Social Control of the Brain

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Keywords

Abstract

In the course of evolution, social behavior has been a strikingly potent selective force in shaping brains to control action. Physiological, cellular, and molecular processes reflect this evolutionary force, particularly in the regulation of reproductive behavior and its neural circuitry. Typically, experimental analysis is directed at how the brain controls behavior, but the brain is also changed by behavior over evolution, during development, and through its ongoing function. Understanding how the brain is influenced by behavior offers unusual experimental challenges. General principles governing the social regulation of the brain are most evident in the control of reproductive behavior. This is most likely because reproduction is arguably the most important event in an animal's life and has been a powerful and essential selective force over evolution. Here I describe the mechanisms through which behavior changes the brain in the service of reproduction using a teleost fish model system.

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INTRODUCTION

In many species, social context modulates interactions among animals, which then tune their behavior accordingly. Social interactions clearly influence the brain and circulating hormonal levels, but how does the social environment regulate the physiological, cellular, and molecular processes of the brain? Elucidating this connection is critically important because social interactions, especially those related to reproduction, are essential for the evolutionary success of all species. Social regulation of vertebrate reproduction offers a unique opportunity to understand how behavior influences the brain for two reasons. First, reproductive behaviors are often stereotypic, making them relatively easy to observe and quantify. Second, central control of reproduction is lodged in the brain-pituitary-gonadal (BPG) axis with the hypophysiotropic gonadotropin-releasing hormone (GnRH1) neurons as its final output path. Thus the neuronal circuit that produces the GnRH1 signaling peptide is the key locus for integrating the external and internal factors that control reproduction.

Understanding behavioral regulation of the brain requires an animal model in which (*a*) social interchange is essential for reproductive success; (*b*) animals can be studied in a seminatural context; (*c*) key molecular, cellular, and physiological processes are accessible; and (*d*) behavior and physiology of both individuals and groups of animals can be readily analyzed.

CHOICE OF FISH SPECIES FOR STUDY

In considering experimental systems for studies of the brain that focus on social behavior, it is important to select a system that allows a reasonable replication of the native social and environmental habitat. Although primates are an obvious choice of an experimental animal species that is closely related to humans, fish offer an interesting chance to understand how the brain controls behavior for several reasons. Fish are the largest vertebrate group, with more species than all other vertebrates combined, occupying ecological niches from freezing water to hot soda springs. Moreover, they represent more than 400 million years of vertebrate evolution, and their taxonomic dimensions exceed the distance between frogs and humans (Romer 1959). The variety of sensory modalities required for aquatic life, aside from vision, olfaction, taste, and hearing, include mechanosensory systems (e.g., lateral line), external taste buds, and numerous electroreceptor systems that have led to extensive variation in brain structures. Moreover, it is not an exaggeration to say that essentially every known kind of social system has evolved in fish species from monogamy to harems to sex-changing animals.

Given the wide variety of ecological niches exploited, appropriate species comparisons among fish offer the potential for understanding the relative contributions of environmental and social factors to brain evolution. Even more appealing, fish offer the promise of discovering mechanisms through which the brain controls social activities in ecologically meaningful contexts (Bshary et al. 2002).

Studies of animal behavior fall roughly into two groups that have quite different goals (Shettleworth 1993, Kamil 1998). Some investigators seek to identify human-like skills in other species, a thread derived broadly from a search for general cognitive abilities (Hodos & Campbell 1969). This approach has been termed the anthropocentric perspective and may, in fact, be an indirect descendent of Aristotle's *scala naturae*, a view reinforced by comparative brain research. Another camp treats cognition as strictly biological, best elucidated through observations and experiments directed at understanding adaptive modifications crafted by evolution to regulate social interactions (Robinson et al. 2008). Such adaptations typically produce cognitive skills that animals need and use in nature to navigate their social worlds. There are several ways to parse these general classes of investigation in other terms, for example, understanding aspects of human behavior using animal models versus understanding animals in meaningful biological contexts for their own sake.

Fish Have Significant Cognitive Abilities

Cognitive skills in fish species offer an opportunity to study basic skills in a tractable animal that can be kept in a seminatural environment where the whole social system can be well mimicked. The following is a brief summary of the range of cognitive capacities that could be tapped in a fish model system.

Numerosity. Counting is an important form of abstraction that led to the development of mathematics. Since the discovery in 1904 that Hans, the famous Russian trotting horse

could not really count or do mathematical calculations (or read either German or musical notation) but rather responded to his owner's cues (Candland 1993), scientists have used more rigorous methods to investigate whether and how animals can keep track of quantities. Can some fish species keep track of amounts, and when might they need to count something? Numerical abilities in a fish species appear to be handy when choosing which group to join in times of danger. "Safety in numbers" predicts that fish should select the larger group when given a choice. In fact, three-spined sticklebacks (*Gasterosteus aculeatus*), when threatened with a simulated aerial predator, chose to join larger shoals when equidistant from small shoals but made a trade-off between distance to the shoal and its numbers when given that option (Tegeder & Krause 1995). Because the number of fish in larger shoals covaries with several physical attributes of the group (e.g., area, contour, density), sophisticated experiments are required to show which feature of shoal size is actually being discriminated. These types of experiments can be done when the stimuli are presented in succession, rather than in aggregation. In one case, item-by-item presentation showed that the mosquitofish (*Gambusi holbrooki*) can distinguish small (three versus two) and large (eight versus four) shoals independent of other factors (Agrillo et al. 2009). Such numerical skills likely evolved in species in which antipredator benefits of group assemblies have evolved. We can predict that similar capacities will be found in other fish species that aggregate during predation threats.

Recognition of individuals. When an animal encounters another individual, it likely compares sensory information with a template to categorize that individual as conspecific, heterospecific, threatening, or nonthreatening. It may also recognize the individual. Recognition of individuals is a prerequisite for many behavioral interactions and has been demonstrated in a wide range of taxa. In particular, individual recognition is essential for kin recognition and hence required for any kin-selected behavior.

Individuals can be identified using multiple sensory modalities depending on the species and ecological circumstances. For fish, novel sensory systems, including electroreception, pressure reception, and polarization vision, may be important for recognizing individuals.

How many individuals would a fish need to know in some way? Sampling natural populations, Ward et al. (2005) estimated that three-spined sticklebacks living in ∼20 m of a channel in a freshwater lake could meet with 900 conspecifics regularly and showed that direct experience and social cues led to relatively quick learning about the categories of individuals. However, the total number of conspecifics that stickleback's remember or whether they recognize individuals was not established (Ward et al. 2005). Bshary et al. (2002) report that some cleaner fish species can probably distinguish ∼100 individuals by observing their behavior toward clients.

One of the most important realms for individual recognition is in mating pairs of fish. Noble & Curtis (1939) first described recognition between mated pairs in a cichlid fish with biparental care of the young, *Hemichromis bimaculatus*. Much later, Fricke (1973) performed elegant field experiments on fish (*Amphiprion bicinctus*) that live together among the tentacles of anemones, showing that mated individuals recognized one another on the basis of individual body color patterns rather than mutually recognizing the anemone. Moreover, after arbitrarily pairing a male and female, anemone fish could learn the identity of the new partner in 24 h and could also recognize that individual after 10 days of isolation. Given the high rates of predation on *A. bicinctus*, the ability to identify a new partner rapidly would allow animals to continue reproducing despite the loss of a familiar partner. In cichlids living in clear water habitats, individuals used primarily visual cues to recognize other individuals (Noble & Curtis 1939, Fricke 1973, Balshine-Earn & Lotem 1998).

Differences in mating systems and ecology may result in the evolution of different recognition abilities among species. For example, guppies can recognize conspecifics individually as well as distinguish among groups of conspecifics on the basis of cues about resource use and habitat (Ward et al. 2009). In contrast, sticklebacks do not recognize individuals in a social context despite prior interactions, though they do have general recognition capacities based on resource use (Ward et al. 2009) that are considered "familiarity" rather than individual recognition. This cognitive skill seems to increase the chances of grouping together and improving foraging (Ward et al. 2005, 2007). More recently, Ward et al. (2009) suggested that sticklebacks may rely on habitat information, specifically odors, to identify particular groups of individuals.

A second important function for individual recognition is to reduce the costs of contesting resources. This has been demonstrated in sea trout (*Salmo trutta*) in which familiarity with conspecifics enhanced growth (Höjesjö et al. 1998). In a twist on this skill, European minnows (*Phoxinus phoxinus*) recognized and preferred to group together in a shoal with poor competitors, although how they recognized poor competitors is unknown (Metcalfe & Thomson 1995). Evidence also indicates that kin recognition is widespread among fish species, particularly those that school (Quinn & Hara 1986, Havre & FitzGerald 1988, Olsen 1989), and that this skill requires individual recognition.

As in all laboratory experiments, individual recognition may be a consequence of artificially extended interactions among individuals. However, most data cited here were from field experiments and hence provide more convincing examples of individual recognition in fish (see also discussion below on transitive inference data: Assessing Male Fighting Abilities).

Deception

Do fish communicate honestly or can they deceive? Deception is a fundamental issue in animal communication (Maynard Smith & Harper 2003), so can fish deceive? Several authors beginning with Byrne & Whiten (1988) have distinguished between functional and intentional

deception. Functional deception is widespread and includes many examples that do not require cognitive skill (e.g., mimicry, crypsis, although see Chittka & Osorio 2007), whereas intentional deception implies behavior based on intentional states (e.g., beliefs, desires). As cogently discussed by Shettleworth (1998), translating anthropocentric concepts into predictions and experiments that are testable is a serious challenge. Suitable experiments have been described for chimpanzees (Hare et al. 2000, Hare & Tomasello 2001), scrub jays (Dally et al. 2006), and ravens (Bugnyar & Heinrich 2006) with a test to demonstrate an ultimate fitness benefit of deception to the deceiver and the cost to the deceived (Hauser 1997).

Perhaps the cleanest example of deception has been described for the cleaner wrasse, *Labroides dimidiatus*. This marine cleaner fish removes ectoparasites from visiting reef fish clients. This relationship is mutual because the client gets cleaned of ectoparasites and the cleaner gets a meal, the parasite, delivered. But a problem exists: Cleaner fish prefer the client's tasty layer of mucus to its ectoparasites (Grutter & Bshary 2003). Because cleaner fish service up to 2,000 clients every day (Grutter 1997) and many of these encounters happen in the presence of observing bystanders, including future clients, does the presence of bystanders alter the cleaner's behavior? Pinto et al. (2011) used two species of client fish to ask whether being watched matters. Cleaners were tested on clients, and the introduction of a bystander led to an immediate increase in cooperation by the cleaner fish: The cleaners spent more time removing ectoparasites than eating mucus when being watched. This brief discussion of the social skills of teleost fish reveals why they are such useful model systems for understanding the neural bases of social behavior.

## SOCIAL CONTROL OF THE BRAIN: WHY STUDY THE CICHLID FISH, *ASTATOTILAPIA BURTONI*?

Astatotilapia (Haplochromis) burtoni, the African cichlid fish model system we developed, has numerous social skills and, perhaps most importantly, social interactions related to the fact that social dominance tightly controls reproductive physiology. By manipulating the social system we can essentially turn on or off an animal's reproductive competence, mimicking natural changes to identify key regulatory processes. This fish model system offers several important advantages for understanding how social behavior changes the brain: (*a*) The social system of this fish can be easily replicated in the laboratory; (*b*) male status is signaled by obvious rapid color changes, making it easy to detect and quantify; (*c*) GnRH1 neurons are directly regulated by male social status and hence are causally related to behavior; (*d*) *A. burtoni* offers easy access to the brain, allowing sampling of cells and molecules of interest; and (*e*) the *A. burtoni* genome has been sequenced, enabling a class of experiments not previously possible (**http://www.genome.gov/11007951**). Taken together, these attributes make *A. burtoni* uniquely useful for studying social regulation of reproduction. Using this system, we have manipulated the social situation to produce phenotypic change in a variety of ways and have measured relevant molecular, neural, and hormonal systems.

A. burtoni males exist as one of two socially controlled, reversible phenotypes: reproductively competent dominant (D) males and reproductively incompetent nondominant (ND) males (see **Figure 1**).

D males display bright coloration, aggressively defend territories, and court females, whereas ND males display dull gray coloration, mimic females, and limit their behavior to schooling and fleeing. The major differences between these two phenotypic states of male *A. burtoni* can be summarized as follows.

Social signals regulate GnRH1 cell size, peptide level, GnRH1, and gonadotropin-releasing hormone (GnRH) mRNA receptor levels. When a D male is moved into a social system with larger (>5% in length) D males, it abruptly loses its color (<1 min) and joins other ND males and females in a school. Its GnRH1-containing neurons in the preoptic
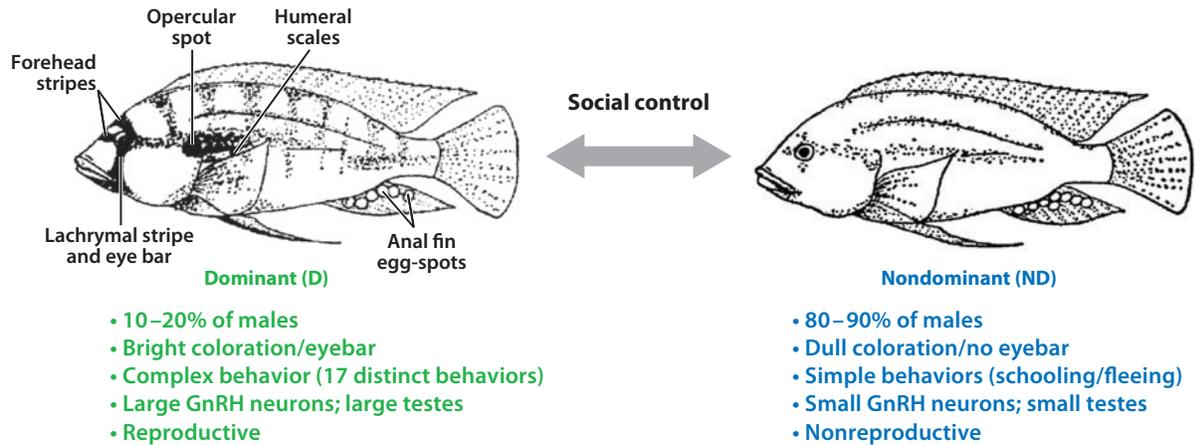
Figure 1

Socially regulated differences between dominant (D) and nondominant (ND) males. Dominant males are brightly colored yellow or blue, express complex behaviors, are reproductively competent, and comprise a small fraction of the population, whereas ND males have dull coloration, express only a few behaviors, and are reproductively incompetent.

area (POA) shrink to one-eighth their volume and produce less GnRH1 mRNA and peptide, causing hypogonadism and loss of reproductive competence (∼2 weeks) (Davis & Fernald 1990, Francis et al. 1993, White et al. 2002). Similarly, androgen, estrogen, and GnRH receptor mRNA expression levels depend on social status (Au et al. 2006, Burmeister et al. 2007, Harbott et al. 2007) as do electrical properties of the GnRH1 neurons (Greenwood & Fernald 2004). Conversely, when an ND male is moved into a social system in which it is larger than other males, these changes are reversed. The male quickly (<20 s) assumes a bright territorial coloration, engages in aggressive encounters, and acquires a territory. We know that ascending animals rapidly (∼20 min) activate the molecular processes related to the subsequent neural transformations (Burmeister et al. 2005).

HOW DOES SOCIAL INFORMATION INFLUENCE BEHAVIOR AND THE BRAIN?

Social living requires sophisticated cognitive abilities because successful social individuals must collect information to guide their future behavior. We have tested the abilities of *A. burtoni* to understand what they know and

how they know it about their social world, and more importantly, how this knowledge affects their brain and subsequent behavior. Knowledge of how conspecifics act in key social situations would be a useful guide to predict future behavior. Consequently, in social settings, individuals gather and use information about others' behavior (Brown & Laland 2003) to regulate their own behavior. But how do animals collect social information (McGregor 2005, Brown et al. 2006), and what do they learn as a result? Here we describe several experiments in which we tested individuals' responses after social observations.

Female Mate Choice

People often assume that females choose males displaying the most exaggerated sexual traits—whether behavioral, morphological, or material, such as food and shelter. However, other factors may also contribute importantly to female mate-choice decisions. A wide range of subtle and complex external factors has been shown to influence female mate choice, suggesting sophisticated integration of cues by females. Less well understood are the physiological substrates that are likely also crucial for successful female reproductive

choice. Choice of a mate by a female is very important and is dictated by a variety of factors. For example, genetic and epigenetic factors, circulating hormones, and learned behavior can contribute to a female's final mate choice (see review by Argiolas 1999). In addition to their role in solicitation behavior, hormones are intimately involved in establishing a preference for conspecifics of the opposite sex during ontogeny (e.g., Adkins-Regan 1998).

Although manipulating hormone levels experimentally can be informative, we took advantage of the naturally fluctuating levels of hormones in the female reproductive cycle to discover whether and how decisions to affiliate with males of different reproductive quality change as a function of the female's stage in the reproductive cycle. We showed in *A. burtoni* that gravid females preferentially associated with D males, whereas nongravid females showed no preference and that preference did not depend on male size (Clement et al. 2005). These data suggest that females use a hierarchy of internal and external cues in deciding on a mate.

Females who choose an inappropriate mate may pay a high cost in lost reproductive opportunity. But which cues should they use to select a mate that might be a successful reproductive partner? In general, females should be choosier about prospective mates than should males because bad mating decisions typically result in higher costs for females than for males (Trivers 1972). Consequently, studies measuring female assessment of male characteristics have produced conceptual, theoretical, and empirical hypotheses suggesting key factors that may mediate female mate choice (for reviews, see Ryan 1980, Andersson & Simmons 2006). Perhaps unsurprisingly, some evidence indicates that females may use information about male–male social interactions in their mate-choice decisions (Otter et al. 1999, Doutrelant & McGregor 2000, Mennill et al. 2002, Earley & Dugatkin 2005), but little is known about how the brain responds to this kind of information. Specifically, what are the consequences for mate choice after collecting key information? Male–male social interactions may affect female mate choice because information about a potential mate triggers changes in female reproductive physiology.

Using immediate early gene (IEG) expression as a proxy for brain activity, we asked whether social information about a preferred male influenced neural activity in females (Desjardins et al. 2010). After a gravid female *A. burtoni* chose between two socially and physically equivalent males, we staged a fight between these males. Her preferred male either won or lost. We then measured IEG expression levels in several brain nuclei including those in the vertebrate social behavior network (SBN), a collection of brain nuclei known to be important for social behavior (Newman 1999, Goodson 2005). When the female saw her preferred male win a fight, SBN brain nuclei associated with reproduction were activated, but when she saw her preferred male lose a fight, the lateral septum, a nucleus associated with anxiety, was activated instead. Thus social information alone, independent of actual social interactions, activated specific brain regions that differ significantly depending on what the female sees. These effects are seen only in gravid females, consistent with our earlier data showing that hormones are important for female mate choices.

These experiments, assessing the role of mate-choice information in the brain using a paradigm of successive presentations of mate information, suggest a method for identifying the neural consequences of social information on animals using IEG activation (Desjardins et al. 2010). IEGs are the earliest genomic responses to stimuli and require no prior activation by any other gene (Clayton 2000). This response, however, is the tip of the genetic activation iceberg because the total number of genes that comprise one neuron's inducible genomic response has been estimated from tens to hundreds (Nedivi et al. 1993); likewise, the set of rapidly inducible genes in any particular cell in the brain may be still larger (Miczek 1977), meaning that the IEG expression measured here is likely only a tiny fraction of the

total gene expression. Nonetheless, this glimpse of the genetic response to social information shows not only that females attend to the information received from watching males interact but also that such information has dramatic effects on their brains in key nuclei rather than producing widespread, general arousal, generating the genetic substrate for subsequent behavioral responses.

Assessing Male Fighting Abilities

A second example of social information being used by *A. burtoni* is the process of drawing inferences through observation. Because males in this species need to be dominant and defend a territory to reproduce, individuals are innately driven to acquire a territory through fighting with an incumbent male. Males engage in vigorous aggressive fighting bouts that determine their access to a territory and subsequent mating opportunities. However, in a colony containing ∼60 D males, it would take a large number of pairwise fights for a male to figure out which dominant individual is vulnerable for a territorial takeover. Plus, the cost to an individual male to engage in repeated conflicts would be substantial. The process of transitive inference (TI) could shorten this process significantly if the animals could infer their chances of winning a fight in advance. TI involves using known relationships to deduce unknown ones. For example, using A > B and B > C to infer A > C allows an individual to acquire hierarchical information essential to logical reasoning. First described as a developmental milestone in children (Piaget 1928), TI has since been reported in nonhuman primates (Gillian 1981, McGonigle & Chalmers 1977, Rapp et al. 1996), rats (Davis 1992, Roberts & Phelps 1994), and birds (Bond et al. 2003, Steirn et al. 1995, von Fersen et al. 1991). Still, how animals acquire and represent transitive relationships and why such abilities might have evolved remain unknown.

We have shown that *A. burtoni* males can draw inferences about a hierarchy implied by pairwise fights between rival males, demon-

strating TI. These fish learned the implied hierarchy vicariously as bystanders watching fights between rivals (Grosenick et al. 2007) and can use TI when trained on socially relevant stimuli. Note that they can make such inferences using indirect information alone. The key to this experiment was to show bystanders staged fights between matched animals that assure the outcomes (see Grosenick et al. 2007 for details). Testing the animals' choice robustly demonstrated TI in both the home tank and a novel tank.

As noted above, social interactions require knowledge of the environment and status of others that can be acquired indirectly by observing others' behavior. When being observed, animals can also alter their signals on the basis of who is watching. We measured how male *A. burtoni* behave when being watched in two different contexts. In the first, we showed that aggressive and courtship behaviors displayed by subordinate males depend critically on whether D males can see them; in the second, we manipulated who was watching aggressive interactions and showed that D males will change their behavior depending on audience composition. In both cases, when a more dominant individual is out of view and the audience consists of more subordinate individuals, those males signal key social information to females by displaying courtship and dominant behaviors. In contrast, when a D male is present, males cease both aggression and courtship. These data suggest that males are keenly aware of their social environment and modulate their aggressive and courtship behaviors strategically for reproductive and social advantage (Desjardins et al. 2012).

FROM SOCIAL INFORMATION TO CHANGES IN THE BRAIN

The brief description of the variety of social interactions found in fish described above offers just a glimpse of the potential mechanisms through which animals sample information from their social environments. But how does that social information change their behavior
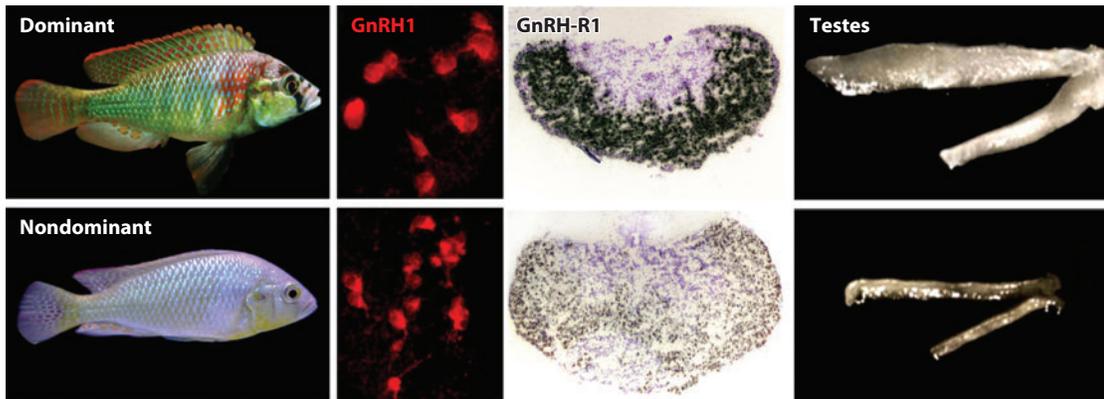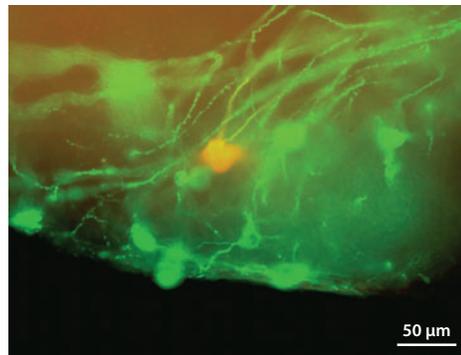
Figure 2

Social regulation of the hypothalamic-pituitary-gonadal axis in *A. burtoni*. Phenotypic characters of reproductively active dominant (D) males (*top row*) and socially suppressed ND males (*bottom row*) are shown. D males have larger GnRH1 neurons (*red*; immunohistochemical staining) in the preoptic area of the brain (Davis & Fernald 1990, White et al. 2002), higher GnRH-R1 levels (*black*, GnRH-R1 in situ hybridization; *purple*, cresyl violet counterstain) in the pituitary gland (Au et al. 2006, Flanagan et al. 2007, Maruska et al. 2011), and larger testes (Fraley & Fernald 1982, Davis & Fernald 1990, Maruska & Fernald 2011) compared with subordinate males (modified from K.P. Maruska & R.D. Fernald 2011). Comparing the dendritic morphology of GnRH1 neurons between D and ND male *A. burtoni* using confocal images provides preliminary evidence that features of the dendritic arbor morphology depend on reproductive state.

and ultimately their brain? More specifically, how does information change circuits and cells to control reproduction, and how does it ultimately reach the organs responsible for it? Although investigators have suggested potential genomic substrates for these processes in several systems (Robinson et al. 2008), the actual circuits and other parts of the responsible nervous system remain unknown.

To approach this problem, we exploit the extreme, reversible phenotypic switch between *A. burtoni* males from D to ND to understand the effects of social environment on reproduction. By combining manipulations of the social milieu with direct intervention and/or measurement of relevant neural and hormonal systems, we have discovered many socially regulated changes that provide insight into the subtle interplay among the factors responsible for causal links to reproductive function. Here I focus on the signaling pathway that begins in the brain with GnRH1 release to the pituitary and ends by controlling reproductive competence and reproduction itself. The macroscopic consequences of a change in phenotype on the reproductive axis is shown in **Figure 2**.

We measured the dendritic extent using laser confocal microscopy and found that the total dendrite length of GnRH1 neurons in D males ($n = 12$, average total length per cell $= 838$ μm) is dramatically greater than the total dendrite length of GnRH neurons in NDs

Figure 3

Individual neurons in the POA were filled with neurobiotin using a microelectrode and immunostained with antibodies to GnRH (*green*) to confirm their identity. Yellow cell is filled with neurobiotin and colabeled with GnRH antibody (A.K. Greenwood and R. Fernald, unpublished).
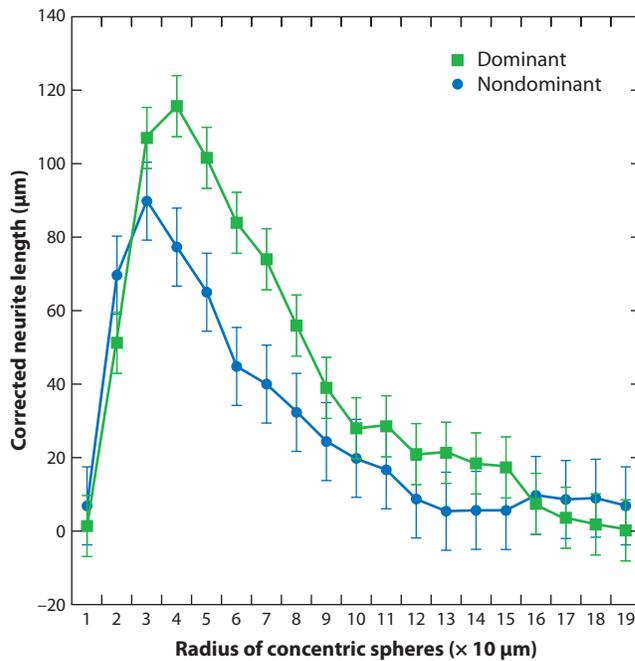
Figure 4

Neurite length measured within each shell of 10 μm concentric spheres (Sholl
analysis). GnRH1 neurons from D males have a greater dendrite length beyond
30 μm from the soma (see text for discussion): D males ($n = 12$; average
length $= 838$ μm), ND males ($n = 8$; average length $= 459$ μm). From M.D.
Scanlon, A.K. Greenwood & R.D. Fernald, unpublished observations.

of the mammalian brain (see Bennett & Zukin
2004 for review). Direct electrical communi-
cation between neurons can give rise to a wide
repertoire of dynamic network outputs, and the
particular network pattern that does arise will
depend on intrinsic cellular properties that af-
fect firing frequencies and heterogeneity across
the population and at the location of the com-
munication (e.g., soma, proximal or distal den-
drite; Roberts et al. 2006).

The role of direct coupling in GnRH neu-
rons is unknown but could be important in the
production of rhythmic GnRH1 output. Fluo-
rescence recovery after photobleaching (FRAP)
(Matesic et al. 1996) and neurobiotin labeling
(Hu et al. 1999) in immortalized GnRH1 neu-
rons (GT1-7 cell line) indicated direct connec-
tions between 20% and 75% of cultured cells.
In GT1-7 cells, gap junctions also contribute to
synchronized pulses (Vazquez-Martinez et al.
2001), and the same group (Bose et al. 2010)
recently reported the necessity of connexin 43
(Cx43) for synchrony. Moreover, gap junction
protein levels appear to be regulated by at
least one intracellular messenger important in
GnRH secretion, cyclic adenosine monophos-
phate (AMP) (Matesic et al. 1996). In the rat,
hypothalamic GnRH neurons express mRNA
for one of the more common connexin pro-
teins (connexin 32), but gap junctions between
GnRH neurons have not been demonstrated di-
rectly in this system (Hosny & Jennes 1998).

Evidence increasingly indicates a role for
gap junctions in several systems related to re-
production. For example, gap junctions have
been shown to be important in the pituitary of
teleost fish (Levavi-Sivan et al. 2005), and they
are important in the rat spinal column motor
nuclei, where they are regulated by testosterone
(Coleman & Sengelaub 2002).

Most studies of electrical communication in
GnRH1 neurons have focused on communica-
tion at the soma. However, two of the above
studies found *in vitro* evidence for the potential
involvement of neurites, some of which could
be rudimentary dendrites. First, Matesic et al.
(1996) reported that pharmacological agents
that increase cAMP also increase connectivity,

$[n = 8$, average total length per cell $= 459$ μm
(Scanlon et al. 2003)].

A Sholl (Sholl 1953) analysis of these data,
which measures the dendrites in concentric cir-
cles, shows significant trends for the overall
difference in dendrite arbor size between D
and ND males and statistically significant dif-
ferences in dendritic lengths between 30 and
80 μm. As can be seen in the graph (**Figure 4**),
the difference in length emerges ∼30 μm from
the cell body, suggesting increased branching
or extension of the dendrite ends rather than an
addition of primary dendrites from the soma.

In some cases, dye from an injected neuron
passed into a second uninjected neuron (e.g.,
unlabeled cell), suggesting that GnRH cells
may be coupled, possibly by electrical synapses.
Coupling by gap junctions is perhaps the most
widely studied mechanism of direct electrical
communication and exists in multiple regions

an effect possibly mediated by dendrites because these treatments increased both the number of neurites and the number of connexin 26 positive neurites. Second, Hu et al. (1999) demonstrated that interactions among neurites could account for at least some of the direct coupling observed in GT1-7 cells, but dendritic coupling of hypothalamic GnRH1 neurons remains to be studied systematically. Nonetheless, emerging evidence in mammalian GnRH neurons is consistent with our findings, namely that GnRH neurons may interact extensively at the dendrite level. Thus, the social cues that drive dendritic remodeling may result in the formation of a dendrite-mediated network of GnRH1 neurons. Modification of dendritic structure by social status is another of the socially regulated parameters in the GnRH1 neurons.

As noted above, in all vertebrates, both development and differences in reproductive state are controlled by the GnRH1 neurons in the basal forebrain (e.g., Gore 2002). In *A. burtoni* these neurons are located in the anterior parvocellular preoptic nucleus (aPPn), which is the most anterior part of the preoptic area in teleosts, a conserved vertebrate brain region (Wullimann & Mueller 2004). Other GnRH peptides exist in all vertebrates (White et al. 1998) as in *A. burtoni*. Specifically, GnRH2 and GnRH3 (White et al. 1995) are expressed in the midbrain tegmentum and the forebrain terminal nerve ganglion, respectively, but neither is found in the pituitary (Powell et al. 1995) nor do they exhibit socially induced neural plasticity in soma size or gene expression (Davis & Fernald 1990, White et al. 2002).

Social modulation of reproductive function is widespread among vertebrates with dominance status as a particularly salient factor. Examples include the suppression of ovulation (e.g., Abbott & Hearn 1978; Rood 1980; Abbott et al. 1978, 1998), control of maturation in social mammals (e.g., Vandenbergh 1973, Lombardi & Vandenbergh 1976, Bediz & Whitsett 1979, Faulkes et al. 1990), delay of first breeding in birds (e.g., Selander 1965, Wiley 1974), control of maturation in fish and other vertebrates (e.g., Sohn 1977, Fraley & Fernald

1982, McKenzie et al. 1983, Leitz 1987), changes in stress levels influencing reproduction (Fox et al. 1997, Abbott et al. 2003), and even sex change (e.g., Robertson 1972, Fricke & Fricke 1977, Cole & Robertson 1988). Thus the mechanistic discoveries from *A. burtoni* may be instructive for understanding the neural control of this process in many other species.

In vertebrates, numerous studies demonstrate activation of the reproductive axis caused by different sensory systems [e.g., olfactory (Gore et al. 2000, Rekwot et al. 2001, Murata et al. 2011), auditory (Bentley et al. 2000, Burmeister & Wilczynski 2005, Maney et al. 2007), tactile (Pfaus & Heeb 1997, Wersinger & Baum 1997), and visual (Castro et al. 2009)]. Changes in the reproductive axis are measured as changes in the number, size, or axonal densities of GnRH1-immunoreactive neurons, alterations in neuronal firing patterns, surges in circulating leutinizing hormone (LH) or steroid levels, increased testicular activity, or increases in sexual arousal and behavior. In addition to sensory channel–specific signals, contextual social interactions with multimodal sensory information such as courtship, mating, exposure to the opposite sex, parental care, and opportunities to rise in social rank are also known to influence GnRH neurons and the hypothalamic-pituitary-gonadal (HPG) axis in many vertebrates (Wu et al. 1992; Dellovade & Rissman 1994; Wersinger & Baum 1997; Rissman et al. 1997; Bakker et al. 2001; Scaggiante et al. 2004, 2006; Burmeister et al. 2005; Cameron et al. 2008; Lake et al. 2008; Mantei et al. 2008; Stevenson et al. 2008). However, despite numerous studies that demonstrate links between important social signals and activation of the reproductive axis, very few experiments examine how these social sensory signals cause changes, either directly or indirectly, within GnRH1 at the neuronal or genomic level.

One method for approaching this problem has been to use IEGs such as *egr-1*, *c-fos*, *jun*, and *arc* to identify activated neurons within reproductive and neuroendocrine circuits (Pfaus & Heeb 1997, Clayton 2000), but neuronal

activation is not always associated with IEG induction. IEGs are typically not expressed in chronically activated neurons, and IEG induction is often not related to challenge-induced neuropeptide expression (Farivar et al. 2004, Hoffman & Lyo 2002, Kovacs 2008, Pfaus & Heeb 1997). Nevertheless, socially relevant reproductive stimuli are known to induce IEG expression within GnRH1 neurons across vertebrates from fishes (Burmeister & Fernald 2005) to mammals (Pfaus et al. 1994, Meredith & Fewell 2001, Gelez & Babre-Nys 2006). Burmeister et al. (2005) showed that in *A. burtoni* the perception of a social opportunity by a subordinate male who then ascends to become a D male produces a rapid (20–30 min) induction of the IEG *egr-1* (a transcription factor–encoding gene; also called *zenk*, *zif-268*, *ngfi-a*, *krox-24*, *tis8*) in the preoptic area and in GnRH1 neurons (Burmeister & Fernald 2005). This molecular response results from the recognition of a social opportunity because it is not elicited in males who are already dominant. Recent studies in *A. burtoni* also suggest that visual cues alone are not sufficient to fully suppress the reproductive axis of subordinate males and that other senses such as olfaction are likely involved (Chen & Fernald 2011, Maruska & Fernald 2012).

SOCIAL REGULATION OF GENE EXPRESSION IN THE PITUITARY: GNRH RECEPTORS AND GONADOTROPIN HORMONES

GnRH1 from the brain travels to the gonadotrope-producing cells in the anterior pituitary gland directly via neuronal projections in fish species in contrast with the specialized vascular system in other vertebrates. Once in the pituitary, GnRH1 binds to its cognate receptors on secretory cells that release LH and follicle-stimulating hormone (FSH), which stimulate steroid production and gamete development in the gonads (testes or ovaries). Multiple forms of GnRH receptors (i.e., types I, II, III) are found in mammals (Millar 2005), amphibians (Wang et al. 2001),

and fishes (Robinson et al. 2001, Lethimonier et al. 2004, Moncaut et al. 2005, Flanagan et al. 2007), and they often show differential distributions, expression patterns (e.g., across season, reproductive stage, or dominance status), and varying responses to regulation by steroids, GnRH, and monoamines, all of which suggest functional specializations (Crowley et al. 1998, Levavi-Sivan et al. 2004, Au et al. 2006, Chen & Fernald 2006, Lin et al. 2010). Although we have considerable information on the signal transduction pathways and how different neurohormones and steroids influence gonadotropin synthesis and release (Bliss et al. 2010, Thackray et al. 2010), little is known about how social information modulates gonadotrope output at the pituitary.

In male *A. burtoni*, pituitary mRNA levels of *GnRH-R1*, but not *GnRH-R2*, are socially regulated such that stable D males have higher levels compared with subordinate males, and the increase during the social transition appears to occur more slowly (days) than do changes in mRNA levels of other genes, which occur within minutes to hours (Au et al. 2006, Maruska et al. 2011). However, pituitary mRNA levels of the IEG *egr-1* and of the β-subunits of LH and FSH are increased at just 30 min after social ascent, suggesting that GnRH1 release has quickly activated the pituitary gland (Maruska et al. 2011).

SOCIAL REGULATION OF GENE EXPRESSION IN THE TESTES: SPERMATOGENESIS AND STEROID PRODUCTION

Although many studies have shown how social information including mating opportunities, female presence or attractiveness, and social status can influence testicular function in terms of sperm quality (e.g., velocity, motility, number) from fishes to humans (Kilgallon & Simmons 2005, Cornwallis & Birkhead 2007, Gasparini et al. 2009, Ramm & Stockley 2009, Maruska & Fernald 2011), less is known about how social cues induce molecular changes in the testes. In *A. burtoni*, however, perception of

social opportunity triggers genomic changes in mRNA levels on both rapid (minutes to hours: FSHR, androgen receptors, corticosteroid receptors) and slower [days: leutinizing hormone releasing hormone (LHR), aromatase, estrogen receptors] time scales (Maruska & Fernald 2011). During the subordinate to D male social transition, the morphological and structural changes in testicular cell composition and relative testes size take several days, whereas many molecular changes in the testes are detected more quickly (Maruska & Fernald 2011). This rapid genomic response in the most distal component of the HPG axis highlights the sensitivity and plasticity of the entire reproductive system to social information. Furthermore, the quick genomic changes in the testes raise the possibility that there may be additional and parallel signaling pathways that perhaps bypass the traditional linear cascade from brain GnRH1 release to pituitary LH/FSH release to a testicular gonadotropin receptor activation scheme.

CONCLUSIONS

Clearly, social information has a profound influence on the function of the reproductive axis in all vertebrates; however, far less is known about how this social information influences the HPG axis at the cellular and molecular levels (e.g., changes in gene expression), and some critical questions about the links between social behaviors, reproductive axis function, and the genome remain unanswered. For example, which signal pathways link reception/ perception of a constellation of social cues that produce changes in gene expression along the HPG axis? It seems clear that the next step is to use the many advances in proteomics, transcriptomics, microtranscriptomics, and epigenomics, combined with comparative systems approaches including single-cell analyses, optogenetics, and transgenic methods. Determining the regulatory roles of epigenetic and small RNAs (e.g., microRNAs) in mediating socially induced changes along the reproductive axis is also an exciting area of future work (Robinson et al. 2005, 2008; Huang et al. 2011; Rajender et al. 2011) that should provide insights into our understanding of the mechanisms governing social and seasonal reproductive plasticity across taxa. The cichlid fish *A. burtoni*, with its complex and experimentally manipulable social system, the wealth of background knowledge on the social control of HPG axis function, and the recently available genomic resources will all become a valuable vertebrate model system for studying how the social environment influences genomic plasticity and function of the reproductive axis.

DISCLOSURE STATEMENT

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LITERATURE CITED

Abbott DH, Hearn JP. 1978. Physical, hormonal and behavioral aspects of sexual development in marmoset monkeys, *Callthrix jaccus*. *J. Reprod. Fertil.* 53:155–66

Abbott DH, Keverne EB, Bercovitch FB, Shively CA, Mendoza SP, et al. 2003. Are subordinates always stressed? A comparative analysis of rank differences in cortisol levels among primates. *Horm. Behav.* 43:67–82

Abbott DH, Saltzman W, Schultz-Darken NJ, Tannenbaum PL. 1998. Adaptations to subordinate status in female marmoset monkeys. *Comp. Biochem. Physiol. C* 119:261–74

Adkins-Regan E. 1998. Hormonal mechanisms of mate choice. *Am. Zool.* 38:166–78

Agrillo C, Dadda M, Serena G, Bisazza A. 2009. Use of number by fish. *PLoS One* 4:e4786

Andersson M, Simmons LW. 2006. Sexual selection and mate choice. *Trends Ecol. Evol.* 21:296–302

Argiolas A. 1999. Neuropeptides and sexual behavior. *Neurosci. Biobehav. Rev.* 23:1127–42

Au TM, Greenwood AK, Fernald RD. 2006. Differential social regulation of two pituitary gonadotropin-releasing hormone receptors. *Behav. Brain Res.* 170:342–46

Bakker J, Kelliher KR, Baum MJ. 2001. Mating induces gonadotropin-releasing hormone neuronal activation in anosmic female ferrets. *Biol. Reprod.* 64:1100–5

Balshine-Earn S, Lotem A. 1998. Individual recognition in a cooperatively breeding cichilid: evidence from video playback experiments. *Behaviour* 135:369–86

Bediz GM, Whitsett JM. 1979. Social inhibition of sexual maturation in male prairie mice. *J. Comp. Physiol. Psychol.* 93:493–500

Bennett MV, Zukin RS. 2004. Electrical coupling and neuronal synchronization in the mammalian brain. *Neuron* 41:495–511

Bentley GE, Wingfield JC, Morton ML, Ball GF. 2000. Stimulatory effects on the reproductive axis in female songbirds by conspecific and heterospecific male song. *Horm. Behav.* 37:179–89

Bliss SP, Navratil AM, Xie J, Roberson MS. 2010. GnRH signaling, the gonadotrope and endocrine control of fertility. *Front. Neuroendocrinol.* 31:322–40

Bond AB, Kamil AC, Balda RP. 2003. Social complexity and transitive inference in corvids. *Anim. Behav.* 65:479–87

Bose SK, Leclerc GM, Vazquez-Martinez R, Boockfor FR. 2010. Administration of connexin43 siRNA abolishes secretory pulse synchronization in GnRH clonal cell populations. *Mol. Cell. Endocrinol.* 314:75–83

Brown C, Laland K. 2003. Social learning in fishes: a review. *Fish Fish.* 4:280–88

Brown C, Laland K, Krause J, eds. 2006. *Fish Cognition and Behavior*. Oxford, UK: Blackwell

Byrne RW, Whiten A, eds. 1988. *Machiavellian intelligence: social complexity and the evolution of intellect in monkeys, apes, and humans*. Oxford, UK: Oxford Univ. Press

Bshary R, Wickler W, Fricke H. 2002. Fish cognition: a primate's eye view. *Anim. Cogn.* 5:1–13

Bugnyar T, Heinrich B. 2006. Pilfering ravens, *Corvus corax*, adjust their behaviour to social context and identity of competitors. *Anim. Cogn.* 9:369–76

Burmeister SS, Fernald RD. 2005. Evolutionary conservation of the egr-1 immediate-early gene response in a teleost. *J. Comp. Neurol.* 481:220–32

Burmeister SS, Jarvis ED, Fernald RD. 2005. Rapid behavioral and genomic responses to social opportunity. *PLoS Biol.* 3:e363

Burmeister SS, Kailasanath V, Fernald RD. 2007. Social dominance regulates androgen and estrogen receptor gene expression. *Horm. Behav.* 51:164–70

Burmeister SS, Wilczynski W. 2005. Social signals regulate gonadotropin-releasing hormone neurons in the green treefrog. *Brain Behav. Evol.* 65:26–32

Cameron N, Del Corpo A, Diorio J, McAllister K, Sharma S, Meaney MJ. 2008. Maternal programming of sexual behavior and hypothalamic-pituitary-gonadal function in the female rat. *PLoS One* 3:e 2210

Candland EJ. 1993. *Feral Children and Clever Animals*. New York: Oxford Univ. Press

Castro AL, Gonçalves-de-Freitas E, Volpato GL, Oliveira C. 2009. Visual communication stimulates reproduction in Nile tilapia, *Oreochromis niloticus* (L.). *Braz. J. Med. Biol. Res.* 42:368–74

Chen CC, Fernald RD. 2006. Distributions of two gonadotropin-releasing hormone receptor types in a cichlid fish suggest functional specialization. *J. Comp. Neurol.* 495:314–23

Chen CC, Fernald RD. 2011. Visual information alone changes behavior and physiology during social interactions in a cichlid fish (*Astatotilapia burtoni*). *PLoS One* 6:e20313

Chittka LA, Osorio D. 2007. Cognitive dimensions of predator responses to imperfect mimicry. *PLoS Biol.* 5:e339

Clayton DF. 2000. The genomic action potential. *Neurobiol. Learn. Mem.* 74:185–216

Clement TS, Parikh V, Schrumpf M, Fernald RD. 2005. Behavioral coping strategies in a cichlid fish: the role of social status and acute stress response in direct and displaced aggression. *Horm. Behav.* 47:336–42

Cole KS, Robertson DR. 1988. Protogyny in the caribbean reef goby, *Coryphopterus personatus*: gonad ontogeny and social influences on sex-change. *Bull. Mar. Sci.* 42:317–33

Coleman AM, Sengelaub DR. 2002. Patterns of dye coupling in lumbar motor nuclei of the rat. *J. Comp. Neurol.* 454:34–41

Cornwallis CK, Birkhead TR. 2007. Changes in sperm quality and numbers in response to experimental manipulation of male social status and female attractiveness. *Am. Nat.* 170:758–70

Crowley MA, Rao A, Wright PJ, Illing N, Millar RP, Clarke IJ. 1998. Evidence for differential regulation of multiple transcripts of the gonadotropin releasing hormone receptor in the ovine pituitary gland; effect of estrogen. *Mol. Cell Endocrinol.* 146:141–49

Dally JM, Emery NJ, Clayton NS. 2006. Food-caching western scrub-jays keep track of who was watching when. *Science* 312:1662–65

Davis H. 1992. Transitive inference in rats (*Rattus norvegicus*). *J. Comp. Psychol.* 106:342–49

Davis MR, Fernald RD. 1990. Social control of neuronal soma size. *J. Neurobiol.* 21:1180–88

Dellovade TL, Rissman EF. 1994. Gonadotropin-releasing hormone-immunoreactive cell numbers change in response to social interactions. *Endocrinology* 134:2189–97

Desjardins JK, Klausner JQ, Fernald RD. 2010. Female genomic response to mate information. *Proc. Natl. Acad. Sci. USA* 107:21176–80

Desjardins JK, Hofmann HA, Fernald RD. 2012. Social context influences aggressive and courtship behavior in a cichlid fish. *PloS ONE.* In press

Doutrelant C, McGregor PK. 2000. Eavesdropping and mate choice in female fighting fish. *Behavioral* 137:1655–69

Earley RL, Dugatkin LA. 2005. Three poeciliid pillars: fighting, mating and networking. See McGregor 2005, pp. 84–113

Farivar R, Zangenehpour S, Chaudhuri A. 2004. Cellular-resolution activity mapping of the brain using immediate-early gene expression. *Front. Biosci.* 9:104–9

Faulkes CG, Abbott DH, Jarvis JUM. 1990. Social suppression of ovarian cyclicity in captive and wild colonies of naked mole-rats, *Heterocephalus glaber*. *J. Reprod. Fertil. Suppl.* 88:559–68

Flanagan CA, Chen CC, Coetsee M, Mamputha S, Whitlock KE, et al. 2007. Expression, structure, function, and evolution of gonadotropin-releasing hormone (GnRH) receptors GnRH-R1SHS and GnRH-R2PEY in the teleost, *Astatotilapia burtoni*. *Endocrinology* 148:5060–71

Fox HE, White SA, Kao MH, Fernald RD. 1997. Stress and dominance in a social fish. *J. Neurosci.* 17:6463–69

Fraley NB, Fernald RD. 1982. Social control of developmental rate in the African cichlid, *Haplochromis burtoni*. *Z. Tierpsychol.* 60:66–82

Francis RC, Soma K, Fernald RD. 1993. Social regulation of the brain-pituitary-gonadal axis. *Proc. Natl. Acad. Sci.* 90:7794–98

Fricke HW. 1973. Individual partner recognition in fish: field studies on *Amphiprion bicinctus*. *Naturwissenschaften* 60:204–5

Fricke HW, Fricke S. 1977. Monogamy and sex change by aggressive dominance in coral reef fish. *Nature* 266:830–32

Gasparini C, Peretti AV, Pilastro A. 2009. Female presence influences sperm velocity in the guppy. *Biol. Lett.* 5:792–94

Gelez H, Fabre-Nys C. 2006. Neural pathways involved in the endocrine response of anestrous ewes to the male or its odor. *Neuroscience* 140:791–800

Gillian DJ. 1981. Reasoning in the chimpanzee: II. Transitive inference. *J. Exp. Psychol. Anim. Behav. Process.* 7:87–108

Goodson JL. 2005. The vertebrate social behavior network: evolutionary themes and variations. *Horm. Behav.* 48:11–22

Gore AC. 2002. Gonadotropin-releasing hormone (GnRH) neurons: gene expression and neuroanatomical studies. *Prog. Brain Res.* 141:193–208

Gore AC, Wersinger SR, Rissman EF. 2000. Effects of female pheromones on gonadotropin-releasing hormone gene expression and luteinizing hormone release in male wild-type and oestrogen receptor-alpha knockout mice. *J. Neuroendocrinol.* 12:1200–4

Greenwood AK, Fernald RD. 2004. Social regulation of the electrical properties of gonadotropin-releasing hormone neurons in a cichlid fish (*Astatotilapia burtoni*). *Biol. Reprod.* 71:909–18

Grosenick L, Clement TS, Fernald RD. 2007. Fish can infer social rank by observation alone. *Nature* 445:429–32

Grutter AS. 1997. Spatio-temporal variation and feeding selectivity in the diet of the cleaner fish *Labroides dimidiatus*. *Copeia* 1997:345–55

Grutter AS, Bshary R. 2003. Cleaner wrasse prefer client mucus: support for partner control mechanisms in cleaning interactions. *Proc. R. Soc. Lond. B* 270(Suppl. 2):242–44

Harbott LK, Burmeister SS, White RB, Vagell M, Fernald RD. 2007. Androgen receptors in a cichlid fish, *Astatotilapia burtoni*: structure, localization, and expression levels. *J. Comp. Neurol.* 504:57–73

Hare B, Call J, Agnetta B, Tomasello M. 2000. Chimpanzees know what conspecifics do and do not see. *Anim. Behav.* 59:771–85

Hare B, Tomasello M. 2001. Do chimpanzees know what conspecifics know? *Anim. Behav.* 61:139–51

Hauser MD. 1997. Minding the behaviour of deception. In *Machiavellian Intelligence II: Extensions and Evaluations*, ed. A Whiten, RW Byrne, pp. 112–43. Cambridge, UK: Cambridge Univ. Press

Havre N, Fitzgerald GJ. 1988. Shoaling and kin recognition in the three-spined stickleback (*Gasterosteus aculeatus*). *Biol. Behav.* 13:190–201

Hodos W, Campbell CBG. 1969. The scala naturae: why there is no theory in comparative psychology. *Psychol. Rev.* 76:337–50

Hoffman GE, Lyo D. 2002. Anatomical markers of activity in neuroendocrine systems: Are we all 'fos-ed out'? *J. Neuroendocrinol.* 14:259–68

Höjesjö J, Johnsson JI, Petersson E, Järvi T. 1998. The importance of being familiar: individual recognition and social behavior in sea trout (*Salmo trutta*). *Behav. Ecol.* 9:445–51

Hosny S, Jennes L. 1998. Identification of gap junctional connexin-32 mRNA and protein in gonadotropin-releasing hormone neurons of the female rat. *Neuroendocrinology* 67:101–8

Hu L, Olson AJ, Weiner RI, Goldsmith PC. 1999. Connexin 26 expression and extensive gap junctional coupling in cultures of GT1-7 cells secreting gonadotropin-releasing hormone. *Neuroendocrinology* 70:221–27

Huang Y, Shen XJ, Zou Q, Wang SP, Tang SM, Zhang GZ. 2011. Biological functions of microRNAs: a review. *J. Physiol. Biochem.* 67:129–39

Kamil AC. 1998. On the proper definition of cognitive ethology. In *Animal Cognition in Nature*, ed. RP Balda, IM Pepperberg, AC Kamil, pp. 1–28. San Diego, CA: Academic

Kilgallon SJ, Simmons LW. 2005. Image content influences men's semen quality. *Biol. Lett.* 1:253–55

Kovacs KJ. 2008. Measurement of immediate-early gene activation—c-fos and beyond. *J. Neuroendocrinol.* 20:665–72

Lake JI, Lange HS, O'Brien S, Sanford SE, Maney DL. 2008. Activity of the hypothalamic-pituitary-gonadal axis differs between behavioral phenotypes in female white-throated sparrows (*Zonotrichia albicollis*). *Gen. Comp. Endocrinol.* 156:426–33

Leitz T. 1987. Social control of testicular steroidogenic capacities in the Siamese fighting fish *Betta splendens*. *J. Exp. Zool.* 244:473–78

Lethimonier C, Madigou T, Muñoz-Cueto JA, Lareyre JJ, Kah O. 2004. Evolutionary aspects of GnRHs, GnRH neuronal systems and GnRH receptors in teleost fish. *Gen. Comp. Endocrinol.* 135:1–16

Levavi-Sivan B, Bloch CL, Gutnick MJ, Fleidervish IA. 2005. Electrotonic coupling in the anterior pituitary of a teleost fish. *Endocrinology* 146:1048–52

Levavi-Sivan B, Safarian H, Rosenfeld H, Elizur A, Avitan A. 2004. Regulation of gonadotropin-releasing hormone (GnRH)-receptor gene expression in tilapia: effect of GnRH and dopamine. *Biol. Reprod.* 70:1545–51

Lin CJ, Wu GC, Lee MF, Lau EL, Dufour S, Chang CF. 2010. Regulation of two forms of gonadotropin-releasing hormone receptor gene expression in the protandrous black porgy fish, *Acanthopagrus schlegeli*. *Mol. Cell Endocrinol.* 323:137–46

Lombardi JR, Vandenbergh JG. 1976. Pheromonally induced sexual maturation in females: regulation by the social environment of the male. *Science* 196:545–46

Maney DL, Goode CT, Lake JI, Lange HS, O'Brien S. 2007. Rapid neuroendocrine responses to auditory courtship signals. *Endocrinology* 148:5614–23

Mantei KE, Ramakrishnan S, Sharp PJ, Buntin JD. 2008. Courtship interactions stimulate rapid changes in GnRH synthesis in male ring doves. *Horm. Behav.* 54:669–75

Maruska KP Fernald RD. 2011. Social regulation of gene expression in the hypothalamic-pituitary-gonadal axis. *Physiology* 26:412–23

Maruska KP, Fernald RD. 2011. Plasticity of the reproductive axis caused by social status change in an African cichlid fish: II. Testicular gene expression and spermatogenesis. *Endocrinology* 152:291–302

Maruska KP, Fernald RD. 2012. Contextual chemosensory signaling in an African cichlid fish. *J. Exp. Biol.* 215:68–74

Maruska KP, Levavi-Sivan B, Biran J, Fernald RD. 2011. Plasticity of the reproductive axis caused by social status change in an African cichlid fish: I. Pituitary gonadotropins. *Endocrinology* 152:281–90

Matesic DF, Hayashi T, Trosko JE, Germak JA. 1996. Upregulation of gap junctional intercellular communication in immortalized gonadotropin-releasing hormone neurons by stimulation of the cyclic AMP pathway. *Neuroendocrinology* 64:286–97

Maynard Smith J, Harper D. 2003. *Animal Signals*. Oxford, UK: Oxford Univ. Press

McGonigle BO, Chalmers M. 1977. Are monkeys logical? *Nature* 267:694–96

McGregor PK. 2005. *Animal Communication Networks*. Cambridge, UK: Cambridge Univ. Press

McKenzie WDJ, Crews D, Kallman KD, Policansky D, Sohn JJ, et al. 1983. Age, weight, and the genetics of sexual maturation in the platyfish, *Xiphophorus maclatus*. *Copeia* 1983:770–73

Mennill DJ, Ratcliffe LM, Boag PT. 2002. Female eavesdropping on male song contests in songbirds. *Science* 296:873

Meredith M, Fewell G. 2001. Vomeronasal organ: electrical stimulation activates Fos in mating pathways and in GnRH neurons. *Brain Res.* 922:87–94

Metcalfe NB, Thomson BC. 1995. Fish recognize and prefer to shoal with poor competitors. *Proc. R. Soc. Lond. B* 259:207–10

Miczek KA. 1977. Effects of L-dopa, d-amphetamine and cocaine on intruder-evoked aggression in rats and mice. *Prog. Neuro-Pharmacol.* 1:271–77

Millar RP. 2005. GnRHs and GnRH receptors. *Anim. Reprod. Sci.* 88:5–28

Moncaut N, Somoza G, Power DM, Canario AV. 2005. Five gonadotrophin-releasing hormone receptors in a teleost fish: isolation, tissue distribution and phylogenetic relationships. *J. Mol. Endocrinol.* 34:767–79

Murata K, Wakabayashi Y, Sakamoto K, Tanaka T, Takeuchi Y, et al. 2011. Effects of brief exposure of male pheromone on multiple-unit activity at close proximity to kisspeptin neurons in the goat arcuate nucleus. *J. Reprod. Dev.* 57:197–202

Nedivi E, Hevroni D, Naot D, Israeli D, Citri Y. 1993. Numerous candidate plasticity-related genes revealed by differential cDNA cloning. *Nature* 363:718–22

Newman SW. 1999. The medial extended amygdala in male reproductive behavior. A node in the mammalian social behavior network. *Ann. N. Y. Acad. Sci.* 877:242–57

Noble GK, Curtis B. 1939. The social behavior of the jewel fish, *Hemichromis bimaculatus* (Gill). *Am. Mus. Nat. Hist.* 76:1–46

Olsen KH. 1989. Sibling recognition in juvenile Arctic charr, *Salvelinus alpinus*. *J. Fish Biol.* 34:571–81

Otter K, McGregor PK, Terry AMR, Burford FRL, Peake TM, Dabelsteen T. 1999. Do female great tits (*Parus major*) assess males by eavesdropping? A field study using interactive song playback. *Proc. Biol. Sci.* 266:1305–9

Pfaus JG, Heeb MM. 1997. Implications of immediate-early gene induction in the brain following sexual stimulation of female and male rodents. *Brain Res. Bull.* 44:397–407

Pfaus JG, Jakob A, Kleopoulos SP, Gibbs RB, Pfaff DW. 1994. Sexual stimulation induces Fos immunoreactivity within GnRH neurons of the female rat preoptic area: interaction with steroid hormones. *Neuroendocrinology* 60:283–90

Piaget J. 1928. *Judgement and Reasoning in the Child*. London: Routledge & Kegan Paul

Pinto A, Oates J, Grutter AS, Bshary R. 2011. Cleaner wrasses (*Labroides dimidiatus*) are more cooperative in the presence of an audience. *Curr. Biol.* 21:1140–44

Powell JF, Fischer WH, Park M, Craig AG, Rivier JE, et al. 1995. Primary structure of solitary form of gonadotropin-releasing hormone (GnRH) in cichlid pituitary; three forms of GnRH in brain of cichlid and pumpkinseed fish. *Regul. Pept.* 57:43–53

Quinn TP, Hara TJ. 1986. Sibling recognition and olfactory sensitivity in juvenile coho salmon (*Oncorhynchus kisutch*). *Can. J. Zool.* 64:921–25

Rajender S, Avery K, Agarwal A. 2011. Epigenetics, spermatogenesis and male infertility. *Mutat. Res.* 727:62–71

Ramm SA, Stockley P. 2009. Adaptive plasticity of mammalian sperm production in response to social experience. *Proc. Biol. Sci.* 276:745–51

Rapp PR, Kansky MT, Eichenbaum H. 1996. Learning and memory for hierarchical relationships in the monkey: effects of aging. *Behav. Neurosci.* 110:887–97

Rekwot PI, Ogwu D, Oyedipe EO, Sekoni VO. 2001. The role of pheromones and biostimulation in animal reproduction. *Anim. Reprod. Sci.* 65:157–70

Rissman EF, Li X, King JA, Millar RP. 1997. Behavioral regulation of gonadotropin-releasing hormone production. *Brain Res. Bull.* 44:459–64

Roberts CB, Best JA, Suter KJ. 2006. Dendritic processing of excitatory synaptic input in hypothalamic gonadotropin releasing-hormone neurons. *Endocrinology* 147:1545–55

Roberts WA, Phelps MT. 1994. Transitive inference in rats—a test of the spatial coding hypothesis. *Psychol. Sci.* 5:368–74

Robertson DR. 1972. Social control of sex reversal in a coral-reef fish. *Science* 177:1007–9

Robinson GE, Fernald RD, Clayton DF. 2008. Genes and social behavior. *Science* 322:896–900

Robinson GE, Grozinger CM, Whitfield CW. 2005. Sociogenomics: social life in molecular terms. *Nat. Rev. Genet.* 6:257–70

Robison RR, White RB, Illing N, Troskie BE, Morley M, et al. 2001. Gonadotropin-releasing hormone receptor in the teleost *Haplochromis burtoni*: structure, location, and function. *Endocrinology* 142:1737–43

Romer AS. 1959. *The Vertebrate Story*. London: Univ. Chicago Press

Rood JP. 1980. Mating relationships and breeding suppression in the dwarf mongoose. *Anim. Behav.* 23:143–50

Ryan MJ. 1980. Female mate choice in a neotropical frog. *Science* 209:523–25

Scaggiante M, Grober MS, Lorenzi V, Rasotto MB. 2004. Changes along the male reproductive axis in response to social context in a gonochoristic gobiid, *Zosterisessor ophiocephalus* (Teleostei, Gobiidae), with alternative mating tactics. *Horm. Behav.* 46:607–17

Scaggiante M, Grober MS, Lorenzi V, Rasotto MB. 2006. Variability of GnRH secretion in two goby species with socially controlled alternative male mating tactics. *Horm. Behav.* 50:107–17

Scanlon MD, Greenwood AK, Fernald RD. 2003. Dendritic plasticity in gonadotropin-releasing hormone neurons following changes in reproductive status. *Soc. Neurosci. Abstr.* No. 828.20

Selander RK. 1965. On mating systems and sexual selection. *Am. Nat.* 99:129–41

Shettleworth SJ. 1993. Varieties of learning and memory in animals. *J. Exp. Psychol. Anim. Behav. Process* 19:5–14

Shettleworth SJ. 1998. *Cognition, Evolution and Behaviour*. New York: Oxford Univ. Press

Sholl DA. 1953. Dendritic organization in the neurons of the visual and motor cortices of the cat. *J. Anat.* 87:387–406

Sohn JL. 1977. Socially induced inhibition of genetically determined maturation in the platyfish, *Xiphophorus macalatus*. *Science* 195:199–201

Steirn JN, Weaver JE, Zentall TR. 1995. Transitive inference in pigeons: simplified procedures and a test of value transfer theory. *Anim. Learn. Behav.* 23:76–82

Stevenson TJ, Bentley GE, Ubuka T, Arckens L, Hampson E, MacDougall-Shackleton SA. 2008. Effects of social cues on GnRH-I, GnRH-II, and reproductive physiology in female house sparrows (*Passer domesticus*). *Gen. Comp. Endocrinol.* 156:385–94

Tegeder RW, Krause J. 1995. Density dependence and numerosity in fright stimulated aggregation behaviour of shoaling fish. *Philos. Trans. R. Soc. Lond. B* 350:381–90

Thackray VG, Mellon PL, Coss D. 2010. Hormones in synergy: regulation of the pituitary gonadotropin genes. *Mol. Cell Endocrinol.* 314:192–203

Trivers RL. 1972. Parental investment and sexual selection. In *Sexual Selection and the Descent of Man*, ed. B Campbell, pp. 136–79. Chicago: Aldine

Vandenbergh JG. 1973. Acceleration and inhibition of puberty in female mice by pheromones. *J. Reprod. Fertil. Suppl.* 19:411–19

Vazquez-Martinez R, Shorte SL, Boockfor FR, Frawley LS. 2001. Synchronized exocytotic bursts from gonadotropin-releasing hormone-expressing cells: dual control by intrinsic cellular pulsatility and gap junctional communication. *Endocrinology* 142:2095–101

von Fersen L, Wynne CDL, Delius JD, Staddon JER. 1991. Transitive inference formation in pigeons. *J. Exp. Psychol. Anim. Behav. Process* 17:334–41

Wang L, Bogerd J, Choi HS, Seong JY, Soh JM, et al. 2001. Three distinct types of GnRH receptor characterized in the bullfrog. *Proc. Natl. Acad. Sci. USA* 98:361–66

Ward AJW, Holbrook RI, Krause K, Hart PJB. 2005. Social recognition in sticklebacks: the role of direct experience and habitat cues. *Behav. Ecol. Sociobiol.* 57:575–83

Ward AJW, Webster MM, Hart PJB. 2007. Social recognition in wild fish populations. *Proc. R. Soc. B* 274:1071–77

Ward AJW, Webster MM, Magurran AE, Currie S, Krause J. 2009. Species and population differences in social recognition between fishes: a role for ecology. *Behav. Ecol.* 20:511–16

Wersinger SR, Baum MJ. 1997. Sexually dimorphic processing of somatosensory and chemosensory inputs to forebrain luteinizing hormone-releasing hormone neurons in mated ferrets. *Endocrinology* 138:1121–29

White RB, Eisen JA, Kasten TL, Fernald RD. 1998. Second gene for gonadotropin releasing hormone in humans. *Proc. Natl. Acad. Sci.* 95:305–9

White SA, Kasten TL, Bond CT, Adelman JP, Fernald RD. 1995. Three gonadotropin-releasing hormone genes in one organism suggest novel roles for an ancient peptide. *Proc. Natl. Acad. Sci. USA* 92:8363–67

White SA, Nguyen T, Fernald RD. 2002. Social regulation of gonadotropin-releasing hormone. *J. Exp. Biol.* 205:2567–81

Wiley RH. 1974. Effects of delayed reproduction on survival, fecundity, and the rate of population increase. *Am. Nat.* 108:705–9

Wu TJ, Segal AZ, Miller GM, Gibson MJ, Silverman AJ. 1992. FOS expression in gonadotropin-releasing hormone neurons: enhancement by steroid treatment and mating. *Endocrinology* 131:2045–50

Wullimann MF, Mueller T. 2004. Teleostean and mammalian forebrains contrasted: evidence from genes to behavior. *J. Comp. Neurol.* 475:143–62