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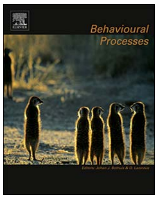

Review

Song practice as a rewarding form of play in songbirds

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ABSTRACT

In adult songbirds, the primary functions of song are mate attraction and territory defense; yet, many songbirds sing at high rates as juveniles and outside these primary contexts as adults. Singing outside primary contexts is critical for song learning and maintenance, and ultimately necessary for breeding success. However, this type of singing (i.e., song "practice") occurs even in the absence of immediate or obvious extrinsic reinforcement; that is, it does not attract mates or repel competitors. Here we review studies that support the hypothesis that song practice is stimulated and maintained by intrinsic reward mechanisms (i.e., that it is associated with a positive affective state). Additionally, we propose that song practice can be considered a rewarding form of play behavior similar to forms of play observed in multiple young animals as they practice sequences of motor events that are used later in primary adult reproductive contexts. This review highlights research suggesting at least partially overlapping roles for neural reward systems in birdsong and mammalian play and evidence that steroid hormones modify these systems to shift animals from periods of intrinsically rewarded motor exploration (i.e., singing in birds and play in mammals) to the use of similar motor patterns in primary reproductive contexts.

1. Introduction

Birdsong consists of species-typical sequences of vocalizations that are learned from adult tutors, refined and maintained through practice, and then used primarily within reproductive contexts to attract mates and defend breeding territories (Catchpole and Slater, 2008; Bradbury and Vehrencamp, 2011). In reproductive contexts, there are clear extrinsic factors that powerfully reinforce singing behavior. For example, male courtship song can be positively reinforced through mate attraction and copulation, whereas territorial song can be negatively reinforced by the departure of a rival. In contrast, much less is known about the factors that reinforce singing behavior during development and in non-sexual contexts in adulthood when many birds sing in flocks or when alone. Singing in these non-sexual contexts is critical for song learning and maintenance, and ultimately necessary for breeding success. However, song in these contexts occurs even in the absence of immediate or obvious extrinsic reinforcement (i.e., it does not attract mates or repel competitors). The mechanisms that ensure that birds continue singing in contexts in which there is no immediate, essential function or obvious extrinsic consequence are not known.

In this review, we explore the possibility that birds sing A) when young and B) outside territorial or reproductive contexts as adults because the act of singing is both facilitated and maintained by intrinsic reward mechanisms (i.e., that singing in these contexts is tightly coupled to a positive affective state). This is not to say that song in non-sexual contexts is completely uninfluenced by social factors (as reviewed below), but that extrinsic reward is not the sole or primary driver of song in these contexts. Moreover, we suggest that song practice can be considered a rewarding form of play behavior similar in many ways to that observed in a variety of young animals as they practice sequences of motor events that are used later in primary adult reproductive contexts.

2. Birdsong outside primary reproductive contexts is needed to develop critical motor behaviors and may be intrinsically reinforced

During song learning, young birds first listen to song from an adult tutor. They then begin to produce "subsong", which is similar to babbling in human infants. This is followed by a period of vocal plasticity consisting of vocal-motor exploration during which birds produce, repeat, reorder, add, and drop vocal elements until they eventually match a stored template or memory for the song of an adult tutor. At this stage song becomes stereotyped or "crystallized" (Marler, 1991; Williams, 2004). Some species do this once during a critical period in which they learn the songs that they will sing throughout their adult lives (e.g., zebra finches; (Bohner, 1990; Marler, 1987; Beecher and Brenowitz, 2005)). Other species return to periods of vocal-motor exploration outside the breeding season as adults when they re-sequence song elements for use during the next breeding period (e.g., canaries;

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(Beecher and Brenowitz, 2005; Nottebohm et al., 1986)). Still other songbirds appear capable of learning and incorporating entirely new elements into their songs throughout the year but concentrate periods of vocal-motor exploration outside the breeding season (e.g., European starlings; (Alger et al., 2016)). Even birds that learn song only during a single critical period engage in periods of singing outside reproductive contexts, and depriving birds of this form of song practice can result in degraded song structure (Woolley and Rubel, 1997). Thus singing outside a primary reproductive context is necessary across multiple species for both song learning and maintenance, yet unlike song that is used to attract mates or repel intruders, the factors that facilitate and reinforce what we will refer to here as song "practice" are not known.

During song learning, vocal output is proposed to be positively reinforced by sensory feedback when it matches the stored template of adult tutor song (reviewed in (Fee and Goldberg, 2011)). This type of reinforcement is needed to learn precise species-typical song repertoires, but it does not explain why birds initiate singing, why they continue to sing during periods when songs fail to match the learned template, or the fact that deafened birds sing during developmental periods of song learning (Konishi, 1965; Marler and Sherman, 1983). Furthermore, even after adult song has been crystallized, birds continue to practice and to produce songs that are less stereotyped than those used in reproductive contexts (Leblois et al., 2010). Rather than template matching, the focus of this review is on mechanisms that ensure that birds continue to practice during early song learning or in adulthood after a song template has already been learned.

3. Practicing developmentally critical motor behaviors is rewarding

There are not many behaviors without immediately essential or obvious functions that animals perform at high rates. A notable exception is play behavior (Pellis and Pellis, 2017; Panksepp et al., 1984; Trezza et al., 2010; Burghardt, 2005). Different forms of play behavior, ranging from solitary object manipulation or locomotion to rough-and-tumble social play, are critical for the development of functionally distinct physical, cognitive and/or social skills across a range of species (Vanderschuren and Trezza, 2014; Pellis et al., 1993; Himmler et al., 2013; Burghardt, 2005; Nunes et al., 2004; Marks et al., 2017). For example, by engaging in rough-and-tumble play outside the primary contexts of mating and aggression, animals develop physical, cognitive, and social skills that can be used in later reproductive contexts (Vanderschuren and Trezza, 2014; Pellis et al., 1993; Himmler et al., 2013). These behaviors are developmentally critical; however, the immediate factors that facilitate and reinforce these behaviors are not clear.

Studies in rats suggest that intrinsic reward associated with social play is essential for stimulating and maintaining this form of developmentally critical motor exploration. For example, juvenile rats readily learn mazes for the opportunity to play (Humphreys and Einon, 1981; Normansell and Panksepp, 1990). Juvenile rats also develop a preference for a place in which they previously had been allowed to play (i.e., a conditioned place preference, which is considered a reflection of reward) (Calcagnetti and Schechter, 1992; Achterberg et al., 2016; Trezza et al., 2009), and the magnitude of this preference correlates positively with the number of 50 kHz vocalizations produced during play, which are vocalizations that indicate a positive affective state (Knutson et al., 1998; Burgdorf et al., 2008).

Engaging in behaviors because they are intrinsically rewarding is nearly synonymous with "play". Social play is facilitated by reunion with social partners, and it is initiated when an animal is fed, healthy and free from stress (e.g., in the absence of predators (Siviy et al., 2006; Panksepp and Beatty, 1980; Burghardt, 2005)). This suggests that safety and the presence of social contacts may induce a positive affective/motivational state that is conducive to play, which may then be maintained by reward induced by the act of playing.

4. Is birdsong practice a form of rewarding play?

Play behavior in birds (e.g., play fighting, acrobatics, and object manipulation) has been estimated to be present in only 1% of approximately 10,000 bird species (Emery and Clayton, 2015); however, it also may be that singing outside a breeding context is a prevalent form of play exhibited by an estimated 4500+ species of oscine songbirds (Sibley and Monroe, 1990). Indeed, it has been suggested that the muted, rambling, plastic vocalizations produced during subsong may be a form of vocal play in young songbirds (Hartshorne, 1973; Ficken, 1977; Thorpe, 1956; Burghardt, 2005; Fagen, 1981); however, until recently this had not been investigated experimentally.

Play can easily be confused with other behaviors. Burghardt suggests that five criteria can be used to distinguish play behavior from other behaviors (Burghardt, 2005). In brief, play behavior must be 1) not fully functional, 2) spontaneous and rewarding, 3) structurally or temporally modified, 4) performed repeatedly during parts of an animal's ontogeny, and 5) initiated when an animal is free from stress. With the exception of being "rewarding", the data reviewed above demonstrate that song practice meets each of these criteria.

Given that playing involves engaging in behaviors because they induce a positive affective state, if song practice is a form of play, then it should be rewarding. Indeed, Darwin proposed that although the main function of male birdsong during the breeding season is mate attraction, "birds continue singing for their own amusement after the season for courtship is over" (Darwin, 1871). The possibility that young birds may sing for enjoyment or that song learning may be "self-reinforcing" without the requirement of extrinsic reward was also proposed in the 1950s and 70s (Marler, 1970; Hartshorne, 1973; Thorpe, 1956). However, it is only recently that studies have been done to explicitly test the hypothesis that singing outside a primary reproductive context is intrinsically rewarding.

It is challenging to ask a bird if singing "feels good". To do this, our lab uses a conditioned place preference (CPP) test of reward, a method that is commonly used in rat studies to evaluate reward induced by feeding, mating, and the use of drugs of abuse (Tzschentke, 2007; Paredes, 2009; Bardo and Bevins, 2000). This is also a method that has been used to show that social play is rewarding in rats (Calcagnetti and Schechter, 1992; Achterberg et al., 2016; Trezza et al., 2009). In songbirds, the presence of a social flock facilitates singing in non-sexual contexts in many species, including our study species, European starlings and zebra finches (Jesse and Riebel, 2012; Gochfeld, 1977; Petrinovich, 1988; Eens, 1997). In these flocks, starlings and zebra finches sing at high rates but often while facing away from other flock mates. These songs also appear to be ignored by potential recipients and are commonly referred to as "undirected" songs in studies of zebra finches (Zann, 1996; Feare, 1984). This type of song is important for song maintenance and learning, and it may play a role in flock cohesion; however, adding birds to or removing birds from a flock does not alter singing (Riters et al., 2000), suggesting that the function is not to immediately attract or repel other birds. Thus, unlike song in a mating context, there is no obvious, immediate survival or reproductive function for this type of song. We propose that similar to play behavior, this type of singing behavior may be stimulated by a positive affective state and maintained by reward induced by the act of singing.

To test this hypothesis, we used a CPP test of song-associated reward. In brief, we allowed males to sing in social flocks for 30 min, placed them singly into one of two distinctly decorated compartments of a standard bird cage for 30 min, and afterwards returned them to home aviaries. The following day (Test Day) we removed a partition separating the two compartments of the conditioning cage, placed males into the cage, and recorded the amount of time males spent on the previously song-paired versus the non-song-paired sides of the cage for 30 min. Both male starlings and zebra finches developed a strong preference for the previously song-paired side of the cage (Riters et al., 2014; Riters and Stevenson, 2012; Hahn et al., 2017) with the number

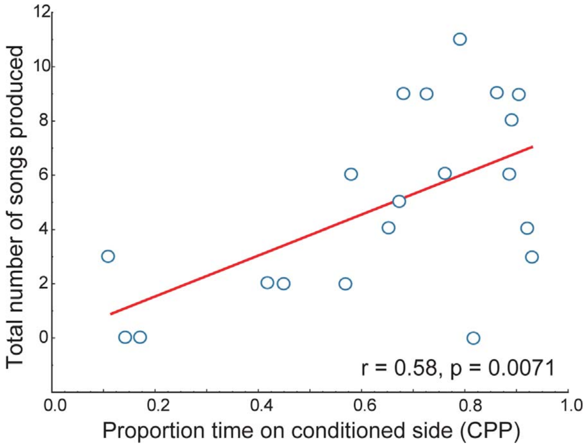

Fig. 1. Song practice is positively correlated with an intrinsic reward state. Correlation between the number of songs produced by male starlings during song practice and a CPP measure of song-associated reward (measured as the proportion of time on Test Day spent on the conditioned/previously song-paired side of the apparatus); $n = 20$. Line indicates a significant correlation.
Redrawn from data presented in Riters et al. (2014).

of songs produced correlating linearly to measures of song-associated reward (i.e., CPP; Fig. 1). These findings parallel the correlations observed between 50 kHz vocalizations and play-associated CPP described above for rats (Burgdorf et al., 2008). This indicates that song production in this context is associated with a positive affective/reward state, similar to what has been observed for rat social play.

We also ran a similar experiment but in males singing in contexts in which song is used primarily to attract females or repel males (Riters and Stevenson, 2012). Males singing in these contexts did not develop a preference for the song-paired side of the cage. In fact, male starlings that sang but were rejected by females developed an aversion for the song-associated side of the cage. This indicates that the act of singing in this context is not tightly coupled to intrinsic reward but is instead extrinsically reinforced by the responses of other birds (in this case, punished by female rejection). In these studies, males and females did not remain together long enough for copulation to occur; however, we predict that if male song successfully attracted females and led to copulation, these males would have developed a place preference, as has been observed in multiple studies of male sexual behavior in rats (Tenk et al., 2009; Pfaus et al., 2001).

Collectively, these findings indicate that song in a non-reproductive context (i.e., song important for learning and maintenance) is tightly coupled in a linear fashion to an intrinsic reward state, whereas song in a primarily reproductive context is not, as proposed by Darwin over 140 years ago. Moreover, these studies are the first to support the previously untested, but key, requirement of the hypothesis that song practice is a form of play behavior (i.e., that singing is tightly coupled to a positive affective state). Similar to what has been proposed for play behavior (Panksepp and Beatty, 1980; Burghardt, 2005; Siviy et al., 2006), we propose that the safety of a flock, the absence of predators, and the availability of basic resources such as food and water induce a positive affective state that stimulates song practice. We further suggest that the act of song practice also induces a positive affective state to maintain singing in this context.

5. Contributions of extrinsic reinforcement

Although extrinsic reinforcement does not appear to be necessary for song learning and practice, this should not be taken to suggest that extrinsic reinforcement is irrelevant. For example, male cowbirds adjust song structure in response to female behavioral responses to specific elements of song (Smith et al., 2000; King and West, 1983; West and King, 1988), and white-crowned sparrows and zebra finches learn song better from live socially interacting tutors than from exposure to song playback (Chen et al., 2016; Eales, 1989; Deregnaucourt et al., 2013). Research on whether parental responses to vocal practice shape song development in young birds, as parental responses to vocal behavior in children (i.e., responses to babbling in human infants) shape speech, is ongoing (Goldstein et al., 2003; Goldstein and Schwade, 2008). However, there is evidence that adult male zebra finches change the temporal structure of song when singing to juveniles in a manner that is similar to the way that humans modify speech when directing it to infants (Fernald et al., 1989; Chen et al., 2016). Thus behavioral studies to date indicate that birds engage in periods of intrinsically-rewarded motor exploration during which they learn and practice singing (similar to solitary babbling during language learning in human infants (Kuczaj, 1983)). Songs are then further shaped and refined by social responses by conspecifics (e.g., potential mates or parents), a form of vocal plasticity termed “action-based learning” (Marler and Nelson, 1993).

6. Both social play and song practice are coupled to neuromodulators underlying reward

The behavioral data reviewed so far suggest that song practice may be a form of rewarding play similar to other forms of play (e.g., rough-and-tumble social play, locomotor play or object manipulation). Given that important behaviors observed across species are commonly regulated by shared neural systems (O’Connell and Hofmann, 2011; Goodson, 2005), song practice and play behavior may be regulated by an evolutionarily conserved, core neural system that facilitates developmentally important behaviors that lack obvious, immediate endpoints across species. If this hypothesis is correct, then song practice in songbirds and play in birds and other vertebrates should be regulated by similar reward systems. Accumulating evidence from studies of birdsong and rodent social play (which is the form of play best studied to date, with respect to neural mechanisms) supports this prediction.

Across vertebrates, reward-related behaviors, including birdsong and rodent social play, are regulated by dopamine (Kubikova and Kostal, 2010; Merullo et al., 2016; Riters, 2012); however, a growing body of research indicates that dopamine strengthens reward-related memories (Wise, 2004) and underlies motivated responses to rewarding stimuli rather than pleasure per se (Berridge and Kringelbach, 2008; van Furth et al., 1995; Barbano and Cador, 2007). Other neuromodulators, including opioids and endocannabinoids, are considered to be the primary neuromodulators underlying positive affective states (Le Merrer et al., 2009; Kelley and Berridge, 2002; Fields and Margolis, 2015; Solinas et al., 2008; Fattore et al., 2010). These modulators act in brain areas comprising the well-studied mesolimbic reward system, which includes projections from the ventral tegmental area (VTA) to the nucleus accumbens (NAc), as well as other regions involved in reward that reciprocally interact with the mesolimbic system, including the medial preoptic nucleus (mPOA). As reviewed next, studies of birdsong and rodent social play are beginning to reveal similar roles for opioids and endocannabinoids in the regulation of song- and play-associated reward, yet whether these modulators are acting in the same brain regions to influence song practice and social play has not yet been tested.

6.1. *Opioids, reward, playing and singing*

Endogenous opioids are the most extensively studied neuromodulators of social play-associated reward in juvenile rats and song-associated reward in songbirds. The mu opioid receptor is the primary subtype that mediates pleasure (Fields and Margolis, 2015), and a body of work indicates that peripheral injections of opioid receptor agonists that target mu opioid receptors stimulate social play in juvenile rats; whereas, antagonists suppress play behavior (e.g., (Panksepp et al., 1980, 1985; Manduca et al., 2014; Vanderschuren et al., 1995a; Trezza et al., 2011)). Similarly in songbirds, peripheral administration of the opioid receptor antagonist naloxone dose-dependently suppressed song in male zebra finches singing in isolation (i.e., birds presumed to be practicing song) (Khurshid et al., 2010), suggesting that opioids facilitate both social play and song practice.

The activation of mu opioid receptors in multiple brain regions can induce reward (Le Merrer et al., 2009). With respect to NAc, play, and reward, infusion of mu opioid receptor agonists into NAc induces reward as measured using a CPP test (Olmstead and Franklin, 1997). Infusion of mu receptor agonists into NAc also facilitates social play behavior; whereas, blocking mu opioid receptors in NAc prevents the development of a play-associated CPP (Trezza et al., 2011). These studies thus establish the NAc as a central site in which opioids released in association with social play act to induce reward.

Although a region in birds has been identified that is neurochemically and hodologically similar to NAc in mammals (Husband and Shimizu, 2011; Balint et al., 2011; Balint and Csillag, 2007), the role of this region in social reward in birds remains to be tested. Instead, studies of birdsong and reward have focused on the mPOA, another region in which opioids (mu receptor agonists and the opioid met-enkephalin) act to induce reward (Agmo and Gomez, 1991, 1993; Garcia-Horsman et al., 2008). Singing behavior produced by male starlings in a non-reproductive context (i.e., when they are learning/practicing new songs) correlates positively with mRNA expression for mu opioid receptors, the opioid precursor pre-proenkephalin, and measures of met-enkephalin protein labeling in mPOA (Riters et al., 2005, 2014). Mu opioid receptor labeling in mPOA is also related to song practice in an inverted U-shaped pattern (Kelm-Nelson and Riters, 2013). Mu opioid receptor agonists, such as met-enkephalin, downregulate mu opioid receptors (Tien et al., 2007; Chakrabarti et al., 1997), suggesting that high levels of enkephalin released in association with song practice may bind to and downregulate mu opioid receptors.

The correlations between opioid markers in mPOA and song practice in starlings suggest that the mPOA may be a site in which opioids act to facilitate song practice, and because enkephalin infusion and mu opioid receptor stimulation in the mPOA induces reward in other species (Agmo and Gomez, 1991, 1993; Garcia-Horsman et al., 2008), it is possible that opioid activity in mPOA underlies song-associated reward. To begin to explore this possibility, song-associated reward was studied using the CPP methods detailed above, and opioid-related mRNA expression was measured in mPOA (Riters et al., 2014). Results showed positive linear couplings between song practice, song-associated CPP, and expression of both preproenkephalin and mu opioid receptors (Fig. 2). This is the first time that all three measures (song practice, reward, and opioid markers in mPOA) have been examined in a single set of birds, and the findings offer support for the hypothesis that opioid release in mPOA underlies song-associated reward.

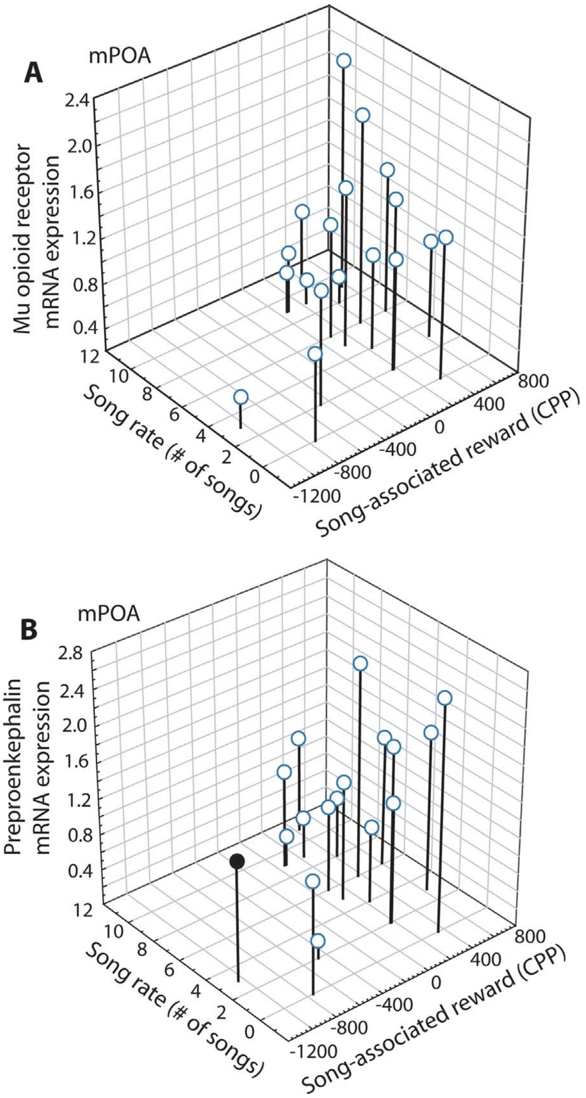

Fig. 2. Scatterplots illustrating positive relationships between song practice, opioid-marker mRNA expression in mPOA, and reward state. For both panels A and B, the Y axis indicates the number of songs produced by male starlings just prior to being placed in one side of a CPP apparatus (the song-paired side). The X axis represents reward associated with singing behavior as reflected in the development of a preference for the previously song-paired side of the apparatus (i.e., secs spent on the previously song-paired side of the apparatus on Test Day minus secs spent on that side during a habituation prior to conditioning). The Z axis in panel A represents mu opioid receptor expression. The Z axis in panel B represents preproenkephalin expression. Each point within a panel represents data from a single male. The filled point in panel B was a statistical outlier that was not included in the analysis.
Data from Riters et al. (2014).

The mPOA was also one of the first regions in which correlational data implicated opioids in social play in rats (Panksepp and Bishop, 1981). However, a later study that used slightly different methods from the first and tested rats at a much younger age (well before maximal play behavior (Thor and Holloway, 1984)), did not show relationships between opioids in mPOA and play (Vanderschuren et al., 1995b). Future studies are thus needed to elucidate the extent to which opioids in mPOA have similar effects on social play in rats and song practice in birds.

6.2. *Cannabinoids, reward, playing and singing*

The endocannabinoid system is also receiving attention for its role in reward, social play, and song practice (Friemel et al., 2014; Hahn et al., 2017; Trezza et al., 2012). Pharmacology studies demonstrate that treatments that increase cannabinoid binding to receptors by preventing the breakdown of cannabinoids (i.e., indirect agonists) enhance social play in juvenile rats through interactions with opioid and dopamine receptor activity (Trezza and Vanderschuren, 2008a,b, 2009). Indirect agonist treatment also increases the number of times rats push levers for the opportunity to play (Achterberg et al., 2016), indicating that cannabinoids are involved in the motivation to engage in rewarding play behavior. Although this treatment did not increase social play-associated CPP, which is considered a reflection of the magnitude of reward induced by play, the authors suggest that this may be the result of a ceiling effect.

In songbirds, the effects of indirect endocannabinoid agonists on song practice have not been studied; however, a receptor agonist that binds directly to cannabinoid receptors (i.e., a direct agonist) suppressed song produced by adult zebra finches singing in isolation (i.e., birds presumed to be practicing song) (Soderstrom and Johnson, 2001) and disrupted vocal learning in young birds (Soderstrom and Johnson, 2003). These results appear to be contrary to the stimulatory effects of indirect cannabinoid receptor agonists on social play; however, in rats direct agonists (like those used to study song practice) also reduce social play (Trezza and Vanderschuren, 2008a,b, 2009). The contradictory effects of direct versus indirect agonists on play were interpreted to reflect the fact that direct agonists bind to receptors throughout the brain, including in regions in which they inhibit play. In contrast, indirect agonists act to maintain cannabinoids in synapses in which they were already locally released, presumably in regions in which they act to facilitate play. Thus it is proposed that cannabinoids acting in specific brain regions stimulate play behavior (Trezza and Vanderschuren, 2008a,b; Vanderschuren et al., 2016), a hypothesis supported by site-directed pharmacological manipulations reviewed next.

Cannabinoids act in multiple brain regions to induce reward, including the NAc, which is the focus of studies on cannabinoids and play, and the VTA (Zangen et al., 2006). There is a direct projection pathway from NAc to VTA, and it is becoming clear that cannabinoid receptor agonists induce reward at the level of NAc primarily by inhibiting GABAergic control of VTA to increase activity of dopaminergic afferents from VTA (Oleson and Cheer, 2012; Parsons and Hurd, 2015). This circuitry, which appears to be similar in birds and mammals (Ding and Perkel, 2014), along with the mPOA, is the focus of studies on cannabinoids and song practice. In juvenile rats, social play increases levels of the endocannabinoid anandamide in NAc (Trezza et al., 2012), and infusion of URB597, an indirect cannabinoid agonist, into NAc increases social play in rats (Trezza et al., 2012). Additionally, the endocannabinoid 2-arachidonoylglycerol (2-AG) plays a role in social play. Treatment with JZL184, a 2-AG hydrolysis inhibitor (i.e., an indirect agonist of 2-AG), enhances social play, an effect prevented by direct infusion of a CB$_1$ receptor antagonist into the NAc (Manduca et al., 2016a). NAc dopaminergic neurotransmission also modulates the endocannabinoid-mediated increase in social play. Specifically, it was shown that intra-NAc infusion of α-flupenthixol, a dopamine receptor antagonist, blocked the play-enhancing effects of the indirect cannabinoid agonist, URB597, on social play (Manduca et al., 2016b). Taken together, results of these studies suggest a possible role for endocannabinoinds in NAc, including the modulation of dopamine-related reward, in regulating the rewarding properties of play in rats, although this must now be tested directly.

Studies on brain regions in which cannabinoids impact song practice have mostly focused on regions involved in vocal learning and production, rather than in motivation and reward (e.g., (Soderstrom et al., 2011, 2004; Soderstrom and Tian, 2006; Soderstrom and Wilson, 2013)). However, recently we conducted a study examining relationships between song-associated reward and endocannabinoid expression in VTA and mPOA. Using a song-associated CPP procedure similar to that described above, we found that song practice in male starlings correlated positively with a CPP measure of reward (Hahn et al., 2017), as in previous studies reviewed above (Riters et al., 2014; Riters and Stevenson, 2012). In addition, expression of the endocannabinoid transporter FABP7 in mPOA and CB$_1$ receptor expression in VTA positively related to the CPP measures of song-associated reward (Fig. 3). These data suggest that endocannabinoids may act in these regions to stimulate, maintain, and reward song practice. Studies are now needed to determine the extent to which blocking endocannabinoid activity directly in specific brain regions, such as mPOA and VTA disrupts associations between song practice and reward and to determine the extent to which these manipulations have similar effects on play in rats. In addition, given that cannabinoid indirect agonists induce reward at the level of NAc by increasing activity of dopaminergic afferents from VTA (Oleson and Cheer, 2012); future work should examine how dopamine and cannabinoids in this circuitry influence reward associated with social play in rats and song practice in songbirds.

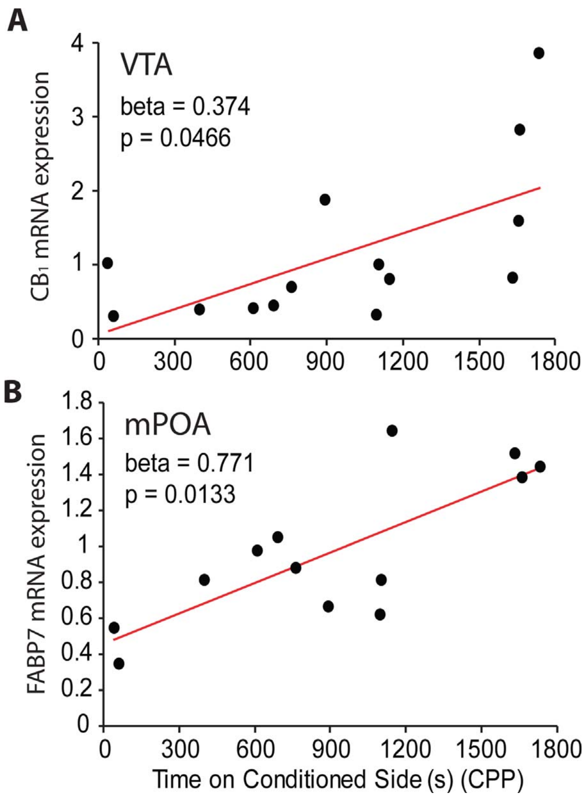

Fig. 3. Song-associated reward is positively coupled to endocannabinoid-related mRNA expression in VTA and mPOA. Relationships between song-associated reward (CPP; measured as the amount of time (s) on Test Day spent on the conditioned side of the apparatus) and (A) CB$_1$ mRNA expression in VTA and (B) FABP7 mRNA expression in mPOA. Beta and p values were determined with a multiple regression model. Linear regression lines indicate a significant relationship ($p < 0.05$).
Data from Hahn et al. (2017).

7. Both song practice and social play are highest when steroids are low

In songbirds, steroid effects on male song learning have been well studied. These studies show that the plastic period of juvenile song learning closes when birds mature and concentrations of testosterone rise (Nottebohm et al., 1987; Marler et al., 1988; Williams et al., 2003). The rise in testosterone causes song to crystallize into a stable, stereotyped form that a male bird will use to attract mates and defend territories. In seasonally breeding songbirds, at the end of each breeding season, testosterone drops and males again enter periods of vocal motor exploration that are characterized by the production of less stereotyped songs (and in the case of open-ended learners such as starlings the learning of new, or rearrangement of old, sequences of song) (Nottebohm et al., 1987; Alger et al., 2016). Testosterone thus causes a shift from song practice (which we propose to be a form of play behavior) to conspecific-directed extrinsically-rewarded singing behavior. Although, activational effects of testosterone do not appear to suppress play in rats (Smith et al., 1996), the pubertal increase in steroid hormones (testosterone in males and estradiol in females) facilitates sexual and agonistic behaviors and in this way contributes to the transition from playful behavior to extrinsically-rewarded sexually- and agonistically-motivated behaviors (Thor and Holloway, 1984; Baum, 1972). Thus testosterone (or its metabolites) may modify motivation and reward systems to induce the shift from singing/playing for "amusement" to producing similar, yet more stereotyped motor behaviors in reproductive, extrinsically-rewarded contexts.

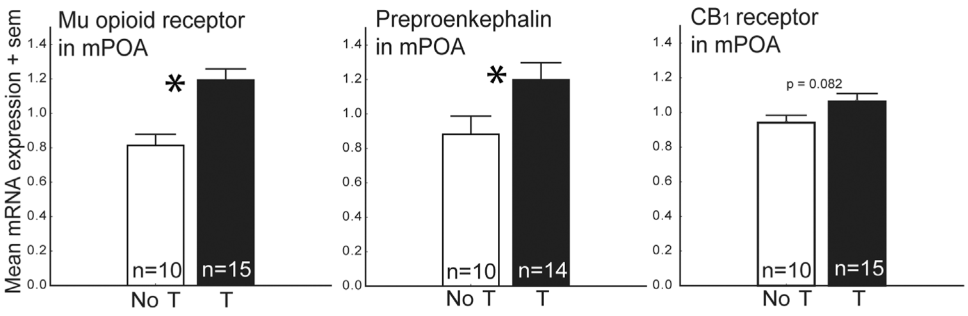

Fig. 4. Evidence that testosterone may modify opioid and endocannabinoid reward systems to shift birds from song practice to the production of more stereotyped song in primary contexts. mRNA measures of mu opioid receptors, preproenkephalin, and CB$_1$ receptors in the mPOA of castrated male starlings treated for 10 days with empty or testosterone (T)-filled subcutaneous silastic implants. Asterisks indicate $p < 0.05$. Opioid findings are from reanalysis of data presented in (Spool et al., 2016). CB$_1$ findings are from an unpublished pilot study.

8. Testosterone modifies neural systems involved in reward

In rats, studies show that testosterone and its metabolite estradiol modify behavioral responses to opioids (e.g., morphine) and cannabinoids (e.g., Δ^9-tetrahydrocannabinol) (Stewart and Rodaros, 1999; Marusich et al., 2015). Past studies also show that relatively low opioid activity is present in mPOA when rats are in endocrine conditions that facilitate play behavior. For example, enkephalin and mu opioid receptor markers in NAc and mPOA are lower in female rats with low estradiol compared to those treated with estradiol (e.g., (Holland et al., 1998; Watson et al., 1986; Mateo et al., 1992; Peckham et al., 2011; Roman et al., 2006; Le Saux and Di Paolo, 2005; Hammer et al., 1994)). Estradiol treatment also increases mu opioid receptor binding and internalization in mPOA (Eckersell et al., 1998). Our work in starlings similarly shows that testosterone treatment in castrated males increases preproenkephalin and mu opioid receptor mRNA expression in mPOA (Fig. 4) (Spool et al., 2016). As part of a pilot project, we also measured CB$_1$ receptor expression in mPOA in the same birds and observed a trend for expression to be higher in testosterone treated compared to castrated males ($p = 0.08$) (Fig. 4). Thus, when birds are in endocrine conditions in which they engage in high rates of motor exploration (i.e., song practice), opioid markers in mPOA are relatively low. Cannabinoids may also be impacted by steroid hormones, but this requires further study.

The findings that opioids are relatively low during periods of play and song practice may seem counterintuitive to the idea that opioids facilitate these behaviors. However, high levels of opioid activity are known to inhibit behavior (e.g., (Kelm-Nelson et al., 2013)). Therefore it may be that the relatively low level of opioid-related mRNA that is present when circulating steroid concentrations are low results in a low level of opioid activity (i.e., release and binding) which facilitates and rewards song practice and play. This would be similar to “hedonic” feeding which is facilitated and rewarded by relatively low levels of opioid release, but suppressed by higher levels (DiFeliceantonio et al., 2012; Doyle et al., 1993; Evans and Vaccarino, 1990; Sanger and McCarthy, 1981). Studies are now needed to determine the extent to which steroids modify opioids and endocannabinoids in the same brain regions in songbirds and mammals to shift animals from periods of high song practice/social play to periods of high sexual/agonistic activity.

9. Conclusions

By necessity, this review focuses on studies of play in rats, because studies of play-associated reward and the brain have been run mostly in rats. However, play (or play-like) behavior has been identified in a range of animals (from invertebrates to fish to birds to mammals) with birds such as magpies, ravens, and parrots engaging in extremely high levels of play behavior (reviewed in (Burghardt, 2005)). Furthermore, song-associated reward has only been studied to date in starlings and zebra finches. This limits the extent to which findings can be generalized to other species. Thus, future studies involving a wider range of species are necessary to expand the breadth of this research.

There are certainly differences in many aspects of play and birdsong practice. For example, rough-and-tumble play in rats is dependent upon the presence of a social partner and involves sensory-motor contact in the form of touch between playing individuals. In contrast, although song practice in birds is facilitated by the presence of social flock mates, it is not strictly dependent upon the presence of a social partner (i.e., it can be produced by isolated birds) and involves acoustic sensory-motor contact. Nonetheless, we note several striking parallels between social play in mammals and song practice in songbirds. 1) Both involve adding, dropping, and resequencing motor behaviors in non-sexual contexts. 2) In both cases, these behaviors are performed outside primary reproductive contexts but are developmentally preparing animals to engage in these contexts. 3) In both cases, engaging in these patterns of motor exploration does not result in any obvious, immediate external reward. 4) There is strong evidence that both activities are tightly coupled to intrinsic reward based on studies using similar CPP methods. 5) Both social play and song practice are tightly coupled to opioid and endocannabinoid activity. 6) Finally, both social play in rats and song practice in birds are highest when testosterone is low. This list both fulfills criteria proposed by Burghardt to distinguish play from other behaviors (Burghardt, 2005) and offers novel neurophysiological support to the hypothesis that song practice is a rewarding form of play.

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