Dopaminergic Dynamics Contributing to Social Behavior

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Social interaction is a complex behavior that is essential for the survival of many species, and it is impaired in a broad range of neuropsychiatric disorders. Several cortical and subcortical brain regions have been implicated in a variety of sociosexual behaviors, with pharmacological studies pointing to a key role of the neurotransmitter dopamine. However, little is understood about the real-time circuit dynamics causally underlying social interaction. Here, we consider current knowledge on the role of brain reward circuitry in same-sex social behavior and describe findings from new methods for probing how this circuitry governs social motivation in health and disease.

Social interaction is a challenging and highly integrative cognitive behavior that is essential for many mammalian species, and it is impaired in major psychiatric disorders such as autism, schizophrenia, social anxiety, and depression, with a broad range of potential etiologies. Several cortical and subcortical brain regions have been implicated in controlling social behavior, such as the prefrontal cortex, amygdala, striatum, dorsal raphe, and hypothalamus (Gingrich et al. 2000; Young et al. 2001; Leypold et al. 2002; Robinson et al. 2002; Liu and Wang 2003; Young and Wang 2004; Curtis and Wang 2005; Aragona et al. 2006; Lin et al. 2011; Robinson et al. 2011; Dölen et al. 2013; Yang et al. 2013; Felix-Ortiz and Tye 2014; Hong et al. 2014; Unger et al. 2015). In rodents, the majority of these studies have focused on sociosexual behaviors, such as pair bonding, aggression, and other behaviors related to sexual competition. However, comparatively little is known about the neural circuitry regulating adult same-sex, nonaggressive social interaction, which is of relevance for understanding circuits that may go awry in social-function disorders. Here, we discuss the role of dopaminergic circuitry in same-sex social interaction, highlighting recent findings from new optogenetic methods for probing endogenous and causal circuit dynamics underlying social motivation.

MESOLIMBIC CIRCUITRY IN NORMAL SOCIAL BEHAVIOR

The neurotransmitter dopamine (DA), produced in the ventral tegmental area (VTA), has long been known to play a role in the processing of both natural and conditioned rewards. The terminal region with the densest VTA DA projections is the ventral striatum, or nucleus accumbens (NAc), which is thought to encode reward-related signals from the VTA. The NAc comprises pri-

marily the inhibitory projection neurons called medium spiny neurons (MSNs) that can be differentiated by the type of DA receptor they express: D1 or D2. These two subpopulations of NAc MSNs are thought to bidirectionally control reward (Lobo et al. 2010) and have been pharmacologically implicated in affiliative behaviors (Puglisi-Allegra and Cabib 1997; Young and Wang 2004). The NAc also receives inputs from other regions implicated in social behavior, such as the dorsal raphe, hypothalamus, and prefrontal cortex, as well as sensory inputs, and is thus poised to orchestrate the integration of diverse streams of socially relevant information into behavioral output.

Human genetic studies have shown a role for genes involved in the dopamine pathway in modulating social behavior. The nine-repeat allele of the DA transporter DAT1, thought to result in increased striatal DA, was associated with stronger social approach tendency in an implicit social approach-avoidance task (Enter et al. 2012). Interestingly, the authors observed a significantly stronger approach to images of happy faces, whereas avoidance of angry faces was not affected, consistent with a role for striatal DA in approach of appetitive socially relevant stimuli. Another study showed that administration of L-DOPA, a DA precursor, improved the ability of 10-repeat genotype subjects, assumed to have lower endogenous striatal DA, to learn about a partner's prosocial preferences (Eisenegger et al. 2013). In rats, studies using fast-scan cyclic voltammetry to record temporally precise DA release in postsynaptic targets found a sixfold increase in the frequency of DA transients throughout the dorsal and ventral striatum of rats investigating a novel conspecific (Robinson et al. 2002). Recording specifically from the NAc, they observed DA release upon orientation toward and initial contact with the conspecific, an effect that habituated upon subsequent presentations of the same conspecific (Robinson et al. 2011).

These studies, although largely correlative, suggest that DA may be involved in encoding or modulating social behavior.

SOCIAL COGNITION VERSUS SOCIAL MOTIVATION THEORIES OF AUTISM

Examining the changes that occur in the brains of patients with social-function disorders can inform us about the circuitry underlying normal behavior. One of the classical hypotheses put forward to explain the social deficits in autism spectrum disorders (ASDs) is the notion of a dysfunction in social cognition or executive control, with specific deficits in theory of mind, the ability to understand and ascribe mental states to others to explain and predict their behavior. These deficits in social cognition are thought to arise from abnormal information processing in higher-level executive control regions, such as the frontal cortex. For example, recent studies in human genetics and development have implicated cortical abnormalities in ASD (e.g., Willsey et al. 2013), and direct optogenetic modulation of neocortical excitation–inhibition balance was found to disrupt social behavior in mice (Yizhar et al. 2011). However, the idea of autism as a deficit in reward-related social motivation may be distinct and complementary to processes involved in cortical information processing, and thus is likely in its own right to be relevant to etiology, genetics, diagnosis, and investigation of potential avenues for treatment.

Social motivation encompasses the drive to seek social interaction and take pleasure in it. Many species, from humans to rodents, find social interaction rewarding, independent of familial or reproductive motivations. Subjects playing economic games take pleasure in cooperation and collaboration and will work to obtain social rewards even at the cost of higher individual economic outcome (Fehr and Camerer 2007). Neuroimaging during tasks such as the prisoner's dilemma show that the reward value of mutual cooperation with a human partner is associated with increased activation of the ventral striatum compared with cooperation with a computer partner, despite identical monetary gain in both situations (Fehr and Camerer 2007). Even toddlers show a strong preference for collaborative over individual access to reward (Chevallier et al. 2012). There is also evidence from animal studies suggesting that mice find social interaction rewarding outside the context of reproduction or parental care. Juvenile mice are equally motivated to investigate conspecifics regardless of their sex, and social conditioned place preference tests have shown that adolescent mice will strongly prefer an environment that has previously been paired with a conspecific to one without a conspecific, suggesting that a brief episode of social contact can have positive conditioning value even before animals reach sexual maturity (Panksepp et al. 2007).

The social motivation hypothesis of autism postulates that children with ASD do not find social stimuli rewarding, a primary deficit leading to later abnormal development of social skills and social cognition as a consequence

of lacking social interest. This theory points to the dysregulation of subcortical circuits such as the mesolimbic pathway in the etiology of the disorder. Several neuroimaging studies have supported the notion of lacking social reward in ASD, accompanied by changes in striatal circuitry implicated in motivation. Several studies showed pronounced impairment in learning to choose social rewards compared with monetary rewards in ASD, which was associated with decreased frontostriatal response during social but not monetary reward learning (Scott-Van Zeeland et al. 2010; Lin et al. 2012). In typically developing children, the authors also found a positive correlation between ventral striatal activity and social reciprocity (Scott-Van Zeeland et al. 2010). Yet another study showed that oxytocin, a prosocial neuropeptide being explored as a potential therapy for ASD, enhances VTA activation to social reward and social punishment cues (Groppe et al. 2013). Genetic studies have also suggested that mutations in genes along the mesolimbic DA pathway are associated with ASD. A dopamine D1 receptor (DRD1) haplotype as well as DRD3 single-nucleotide polymorphisms have been associated with increased risk for ASD (Hettinger et al. 2008; Staal 2014). Mutations in the dopamine transporter (DAT) have also been associated with ASD (Bowton et al. 2014); DAT mutations that result in increased expression of the transporter, and thus likely lower synaptic levels of DA, are associated with increased social anxiety in ASD children (Gadow et al. 2008). Together, these data suggest a deficit in social reward processing in ASD accompanied by genetic and functional abnormalities in the mesolimbic DA pathway. An intriguing hypothesis arising from this research is that increasing social reward responsiveness in ASD, perhaps via manipulation of the dopaminergic mesolimbic pathway, may improve social learning and prevent the emergence of social cognitive deficits.

A CIRCUIT-BASED APPROACH TO SOCIAL MOTIVATION

However, DA pathway genetic polymorphisms are present in only a small fraction of ASD cases, and human neuroimaging studies are purely correlative in nature. To gain a better mechanistic understanding of the role of mesolimbic circuitry in normal and pathological social behavior, we can take advantage of the genetic tools available in mice. Previous behavioral pharmacology studies have shown that dopamine receptor agonists and antagonists can bidirectionally modulate social interaction (Puglisi-Allegra and Cabib 1997), suggesting a causal role of the neurotransmitter in social behavior. However, a circuit-level understanding of which DA cells, projections, and postsynaptic targets mediate these effects and how they interact in real time during behavior has remained largely unknown. This problem was recently addressed using all-optical readout and control of DA neurons in socializing mice to understand how genetically specified cells and projections are causally involved in driving social behavior (Gunaydin et al. 2014).

To observe socially relevant native patterns of neural activity in real time, the genetically encoded Ca^{2+} indicator GCaMP5, which changes its fluorescence properties upon elevation of Ca^{2+} levels inside the cell (a well-established proxy for neural activity), was used to record temporally precise Ca^{2+} transients (Akerboom et al. 2012; Chen et al. 2013) in VTA DA neurons (Gunaydin et al. 2014). To selectively target dopaminergic neurons in the VTA, a virus carrying Cre-dependent GCaMP5 was injected into the VTA of mice expressing Cre recombinase under the tyrosine hydroxylase (TH) promoter (TH::Cre mice). Developing and using a novel technique called fiber photometry, the investigators implanted a single optical fiber just above the VTA, which was used both to deliver excitation light and to collect bulk activity-dependent GCaMP fluorescent transients in the freely behaving animal. Excitation and emission fluorescence were spectrally separated using a dichroic, passed through a single band filter, and focused onto a photodetector to record real-time VTA activity as animals socialized with a novel conspecific in their home cage (Fig. 1A). There was a marked increase in VTA GCaMP signal as the test subject investigated the conspecific, specifically time-locked to appetitive approach and contact investigation of the other mouse, which habituated over time (Fig. 1B). These data show for the first time the real-time dynamics of VTA DA neurons during a complex social behavior, and although correlative, they suggested that experimentally prolonging these habituating VTA signals might be a way to increase the animal's social behavior.

Optogenetics enables us to causally link VTA DA activity to social interaction by expressing a Cre-dependent light-gated cation channel, channelrhodopsin-2 (ChR2), in the VTA of TH::Cre mice to enable temporally precise control over their activity using pulses of 473-nm blue light. Precise patterns of phasic photostimulation of these cells, which had previously been shown to evoke maximal levels of downstream DA release (Adamantidis et al. 2011), significantly increased the amount of time mice spent investigating a novel conspecific. This effect was

blocked by DA receptor antagonism (although no genetic targeting strategy resolves cell types with complete specificity, these results confirmed DA dependence of the behavioral result, supporting prior immunostaining-based validation of this targeting methodology; Tsai et al. 2009). Conversely, inhibition of VTA DA neurons using the inhibitory chloride pump halorhodopsin (eNpHR3.0) significantly decreased interaction, showing bidirectional control of social behavior by VTA DA neurons (Fig. 2A,B). Importantly, modulation of VTA DA activity did not affect time spent investigating a novel inanimate object (Fig. 2C). These data showed for the first time an endogenous and causal role of VTA DA activity in driving social approach behavior.

Previous human and animal studies have suggested that the ventral striatum (or NAc), a primary target of reward-related VTA DA neurons, may be a key downstream region relevant to the processing of social reward and one dysregulated in autism. Selective optogenetic stimulation of the VTA-to-NAc projection was sufficient to reproduce the prosocial effect of VTA DA cell body stimulation, whereas stimulation of other VTA DA projections, such as to the PFC, did not affect social behavior, pointing to a critical role specifically for the VTA-NAc circuit (Fig. 2D,E). Electrophysiologically, the stimulation parameters that increased social behavior increased firing rate in the NAc (Fig. 3A,B). Animals were then exposed to the three-chamber test, an apparatus consisting of one “social chamber” with a caged novel conspecific on one side and a “neutral chamber” containing a caged inanimate object on the other, separated by an empty middle chamber. Recording in vivo during this behavioral test, higher NAc activity was also found when animals chose to explore the social chamber compared with the neutral one (Fig. 3C,D), suggesting that increased NAc activity is a correlate of native prosocial behavior independent of any exogenous neural manipulation, corroborating previous reports from human neuroimaging (Scott-Van Zee et al. 2010).

These electrophysiological recordings suggested that the increased NAc activity observed during prosocial

Figure 1. Optical recording of dopaminergic dynamics during social interaction. (A, Left) Fiber photometry setup. Light path for GCaMP fluorescence excitation and emission is through a single optical fiber implanted in the VTA. (Right) viral targeting of GCaMP5 to VTA DA neurons. (B, Top) Example trace of VTA DA activity in social behavior. Red dashes indicate interaction bouts. (Bottom) zoom-in of dashed interval relating VTA DA GCaMP signal and social interaction (red boxes). (Adapted from Gunaydin et al. 2014.)

Figure 2. VTA modulation of social behavior. (A) Optical stimulation parameters for home cage interaction. For excitation, phasic bursts of blue light were delivered every 5 sec. For inhibition, continuous yellow light was delivered. (B) Summary of light-evoked changes in social interaction after bidirectional control of VTA DA neurons. Phasic stimulation of VTA cell bodies increased social interaction, whereas inhibition of VTA cell bodies decreased interaction. (C) Neither stimulation nor inhibition of VTA cell bodies significantly affected investigation of a control novel inanimate object. (D) Phasic stimulation of VTA-NAc projections increased social interaction in ChR2 animals (purple) compared with controls (gray). (E) Phasic stimulation of VTA-PFC projections had no effect on social interaction in ChR2 animals (blue) or controls (gray). (Adapted from Gunaydin et al. 2014.)

Figure 3. NAc electrophysiological correlates of increased social behavior. (A) Increase in NAc activity (red) evoked by VTA stimulation (black). (B) PSTH showing light-evoked increase in NAc firing with one burst of VTA stimulation. (C) Heat map showing firing rate of NAc neurons in freely moving animals exploring neutral and social environments. Warmer colors indicate higher firing rate. (D) NAc spiking is higher in the social environment. (Adapted from Gunaydin et al. 2014.)

Figure 4. Fiber photometry of DA projection activity in NAc during social interaction. (A) Fiber photometry of VTA projections in NAc. (B) VTA projection activity during social (*top*) and novel object investigation (*bottom*; interaction bouts in red). (C) Heat maps (*top*) and peri-event plots (*bottom*) of NAc projection fluorescence aligned to start of interaction bout for social or novel object investigation. For heat maps, warmer colors indicate higher fluorescence signal; for peri-event plots, warmer colors indicate earlier interaction bouts. (D) NAc projections largely recapitulate social signals in VTA, with lower response to a novel object. (Adapted from Gunaydin et al. 2014.)

behavior was likely driven by increased VTA input. However, until the advent of fiber photometry, no technique existed to directly measure activity in a set of genetically defined afferent projections to a region. By expressing GCaMP5 in the VTA and implanting the recording fiber-optic in the NAc (Fig. 4A), fluorescent transients were detected in VTA-NAc projections during epochs of social interaction, recapitulating the increased activity seen in VTA cell bodies, and demonstrating for the first time the activity of genetically defined, projection-specific inputs to a region during social behavior (Fig. 4B–D). Further pharmacological and optogenetic investigation showed that downstream D1 neurons in the NAc mediated this prosocial effect of increased VTA input. This work showed a causal role for reward circuitry in driving social behavior and opened the door to further investigation of specific mechanisms within the VTA-NAc circuit that may go awry in social-function disorders such as autism and could potentially one day be harnessed therapeutically to augment the rewarding nature of social stimuli in these disorders.

INTEGRATING MOTIVATIONAL AND COGNITIVE CONTROL OF SOCIAL BEHAVIOR

In addition to motivational factors, social behavior requires rapid integration and updating of complex stimuli that are used to guide appropriate actions for initiation and maintenance of interaction, likely mediated by higher-

level cognitive areas such as the prefrontal cortex (PFC). Another optogenetic study using direct manipulation of prefrontal microcircuit elements showed a crucial role of this region in regulating social behavior. Yizhar et al. (2011) developed a novel channelrhodopsin variant called the stabilized step-function opsin (SSFO) for long-timescale modulation of cortical activity using a brief pulse of blue light before assessing social interaction. One advantage of using the SSFO to study the causal relationships between PFC circuit elements and behavior was that its long-lasting depolarization facilitated social behavioral assessment without requirement for the fiber-optic during behavior, because a single pulse of blue light before behavioral testing is sufficient to cause activation of cells for the duration of the assay. They found that activating excitatory neurons in the mPFC with the SSFO caused a dramatic impairment in social behavior, as stimulated animals spent significantly less time investigating a novel conspecific. This social impairment was accompanied by an increase in power of high-frequency γ oscillations in the mPFC, a pathological signature observed in patients with autism (Orekhova et al. 2007). Concurrent elevation of activity in inhibitory parvalbumin (PV)-expressing local interneurons partially rescued the social deficit, demonstrating that excitatory/inhibitory balance in mPFC plays a causal role in modulating social interaction.

Although activation of the mesolimbic DA pathway drove an increase in social behavior, activation of the mesocortical pathway interestingly had no effect on social

behavior, but instead drove aversion and anxiety-related behaviors (Gunaydin et al. 2014). Accordingly, there is no current evidence that VTA projections play a causal role within the PFC in modulating the PFC's important role in social behavior regulation, although certainly this mesocortical circuit could provide subthreshold modulation of the relevant circuitry or other glutamatergic cortical inputs, whereas under these conditions, activation alone is not sufficient to alter social behavior. It is also possible that in situations of high stress and anxiety, this circuit may serve to negatively regulate social behavior. Future studies are certainly needed to better understand how subcortical and cortical circuits work together to control social motivation and cognition, and which specific aspects of social interaction (e.g., initiation, maintenance, and reward) are controlled by each circuit and cell type. In this regard, fiber photometry and optogenetics together will be useful for combinatorial readout and control of multiple independent cell populations in behaving animals and hold great promise for beginning to unravel how other subcortical regions work in a coordinated fashion to regulate normal and pathological social behavior.

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REFERENCES

- Adamantidis AR, Tsai HC, Boutrel B, Zhang F, Stuber GD, Budygin EA, Touriño C, Bonci A, Deisseroth K, de Lecea L. 2011. Optogenetic interrogation of dopaminergic modulation of the multiple phases of reward-seeking behavior. *J Neurosci* **31**: 10829–10835.
- Akerboom J, Chen TW, Wardill TJ, Tian L, Marvin JS, Mutlu S, Calderón NC, Esposti F, Borghuis BG, Sun XR, et al. 2012. Optimization of a GCaMP calcium indicator for neural activity imaging. *J Neurosci* **32**: 13819–13840.
- Aragona BJ, Liu Y, Yu YJ, Curtis JT, Detwiler JM, Insel TR, Wang Z. 2006. Nucleus accumbens dopamine differentially mediates the formation and maintenance of monogamous pair bonds. *Nat Neurosci* **9**: 133–139.
- Bowton E, Saunders C, Reddy IA, Campbell NG, Hamilton PJ, Henry LK, Coon H, Sakrikar D, Veenstra-VanderWeele JM, Blakely RD, et al. 2014. SLC6A3 coding variant Ala559Val found in two autism probands alters dopamine transporter function and trafficking. *Transl Psychiatry* **4**: e464.
- Chen TW, Wardill TJ, Sun Y, Pulver SR, Renninger SL, Baohan A, Schreier ER, Kerr RA, Orger MB, Jayaraman V, et al. 2013. Ultrasensitive fluorescent proteins for imaging neuronal activity. *Nature* **499**: 295–300.
- Chevallier C, Kohls G, Troiani V, Brodtkin ES, Schultz RT. 2012. The social motivation theory of autism. *Trends Cogn Sci* **16**: 231–239.
- Curtis JT, Wang Z. 2005. Ventral tegmental area involvement in pair bonding in male prairie voles. *Physiol Behav* **86**: 338–346.
- Dölen G, Darvishzadeh A, Huang KW, Malenka RC. 2013. Social reward requires coordinated activity of nucleus accumbens oxytocin and serotonin. *Nature* **501**: 179–184.
- Eisenegger C, Pedroni A, Rieskamp J, Zehnder C, Ebstein R, Fehr E, Knoch D. 2013. DAT1 polymorphism determines L-DOPA effects on learning about others' prosociality. *PLoS One* **8**: e67820.
- Enter D, Colzato LS, Roelofs K. 2012. Dopamine transporter polymorphisms affect social approach-avoidance tendencies. *Genes Brain Behav* **11**: 671–676.
- Fehr E, Camerer CF. 2007. Social neuroeconomics: The neural circuitry of social preferences. *Trends Cogn Sci* **11**: 419–427.
- Felix-Ortiz AC, Tye KM. 2014. Amygdala inputs to the ventral hippocampus bidirectionally modulate social behavior. *J Neurosci* **34**: 586–595.
- Gadow KD, Roohi J, DeVincent CJ, Hatchwell E. 2008. Association of ADHD, tics, and anxiety with dopamine transporter (DAT1) genotype in autism spectrum disorder. *J Child Psychol Psychiatry* **49**: 1331–1338.
- Gingrich B, Liu Y, Cascio C, Wang Z, Insel TR. 2000. Dopamine D2 receptors in the nucleus accumbens are important for social attachment in female prairie voles (*Microtus ochrogaster*). *Behav Neurosci* **114**: 173–183.
- Groppe SE, Gossen A, Rademacher L, Hahn A, Westphal L, Gründer G, Spreckelmeyer KN. 2013. Oxytocin influences processing of socially relevant cues in the ventral tegmental area of the human brain. *Biol Psychiatry* **74**: 172–179.
- Gunaydin LA, Grosenick L, Finkelstein JC, Kauvar IV, Fenno LE, Adhikari A, Lammel S, Mirzabekov JJ, Airan RD, Zalocusky KA, et al. 2014. Natural neural projection dynamics underlying social behavior. *Cell* **157**: 1535–1551.
- Hettinger JA, Liu X, Schwartz CE, Michaelis RC, Holden JJ. 2008. A DRD1 haplotype is associated with risk for autism spectrum disorders in male-only affected sib-pair families. *Am J Med Genet B Neuropsychiatr Genet* **147B**: 628–636.
- Hong W, Kim DW, Anderson DJ. 2014. Antagonistic control of social versus repetitive self-grooming behaviors by separable amygdala neuronal subsets. *Cell* **158**: 1348–1361.
- Leybold BG, Yu CR, Leinders-Zufall T, Kim MM, Zufall F, Axel R. 2002. Altered sexual and social behaviors in trp2 mutant mice. *Proc Natl Acad Sci* **99**: 6376–6381.
- Lin D, Boyle MP, Dollar P, Lee H, Lein ES, Perona P, Anderson DJ. 2011. Functional identification of an aggression locus in the mouse hypothalamus. *Nature* **470**: 221–226.
- Lin A, Rangel A, Adolphs R. 2012. Impaired learning of social compared to monetary rewards in autism. *Front Neurosci* **6**: 143.
- Liu Y, Wang ZX. 2003. Nucleus accumbens oxytocin and dopamine interact to regulate pair bond formation in female prairie voles. *Neuroscience* **121**: 537–544.
- Lobo MK, Covington HE III, Chaudhury D, Friedman AK, Sun H, Dames-Werno D, Dietz DM, Zaman S, Koo JW, Kennedy PJ, et al. 2010. Cell type-specific loss of BDNF signaling mimics optogenetic control of cocaine reward. *Science* **330**: 385–390.
- Orehova EV, Stroganova TA, Nygren G, Tsetlin MM, Posikera IN, Gillberg C, Elam M. 2007. Excess of high frequency electroencephalogram oscillations in boys with autism. *Biol Psychiatry* **62**: 1022–1029.
- Panksepp JB, Jochman KA, Kim JU, Koy JJ, Wilson ED, Chen Q, Wilson CR, Lahvis GP. 2007. Affiliative behavior, ultrasonic communication and social reward are influenced by genetic variation in adolescent mice. *PLoS One* **2**: e351.
- Puglisi-Allegra S, Cabib S. 1997. Psychopharmacology of dopamine: The contribution of comparative studies in inbred strains of mice. *Prog Neurobiol* **51**: 637–661.
- Robinson DL, Heien ML, Wightman RM. 2002. Frequency of dopamine concentration transients increases in dorsal and ventral striatum of male rats during introduction of conspecifics. *J Neurosci* **22**: 10477–10486.
- Robinson DL, Zitzman DL, Smith KJ, Spear LP. 2011. Fast dopamine release events in the nucleus accumbens of early adolescent rats. *Neuroscience* **176**: 296–307.

- Scott-Van Zeeland AA, Dapretto M, Ghahremani DG, Poldrack RA, Bookheimer SY. 2010. Reward processing in autism. *Autism Res* **3**: 53–67.
- Staal WG. 2014. Autism, DRD3 and repetitive and stereotyped behavior, an overview of the current knowledge. *Eur Neuropsychopharmacol* doi: 10.1016/j.euroneuro.2014.08.011.
- Tsai HC, Zhang F, Adamantidis A, Stuber GD, Bonci A, de Lecea L, Deisseroth K. 2009. Phasic firing in dopaminergic neurons is sufficient for behavioral conditioning. *Science* **324**: 1080–1084.
- Unger EK, Burke KJ CF Jr, Bender KJ, Fuller PM, Shah NM. 2015. Medial amygdalar aromatase neurons regulate aggression in both sexes. *Cell Rep* **10**: 453–462.
- Willsey AJ, Sanders SJ, Li M, Dong S, Tebbenkamp AT, Muhle RA, Reilly SK, Lin L, Fertuzinhos S, Miller JA, et al. 2013. Coexpression networks implicate human midfetal deep cortical projection neurons in the pathogenesis of autism. *Cell* **155**: 997–1007.
- Yang CF, Chiang MC, Gray DC, Prabhakaran M, Alvarado M, Juntti SA, Unger EK, Wells JA, Shah NM. 2013. Sexually dimorphic neurons in the ventromedial hypothalamus govern mating in both sexes and aggression in males. *Cell* **153**: 896–909.
- Yizhar O, Fenno LE, Prigge M, Schneider F, Davidson TJ, O'Shea DJ, Sohal VS, Goshen I, Finkelstein J, Paz JT, et al. 2011. Neocortical excitation/inhibition balance in information processing and social dysfunction. *Nature* **477**: 171–178.
- Young LJ, Wang Z. 2004. The neurobiology of pair bonding. *Nat Neurosci* **7**: 1048–1054.
- Young LJ, Lim MM, Gingrich B, Insel TR. 2001. Cellular mechanisms of social attachment. *Horm Behav* **40**: 133–138.

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