Check for updates

Neural mechanisms of aggression across species

Julieta E. Lischinsky[1] and Dayu Lin [1,2,3] ✉

Aggression is a social behavior essential for securing resources and defending oneself and family. Thanks to its indispensable function in competition and thus survival, aggression exists widely across animal species, including humans. Classical works from Tinbergen and Lorenz concluded that instinctive behaviors including aggression are mediated by hardwired brain circuitries that specialize in processing certain sensory inputs to trigger stereotyped motor outputs. They further suggest that instinctive behaviors are influenced by an animal's internal state and past experiences. Following this conceptual framework, here we review our current understanding regarding the neural substrates underlying aggression generation, highlighting an evolutionarily conserved 'core aggression circuit' composed of four subcortical regions. We further discuss the neural mechanisms that support changes in aggression based on the animal's internal state. We aim to provide an overview of features of aggression and the relevant neural substrates across species, highlighting findings in rodents, primates and songbirds.

Aggression is defined as hostile behaviors toward other animals of the same species[1,2]. While the exact form of aggression differs widely across species, all aggressive actions share the common goal of overpowering the opponent, often by inflicting pain and harm[1]. Aggression is metabolically costly and potentially risky. In extreme cases, it is fatal. Yet aggression exists in nearly all species, ranging from invertebrates to vertebrates, from animals swimming in the ocean to those soaring in the sky, denoting its important functionality[1] (Box 1).

In humans, a popular framework for understanding aggression is called the general aggression model (GAM)[3]. In this model, an aggression-provoking situation (input) alters the internal state of the individual (route), which in turn affects appraisal and decision processes that lead to aggressive or nonaggressive outcomes (outcome). In animals, similar frameworks can be applied to understand the generation of aggression (Fig. 1). Upon detection of an aggression-provoking stimulus, for example, the intrusion of a conspecific competitor, aggressive arousal—an internal state that favors the generation of aggression—increases. Aggressive arousal is influenced by many internal and experiential factors, such as circadian state, stress level, reproductive state and winning and losing experience. When the aggressive arousal reaches a certain threshold, the animal initiates the motor execution of aggression, for example, attack. Here we will review the main neural substrates relevant for each stage of aggression generation.

Aggression-provoking cue detection circuits

The first step in the generation of aggression is the detection of an aggression-provoking stimulus. For humans, such stimuli can be in various sensory modalities, ranging from physical acts to verbal insults. For other animals, the aggression-provoking stimuli are often more stereotypical and conveyed primarily through one sensory modality. For example, rodents rely heavily on the olfactory cues to determine the sex, age, physical condition, familiarity and dominance status of an intruder[4]. Aggression is largely absent in mice without a functional nose[4,5]. Two parallel olfactory systems detect and process olfactory cues in rodents. In the main olfactory system, the main olfactory epithelium detects volatiles and projects to the main olfactory bulb (MOB), which then projects to several areas including piriform cortex and cortical amygdala (CoA)[4].

CoA then projects to the medial amygdala (MeA), an essential region for aggression generation, as detailed below[6]. In the accessory olfactory system, the vomeronasal organ detects non-volatile pheromones and projects to the accessory olfactory bulb (AOB), which then projects directly to MeA[4]. Thus, MeA is the first brain region where all olfactory information converges (Fig. 2).

In songbirds, olfaction plays a less important role (but see ref. [7]). Instead, auditory input, specifically the song of another conspecific, contains pivotal information regarding the identity of the individual and is an important trigger of aggression[8,9]. Playing back the song of an intruder paired to a decoy toy or a caged conspecific is sufficient to result in direct (physical attacks) or indirect (soft song) aggressive responses[9]. The auditory pathway in songbirds in the context of vocal learning and song production is well understood[10]. After the song is detected by the inner ear, the auditory information travels to the cochlear nucleus (CN) in the medulla, the dorsal lateral nucleus of the mesencephalon (MLd; analogous to inferior colliculus in mammals), the nucleus ovoidalis (Ov) of thalamus (analogous to auditory thalamus) and eventually reaches song perception and production regions in the forebrain[10]. While the interactions between the auditory pathway and the aggression circuit (see next section) are less well understood, tracing studies suggest that auditory information in songbirds can be relayed to the aggression circuit at the subcortical level. Specifically, nucleus taenia of the amygdala (Nt; homolog to mammalian MeA) receives inputs from the ovoidalis shell, a subdivision of avian auditory thalamus[11,12] while the ventromedial hypothalamus—an essential hypothalamic regions for aggression—receives inputs from Ov[13] (Fig. 3). Thus, in animals whose aggression can be triggered by stereotypical stimuli, there likely exist species-specific and developmentally hardwired circuits that route this information to the core aggression circuit (CAC) as proposed and detailed below.

The core aggression circuit

Once the aggression-provoking cue is detected, it is passed onto the CAC, the activity of which determines the overall aggressive arousal and likelihood of attack. The proposed CAC is composed of several interconnected nuclei, including MeA, bed nucleus of stria terminalis (BNST), ventrolateral part of the ventromedial hypothalamus (VMHvl) and ventral part of the premammillary nucleus (PMv).

[1]Neuroscience Institute, New York University School of Medicine, New York, NY, USA. [2]Department of Psychiatry, New York University School of Medicine, New York, NY, USA. [3]Center for Neural Science, New York University, New York, NY, USA. ✉e-mail: Dayu.Lin@nyulangone.org

---

Box 1 | Aggressive actions vary across species

In this Review, we define aggression as actions to overpower a conspecific opponent, which include both physical attacks and non-physical threats. As aggression exists in nearly all species, its form of expression varies widely with species-specific anatomical features. Here we discuss aggressive behaviors in mice, songbirds and humans.

Mice

Aggression is readily observed in laboratory male mice using a resident–intruder assay. In this assay, a strange male is introduced into the home cage of a singly-housed 'resident' male mouse. Upon detecting the intruder, the resident often initiates aggressive actions, including both threat display and physical attack. Tail rattling, a rapid vibration of the tail, is the most noticeable form of threat display[132], and biting is the main component of the physical attack. The specific pattern of biting varies with the relative strength of the animals: strong and offending animals tend to bite on the back of the opponent, whereas weak and defending animals tend to bite on the ventral surfaces and head[49]. Other movements, such as lunging and chasing, are common tactics to gain access to the preferred biting targets.

Songbirds

There are approximately 5,000 songbird species, many of which are migratory[133]. When a male songbird arrives at the breeding grounds, it competes, by singing, to obtain the most valuable resource: a territory. A high-quality territory is a guarantee of reproductive success, as it attracts females and provides nesting areas and food. A male songbird will choose a centrally located perch and sing loudly and repeatedly to advertise its presence to both its competitors and potential mates. Once a territory is established, the males will also sing at the territorial borders to ascertain their ownership[133].

If a male stranger ignores the singing and enters the territory, the resident will escalate its aggressive acts. Paradoxically, resident songbird will sing 'soft songs' to signal its intent to attack[133]. The resident will also 'puff' its feathers and quiver its wings, followed by arduously pecking on a near-by object. If the intruder refuses

to leave, the final resort is to exert physical attacks in which the resident will fly over the intruder, chase it and eventually pounce or vigorously peck its head or body[9]. During the non-breeding season, many songbird species do not maintain territories, but instead form a flock with a hierarchical order. Physical fighting will occur during hierarchy formation but is rare afterwards[133].

In laboratory settings, the majority of the studies on songbird aggression use a paradigm mimicking territorial intrusion. The procedure involves placing a decoy intruder (for example, a painted model of a bird or a live bird in a cage) into the territory of a male songbird, paired with a conspecific song played through a speaker. The resident's responses, such as approaching, singing, wing quivers and flights directed at the decoy, are quantified to indicate the level of aggression[133].

Human primates

Human aggression is complex and can be expressed in numerous ways. Non-physical aggression can be expressed verbally, through gestures or in writing, whereas physical aggression can include punching, kicking, biting, etc. Human aggression also has several features that are largely absent in other species. First, humans can employ weapons to overpower their opponents, and the winner of a fight is thus not necessarily determined by physical strength. Second, human aggression can sometimes be self-directed, with suicide at its extreme[134]. Third, any form of physical aggression, from school bullying to domestic violence, is generally considered bad behavior and condemned by our moral and justice systems. Lastly, humans show proactive aggression much more than any other species. Aggression can be classified as reactive or proactive (instrumental) based on the motive behind the actions. The former is unplanned aggression in response to an immediate trigger, whereas the latter is a planned action involving a seeking phase to gain access to the victim[135]. Although laboratory studies suggest that animals can show simple aggression-seeking behaviors[54], reactive aggression is far more common naturally. Humans are the only species that show proactive aggression with extreme sophistication, with war as an ultimate example.


It partially overlaps with the 'social behavior network' (SBN) that was initially proposed by Sarah Newman in mammals[14] and later expanded to large vertebrate species by James Goodson[15] (Box 2).

Medial amygdala. In mice, MeA is the major downstream of AOB and also receives inputs indirectly from MOB through CoA[4,6]. Correspondingly, cells in this region are strongly activated by olfactory cues from conspecifics[4,16]. Recent studies further demonstrate its direct role in driving aggression. Activating GABAergic cells in the posterodorsal part of MeA (MeApd) is sufficient to evoke attack in male mice[17]. Conversely, inactivating this area suppresses both male and female aggression[17–19]. In songbirds, MeA is among the regions showing increased immediate early gene (IEG) expression after aggressive encounters, but its functional role remains unclear[20,21]. In primates, imaging and lesion studies indicate that the amygdala plays a role in aggression, but these studies generally do not consider specific amygdala subregions[22,23].

Bed nucleus of the stria terminalis. Studies in rodents showed that the posterior part of the BNST (BNSTp) also receives inputs from the AOB[4] and has dense, bidirectional connections to the MeA[24]. Padilla et al. showed that optogenetic activation of axon terminals of MeA NPY-expressing cells in the BNST increased the overall attack duration in mice within a 10-min testing period[19]. Another study demonstrated that acute inhibition or ablation of aromatase-

expressing cells in the BNST suppresses inter-male aggression but does not affect maternal aggression in mice[25]. Recording of BNST aromatase cells in mice showed transient activation of the cells upon male introduction but not during subsequent attacks, suggesting that BNST might be important for aggressive arousal but not moment-to-moment attack[25]. Functional studies regarding a role of BNST in birds remain lacking, although studies in several avian species reported an increase in IEG expression in BNST after aggressive encounters[21].

Ventrolateral portion of the ventromedial hypothalamus. The VMHvl is perhaps the best studied region for aggression in recent years, with the vast majority of the studies done in mice[26]. This subnucleus of the medial hypothalamus receives direct inputs from both BNSTp and MeA[27,28]. In male and female mice, optogenetic activation of VMHvl cells, especially those expressing estrogen receptor alpha (Esr1), elicited time-locked attack toward both natural and suboptimal targets[29–32]. Pharmacogenetic activation of the VMHvl cells expressing progesterone receptor (PR), which overlaps substantially with Esr1, can enhance aggression in male mice regardless of their social status, housing condition or testing context[33]. Inactivating or ablating VMHvl cells abolishes natural inter-male aggression and maternal aggression in mice[29–32,34]. In vivo recording and imaging studies have revealed detailed response patterns of the VMHvl cells during agonistic encounters in male mice[29,31,32,35,36].
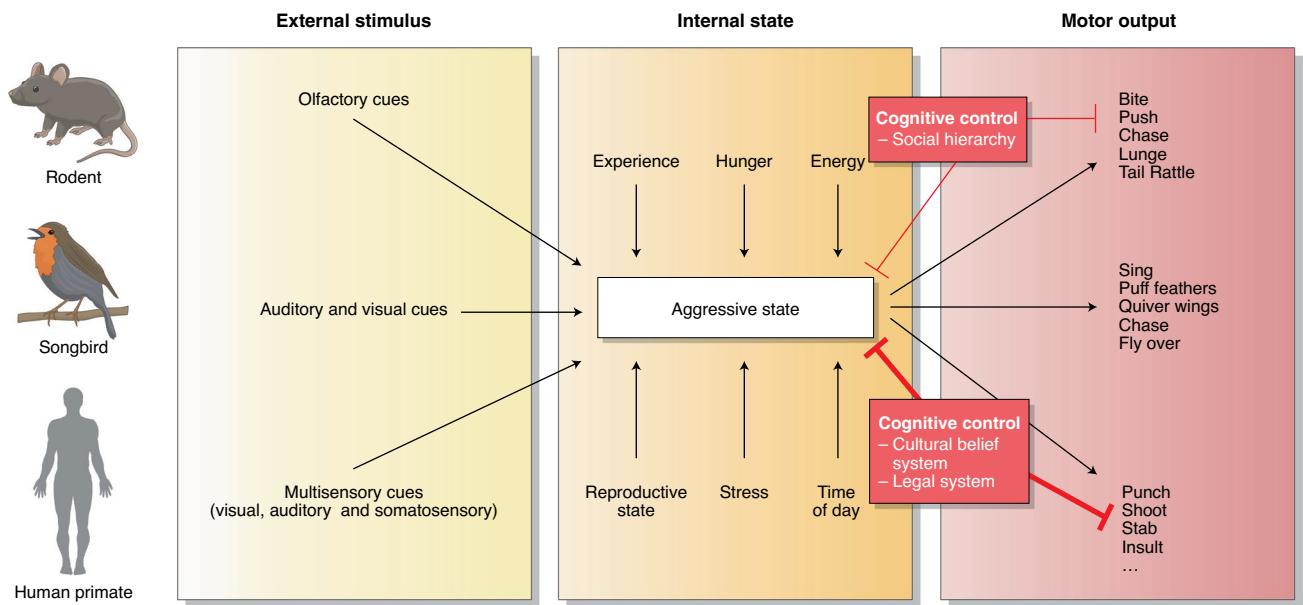
Fig. 1 | A common process that generates aggression in mice, songbirds and humans. Across species, detection of aggression-provoking cues increases aggressive arousal, which is also subject to modulation by other internal states and prior knowledge (for example, social status of an opponent or legal consequence of an assault). A heightened aggressive arousal promotes the motor execution of aggressive actions. While the general process is similar, species differ in the sensory trigger, motor expression and the extent of cognitive control over the behavioral output, i.e., the aggressive act. The strength of cognitive control is denoted by the width of the red lines.
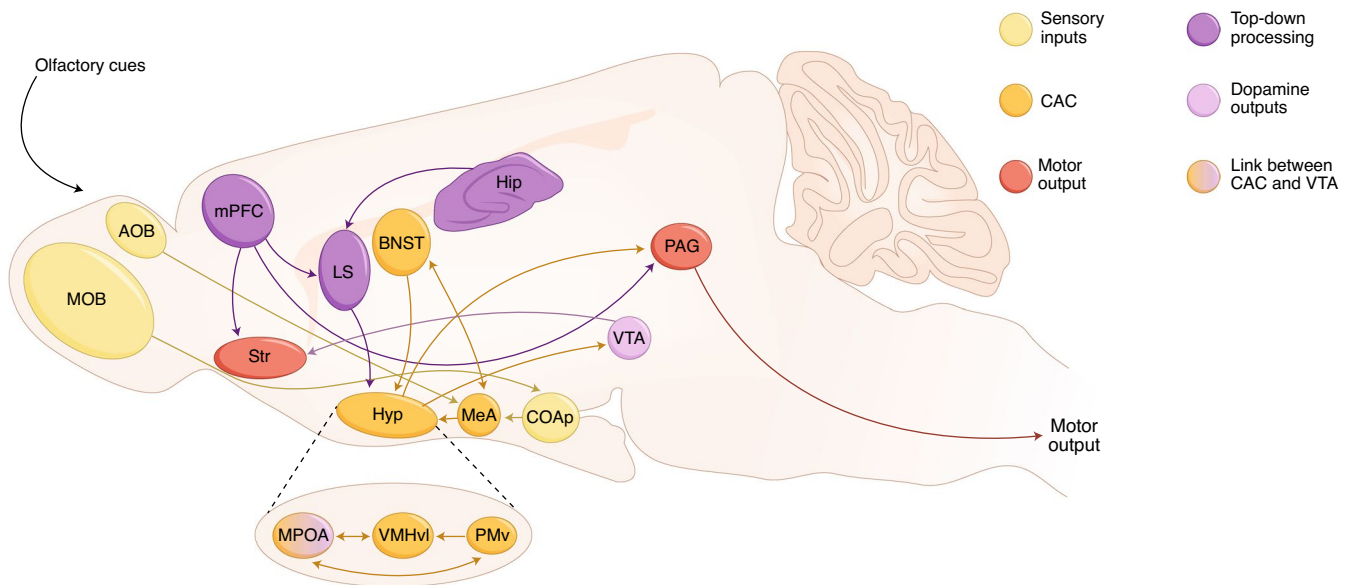
Fig. 2 | Neuroanatomical pathways of aggression in mice. In mice, olfactory sensory information is processed by the accessory and main olfactory bulbs and relayed to the CAC for integration. Hip–LS and mPFC can modulate aggression through their interaction with the CAC. The CAC mediates innate attack through its projection to the PAG and may also facilitate the activation of striatum via its projection to VTA dopamine neurons. Yellow indicates regions for processing sensory inputs; orange indicates regions belonging to CAC; red indicates regions relevant for motor output; purple indicates regions for top-down control and lilac indicates regions where dopamine neurons reside. AOB, accessory olfactory bulb; MOB, main olfactory bulb; CoAp, posterior cortical amygdala nucleus; Hyp, hypothalamus; MPOA, medial preoptic area; Hip, hippocampus; Str, striatum.

Upon male-intruder introduction, VMHvl cells show an elevation in baseline activity, which is sustained throughout the duration of the intruder's presence and minutes after removal of the intruder[26,29,35,36]. During male–male investigation and attack, VMHvl activity increases further, and then returns to the elevated baseline at the offset of the behavioral episode[29,31,32,35]. Thus, the VMHvl

cells appear to carry information regarding aggressive arousal state, aggression-provoking sensory cues and the motor execution of attacks. Furthermore, VMHvl cell activity is flexible. While in naive male mice VMHvl Esr1+ cell responses to males and females overlap substantially, the responses become more distinct after sexual experience[35]. When the mouse learns to associate an arbitrary motor
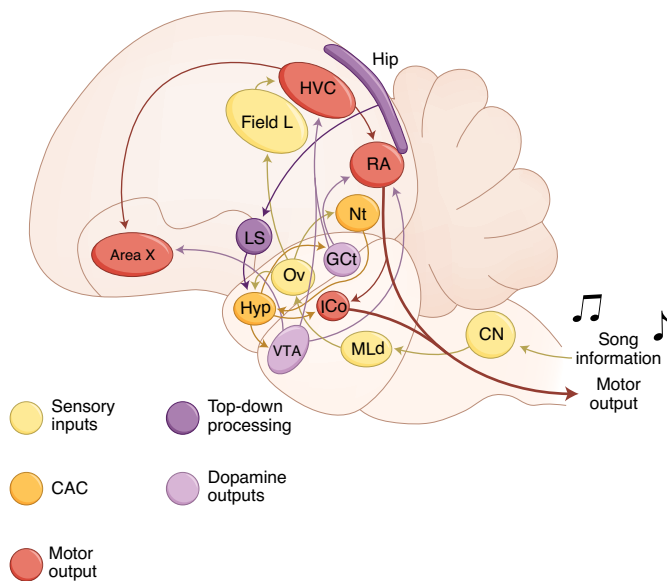
Fig. 3 | Neuroanatomical pathway of aggression in songbirds. In songbirds, auditory information from an intruder's song is relayed to the CAC (MeA and hypothalamus) via CN–MLd–Ov. CAC then promotes the dopamine outputs from the VTA and GCt which in turn project to the song production system to promote singing. CAC also projects to ICo to potentially promote innate vocalization. Hip–LS is the major controller of CAC and aggressive behaviors. Yellow indicates regions for processing sensory inputs; orange indicates regions belonging to CAC; red indicates regions relevant for motor output; purple indicates regions for top down control and lilac indicates regions where dopamine neurons reside. Arrows indicate established connections. CN, cochlear nucleus; MLd, dorsal lateral nucleus of the mesencephalon; Ov, ovoidalis; Field L, fields L1, L2 and L3; HVC, a letter-based name; RA, the robust nucleus of the arcopallium; Nt, nucleus taenia (homolog to MeA in rodents); GCt, midbrain central gray (homolog to PAG, in this case excluding the ICo); ICo, intercollicular nucleus (homolog to dorsal PAG in rodents); Area X, area X of the striatum; Hip, hippocampus; Hyp, hypothalamus.

action, for example, nose poke, with future opportunities to attack, VMHvl cells start to increase activity before poking[31]. Notably, VMHvl can be divided into functionally distinct compartments. While the posterior VMHvl is primarily involved in aggression, the anterior VMHvl mediates conspecific self-defense and social fear[37]. In female mice, the posterior VMHvl contains medial and lateral compartments that are relevant for aggression and sexual behaviors, respectively[32]. Most recently, single-cell RNA sequencing revealed the diverse molecular make-up of mouse VMHvl cells. Specifically, there are three major clusters, characterized by the expression of Esr1, Dlk1 or Satb2, respectively. Based on IEG expression, male aggression largely activates the Esr1+ population, while mating activates Dlk+ cells[38]. Future recordings from specific molecularly defined subpopulations will help elucidate the relationship between gene expression and functions of VMHvl cells.

There is also much evidence supporting a role of VMHvl in aggression in other species. Electrical stimulation or pharmacological manipulation in the VMHvl can elicit aggression in cats, chickens, opossums and monkeys[39–42]. When a male songbird is exposed to a male conspecific, VMHvl shows an increase in IEG expression, and this increase is higher in territorial finches than in gregarious species, consistent with its function in driving aggression[21]. Due to the small size of the VMHvl in humans, it has been difficult to examine its activity pattern during aggression. Nevertheless, several case reports provide a glimpse of the medial hypothalamus function

in human aggression. In patients showing extreme aggression (including self-directed), deep brain stimulation-induced inhibition of posterior medial hypothalamus reportedly suppressed or eliminated aggression[43] (Fig. 4). Thus, VMHvl is a key node for aggression likely across all vertebrate species.

Ventral premammilary nucleus. Posterior to the VMHvl is a small hypothalamic region, the ventral premammilary nucleus (PMv). It provides strong excitatory projections to the VMHvl and shows a consistent increase in IEG expression after aggressive encounters in mice[29,44,45]. Lesioning the PMv in female rats abolished aggression-provoking cue-induced IEG expression in the VMHvl, indicating that activation of VMHvl is dependent on the PMv input[44]. Additionally, optogenetic activation revealed a causal role of PMv dopamine transporter (DAT)-expressing cells in inter-male aggression[46]. Notably, PMv DAT-expressing cells were quiescent and hyperpolarized in nonaggressive mice and became spontaneously active and depolarized in aggressive mice[46]. This finding suggests that the aggressiveness of an animal may be encoded by the biophysical properties of cells in the aggression circuit. In birds, PMv cells are photosensitive and relevant for the day-length-induced seasonal rhythms of endocrine and metabolic events[47]. As the overall aggression level of seasonal breeders increases at the onset of the breeding season, PMv may play a role in adjusting an animal's aggressiveness according to seasonal cues.

Summary of the core aggression circuit. Unlike the sensory-detection regions, regions in the core aggression circuit are more specialized for aggression: activating any of those regions evokes attack, often in a time-locked manner, while inactivating any of those regions impairs or even abolishes natural aggression. The fact that aggression can be triggered as well as blocked from each of those regions supports the idea that these regions form one integrated circuit. Indeed, MeA, BNST, VMHvl and PMv are highly interconnected, with the former two providing more projections to the latter two regions than the other way around[27,28,45,48]. It is worth noting that aggression is often sexually dimorphic due to the higher reproduction-selection pressure in males (Box 3). However, the core aggression circuit appears to be largely similar in males and females, based on recent studies in mice[49]. Finally, much of our knowledge regarding this CAC was gained in the last 10 years thanks to the fast development of precise functional manipulation, tracing and recording tools. It is likely that new members of the CAC will continue to emerge based on future studies.

Motor output circuit to execute aggression

Depending on the species, the motor execution of attack can be composed of innate and stereotypical actions such as biting, or learned skilled actions such as singing (Box 1). A key site for expressing innate aggressive actions is the periaqueductal gray (PAG) in the midbrain (Fig. 2). Across species, PAG receives massive inputs from the hypothalamus, especially VMHvl[34,48], and projects to motor-control neurons in the spinal cord[50]. Our recent study in mice showed that PAG cells project to jaw muscles used for biting and increase spiking activity immediately before biting during attacks[51]. When the PAG is inhibited pharmacologically in male mice, the mice appear to remain intensely interested in the opponent and sometimes show lunge-like behavior, but fail to bite the opponent. In addition to biting, various innate vocalizations, including threatening calls, can be elicited from PAG in rodents and primates[52,53], indicating a conserved role of PAG in driving innate aggressive actions.

Although attacks in mice are innate, mice can learn to perform arbitrary motor actions, for example, nose poking or lever pressing, that lead to the opportunity to attack[54]. This learned aggression-seeking behavior is the key to distinguish reactive

## Box 2 | The social behavior network and the core aggression circuitry

In 1999, Sarah Newman proposed the existence of a social behavior network (SBN) that mediates innate social behaviors in mammals[14]. The SBN includes six subcortical areas: medial extended amygdala (MeA and BNST), medial preoptic area (MPOA), anterior hypothalamus (AH), LS, VMH, and midbrain (PAG and tegmentum). These regions were selected based on three criteria: (i) all areas are implicated in one or more social behaviors; (ii) all areas are enriched in gonadal hormone receptors; (iii) all areas are reciprocally connected[14].

How does the SBN encode diverse social behaviors? Newman suggested that each node of SBN responds to a variety of social stimuli, and the relative activities of these seven areas determine the exact type of social behavior to be displayed. For example, sexual behavior is associated with a pattern of high activity in MPOA, BNST and MeA and relatively low activity in other nodes, whereas aggressive behavior is associated with moderate activation of all nodes exHcept MPOA[14]. She also suggested that changes in the levels of gonadal hormones, principally estradiol, across regions shape the circuitry during both development and adulthood.

In 2005, James Goodson extended this network to non-mammalian vertebrate species based on his studies in birds and teleost (bony) fish[15]. Through a series of IEG mapping, anatomical tracing, histochemistry and lesion studies[15], he concluded that a homologous SBN exists in non-mammalian vertebrate species. Similar to the mammalian SBN, regions of the non-mammalian SBN express high levels of sex hormone receptors, are activated by various social behaviors and are reciprocally connected. James further noted that neuropeptide distribution in the mammalian and non-mammalian SBN is conserved and could play similarly important roles in generating species-specific social behaviors. For example, the distinct oxytocin and vasopressin signaling in prairie voles and montane voles have been linked to the widely different affiliative behaviors of these two species[136]. James found that injecting vasotocin (AVT), an avian homolog to vasopressin and oxytocin, into the LS elicited opposing changes in aggression in territorial vs gregarious songbird species[91,137].

Lauren O'Connel and Hans Hoffman further proposed a vertebrate social decision-making network (SDM) composed of SBN and the mesolimbic reward systems[138]. They compared gene expression profiles related to dopamine systems, sex steroid signaling and nonapeptide systems across 88 species and concluded that the neurochemical profiles of the SDM network have been remarkably conserved throughout vertebrate evolution. MPOA appears to be the most conserved region with identical neurochemical profiles across all species, while small differences in neurochemical distributions are found in other nodes of the SDM. These studies collectively suggest that social behaviors are mediated by a highly ancient and conserved set of brain regions and that subtle tweaks in neurochemical systems may lead to a large change in social behaviors among closely-related species[138].

Our proposed CAC could be considered as a subnetwork of the SBN that is specialized for aggression (**Box Figure**). Based on studies mainly in rodents, we suggest that CAC includes the MeA, VMHvl, PMv and BNST. Considering that the SBN is highly conserved across vertebrate lineages, we expect that the same CAC will exist in songbirds and primates, although detailed functional evidence for some regions remains lacking. All CAC regions except PMv are included in the SBN. The PMv might have been overlooked by earlier researchers due to its relatively small size. LS is a part of the SBN, but here we consider it a top-down modulatory region rather than a core aggression-generating region. PAG is also a part of the SBN, but is in this Review considered a premotor region for aggressive actions[51]. It is important to note that unlike regions in the CAC, PAG is highly heterogeneous and mediates the motor execution of a wide range of social and nonsocial behaviors[139]. MPOA is not included in the CAC, as its primary function is for parental care and sexual behaviors[5,57]. Lastly, although earlier studies in hamsters suggested a role for AHN in aggression[140,141], later IEG mapping, circuit tracing and functional experiments in other rodent species support it being a part of the predator-defense circuit[142,143]. It is likely that AHN contains functionally heterogeneous populations, and future studies will help elucidate its role in aggression.
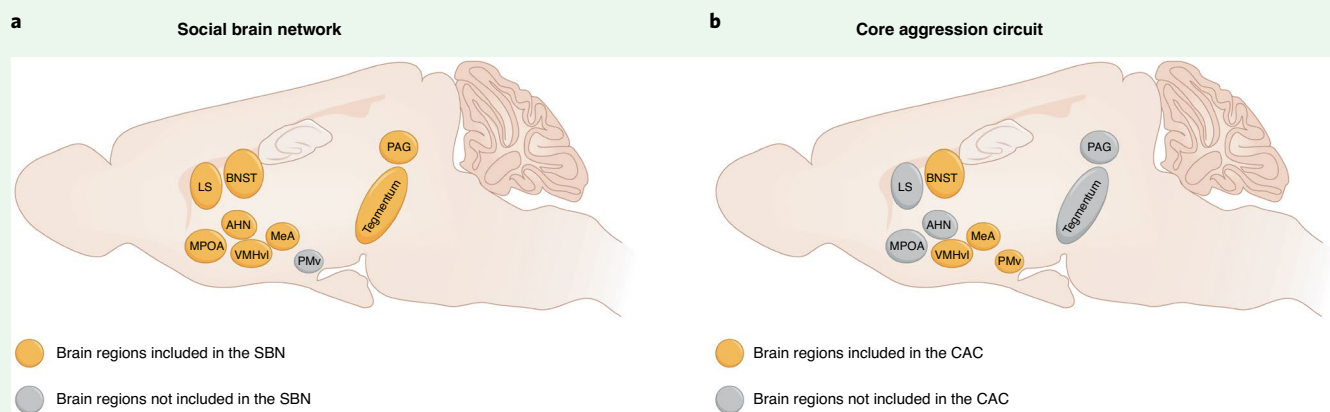
Box Figure Comparison between brain regions that belong to SBN and CAC.

aggression from proactive aggression (Box 1). Our recent study suggests that the VMHvl is an important site for mediating learned aggression-seeking actions, as inactivation of VMHvl reduced nose poking rate leading to attack opportunity[31]. In vivo electrophysiology recordings revealed a ramped-up activity of VMHvl

preceding nose poking, although the origin of this signal remains unclear[31]. Other studies pointed to dopamine signaling in the striatum as an essential player for learned aggression-seeking actions. In well-trained mice, blocking D1 or D2 receptors in the nucleus accumbens (NAc) reduced nose-poking rate at dosages that did
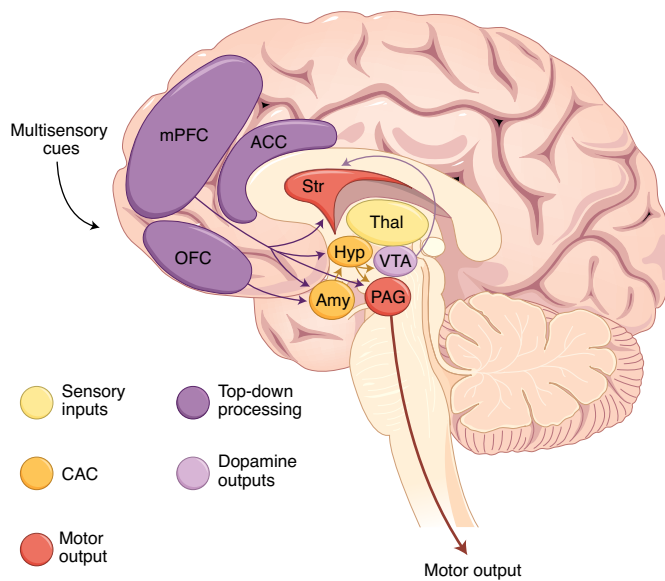
Fig. 4 | Neuroanatomical pathways of aggression in human primates.
In humans, multisensory inputs from the environment are processed by
the thalamus and then reach CAC to promote aggressive actions via its
influence on the basal ganglia circuit. The prefrontal cortex projections to
multiple CAC regions play an important role in controlling the CAC activity
and aggressive actions. Yellow indicates regions for processing sensory
inputs; orange indicates regions belonging to CAC; red indicates regions
relevant for motor output; purple indicates regions for top down control
and lilac indicates regions where dopamine neurons reside. Arrows indicate
established connections. Amy, amygdala; Hyp, hypothalamus; Str, striatum;
Thal, thalamus; OFC, orbitofrontal cortex; ACC, anterior cingulate cortex.

not compromise locomotion or attack itself[55]. A recent fur-
ther showed that inhibiting the D1 receptor-expressing cells in the
NAc reduced the rate of lever pressing leading to attack[56]. Does
the CAC connect to striatum in any way? Tracing studies revealed
that VMHvl project to the ventral tegmental area (VTA), the major
source of dopamine in NAc, both directly and indirectly through
the medial preoptic nucleus (MPN)[48,57].

Songbirds, unsurprisingly, primarily use songs to signal aggres-
sion (Box 1). How does the aggressive arousal promote singing, a
highly skilled and learned motor action? In a simple scenario, the
CAC may provide direct inputs to the song-production system.
Tracing studies reveal that ventromedial hypothalamus (VMH)
projects densely to intercollicular nucleus (ICo), the midbrain vocal
center[13,58,59] (Fig. 2). Although this pathway may drive simple calls,
it is unlikely to be sufficient for producing elaborate songs, which
requires the participation of forebrain regions[58]. As in rodents, the
dopaminergic cells appear to be the key link between CAC and
brain regions mediating learned aggressive action, in this case,
singing. Tracing studies revealed that the VMH projects to two
dopamine-producing regions—VTA and dorsomedial nucleus of
the GCt (equivalent to a subregion of the PAG)—either directly
or indirectly via MPN[13,59,60]; VTA and GCt (mesencephalic cen-
tral gray) in turn project to HVC (the songbird premotor region
for singing), RA (robust nucleus of the arcopallium) and Area X
(the songbird striatum), three key regions for song production[61–63]
(Fig. 2). Several lines of evidence support a role for dopaminergic
cells in aggression-driven, and more broadly socially driven, song
production. After a simulated territorial intrusion, the number
of IEG-positive dopaminergic cells correlates with the number of
male-directed songs[64]. Furthermore, when males sing to females,
VTA dopamine cells increase spiking activity, resulting in elevation
in dopamine levels in Area X[65,66]. Unilateral damage of dopaminergic

inputs to Area X causes a reduction in female-directed but not
undirected songs[67]. When juvenile finches are learning songs,
dopaminergic cells in GCt are activated by songs from a live tutor,
causing a dopamine increase in the HVC; this process is required
for song copying[68]. Thus, during socially motivated situations, such
as defending territory, the CAC likely increases activity in striatal
motor circuit to promote singing through its inputs to the midbrain
dopaminergic cells.

Based on the evidence from both rodents and songbirds, we
propose that two parallel pathways transform aggressive arousal
to aggressive actions (Fig. 5). In the direct pathway, the CAC—
mainly the VMHvl and to a lesser extent other regions—projects
to the midbrain premotor areas to drive innate aggressive acti-
ons[27,28,45,48]. In the indirect pathway, the CAC energizes the striatal
motor circuit and promotes learned aggressive actions by activat-
ing the midbrain neuromodulatory systems. While dopamine is
the best studied so far, other neuromodulators, for example, nor-
epinephrine, may also play a role in this 'bottom up' modulation[62].
Considering that human aggression can be expressed diversely,
the indirect pathway may be particularly important for enacting
aggression in humans.

A circuit for aggression-mediated associative learning
Mice can learn to perform arbitrary actions for the sole purpose
of obtaining an opportunity to attack, and they develop a prefer-
ence for the cues that are associated with winning[54]. Thus, like other
innate social behaviors, such as sexual behaviors and maternal
behaviors, the successful execution of aggressive behaviors is intrin-
sically rewarding and can serve as an unconditional stimulus for
associative learning.

VTA dopamine cells are key to reward-based associative learn-
ing[69]. Recent studies suggest that winning-mediated associative
learning also involve these cells[70]. First, NAc dopamine levels
increase following repeated aggression[71], possibly through the
VMHvl–VTA–NAc pathway, as discussed earlier. Second, a recent
study showed that overexpressing ΔFosB, encoded by a key gene
for brain plasticity, in NAc D2 receptor-expressing cells prevented
the development of preference for the aggression-paired context[72].
Third, Golden et al. demonstrated that artificial inactivation of the
lateral habenula (LHb) blocks the preference for winning-associated
context[73]. Since LHb strongly suppresses VTA dopaminergic cells,
this manipulation likely results in reduced dopaminergic signaling
in the NAc[74]. How does the aggression-driven dopamine release
in the NAc facilitate associative learning? This is likely achieved
through dopamine-mediated synaptic plasticity[75]. A burst of dopa-
mine and glutamate activate D1 and NMDA receptors which in turn
activate the G-protein-coupled receptor (GPCR) signaling pathway
and alter the glutamatergic synaptic strength[76]. When a neutral
stimulus, for example, a context, is paired with winning-induced
dopamine release, the glutamate synapses carrying the contextual
information to the NAc could be strengthened and result in a pref-
erence for the context in subsequent encounters.

In addition to supporting associate learning, winning also
reinforces aggression itself, a phenomenon referred to as the win-
ner effect. Dopamine may also play an important role in the
self-reinforcing nature of winning. In California mice, blocking
dopamine signaling after winning abolishes increases in aggres-
sion[77], whereas increasing synaptic dopamine levels through
injection of methamphetamine (a dopamine reuptake inhibitor)
increases aggression even 20 h later, suggesting that a high level
of dopamine is sufficient to induce a long-term shift in aggression
level[78]. However, it remains unclear whether the NAc is the key site
for dopamine action in reinforcing aggression. Additionally, win-
ning a fight is accompanied by a surge of testosterone[79] that is likely
to impact all regions in the CAC and thus enhance aggression in
future encounters (see more details below).

In many species, males typically exhibit higher levels of aggression than females and often have larger body sizes; some males have even developed specialized 'weaponry' body parts to increase their attacking power[144]. This male-biased dimorphism is considered to be a result of sexual selection. Due to the imbalance in reproduction cost and parental investment between sexes, females are the limiting resource for reproduction. Thus, males who have better fighting ability and compete more aggressively for healthy and fertile females prevail[144]. According to this theory, the degree of sexual selection pressure should correlate with the extent of male aggressiveness. Consistent with this hypothesis, males in polygamous species are under higher sexual selection pressure and are generally larger and more aggressive than females. In contrast, sexual selection pressure is largely absent in monogamous species, and males and females in those species often have similar body size and aggression levels[144]. For example, laboratory mice (*Mus musculus*) are polygamous, with males weighing approximately 13% more than females and expressing higher levels of aggression[145], whereas California mice (*Peromyscus californicus*) are strictly monogamous, and males and females weigh similarly and express similar levels of aggression toward an intruder[146].

Evidence of sexual selection is also prevalent in primate species. Male rhesus macaques weigh approximately 40% more than females and possess large and sharp canine teeth that can inflict severe injuries to their opponents[144]. Among primate species, humans show the least degree of sexual dimorphism in terms of body size differences (human average male/female: 1.07; primate average male/female: 1.28), indicating that sexual selection pressure decreased over our evolution[144]. Nevertheless, human

males are on average taller and heavier than females and express higher levels of aggression[147]. Males commit most of the violent acts in the world and constitute approximately 85–90% of the prison population[148]. In addition, males and females differ in their means to express aggression. Males commonly resort to physical aggression, whereas females are more prone to non-physical aggression[149].

In songbirds, although the majority of the species are monogamous, male-biased aggression is common for songbirds in temperate climates like North America and Europe[133]. This is because males in these species are responsible for establishing territories, a process that requires good fighting ability. Since only males with high-quality territories can attract females and propagate their genes, more-aggressive males are evolutionarily favored. As singing is a major means of expressing aggression in songbirds, males are the primary if not exclusive singers in many temperate songbird species[133]. Like humans, male songbirds are also more likely to carry out physical attacks than females[133]. In contrast, in tropical rainforests and Australia, songbirds maintain their territory year-round, and it is common for both female and male songbirds to sing in response to territorial intrusions[150]. Taken together, sexual selection has created a wide range of sexual dimorphism in physical traits and aggressive acts to best suit the competition needs of each species.

Although the extent of aggression differs between sexes, the CAC appears to be qualitatively similar in males and females—all regions relevant for male aggression are found to be relevant for female aggression in mice. However, the detailed organization and the number of aggression-related cells in each region could differ between sexes, as reviewed in detail recently[49].

Taken together, these findings suggest that dopamine signaling in the striatal circuit serves dual functions. First, it promotes the expression of learned motor actions that signal or lead to aggression, for example, singing and nose poking. Second, it reinforces actions and cues associated with the successful execution of aggression, likely through synaptic plasticity.

Internal states modulate the aggression circuit

Tinbergen argued that behavioral decisions are not solely determined by extrinsic stimuli, but are also influenced by the animals' internal state[2]. Indeed, an individual's tendency to aggress can be affected by stress level, reproduction state, energy state and circadian state, among others. Any state could affect aggression through its impact on any node along the sensorimotor circuit that generates the behavior, although modulating the CAC will be the most specific and effective way. As different states vary at different time scales (for example, energy state varies over hours while reproductive state varies over days or months), it is likely that several mechanisms are employed to modulate aggression. The slow-varying states likely induce long-lasting changes in the aggression circuit to cause a change in 'aggressiveness', a trait independent of moment-to-moment aggression, whereas the fast-varying states likely induce more transient changes in the circuit. Here we discuss how the fast- and slow-varying internal states may modulate the CAC to alter the propensities of the behavior output.

Aggression modulation by energy state. Aggression, as a critical means to secure resources, is modulated by the energy state of the animal. Across species, aggression levels were found to increase when the animals are in an energy-deficient state, such as

hunger[80–82]. During hunger, the empty stomach releases the gastric peptide ghrelin, while the low levels of blood glucose and lipids block the release of insulin and leptin from pancreas and fat cells, respectively. Although the main function of these hormones is to modulate feeding through their actions on the feeding-related hypothalamic regions, for example, arcuate nucleus (Arc), they can also affect the activity of the CAC. In particular, both VMHvl and PMv are enriched in various receptors detecting these energy-signaling peptides[83,84]. In vitro electrophysiology recordings demonstrated that the hunger hormone ghrelin can directly activate VMH cells, whereas insulin inhibits VMH activity[85,86]. Consistent with an effect of ghrelin in activating the aggression circuit, central infusion of ghrelin promotes inter-male attack[87]. Furthermore, VMH is one the few brain regions that contains glucose-sensing neurons[88]. In fact, all VMHvl Esr1+ cells are responsive to glucose, with approximately 60% inhibited by glucose and 40% excited by glucose[88]. Lastly, hunger signals may also be relayed to the CAC through the feeding circuit: AGRP-expressing cells in the Arc project to the MeA, which in turn projects to the BNST to modulate aggression[19]. Thus, the CAC is well equipped to detect the energy state and can adjust its own output accordingly.

Aggression modulated by circadian clock. Throughout the day, the propensity of aggression fluctuates. In rodents, the aggression level is the highest at the beginning of the night and the lowest at the onset of daytime[89]. In patients with Alzheimer's disease, 20% show increases in aggression and anxiety in the early evening hours, a phenomenon known as 'sundowning'[90]. The master controller of the brain's circadian state is the suprachiasmatic nucleus (SCN), a small hypothalamic region that shows genetically based
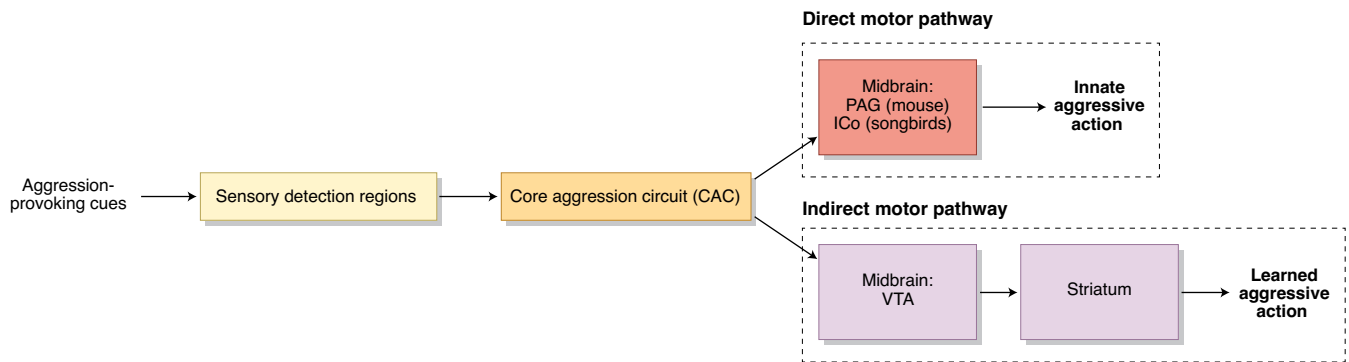
Fig. 5 | Direct and indirect pathways for aggressive motor outputs. We propose the existence of two parallel pathways for generating aggressive actions in vertebrates. In both pathways, aggression-provoking cues are processed by sensory detection regions (yellow) and passed to the CAC (orange). Then, through the direct pathway, CAC sends the information to the midbrain (red) to generate innate aggressive actions. Simultaneously, through the indirect pathway, CAC activates the dopaminergic cells in the VTA which in turn facilitate the activation of the striatum (purple) to promote learned aggressive actions.

near 24-h rhythms. Recently, Todd and colleagues found, in mice, that the diurnal variation in aggression is mediated by a circuit linking SCN to VMHvl. SCN neurons expressing vasoactive intestinal polypeptide (VIP) project to subparaventricular zone (SPZ), which in turn send inhibitory projections to VMH[89]. Since SPZ cells are most active during the beginning of the daytime, they provide the strongest inhibitory control of VMH cells and reduce the level of aggression at that time. Eliminating the GABAergic transmission of the SPZ cells abolished the diurnal variation of aggression propensity. In this study, it remained undetermined whether VIP is the key signal between the SCN and SPZ, in other words, whether the diurnal variation of aggression is ultimately caused by fluctuations of VIP release in the SCN. Interestingly, studies in birds identified VIP as an important regulator of aggression[91,92]. Infusions of VIP into the anterior hypothalamus (AHN), a region adjacent to the VMHvl, in violet-eared waxbill finches, facilitates male aggression[91], while blocking the production of VIP abolishes aggression[92]. Whether the natural function of VIP in avian aggression modulation is related to circadian rhythm remains to be addressed in future studies.

Aggression modulated by reproductive state. Aggression is also strongly influenced by the animal's reproductive state. For seasonal breeders, male aggression level dramatically increases during the mating season and plummets during the non-breeding season[93]. According to the 'challenge hypothesis', male testosterone levels are low during the non-breeding season, increase at the beginning of the breeding season as a result of external cues (for example, changes in day length)—which results in the development of secondary sex characteristics and expression of reproductive behaviors—and further increase in response to challenges from other conspecific males over territory and mates so as to promote aggression and success in competition[93]. The important role of testosterone in eliciting long-term increases of aggression is also manifested in the winner effect. Repeated winning causes an increase in aggressiveness across a wide range of species and is critically dependent on a post-winning testosterone surge[79]. While female aggression is generally lower than that of males, lactating females show a dramatic increase in aggression for the purpose of protecting their young, a widespread phenomenon termed 'maternal aggression'. The hormonal mechanisms underlying maternal aggression are not yet fully understood, but the orchestrated waves of sex steroids, including estrogen and progestogen, are likely to be critical for the onset of maternal aggression[49].

How do sex steroids modulate the aggression circuit? This occurs presumably through activation of the sex hormone receptors, such as androgen receptors, estrogen receptors and progesterone receptors. All sex steroid receptors are nuclear receptors that can directly bind to DNA and regulate gene expression. Thus, changes in the levels of sex hormones could alter the protein composition of a cell, which in turn could control cell morphologies and electrophysiological properties[94]. Indeed, numerous studies in rodents have found impacts of sex hormones on VMHvl cell spiking activity and morphology within the context of female sexual behavior, a behavior for which the VMHvl is known to be relevant[5]. In songbirds, the effects of sex hormones on seasonal changes of the song control nuclei (SCNuc) are well understood. The volume of the entire SCNuc dramatically increases during the breeding season to support song production, and these volumetric changes require increases in plasma testosterone levels. Testosterone or estrogen administration can mimic seasonal growth of SCNuc, including increases in neuronal size, dendritic length and cell numbers[95], whereas blocking aromatase prevents this seasonal growth[96]. As the CAC is enriched in androgen, estrogen and progesterone receptors, sex hormones should readily adjust the responsiveness and communications of neurons in the circuit and induce a long-lasting increase in aggression during mating season or lactating period.

Forebrain control of the aggression circuit
Aggression is costly and risky and thus its expression is tightly controlled. Early experiments in cats found that when the hypothalamus was dissociated from its anterior structures, the animals showed spontaneous rage, such as hissing and paw strike, without any provocation, suggesting that forebrain regions tonically suppress the hypothalamus to block aggression[97]. Since then, numerous functional and imaging studies have been conducted to identify the 'top-down' controllers. Two important regions, medial prefrontal cortex (mPFC) and lateral septum (LS), have emerged as potential key sites for controlling aggression (Figs. 2, 3 and 4).

Prefrontal control of aggression. The prefrontal cortex (PFC) is the most studied region for top-down control of aggression in humans and possibly also in rodents, although rodents only have mPFC, which includes prelimbic cortex (PL), infralimbic cortex (IL) and anterior cingulate cortex (ACC)[98].

At least four lines of evidence indicate a role for mPFC in aggression control in humans. First, humans with frontal brain injury show increased levels of aggression[99,100]. A widely cited example is Phineas Gage, a railroad constructor who, after his frontal lobe was injured by an iron rod, radically changed from "the most efficient and capable foreman" to "capricious, hostile and irresponsible"[100].

Furthermore, patients suffering from psychiatric disorders with a history of violence have a smaller PFC or show a blunted PFC response to emotionally salient stimuli such as angry faces[101,102]. Second, increasing mPFC activity is sufficient to suppress aggression. In humans, bilateral transcranial direct-current stimulation (tDCS) of PFC decreases self-reported aggressiveness in imprisoned violent offenders[103]. Third, imaging studies in humans have demonstrated a positive correlation between PFC activity and self-imposed emotional control; for example, when study participants were instructed to reappraise highly negative arousing images, PFC activation correlated with the decrease in negative affect[104,105]. Lastly, PFC function has also been studied in the context of serotonin, which is considered a key inhibitor of aggression since the initial reports of a low level serotonin metabolite in suicidal individuals[106]. While serotonins' influence on the brain is extremely complex, given its 14 different and widely expressed receptors, mPFC has emerged as a key site for the inhibitory effect of serotonin on aggression. For example, patients with exaggerated aggression showed reduced prefrontal activation when challenged with d,l-fenfluramine, a drug that induces serotonin release, suggesting a deficiency in serotonin signaling in the mPFC[107].

mPFC has also been shown to modulate aggression in rodents. Optogenetic inhibition of the mPFC is sufficient to increase aggression in mice[108], whereas optogenetic activation of mPFC reduces inter-male aggression[108] (but see ref. [109]). Serotonin levels in the mPFC decreases after both acute attack and repeated victories[71,110], and agonizing the 5HT1B or 5HT1A receptors in the mPFC suppresses both male and female mouse aggression[111,112].

Thus, there is clear evidence for a role of mPFC in modulating aggression in mammals. However, many questions remain. What kind of information is encoded in the mPFC in the context of aggression? When does mPFC exert its top-down control? Through which pathway does mPFC modulate aggression? Here, we attempt to offer some speculations, based on the role of mPFC outside aggression contexts. In 2011, Alexander et al. proposed an action–outcome predictor model in which the key function of mPFC is learning to anticipate the various possible outcomes of an action and represent them with corresponding probabilities[113]. If the outcome violates the initial prediction, mPFC updates the probability of outcomes for future actions.

This is a particularly attractive model given that aggression is highly consequential. For animals, the cost of losing a fight could be hefty; it is thus essential to determine the likelihood of a win or a loss before a fight. In humans, in addition to the immediate outcomes of an aggressive action, there are also consequences imposed by our moral and legal systems (Fig. 1). These consequences are uniformly negative and discourage the expression of aggressive actions. In people with blunted activity of the mPFC, the ability to properly evaluate the action–outcome relationship could be compromised and lead to disinhibition of aggression[114]. Although it remains unknown whether and how the anticipated outcomes of aggression are encoded in the mPFC, recent studies in mice reveal that mPFC neurons carry information regarding the social status of a conspecific opponent. Specifically, mPFC neurons in male mice represent the behaviors of dominant animals more so than those of subordinate animals[115]. Social ranking information is essential for estimating the outcomes of a fight and so likely influences the decision to attack. As an example, when 12 male mice are housed together in a laboratory setting, they form a linear hierarchy and each animal primarily initiates attacks toward others that are below but not above its own ranking[116]. Remarkably, when the synaptic strength in the mPFC cells was artificially enhanced or when the mPFC was optogenetically activated in male mice, the manipulated animals rose in their social ranking, as measured by the probability of winning a staged competition, for example, competing for a warm spot in a cold room or going through a narrow tube[117,118]. Does an increase in mPFC activity alter the assessment of the relative strength of oneself and one's opponent? Can this falsely perceived strength change the action–outcome prediction and increase the willingness to fight? Answers to these questions remain unclear and will require a better understanding of social information encoded in the mPFC.

How does the mPFC interact with the CAC to control aggression? In rodents, mPFC sends projections mainly to the basolateral amygdala complex and lateral hypothalamus, whereas direct inputs to aggression-related hypothalamic and amygdalar regions are scarce (Fig. 2)[119]. By contrast, the primate mPFC—especially area 25 (equivalent to infralimbic area in rodents)—provides dense inputs to the medial hypothalamus, including VMHvl, and moderate inputs to the MeA[120,121]. Although the functional importance of this primate-specific hypothalamic projection remains unclear, it raises an intriguing possibility that mPFC may exert greater control on aggression through its hypothalamic projection in primates than in rodents (Fig. 1).

Another potential node through which the mPFC could control aggression is the PAG. In both rodents and primates there is a moderate and topographically organized connection between the mPFC and PAG[122,123]. A recent study using channelrhodopsin (ChR2)-assisted circuit mapping revealed that mPFC axons projecting to PAG exclusively target glutamatergic cells[124]. Surprisingly, although only a small fraction of glutamatergic cells in PAG receive monosynaptic inputs from the mPFC, activating mPFC axons induced a long-lasting decrease in excitatory post-synaptic current (EPSC) frequency in the majority of glutamatergic cells in PAG[124]. These results suggest that mPFC activation can reduce the excitatory drive onto the PAG, decreasing PAG cell spiking activity and ultimately blocking attack. Importantly, as PAG mainly controls the motor execution of aggression, blocking PAG activity will likely leave the aggressive arousal unaltered.

Septal control of aggression. The septum is a midline structure composed of a middle and lateral part, namely the medial septum and LS, respectively[98]. Studies in mice[125], rats[126] and songbirds[127] have shown that lesions or chemical perturbation of the LS cause a dramatic increase in aggression, a phenomenon termed 'septal rage'. A study in songbirds showed an inverse correlation between the number of IEG-positive cells in the LS and aggression levels, suggesting an inhibitory role of the LS in aggression[20]. In mice, LS can suppress aggression through its strong monosynaptic inhibitory inputs to the VMHvl glutamatergic cells[125], and optogenetic activation of this pathway effectively terminates ongoing attacks[125].

What kind of aggression-relevant information is encoded in the LS? Answers to this question remain elusive. LS receives the densest inputs from hippocampus and thus is well positioned to relay experiential and contextual information to the hypothalamus[128]. Indeed, a recent study showed that CA2 pyramidal neurons project to the dorsal LS, which inhibits the ventral LS, resulting in disinhibition of the VMHvl to promote aggression[129]. As CA2 is a key site for encoding social memory[130], an intriguing hypothesis is that memories of social interactions may influence future decisions to attack through the CA2–LS–VMHvl pathway[129].

There is limited evidence regarding LS modulation of aggression in humans[131]. Tumors of the septum pellucidum (a fiber track dorsal to the septum) have been associated with irritability and, in some instances, violent and angry outbursts, but it is unclear whether the septum itself was affected by such tumors[131]. Imaging studies similarly provide no clues regarding a role of LS in human aggression, possibly due to its small size, odd shape and awkward position. We speculate that in animals with rudimental or no PFC, hippocampal–septal systems are likely to play a major role in aggression control, and that in primates the top-down control of aggression might be largely carried out by mPFC.

Concluding remarks

The past decade has seen significant advances in our understanding of the neural mechanisms underlying the generation of aggression. A conserved subcortical CAC emerges as the core substrate for encoding aggressive arousal and promoting aggressive actions across species. On the sensory end, species-specific pathways carry the aggression-provoking sensory cues to the CAC. On the motor end, the CAC promotes stereotypical innate aggressive actions through its projections to the midbrain premotor area and simultaneously promotes learned, aggression-relevant motor actions by energizing the striatum through activating dopaminergic cells. Given the high cost of aggression, CAC is under tight top-down control. A hippocampus–LS pathway and the mPFC are likely the two key controlling systems, with mPFC playing a more important role in primates than in rodents. Various internal-state variables could also influence aggression output by modulating the responsiveness and communication efficiency of the CAC. Much work remains to be done to validate and elaborate this general framework. It is worth noting that aggression is a prevalent social behavior but differs widely across species. Adopting a cross-species comparative approach will be central to revealing the general principles underlying the generation of aggression, as well as the neural mechanisms that enable its unprecedented complexity in humans.

References

1. Lorenz, K. *On Aggression.* (Routledge, 2005).
2. Tinbergen, N. *The Study of Instinct* (Oxford Univ. Press, 1951).
3. Allen, J. J., Anderson, C. A. & Bushman, B. J. The general aggression model. *Curr. Opin. Psychol.* **19**, 75–80 (2018).
4. Dulac, C. & Torello, A. T. Molecular detection of pheromone signals in mammals: from genes to behaviour. *Nat. Rev. Neurosci.* **4**, 551–562 (2003).
5. Hashikawa, K., Hashikawa, Y., Falkner, A. & Lin, D. The neural circuits of mating and fighting in male mice. *Curr. Opin. Neurobiol.* **38**, 27–37 (2016).
6. Keshavarzi, S., Power, J. M., Albers, E. H., Sullivan, R. K. & Sah, P. Dendritic organization of olfactory inputs to medial amygdala neurons. *J. Neurosci.* **35**, 13020–13028 (2015).
7. Caro, S. P., Balthazart, J. & Bonadonna, F. The perfume of reproduction in birds: chemosignaling in avian social life. *Horm. Behav.* **68**, 25–42 (2015).
8. Stoddard, P. K., Beecher, M. D., Horning, C. L. & Campbell, S. E. Recognition of individual neighbors by song in the song sparrow, a species with song repertoires. *Behav. Ecol. Sociobiol.* **29**, 211–215 (1991).
9. Searcy, W. A., Anderson, R. C. & Nowicki, S. Bird song as a signal of aggressive intent. *Behav. Ecol. Sociobiol.* **60**, 234–241 (2006).
10. Theunissen, F. E. & Shaevitz, S. S. Auditory processing of vocal sounds in birds. *Curr. Opin. Neurobiol.* **16**, 400–407 (2006).
11. Durand, S. E., Tepper, J. M. & Cheng, M. F. The shell region of the nucleus ovoidalis: a subdivision of the avian auditory thalamus. *J. Comp. Neurol.* **323**, 495–518 (1992).
12. Cheng, M., Chaiken, M., Zuo, M. & Miller, H. Nucleus taenia of the amygdala of birds: anatomical and functional studies in ring doves (*Streptopelia risoria*) and European starlings (*Sturnus vulgaris*). *Brain Behav. Evol.* **53**, 243–270 (1999).
13. Wild, J. M. The ventromedial hypothalamic nucleus in the zebra finch (*Taeniopygia guttata*): afferent and efferent projections in relation to the control of reproductive behavior. *J. Comp. Neurol.* **525**, 2657–2676 (2017).
14. Newman, S. W. The medial extended amygdala in male reproductive behavior. A node in the mammalian social behavior network. *Ann. NY Acad. Sci.* **877**, 242–257 (1999).
15. Goodson, J. L. The vertebrate social behavior network: evolutionary themes and variations. *Horm. Behav.* **48**, 11–22 (2005).
16. Lischinsky, J. E. et al. Embryonic transcription factor expression in mice predicts medial amygdala neuronal identity and sex-specific responses to innate behavioral cues. *eLife* **6**, e21012 (2017).
17. Hong, W., Kim, D.-W. & Anderson, D. J. Antagonistic control of social versus repetitive self-grooming behaviors by separable amygdala neuronal subsets. *Cell* **158**, 1348–1361 (2014).
18. Unger, E. K. et al. Medial amygdalar aromatase neurons regulate aggression in both sexes. *Cell Rep.* **10**, 453–462 (2015).
19. Padilla, S. L. et al. Agouti-related peptide neural circuits mediate adaptive behaviors in the starved state. *Nat. Neurosci.* **19**, 734–741 (2016).
20. Goodson, J. L., Evans, A. K. & Soma, K. K. Neural responses to aggressive challenge correlate with behavior in nonbreeding sparrows. *Neuroreport* **16**, 1719–1723 (2005).
21. Goodson, J. L., Evans, A. K., Lindberg, L. & Allen, C. D. Neuro-evolutionary patterning of sociality. *Proc. Biol. Sci.* **272**, 227–235 (2005).
22. Meunier, M., Bachevalier, J., Murray, E. A., Málková, L. & Mishkin, M. Effects of aspiration versus neurotoxic lesions of the amygdala on emotional responses in monkeys. *Eur. J. Neurosci.* **11**, 4403–4418 (1999).
23. Coccaro, E. F., McCloskey, M. S., Fitzgerald, D. A. & Phan, K. L. Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. *Biol. Psychiatry* **62**, 168–178 (2007).
24. Dong, H.-W., Petrovich, G. D. & Swanson, L. W. Topography of projections from amygdala to bed nuclei of the stria terminalis. *Brain Res. Brain Res. Rev.* **38**, 192–246 (2001).
25. Bayless, D. W. et al. Limbic neurons shape sex recognition and social behavior in sexually naive males. *Cell* **176**, 1190–1205.e20 (2019).
26. Hashikawa, Y., Hashikawa, K., Falkner, A. L. & Lin, D. Ventromedial hypothalamus and the generation of aggression. *Front. Syst. Neurosci.* **11**, 94 (2017).
27. Pardo-Bellver, C., Cádiz-Moretti, B., Novejarque, A., Martínez-García, F. & Lanuza, E. Differential efferent projections of the anterior, posteroventral, and posterodorsal subdivisions of the medial amygdala in mice. *Front. Neuroanat.* **6**, 33 (2012).
28. Dong, H. W. & Swanson, L. W. Projections from bed nuclei of the stria terminalis, posterior division: implications for cerebral hemisphere regulation of defensive and reproductive behaviors. *J. Comp. Neurol.* **471**, 396–433 (2004).
29. Lin, D. et al. Functional identification of an aggression locus in the mouse hypothalamus. *Nature* **470**, 221–226 (2011).
30. Lee, H. et al. Scalable control of mounting and attack by Esr1+ neurons in the ventromedial hypothalamus. *Nature* **509**, 627–632 (2014).
31. Falkner, A. L., Grosenick, L., Davidson, T. J., Deisseroth, K. & Lin, D. Hypothalamic control of male aggression-seeking behavior. *Nat. Neurosci.* **19**, 596–604 (2016).
32. Hashikawa, K. et al. Esr1+ cells in the ventromedial hypothalamus control female aggression. *Nat. Neurosci.* **20**, 1580–1590 (2017).
33. Yang, T. et al. Social control of hypothalamus-mediated male aggression. *Neuron* **95**, 955–970.e4 (2017).
34. Yang, C. F. et al. Sexually dimorphic neurons in the ventromedial hypothalamus govern mating in both sexes and aggression in males. *Cell* **153**, 896–909 (2013).
35. Remedios, R. et al. Social behaviour shapes hypothalamic neural ensemble representations of conspecific sex. *Nature* **550**, 388–392 (2017).
36. Falkner, A. L., Dollar, P., Perona, P., Anderson, D. J. & Lin, D. Decoding ventromedial hypothalamic neural activity during male mouse aggression. *J. Neurosci.* **34**, 5971–5984 (2014).
37. Wang, L. et al. Hypothalamic control of conspecific self-defense. *Cell Rep.* **26**, 1747–1758.e5 (2019).
38. Kim, D.-W. et al. Multimodal analysis of cell types in a hypothalamic node controlling social behavior. *Cell* **179**, 713–728.e17 (2019).
39. Putkonen, P. T. Attack elicited by forebrain and hypothalamic stimulation in the chicken. *Experientia* **22**, 405–407 (1966).
40. Lipp, H. P. & Hunsperger, R. Threat, attack and flight elicited by electrical stimulation of the ventromedial hypothalamus of the marmoset monkey *Callithrix jacchus*. *Brain Behav. Evol.* **15**, 276–293 (1978).
41. Siegel, A. & Pott, C. B. Neural substrates of aggression and flight in the cat. *Prog. Neurobiol.* **31**, 261–283 (1988).
42. Roberts, W. W., Steinberg, M. L. & Means, L. W. Hypothalamic mechanisms for sexual, aggressive, and other motivational behaviors in the opossium, *Didelphis virginiana*. *J. Comp. Physiol. Psychol.* **64**, 1–15 (1967).
43. Barbosa, D. A. N. et al. The hypothalamus at the crossroads of psychopathology and neurosurgery. *Neurosurg. Focus* **43**, E15 (2017).
44. Motta, S. C. et al. Ventral premammillary nucleus as a critical sensory relay to the maternal aggression network. *Proc. Natl Acad. Sci. USA* **110**, 14438–14443 (2013).
45. Soden, M. E. et al. Genetic isolation of hypothalamic neurons that regulate context-specific male social behavior. *Cell Rep.* **16**, 304–313 (2016).
46. Stagkourakis, S. et al. A neural network for intermale aggression to establish social hierarchy. *Nat. Neurosci.* **21**, 834–842 (2018).
47. Kang, S. W., Thayananuphat, A., Bakken, T. & El Halawani, M. E. Dopamine-melatonin neurons in the avian hypothalamus controlling seasonal reproduction. *Neuroscience* **150**, 223–233 (2007).
48. Lo, L. et al. Connectional architecture of a mouse hypothalamic circuit node controlling social behavior. *Proc. Natl Acad. Sci. USA* **116**, 7503–7512 (2019).
49. Hashikawa, K., Hashikawa, Y., Lischinsky, J. & Lin, D. The neural mechanisms of sexually dimorphic aggressive behaviors. *Trends Genet.* **34**, 755–776 (2018).

50. Cameron, A. A., Khan, I. A., Westlund, K. N. & Willis, W. D. The efferent projections of the periaqueductal gray in the rat: a *Phaseolus vulgaris*-leucoagglutinin study. II. Descending projections. *J. Comp. Neurol.* **351**, 585–601 (1995).

51. Falkner, A. L. et al. Hierarchical representations of aggression in a hypothalamic-midbrain circuit. *Neuron* **106**, 637–648.e6 (2020).

52. Tschida, K. et al. A specialized neural circuit gates social vocalizations in the mouse. *Neuron* **103**, 459–472.e4 (2019).

53. Jürgens, U. & Ploog, D. Cerebral representation of vocalization in the squirrel monkey. *Exp. Brain Res.* **10**, 532–554 (1970).

54. Golden, S. A., Jin, M. & Shaham, Y. Animal models of (or for) aggression reward, addiction, and relapse: behavior and circuits. *J. Neurosci.* **39**, 3996–4008 (2019).

55. Couppis, M. H. & Kennedy, C. H. The rewarding effect of aggression is reduced by nucleus accumbens dopamine receptor antagonism in mice. *Psychopharmacol. (Berl.)* **197**, 449–456 (2008).

56. Golden, S. A. et al. Nucleus accumbens Drd1-expressing neurons control aggression self-administration and aggression seeking in mice. *J. Neurosci.* **39**, 2482–2496 (2019).

57. Fang, Y.-Y., Yamaguchi, T., Song, S. C., Tritsch, N. X. & Lin, D. A hypothalamic midbrain pathway essential for driving maternal behaviors. *Neuron* **98**, 192–207.e10 (2018).

58. Nieder, A. & Mooney, R. The neurobiology of innate, volitional and learned vocalizations in mammals and birds. *Philos. Trans. R. Soc. Lond. B* **375**, 20190054 (2020).

59. Berk, M. L. & Butler, A. B. Efferent projections of the medial preoptic nucleus and medial hypothalamus in the pigeon. *J. Comp. Neurol.* **203**, 379–399 (1981).

60. Riters, L. V. & Alger, S. J. Neuroanatomical evidence for indirect connections between the medial preoptic nucleus and the song control system: possible neural substrates for sexually motivated song. *Cell Tissue Res.* **316**, 35–44 (2004).

61. Lewis, J. W., Ryan, S. M., Arnold, A. P. & Butcher, L. L. Evidence for a catecholaminergic projection to Area X in the zebra finch. *J. Comp. Neurol.* **196**, 347–354 (1981).

62. Appeltants, D., Absil, P., Balthazart, J. & Ball, G. F. Identification of the origin of catecholaminergic inputs to HVc in canaries by retrograde tract tracing combined with tyrosine hydroxylase immunocytochemistry. *J. Chem. Neuroanat.* **18**, 117–133 (2000).

63. Appeltants, D., Ball, G. F. & Balthazart, J. The origin of catecholaminergic inputs to the song control nucleus RA in canaries. *Neuroreport* **13**, 649–653 (2002).

64. Maney, D. L. & Ball, G. F. Fos-like immunoreactivity in catecholaminergic brain nuclei after territorial behavior in free-living song sparrows. *J. Neurobiol.* **56**, 163–170 (2003).

65. Sasaki, A., Sotnikova, T. D., Gainetdinov, R. R. & Jarvis, E. D. Social context-dependent singing-regulated dopamine. *J. Neurosci.* **26**, 9010–9014 (2006).

66. Yanagihara, S. & Hessler, N. A. Modulation of singing-related activity in the songbird ventral tegmental area by social context. *Eur. J. Neurosci.* **24**, 3619–3627 (2006).

67. Hara, E., Kubikova, L., Hessler, N. A. & Jarvis, E. D. Role of the midbrain dopaminergic system in modulation of vocal brain activation by social context. *Eur. J. Neurosci.* **25**, 3406–3416 (2007).

68. Tanaka, M., Sun, F., Li, Y. & Mooney, R. A mesocortical dopamine circuit enables the cultural transmission of vocal behaviour. *Nature* **563**, 117–120 (2018).

69. Glimcher, P. W. Understanding dopamine and reinforcement learning: the dopamine reward prediction error hypothesis. *Proc. Natl Acad. Sci. USA* **108**, 15647–15654 (2011).

70. Yamaguchi, T. & Lin, D. Functions of medial hypothalamic and mesolimbic dopamine circuitries in aggression. *Curr. Opin. Behav. Sci.* **24**, 104–112 (2018).

71. van Erp, A. M. & Miczek, K. A. Aggressive behavior, increased accumbal dopamine, and decreased cortical serotonin in rats. *J. Neurosci.* **20**, 9320–9325 (2000).

72. Aleyasin, H. et al. Cell-type-specific role of ΔFosB in nucleus accumbens in modulating intermale aggression. *J. Neurosci.* **38**, 5913–5924 (2018).

73. Golden, S. A. et al. Basal forebrain projections to the lateral habenula modulate aggression reward. *Nature* **534**, 688–692 (2016).

74. Christoph, G. R., Leonzio, R. J. & Wilcox, K. S. Stimulation of the lateral habenula inhibits dopamine-containing neurons in the substantia nigra and ventral tegmental area of the rat. *J. Neurosci.* **6**, 613–619 (1986).

75. Russo, S. J. et al. The addicted synapse: mechanisms of synaptic and structural plasticity in nucleus accumbens. *Trends Neurosci.* **33**, 267–276 (2010).

76. Shen, W., Flajolet, M., Greengard, P. & Surmeier, D. J. Dichotomous dopaminergic control of striatal synaptic plasticity. *Science* **321**, 848–851 (2008).

77. Becker, E. A. & Marler, C. A. Postcontest blockade of dopamine receptors inhibits development of the winner effect in the California mouse (*Peromyscus californicus*). *Behav. Neurosci.* **129**, 205–213 (2015).

78. Sokolov, B. P. & Cadet, J. L. Methamphetamine causes alterations in the MAP kinase-related pathways in the brains of mice that display increased aggressiveness. *Neuropsychopharmacology* **31**, 956–966 (2006).

79. Moore, I. T., Hernandez, J. & Goymann, W. Who rises to the challenge? Testing the challenge hypothesis in fish, amphibians, reptiles, and mammals. *Horm. Behav.* **123**, 104537 (2020).

80. Fokidis, H. B., Prior, N. H. & Soma, K. K. Fasting increases aggression and differentially modulates local and systemic steroid levels in male zebra finches. *Endocrinology* **154**, 4328–4339 (2013).

81. Janson, C. & Vogel, E. Hunger and aggression in capuchin monkeys. in *Feeding Ecology in Apes and Other Primates* (eds. Hohmann, G., Robbins, M. M. & Boesch, C.) 285–312 (Cambridge Univ. Press, 2006).

82. Rohles, F. H. Jr. & Wilson, L. M. Hunger as a catalyst in aggression. *Behaviour* **48**, 123–130 (1974).

83. Berthoud, H.-R. Multiple neural systems controlling food intake and body weight. *Neurosci. Biobehav. Rev.* **26**, 393–428 (2002).

84. Donato, J. Jr. & Elias, C. F. The ventral premammillary nucleus links metabolic cues and reproduction. *Front. Endocrinol. (Lausanne)* **2**, 57 (2011).

85. Yanagida, H. et al. Effects of ghrelin on neuronal activity in the ventromedial nucleus of the hypothalamus in infantile rats: an in vitro study. *Peptides* **29**, 912–918 (2008).

86. Oomura, Y. & Kita, H. Insulin acting as a modulator of feeding through the hypothalamus. *Diabetologia* **20 Suppl.**, 290–298 (1981).

87. Vestlund, J. et al. Ghrelin and aggressive behaviours-evidence from preclinical and human genetic studies. *Psychoneuroendocrinology* **104**, 80–88 (2019).

88. He, Y. et al. Estrogen receptor-α expressing neurons in the ventrolateral VMH regulate glucose balance. *Nat. Commun.* **11**, 2165 (2020).

89. Todd, W. D. et al. A hypothalamic circuit for the circadian control of aggression. *Nat. Neurosci.* **21**, 717–724 (2018).

90. Bliwise, D. L. What is sundowning? *J. Am. Geriatr. Soc.* **42**, 1009–1011 (1994).

91. Goodson, J. L. Vasotocin and vasoactive intestinal polypeptide modulate aggression in a territorial songbird, the violet-eared waxbill (Estrildidae: *Uraeginthus granatina*). *Gen. Comp. Endocrinol.* **111**, 233–244 (1998).

92. Goodson, J. L., Kelly, A. M., Kingsbury, M. A. & Thompson, R. R. An aggression-specific cell type in the anterior hypothalamus of finches. *Proc. Natl Acad. Sci. USA* **109**, 13847–13852 (2012).

93. Wingfield, J. C., Hegner, R. E., Dufty, A. M. Jr. & Ball, G. F. The "challenge hypothesis": theoretical implications for patterns of testosterone secretion, mating systems, and breeding strategies. *Am. Nat.* **136**, 829–846 (1990).

94. Xu, X. et al. Modular genetic control of sexually dimorphic behaviors. *Cell* **148**, 596–607 (2012).

95. Tramontin, A. D., Wingfield, J. C. & Brenowitz, E. A. Androgens and estrogens induce seasonal-like growth of song nuclei in the adult songbird brain. *J. Neurobiol.* **57**, 130–140 (2003).

96. Soma, K. K., Tramontin, A. D., Featherstone, J. & Brenowitz, E. A. Estrogen contributes to seasonal plasticity of the adult avian song control system. *J. Neurobiol.* **58**, 413–422 (2004).

97. Bard, P. A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system. *Am. J. Physiol.* **84**, 490–515 (1928).

98. Paxinos, G. & Franklin, K.B. *The Mouse Brain in Stereotaxic Coordinates* (Academic Press, 2019).

99. Anderson, S. W., Bechara, A., Damasio, H., Tranel, D. & Damasio, A. R. Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nat. Neurosci.* **2**, 1032–1037 (1999).

100. Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M. & Damasio, A. R. The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science* **264**, 1102–1105 (1994).

101. Best, M., Williams, J. M. & Coccaro, E. F. Evidence for a dysfunctional prefrontal circuit in patients with an impulsive aggressive disorder. *Proc. Natl Acad. Sci. USA* **99**, 8448–8453 (2002).

102. Soloff, P. H. et al. Impulsivity and prefrontal hypometabolism in borderline personality disorder. *Psychiatry Res.* **123**, 153–163 (2003).

103. Molero-Chamizo, A., Martín Riquel, R., Moriana, J. A., Nitsche, M. A. & Rivera-Urbina, G. N. Bilateral prefrontal cortex anodal tDCS effects on self-reported aggressiveness in imprisoned violent offenders. *Neuroscience* **397**, 31–40 (2019).

104. Pietrini, P., Guazzelli, M., Basso, G., Jaffe, K. & Grafman, J. Neural correlates of imaginal aggressive behavior assessed by positron emission tomography in healthy subjects. *Am. J. Psychiatry* **157**, 1772–1781 (2000).

105. Ochsner, K. N., Bunge, S. A., Gross, J. J. & Gabrieli, J. D. Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *J. Cogn. Neurosci.* **14**, 1215–1229 (2002).

106. Mann, J. J. Neurobiology of suicidal behaviour. *Nat. Rev. Neurosci.* **4**, 819–828 (2003).

107. Soloff, P. H., Meltzer, C. C., Greer, P. J., Constantine, D. & Kelly, T. M. A fenfluramine-activated FDG-PET study of borderline personality disorder. *Biol. Psychiatry* **47**, 540–547 (2000).

108. Takahashi, A., Nagayasu, K., Nishitani, N., Kaneko, S. & Koide, T. Control of intermale aggression by medial prefrontal cortex activation in the mouse. *PLoS One* **9**, e94657 (2014).

109. Biro, L. et al. Task division within the prefrontal cortex: distinct neuron populations selectively control different aspects of aggressive behavior via the hypothalamus. *J. Neurosci.* **38**, 4065–4075 (2018).

110. Caramaschi, D., de Boer, S. F., de Vries, H. & Koolhaas, J. M. Development of violence in mice through repeated victory along with changes in prefrontal cortex neurochemistry. *Behav. Brain Res.* **189**, 263–272 (2008).

111. Centenaro, L. A. et al. Social instigation and aggressive behavior in mice: role of 5-HT1A and 5-HT1B receptors in the prefrontal cortex. *Psychopharmacol. (Berl.)* **201**, 237–248 (2008).

112. Veiga, C. P., Miczek, K. A., Lucion, A. B. & Almeida, R. M. Effect of 5-HT1B receptor agonists injected into the prefrontal cortex on maternal aggression in rats. *Braz. J. Med. Biol. Res.* **40**, 825–830 (2007).

113. Alexander, W. H. & Brown, J. W. Medial prefrontal cortex as an action-outcome predictor. *Nat. Neurosci.* **14**, 1338–1344 (2011).

114. Harenski, C. L., Harenski, K. A., Shane, M. S. & Kiehl, K. A. Aberrant neural processing of moral violations in criminal psychopaths. *J. Abnorm. Psychol.* **119**, 863–874 (2010).

115. Kingsbury, L. et al. Correlated neural activity and encoding of behavior across brains of socially interacting animals. *Cell* **178**, 429–446.e16 (2019).

116. So, N., Franks, B., Lim, S. & Curley, J. P. A social network approach reveals associations between mouse social dominance and brain gene expression. *PLoS One* **10**, e0134509 (2015).

117. Zhou, T. et al. History of winning remodels thalamo-PFC circuit to reinforce social dominance. *Science* **357**, 162–168 (2017).

118. Wang, F. et al. Bidirectional control of social hierarchy by synaptic efficacy in medial prefrontal cortex. *Science* **334**, 693–697 (2011).

119. Vertes, R. P. Differential projections of the infralimbic and prelimbic cortex in the rat. *Synapse* **51**, 32–58 (2004).

120. Ongür, D., An, X. & Price, J. L. Prefrontal cortical projections to the hypothalamus in macaque monkeys. *J. Comp. Neurol.* **401**, 480–505 (1998).

121. Freedman, L. J., Insel, T. R. & Smith, Y. Subcortical projections of area 25 (subgenual cortex) of the macaque monkey. *J. Comp. Neurol.* **421**, 172–188 (2000).

122. Hardy, S. G. & Leichnetz, G. R. Frontal cortical projections to the periaqueductal gray in the rat: a retrograde and orthograde horseradish peroxidase study. *Neurosci. Lett.* **23**, 13–17 (1981).

123. An, X., Bandler, R., Ongür, D. & Price, J. L. Prefrontal cortical projections to longitudinal columns in the midbrain periaqueductal gray in macaque monkeys. *J. Comp. Neurol.* **401**, 455–479 (1998).

124. Franklin, T. B. et al. Prefrontal cortical control of a brainstem social behavior circuit. *Nat. Neurosci.* **20**, 260–270 (2017).

125. Wong, L. C. et al. Effective modulation of male aggression through lateral septum to medial hypothalamus projection. *Curr. Biol.* **26**, 593–604 (2016).

126. Albert, D. J. & Chew, G. L. The septal forebrain and the inhibitory modulation of attack and defense in the rat. A review. *Behav. Neural Biol.* **30**, 357–388 (1980).

127. Goodson, J., Eibach, R., Sakata, J. & Adkins-Regan, E. Effect of septal lesions on male song and aggression in the colonial zebra finch (*Taeniopygia guttata*) and the territorial field sparrow (*Spizella pusilla*). *Behav. Brain Res.* **98**, 167–180 (1998).

128. Risold, P. Y. & Swanson, L. W. Connections of the rat lateral septal complex. *Brain Res. Brain Res. Rev.* **24**, 115–195 (1997).

129. Leroy, F. et al. A circuit from hippocampal CA2 to lateral septum disinhibits social aggression. *Nature* **564**, 213–218 (2018).

130. Hitti, F. L. & Siegelbaum, S. A. The hippocampal CA2 region is essential for social memory. *Nature* **508**, 88–92 (2014).

131. Sheehan, T. P., Chambers, R. A. & Russell, D. S. Regulation of affect by the lateral septum: implications for neuropsychiatry. *Brain Res. Brain Res. Rev.* **46**, 71–117 (2004).

132. Scott, J. P. Agonistic behavior of mice and rats: a review. *Am. Zool.* **6**, 683–701 (1966).

133. Maney, D. L. & Goodson, J. L. Neurogenomic mechanisms of aggression in songbirds. *Adv. Genet.* **75**, 83–119 (2011).

134. Conner, K. R., Duberstein, P. R., Conwell, Y. & Caine, E. D. Reactive aggression and suicide: theory and evidence. *Aggress. Violent Behav.* **8**, 413–432 (2003).

135. Wrangham, R. W. Two types of aggression in human evolution. *Proc. Natl Acad. Sci. USA* **115**, 245–253 (2018).

136. Insel, T.R., Winslow, J.T., Wang, Z. & Young, L.J. in *Vasopressin and Oxytocin* (eds Zingg, H. H., Bourque, C. W. & Bichet, D.G.) 215–224 (Springer, 1998).

137. Goodson, J. L. Territorial aggression and dawn song are modulated by septal vasotocin and vasoactive intestinal polypeptide in male field sparrows (*Spizella pusilla*). *Horm. Behav.* **34**, 67–77 (1998).

138. O'Connell, L. A. & Hofmann, H. A. Evolution of a vertebrate social decision-making network. *Science* **336**, 1154–1157 (2012).

139. Benarroch, E. E. Periaqueductal gray: an interface for behavioral control. *Neurology* **78**, 210–217 (2012).

140. Ferris, C. F. et al. Vasopressin/serotonin interactions in the anterior hypothalamus control aggressive behavior in golden hamsters. *J. Neurosci.* **17**, 4331–4340 (1997).

141. Ferris, C. F. & Potegal, M. Vasopressin receptor blockade in the anterior hypothalamus suppresses aggression in hamsters. *Physiol. Behav.* **44**, 235–239 (1988).

142. Gross, C. T. & Canteras, N. S. The many paths to fear. *Nat. Rev. Neurosci.* **13**, 651–658 (2012).

143. Wang, L., Chen, I. Z. & Lin, D. Collateral pathways from the ventromedial hypothalamus mediate defensive behaviors. *Neuron* **85**, 1344–1358 (2015).

144. Lindenfors, P. & Tullberg, B. S. Evolutionary aspects of aggression the importance of sexual selection. *Adv. Genet.* **75**, 7–22 (2011).

145. Eisen, E. J. & Legates, J. E. Genotype-sex interaction and the genetic correlation between the sexes for body weight in *Mus musculus*. *Genetics* **54**, 611–623 (1966).

146. Eisenberg, J. F. Studies on the behavior of *Peromyscus maniculatus gambelii* and *Peromyscus californicus parasiticus*. *Behaviour* **19**, 177–207 (1962).

147. Archer, J. Does sexual selection explain human sex differences in aggression? *Behav. Brain Sci.* **32**, 249–266 (2009). discussion 266–311.

148. Harrendorf, S., Heiskanen, M. & Malby, S., eds. International Statistics on Crime and Justice. HEUNI Publication Series No. 64 (United Nations Office on Drugs and Crime, 2010).

149. Österman, K. et al. Cross-cultural evidence of female indirect aggression. *Aggressive Behav.* **24**, 1–8 (1998).

150. Fedy, B. C. & Stutchbury, B. J. Territory defence in tropical birds: are females as aggressive as males? *Behav. Ecol. Sociobiol.* **58**, 414–422 (2005).

Acknowledgements

Author contributions

D.L. wrote the manuscript and edited figures. J.E.L. co-wrote the manuscript and made the figures.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence should be addressed to D.L.

Peer review information *Nature Neuroscience* thanks Aubrey Kelly and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.