interpreted as representing subjective beliefs when viewed in evolutionary perspective, Section 4 explains how evolution uses hormones to generate complex and context-specific social behavior, Section 5 discusses the concept of evolutionary mismatch within the broader context of dual-process theories in psychology and philosophy, and Section 6 concludes.

2 Ligand-Receptor Systems

Ligand-receptor systems are essential to life. Even single-celled organisms rely on biochemical signaling within the cell to communicate information about the external environment (e.g., pH) and the internal environment (e.g., nutritional status). A *ligand* is a molecule (hormone, peptide, neurotransmitter, etc.)⁷ whose presence in bodily fluid can be specifically detected by a *receptor* (often embedded in a cell wall), typically triggering a cellular response that allows the organism to respond in a way that is appropriate to the situation. The metaphor every young medical student learns is that receptors and ligands are the locks and keys of biological systems, respectively (Helm et al., 1991).

In humans, the existence of the endocrine system—in which endocrine organs secrete hormones into the bloodstream in response to physiological or contextual cues—has long been known. For instance, when one experiences an episode of high blood sugar, the pancreas (sensing this via receptors sensitive to blood sugar) responds by secreting insulin into the bloodstream, which is detected by receptors throughout the body, triggering a cascade of physiological, behavioral, and psychological responses (diversion of sugar to storage as glycogen or body fat, thermogenesis and suppression of appetite via interaction with satiety hormones, etc.) that serve the collective function of bringing blood sugar back down into the normal range (Maratos-Flier, 2013).

It is now well-understood that hormones like insulin are also produced, secreted, detected, and subsequently depleted or removed, all within the human brain (Pert et al., 1985). This happens at a pace and with such dramatic effect

⁶Of course, more invasive methods have been used in animal studies, for instance the measurement of single-neuron activity in studies with monkeys (Long et al., 2009; Tanaka et al., 2019; Stein, 2022).

⁷In what follows I follow the widespread convention of using the term “hormone” to refer generally to ligands, while acknowledging this word is sometimes taken to refer specifically to sex hormones such as testosterone and progesterone. A Venn diagram of various categories of ligand is given in Figure 1.

that hormones have been called “the biological substrate of emotion” and thus can be considered key drivers of behavior (Pert et al., 1985, p820s). Human emotions (broadly defined), in turn, have a natural interpretation as products of our evolutionary history (Frank, 1988; Pert, 1988; Al-Shawaf et al., 2016).

3 Decision Theory in Evolutionary Perspective

Hormones typically have multiple simultaneous effects distributed throughout the brain and body, and are elicited by specific circumstances or situations. The reliable coincidence of these causes and effects naturally lends itself to the generation of testable hypotheses about the adaptive function of a given hormone in the evolutionary history of the species (Smith, 2009; Roney, 2016; Grebe and Gangestad, 2019). For instance: insulin, discussed above, is secreted in response to elevated blood sugar after consuming a carbohydrate-rich meal, but it is also secreted when one *anticipates* a meal (Power and Schulkin, 2011), along with a host of other hormones that prepare the body for digestion. It is not difficult to piece the evidence together to understand the adaptive function of insulin in evolutionary history: it generally occurs in response to circumstances in which active reduction of blood sugar levels is a sensible course of action.

Importantly (for economists), the physiological effects induced by insulin and related hormones are in concordance with the *behavioral* effects (i.e., on appetite and feeding). Interpreted in light of subjective decision theory—in which both subjective *values* (i.e., utilities) assigned to uncertain outcomes and subjective *beliefs* about the likelihood of those outcomes occurring are implicit in one’s choice behavior (Savage, 1954)—a decision theorist might conclude that individuals with elevated insulin levels (and hence decreased appetite for carbohydrate) either momentarily assign lower utility to the consequences of carbohydrate-rich food consumption or harbor a belief that the positive outcomes associated with consuming carbohydrate-rich foods are less likely at this particular moment. In principle, according to subjective expected utility theory, sufficient observation (in which values and probabilities are allowed to vary independently) would allow behavioral scientists to distinguish between the two empirically. Before we can proceed to such empirical tests, however, it is essential to clearly define the essential elements of the decision environment: The *prize space* (outcomes our decision-maker cares about), the *state space* (a list of states of the world), and the *action space* (choices our decision-maker has available, each of which maps to a probabilistic distribution of outcomes across states). For economic theorists, the specification of these elements is arbitrary (in the sense that any given action can be justified by many different combinations of utilities and beliefs), though in practice it is often assumed that objective (“correct”) measures of probability apply, and that the

prize space consists of commodities available for purchase in the marketplace. In any event, the theorist’s specification of these elements of the decision environment generates testable hypotheses subject to empirical falsification.

For the behavioral ecologist, specifying the elements of a decision environment in subjective decision theory is equivalent to identifying the *adaptive problem* ostensibly solved by the behavioral phenomenon in question: that is to say, specifying the circumstances in the evolutionary history of the species in which the behavior in question would have served to maximize expected Darwinian fitness (i.e., survival and reproduction) or some proximate currency thereof. This problem specification is significantly more constrained than that faced by the economic decision theorist, in that it must be consistent with evidence from the natural sciences: the state space must reflect regularities present in the environment in which the species evolved, and the relevant prize space should plausibly relate to fitness cost-benefit trade-offs. Moreover, the sources of empirical validation of a given theory are more diverse in the biological world: a given adaptive problem generates not just predictions about within-species behavioral regularities in particular situations or environments, but also predictions about variation across species and across the lifespan, as well as the likelihood of *evolutionary mismatch*: maladaptive behavior in evolutionarily novel situations (Smith, 2015b).

In the case of insulin, for example, there is evidence from the medical literature that blood sugar levels outside a narrow window can be life-threatening, making homeostatic control a critical adaptive problem. In the modern world, the presence of abundant but evolutionarily novel processed carbohydrates appears to have caused widespread dysfunction in this system, as evidenced by the global epidemics of insulin resistance and diabetes (Diamond, 2003; Smith, 2012; Unnikrishnan et al., 2017).

4 Hormones and the Evolution of Complex Social Behavior

Hormones can be understood to represent subjective beliefs because they evolved to coordinate optimal (behavioral and physiological) responses to specific situations or contexts. Figure 2 sketches a rough schematic of the process, using the peptide hormone oxytocin to illustrate. Oxytocin is thought to have originated in mammals as the hormone responsible for governing maternal care of offspring, and then later co-opted to govern other related social behaviors. Oxytocin is secreted during childbirth and can be used to medically induce labor; for a nursing mother, the sound of a crying baby can induce oxytocin secretion, which causes an increase in milk production. Oxytocin also apparently plays a role in pair-bonding between

sexual partners (e.g., with oxytocin being secreted during orgasm), but there are also contradictory reports, for example of oxytocin levels rising during relationship distress. Grebe and Gangestad (2019) refer to this as the “oxytocin paradox” and suggest the following resolution: oxytocin appears to act selectively, guiding behavior first in ways that protect and nurture one’s infant, and secondarily (in behaviors likely acquired later in prehuman evolutionary history) toward support and care of others within the kin or community group. In other words, oxytocin has distinct effects on behavior depending on social context, including potentially non-prosocial or even aggressive responses toward third parties that represent threats to those with whom one shares close relationships.

No social scientist can invoke evolutionary reasoning to explain human behavior without being accused of telling “just so” stories not susceptible to empirical falsification. But what those hurling these epithets are really saying is that they cannot be bothered to read the literature. The oxytocin story sketched above has been pieced together from an impressive array of evidence: *incidence* of oxytocin across species, the *eliciting conditions* or cues that cause oxytocin to be released into the brain or bloodstream, knowledge of important *adaptive problems*—coinciding with the eliciting conditions—faced by the species in its natural environment, and effect of *exogenous manipulation* of the hormone or its receptor (e.g., via pharmaceutical, genetic, or behavioral intervention) on behavior and physiology. The beauty—and bane—of this naturalistic perspective is that *if* (and only if) your theory is correct, it will bind all this evidence from across the disciplines into a coherent whole.

Biologists refer to the branch of theoretical biology that pieces together the story of how complex behavior arose as *life history theory*.⁸ Grebe and Gangestad (2019, p319) introduce life history theory as follows:

“Energy allocated to one kind of activity is not available for allocation to other kinds...Other limited resources such as micronutrient building blocks, time, and neural or other tissue-specific resources also give rise to allocation problems. Life history theory seeks to identify how selection shapes organisms’ solutions to these allocation problems.

In the language of economics, life history theory suggests that natural selection favors individuals who can identify and solve context-specific constrained optimization problems, without need for conscious contemplation. Endocrine signals make this possible. The eliciting conditions that stimulate hormone release serve as an informative cue, and the hormone itself ensures an optimal re-allocation of resources to the task at hand.

⁸Note that this field is distinct from the life-cycle theory of consumption widely used in economics (Modigliani and Brumberg, 1954).

There is a tendency in behavioral endocrinology—and especially in press reports of new findings—to seek to identify the central function of a given hormone, for example by dubbing oxytocin the “cuddle hormone” or the “trust hormone” (Roney, 2016). A more nuanced life history perspective on this particular molecule should reflect the various context-specific costs and benefits required to maintain and protect social networks in the preindustrial world in which humans evolved. In the modern world, it seems likely that these human tendencies are what make us susceptible to much of the attention-grabbing imagery that makes social media so alluring, and perhaps also to political tribalism in the presence of concerns about terrorism or war or infectious disease.

While oxytocin has received a great deal of attention in recent years, the evidence summarized above should not be taken to imply that other hormones play no role in human social interactions. Machin and Dunbar (2011), for example, argue that the endogenous opioid system plays a key role in social attachment. But opioid-like hormones appear to predate social behavior (possibly dating all the way back to single-celled organisms, and as a result the many functions of this family of hormones today is thought to be quite diverse (Dyakonova, 2001). Interestingly, among the known early functions of endogenous opioids was the regulation of feeding behavior. Smith and Tasnádi (2007) suggest that in modern humans, the opioids play a key role in the identification and consumption of safe and nutritious foods, and among the apparent eliciting conditions they list are social cues. It is not difficult to envision a time in the distant past in which food sharing became important for early primates, and the related adaptive functions of opioids (previously useful in, say, recalling the presence of specific tastes or locations of valued foods) subsequently being co-opted for use in social attachment. Discussions of this sort are necessarily speculative at the outset, but if behavioral scientists are to gain a fuller understanding of the “message being sent” by a given hormone, speculative statements are a necessary first step. I offer just a few in Table 2.

It is important to note that the economist’s phrase “subjective beliefs” (inspired by Savage’s 1954 theory of “personalistic probabilities”) reflects a shortcoming of language. Savage’s elegant theory attempted to overcome the fact that when people make decisions under conditions of uncertainty, they will—contrary to what previous theories of expected utility seemed to assume—typically be unable to state the probabilities involved. Savage showed that being able to make decisions is enough: as noted above, the decision-maker’s “beliefs” about the nature of the uncertainty he faced would necessarily be implicit in the decisions he made. This is important here because if we are to interpret endocrine state as representing information or beliefs, there is no reason to expect our human subjects to be consciously aware of these “beliefs.” This is a widely understood phenomenon

among evolutionary psychologists, and it is not difficult to test empirically. For instance, Brunnlieb et al. (2016) find that in a randomized trial in which subjects were given exogenous vasopressin (a neuropeptide similar in structure to oxytocin) and asked to play the stag hunt game while in an fMRI scanner, vasopressin induced significant changes in both behavior and brain activity, with subjects more likely to engage in “risky cooperation” following vasopressin administration. When subjects were quizzed (again, under the influence of vasopressin or a placebo) about their attitudes toward social cooperation, however, no difference between the two groups was observed.

5 Evolutionary Mismatch: A Dual-Process Theory with Normative Implications

There is an age-old temptation, dating back to the great philosophers, to divide the human psyche in two: the body and the soul, the rational and the emotional, the fast and the slow. These duality or dual-process theories—collectively dubbed “Descartes’ Error” by neuroscientist Antonio Damasio (1994), whose theory of ubiquitous “somatic markers” seems an apt description the endocrine system (Smith, 2015a)—have not been as successful as one might hope in generating an empirically useful theory of human behavior (Grayot, 2020).

If there is a meaningful dividing line between “rational” and “irrational,” I believe it lies in the concept of evolutionary mismatch: the notion that a given behavior can be labeled maladaptive because it plausibly reflects a behavioral strategy that is mis-applied in the modern world. The relevant rationality concept in this view is *ecological rationality*, which is defined as a concurrence of behavioral strategy with the decision environment (Berg and Gigerenzer, 2010; Todd and Gigerenzer, 2012). It has been suggested that many (perhaps even all) of the “behavioral anomalies” that are the subject of much of the field of behavioral economics are most parsimoniously explained as resulting from mismatch (Friedman, 1998; Smith, 2004).⁹

When the human tongue comes into contact with simple sugars, for instance, the sugar receptors in our tongues send signals to our brains, where endogenous opioids are released and short-term feeding behavior is stimulated, while the dopaminergic system is also activated, increasing the chances that the food item at hand becomes a habit, incorporated into our regular diet (Smith and Tasnádi, 2007).

⁹This is not to say that humans exhibited perfect “rationality” in the pre-industrial world, in the sense that they operated without constraints on available information or cognitive capacity. But on average, in that world, we might reasonably expect that natural selection favored decisions that maximised expected fitness for the individuals making them.

In the pre-industrial world, sugar was only to be found in ripe fruit, raw honey, and mother’s milk: it was a perfectly reliable indicator of the presence of valuable micronutrients, and the adaptive thing to do was to seek out foods containing it. In the modern world, our predilection for sugar remains with us despite the fact that—thanks to modern food processing technologies—it no longer carries the informational signaling value it once did. In subjective decision theory, this implies that we are behaving *as if* the outcome we care about is good nutrition and long-term health, and consuming sweet foods improves the odds of achieving this objective.

A simple model that captures the situation described above might assume—for an individual confronted with a novel food item—the binary prize space {healthy, unhealthy}, the binary action space {eat, don’t eat}, and a state space characterized by the conditional probabilities $P(\text{healthy}|\text{eat})$ and $P(\text{healthy}|\text{don’t eat})$. Given that evolution would favor healthy individuals over unhealthy (i.e., $u(\text{healthy}) > u(\text{unhealthy})$), the item will be eaten whenever subjective beliefs are such that $P(\text{healthy}|\text{eat}) > P(\text{healthy}|\text{don’t eat})$. The physical manifestation of this subjective belief is an elevated level of endogenous opioids in the brain.

It is understandable that economic theorists have long been reluctant to write down models in which decision-makers harbor persistent false beliefs: doing so would seem an arbitrary—even lazy—shortcut, one that has the potential to undermine the powerful appeal of our normative (axiomatic) theories. Instead, various quirks of human nature that seem “irrational” have been modeled descriptively as trade-offs between health and pleasure (Grossman, 1972; Becker and Murphy, 1988), or as dynamic inconsistencies that generate self-control problems (Laibson, 1997), or as sensitivity to the presence of cues (Bernheim and Rangel, 2004) or emotional states (Loewenstein, 2000). But the evidence for mismatch—including its implication of false subjective beliefs—is overwhelming, and cannot be denied. In the case of the modern diet, it is clear we systematically fail to make healthy choices because our subjective beliefs are calibrated to a world long past (Smith, 2004). There is no more-parsimonious explanation.

The mismatch problem is not limited to the problem of dietary choice. For most of human evolutionary history, “economic” decisions were rooted in social exchange. Humans are thought to have lived in groups no larger than 150 or so individuals for most of their evolutionary history (Hill and Dunbar, 2003). Biologists tell us that human altruism evolved for purely instrumental purposes: to promote the Darwinian fitness of one’s kin and to facilitate reciprocal exchange with in-group members (Kurzban et al., 2015). But in that “small world” of the past, a randomly encountered stranger would be far more likely to be related, and far more likely to be encountered again (to return a favor) than in today’s modern world. If we accept the biologists’ assertion that pure altruism is not part of

human nature, then evidence of such (e.g., tipping in a restaurant in a distant city you will never visit again) could be interpreted as the product of false subjective beliefs. The same is true of the “dark side” of altruism—spite and vengeance—and the human tendency to categorize others as out-group members on the basis of relatively meaningless cues such as skin color or manner of speech. If human social behavior is indeed the product of a finely tuned context-specific neuroendocrine system shaped by evolutionary history, we should expect it to occasionally misfire in today’s anonymous marketplaces.

Human imperfection is real, and almost certainly has its roots in the discordance between the modern world and our evolutionary past. The good news is that there is a simple way to model evolutionary mismatch, and neuroscience provides new means of empirical validation.

6 Conclusion

It may not (yet) be feasible to obtain detailed real-time data on the spatial dynamics of the hormonal soup that governs the human brain (Ganesana et al., 2017). But there do exist established methods for measuring and manipulating the activity of ligands in human subjects: Testosterone and cortisol, for example, are easily measured in saliva (Dabbs, 1990; Levine et al., 2007; Smyth et al., 2013) and can be manipulated experimentally via behavioral interventions (Birkett, 2011; Apicella et al., 2014). The activity of endogenous opioids can be stimulated by giving subjects a taste of sugar, or blocked by administering the drug naltrexone (an opioid antagonist, which when given to human subjects reportedly makes foods taste less palatable (Yeomans and Gray, 1996)). These are methods economists can employ in experimental labs at reasonably low cost, without need for expensive and cumbersome neural imaging machines.

Imagine, in your role as an experimental economist, having the ability to measure and manipulate (albeit in a limited manner) subjective beliefs. In principle, any measure of subjective beliefs—again, as this phrase is used by economic decision theorists—can instead, given sufficient observation, be inferred from observed behavior. But in practice, any finite set of observations can be explained by an infinite number of theoretical models. Knowledge of endocrine state (interpreted as the physical manifestation of subjective beliefs)—together with knowledge of the natural history of the molecule(s) in question—narrows the field of plausible explanations. Moreover, an evolutionary perspective generates specific testable hypotheses. Consider, for example, an experimenter offering his subjects a choice between a small but immediate cash payment and a larger payment delayed by several weeks. In a context of social exchange, the primary determinant of choice in such a situation is likely to be the extent to which the subject trusts the ex-

perimeter (or perhaps the institution she represents) to in fact deliver the future payment. Our knowledge of the natural history of social exchange also suggests important determinants of trust (e.g., a personal history of reciprocal sharing of food or other social support) as well as a number of candidate molecules (oxytocin? serotonin?) that might represent bonds of trust and friendship. Endocrine state interpreted as subjective beliefs can serve as an anchor but also as a powerful weapon in deciphering the many mysteries of human behavior.

Economists should not live in fear of brains. Our abstract theorizing about preference orderings and subjective beliefs has come to life. The richly descriptive theory of human behavior we have sought is at our fingertips, and a clear and specific vision of human frailty is not far behind.

References

- Al-Shawaf, L., Conroy-Beam, D., Asao, K., and Buss, D. M. (2016). Human emotions: An evolutionary psychological perspective. *Emotion Review*, 8(2):173–186.
- Apicella, C. L., Dreber, A., and Mollerstrom, J. (2014). Salivary testosterone change following monetary wins and losses predicts future financial risk-taking. *Psychoneuroendocrinology*, 39.
- Becker, G. S. and Murphy, K. M. (1988). A theory of rational addiction. *Journal of Political Economy*, 96(4):675–700.
- Berg, N. and Gigerenzer, G. (2010). As-if behavioral economics: Neoclassical economics in disguise? *History of Economic Ideas*, pages 133–165.
- Bernheim, B. D. (2009). On the potential of neuroeconomics: A critical (but hopeful) appraisal. *American Economic Journal: Microeconomics*, 1(2):1–41.
- Bernheim, B. D. and Rangel, A. (2004). Addiction and cue-triggered decision processes. *American economic review*, 94(5):1558–1590.
- Birkett, M. A. (2011). The trier social stress test protocol for inducing psychological stress. *J. Vis. Exp.*, 56:e3238.
- Brunnlieb, C., Nave, G., Camerer, C. F., Schosser, S., Vogt, B., Münte, T. F., and Heldmann, M. (2016). Vasopressin increases human risky cooperative behavior. *Proceedings of the National Academy of Sciences*, 113(8):2051–2056.

- Camerer, C., Loewenstein, G., and Prelec, D. (2005). Neuroeconomics: How neuroscience can inform economics. *Journal of Economic Literature*, 43(1):9–64.
- Camerer, C. F. (2013). Goals, methods, and progress in neuroeconomics. *Annu. Rev. Econ.*, 5(1):425–455.
- Conlisk, J. (2011). Professor zak’s empirical studies on trust and oxytocin. *Journal of Economic Behavior & Organization*, 78(1-2):160–166.
- Dabbs, J. M. (1990). Salivary testosterone measurements: Reliability across hours, days, and weeks. *Physiology and Behavior*, 48(1):83–86.
- Damasio, A. (1994). *Descartes’ Error*. G.P. Putnam’s Sons, New York.
- De Meyts, P. (2004). Insulin and its receptor: structure, function and evolution. *Bioessays*, 26(12):1351–1362.
- Diamond, J. M. (2003). The double puzzle of diabetes. *Nature*, 423(6940):599–602.
- Drewnowski, A., Krahm, D. D., Demitrack, M. A., Nairn, K., and Gosnell, B. A. (1995). Naloxone, an opiate blocker, reduces the consumption of sweet high-fat foods in obese and lean female binge eaters. *The American journal of clinical nutrition*, 61(6):1206–1212.
- Dyakonova, V. (2001). Role of opioid peptides in behavior of invertebrates. *Journal of Evolutionary Biochemistry and Physiology*, 37(4):335–347.
- Frank, R. H. (1988). *Passions Within Reason: The Strategic Role of the Emotions*. W.W. Norton.
- Friedman, D. (1998). Monty hall’s three doors: Construction and deconstruction of a choice anomaly. *The American Economic Review*, 88(4):933–946.
- Ganesana, M., Lee, S. T., Wang, Y., and Venton, B. J. (2017). Analytical techniques in neuroscience: Recent advances in imaging, separation, and electrochemical methods. *Analytical chemistry*, 89(1).
- Geddes, L. (2010). My wedding was a science experiment. *New Scientist*, 205(2747):32–35.
- Giannelis, A. (in press). The association between saving disposition and financial distress: A genetically informed approach.
- Grayot, J. D. (2020). Dual process theories in behavioral economics and neuroeconomics: a critical review. *Review of Philosophy and Psychology*, 11(1):105–136.

- Grebe, N. M. and Gangestad, S. W. (2019). Oxytocin: An evolutionary framework. *The Oxford Handbook of Evolutionary Psychology and Behavioral Endocrinology*, page 317.
- Grossman, M. (1972). The demand for health: A theoretical and empirical investigation. Technical report, National Bureau of Economic Research.
- Gul, F. and Pesendorfer, W. (2008). The case for mindless economics. *The foundations of positive and normative economics: A handbook*, 1:3–42.
- Gul, F. and Pesendorfer, W. (2009). A comment on Bernheim’s appraisal of neuroeconomics. *American Economic Journal: Microeconomics*, 1(2):42–47.
- Hare, T. A., Camerer, C. F., and Rangel, A. (2009). Self-control in decision-making involves modulation of the vmPFC valuation system. *Science*, 324(5927):646–648.
- Harrison, G. W. (2008). Neuroeconomics: A critical reconsideration. *Economics & Philosophy*, 24(3):303–344.
- Hau, M. (2007). Regulation of male traits by testosterone: implications for the evolution of vertebrate life histories. *BioEssays*, 29(2):133–144.
- Helm, C. A., Knoll, W., and Israelachvili, J. N. (1991). Measurement of ligand-receptor interactions. *Proceedings of the National Academy of Sciences*, 88(18):8169–8173.
- Hill, R. A. and Dunbar, R. I. (2003). Social network size in humans. *Human nature*, 14(1):53–72.
- Holmgren, S. and Jensen, J. (2001). Evolution of vertebrate neuropeptides. *Brain research bulletin*, 55(6):723–735.
- Hsu, M., Bhatt, M., Adolphs, R., Tranel, D., and Camerer, C. F. (2005). Neural systems responding to degrees of uncertainty in human decision-making. *Science*, 310(5754):1680–1683.
- Kiser, D., Steimer, S. B., Branchi, I., and Homberg, J. R. (2012). The reciprocal interaction between serotonin and social behaviour. *Neuroscience & Biobehavioral Reviews*, 36(2):786–798.
- Konovalov, A. and Krajbich, I. (2019). Over a decade of neuroeconomics: What have we learned? *Organizational Research Methods*, 22(1):148–173.
- Kosfeld, M., Heinrichs, M., Zak, P. J., Fischbacher, U., and Fehr, E. (2005). Oxytocin increases trust in humans. *Nature*, 435(7042):673–676.

- Kuhn, T. S. (1970). *The structure of scientific revolutions*, volume 111. Chicago University of Chicago Press.
- Kurzban, R., Burton-Chellew, M. N., and West, S. A. (2015). The evolution of altruism in humans. *Annual review of psychology*, 66:575–599.
- Laibson, D. (1997). Golden eggs and hyperbolic discounting. *Quarterly Journal of Economics*, 112(2):443–477.
- Lee, Y. H. and Smith, T. G. (2008). Why are Americans addicted to baseball? An empirical analysis of fandom in Korea and the United States. *Contemporary Economic Policy*, 26(1):32–48.
- Levine, A., Zagoory-Sharon, O., Feldman, R., Lewis, J. G., and Weller, A. (2007). Measuring cortisol in human psychobiological studies. *Physiology and Behavior*, 90(1):43–53.
- Loewenstein, G. (2000). Emotions in economic theory and economic behavior. *American economic review*, 90(2):426–432.
- Long, A. B., Kuhn, C. M., and Platt, M. L. (2009). Serotonin shapes risky decision making in monkeys. *Social cognitive and affective neuroscience*, 4(4):346–356.
- Machin, A. J. and Dunbar, R. I. (2011). The brain opioid theory of social attachment: a review of the evidence. *Behaviour*, 148(9-10):985–1025.
- Maratos-Flier, E. (2013). Appetite regulation and thermogenesis. *Endocrinology Adult and Pediatric: Diabetes Mellitus and Obesity E-Book*, 1.
- Modigliani, F. and Brumberg, R. (1954). Utility analysis and the consumption function: an interpretation of cross-section data. In Kurihara, K., editor, *Post-Keynesian Economics*, pages 829–844. Rutgers University Press.
- Montoya, E. R., Terburg, D., Bos, P. A., and Van Honk, J. (2012). Testosterone, cortisol, and serotonin as key regulators of social aggression: A review and theoretical perspective. *Motivation and emotion*, 36(1):65–73.
- Nave, G., Camerer, C., and McCullough, M. (2015). Does oxytocin increase trust in humans? a critical review of research. *Perspectives on Psychological Science*, 10(6):772–789.
- Pert, C. (1988). The wisdom of the receptors: Neuropeptides, the emotions, and bodymind. *Advances in Mind Body Medicine*, 8(8):8–16.

- Pert, C., Ruff, M., Weber, R., and Herkenham, M. (1985). Neuropeptides and their receptors: a psychosomatic network. *The Journal of Immunology*, 135(2):820–826.
- Pert, C. B. (1997). *Molecules of emotion: Why you feel the way you feel*. Simon and Schuster.
- Power, M. L. and Schulkin, J. (2011). Anticipatory physiological regulation in feeding biology. In *Handbook of Behavior, Food and Nutrition*, pages 829–844. Springer.
- Roney, J. R. (2016). Theoretical frameworks for human behavioral endocrinology. *Hormones and behavior*, 84:97–110.
- Sanfey, A. G., Rilling, J. K., Aronson, J. A., Nystrom, L. E., and Cohen, J. D. (2003). The neural basis of economic decision-making in the ultimatum game. *Science*, 300(5626):1755–1758. PMID: 12805551.
- Sapolsky, R. M., Romero, L. M., and Munck, A. U. (2000). How do glucocorticoids influence stress responses? integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine reviews*, 21(1):55–89.
- Savage, L. J. (1954). *The Foundations of Statistics*. John Wiley & Sons.
- Schipper, B. C. (in press). Sex hormones and choice under risk. *Journal of Economic Psychology*.
- Schmitt, F. O. (1984). Molecular regulators of brain function: a new view. *Neuroscience*, 13(4):991–1001.
- Schultz, W. (2016). Dopamine reward prediction-error signalling: a two-component response. *Nature reviews neuroscience*, 17(3):183–195.
- Smith, A., Bernheim, B. D., Camerer, C. F., and Rangel, A. (2014). Neural activity reveals preferences without choices. *American Economic Journal: Microeconomics*, 6(2):1–36.
- Smith, T. G. (2002). *Toward a Unified Theory of Choice: Case Studies in Dietary Preference*. Doctoral Thesis, University of California, Santa Barbara.
- Smith, T. G. (2004). The McDonald’s equilibrium: Advertising, empty calories, and the endogenous determination of dietary preferences. *Social Choice and Welfare*, 23(3):383–413.

- Smith, T. G. (2009). Reconciling psychology with economics: Obesity, behavioral biology, and rational overeating. *Journal of Bioeconomics*, 11(3):249–282.
- Smith, T. G. (2012). Economic stressors and the demand for ‘fattening’ foods. *American Journal of Agricultural Economics*, 94(2):324–330.
- Smith, T. G. (2015a). Decartes’ error and the emotional brain. In Altman, M., editor, *Real-World Decision Making: An Encyclopedia of Behavioral Economics*, pages 88–89. ABC-CLIO.
- Smith, T. G. (2015b). Evolutionary mismatch. In Altman, M., editor, *Real-World Decision Making: An Encyclopedia of Behavioral Economics*, pages 132–133. ABC-CLIO.
- Smith, T. G. and Tasnádi, A. (2007). A theory of natural addiction. *Games and Economic Behavior*, 59:316–344.
- Smyth, N., Hucklebridge, F., Thorn, L., Evans, P., and Clow, A. (2013). Salivary cortisol as a biomarker in social science research. *Social and Personality Psychology Compass*, 7(9):605–625.
- Stanton, A. A. (2009). Neuroeconomics: A critique of ‘Neuroeconomics: A critical reconsideration’. *Revue française d’économie*, 23(4).
- Stein, A. M. (2022). *Serotonin-dependent Modulation of Working Memory and Decision Activity in Primate Prefrontal Cortex*. PhD thesis, Universität Tübingen.
- Tanaka, S., O’Doherty, J. P., and Sakagami, M. (2019). The cost of obtaining rewards enhances the reward prediction error signal of midbrain dopamine neurons. *Nature communications*, 10(1):3674.
- Todd, P. M. and Gigerenzer, G. E. (2012). *Ecological rationality: Intelligence in the world*. Oxford University Press.
- Unnikrishnan, R., Pradeepa, R., Joshi, S. R., and Mohan, V. (2017). Type 2 diabetes: demystifying the global epidemic. *Diabetes*, 66(6):1432–1442.
- Vera, F., Zenuto, R., and Antenucci, C. D. (2017). Expanding the actions of cortisol and corticosterone in wild vertebrates: A necessary step to overcome the emerging challenges. *General and comparative endocrinology*, 246:337–353.
- Waeltl, P., Dickinson, A., and Schultz, W. (2001). Dopamine responses comply with basic assumptions of formal learning theory. *Nature*, 412:43–48.

- Yeomans, M. R. and Gray, R. W. (1996). Selective effects of naltrexone on food pleasantness and intake. *Physiology and Behavior*, 60(2):439–446.
- Zilioli, S. and Watson, N. V. (2012). The hidden dimensions of the competition effect: Basal cortisol and basal testosterone jointly predict changes in salivary testosterone after social victory in men. *Psychoneuroendocrinology*, 37(11):1855–1865.

Table 1: Glossary of selected terms from neuroendocrinology

antagonist	A drug or other chemical substance that blocks the action of a particular hormone, for example by binding to (but not activating) the target receptor.
blood-brain barrier	A physical barrier preventing the passage of most ions and large-molecular weight compounds from the blood to brain tissue. Many hormones are unable to pass through the barrier, or pass only in small and tightly regulated amounts. For this reason it is often important to distinguish between central (brain) and peripheral (bloodstream) concentrations of a given hormone, as the same hormone could (in theory) have markedly different effects depending on the location in which it occurs.
endocrine system	The system of glands and other structures that—in specific situations—produce hormones that are released directly into the circulatory system, influencing metabolism, behavior, and other biological processes.
ligand	A general term for any molecule that is recognized by a receptor.
monoamine	A class of hormones or neurotransmitters that are derived from a single amino acid. Examples include dopamine, epinephrine, norepinephrine, serotonin, and melatonin.
neuron	Any of the impulse-conducting cells that constitute the brain, spinal column, and nerves in vertebrates. Also called a nerve cell.
neuromodulator	A hormone that affects information processing in the brain indirectly, by altering (“modulating”) the local response of neurons to neurotransmitters. This is one mechanism by which hormone-hormone interactions may take effect.
neuropeptide	Any of a variety of peptides found in neural tissue.
neurotransmitter	A molecule in the brain (or peripheral nervous system) that acts as a ligand, transmitting messages across the synapse between neurons.
peptide	Any of a group of compounds consisting of two or more amino acids linked by chemical bonding. Peptides are the building blocks of protein. Examples of peptide hormones include beta-endorphin, insulin, leptin, and oxytocin.
receptor	A molecular structure on the surface of a cell or within a cell that recognizes and binds with a specific ligand, producing some effect on the cell.
steroid hormone	Any of a class of fat-soluble hormones that includes the sex hormones and the corticosteroids (or “stress hormones”). Examples of steroid hormones include testosterone, estradiol, progesterone, and cortisol.
synapse	The gap or space between the two neurons or between a neuron and a target organ, where neural impulses are transmitted by chemical means. An electrical impulse in the sending neuron causes the release of a neurotransmitter into the synapse, where it can be detected by receptors in the target.

Note: adapted from <https://medical-dictionary.thefreedictionary.com/>, accessed 4 January 2023

Table 2: Examples of Postulated Hormonal “Information States”

Hormone	Relevant Adaptive Problem	Contextual Cues	Information State	References
cortisol	“fight or flight” response	presence of immediate threat to health or well-being	“prepare for physical exertion” “social abuse likely”	Sapolsky et al. (2000), Vera et al. (2017)
dopamine	associative learning	novel situations of significance	“remember this place, you’ll want to come back”	Waeltl et al. (2001), Schultz (2016)
insulin	blood sugar regulation	blood sugar levels outside normal range, anticipation of a carbohydrate-rich meal, urgent need for energetic exertion	“blood sugar is too high”	De Meyts (2004)
leptin	maintenance of body fat depots	body fat stores outside normal range	“you have sufficient fat stores, no need for more”	Smith (2009)
opioids	identification of nutritionally valuable food sources	social food cues, presence of basic tastes (sugar/salt etc.), postingestive experience	“this food is nutritious/scarse, eat more now,” “avoid this food, it is likely to make you ill”	Dyakonova (2001), Smith (2004), Smith and Tasnádi (2007)
oxytocin	original: formation of mother-infant bond; co-opted: classification of others as kin, friend, foe	childbirth, nursing, social touching, coalitional behavior	“shower love upon this person,” “this person threatens my kin”	Grebe and Gangestad (2019)
serotonin	social status/social dominance	presence of supportive friends/kin	“be happy, don’t worry, your future is secure”	Smith (2009), Kiser et al. (2012)
testosterone	competition in the context of mating	competitive environments, especially those involving athletic performance	“in a fight, I would win”	Hau (2007), Lee and Smith (2008)

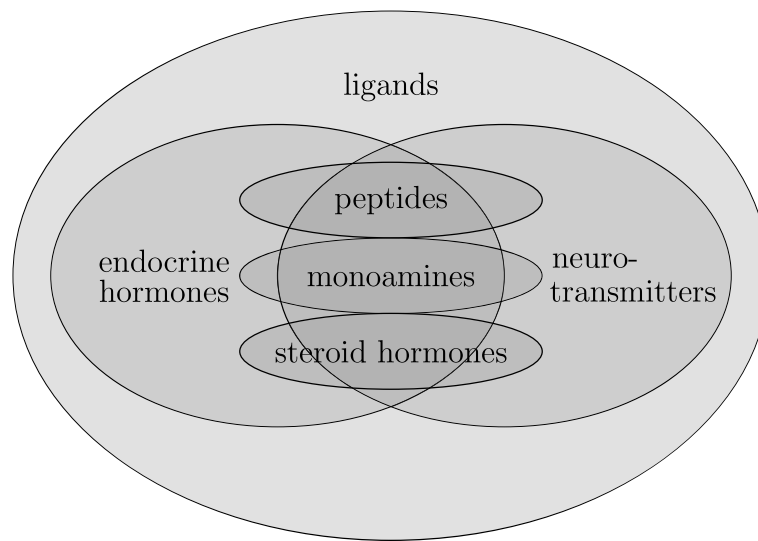


Figure 1: Selected Categories of Signalling Molecules

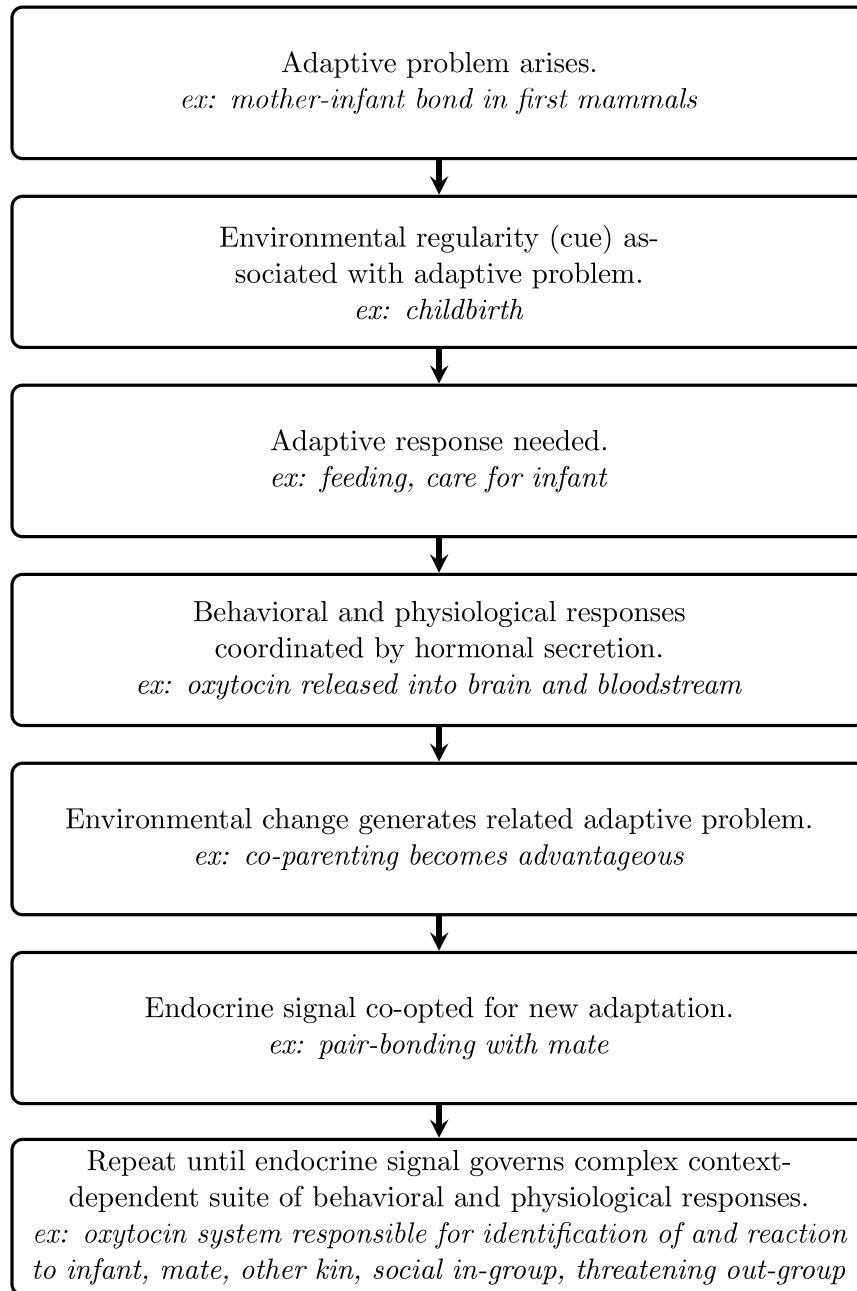


Figure 2: How Hormones Facilitate the Evolution of Complex Behavior