



The role of the amygdala in processing social and affective touch

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The amygdala plays a central role in emotion and social behavior, yet its role in processing social and affective touch is not well established. Longitudinal studies reveal that touch-deprived infants show later in life exaggerated emotional reactivity related to structural and functional changes in the amygdala and other brain structures. The internal organization and connectivity of the amygdala is well-suited to process the sensory features of tactile stimuli and also the socio-cognitive dimensions of the received touch. The convergent processing of bottom-up and top-down pathways that carry information about touch results in the elaboration of context appropriate autonomic responses. Indeed, the positive value of affective touch in humans and social grooming in non-human primates is correlated with vagal tone and the release of oxytocin and endogenous opioids. Grooming, the non-human primate equivalent of affective touch in humans, reduces vigilance, that depends on the amygdala. During touch-induced vagal tone and low vigilance, neural activity in the amygdala is substantially different from activity corresponding to the attentive processing of tactile stimuli. Under these circumstances neurons no longer respond phasically to each touch stimulus, rather they signal a sustained functional state in which the amygdala appears decoupled from monitoring the external environment.

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Introduction

One of the many functions of the amygdala is to detect emotionally and socially salient stimuli, evaluate their momentary significance, and coordinate the most appropriate somatic and autonomic changes in response to these stimuli. We start from the premise that social and affective

touch is almost always salient and the amygdala is expected to process these stimuli. We hypothesize that instead of extracting the sensory features of touch stimuli, the amygdala extracts or processes more abstract overtones of touch, such as the mental state elicited in the receiver by affective touch, as indexed by vagal tone and the level of vigilance. In this perspective article, we review findings that suggest a role of the amygdala in processing affective touch and present evidence from ongoing studies that the amygdala responds to the mental state elicited by touch stimuli and not by the stimuli *per se*.

A century ago, J.B. Watson, the founder of the behaviorist school of thought, discouraged parents from affectionately holding their babies and hugging their toddlers [1]. Instead of affectionate touch, behaviorists suggested verbal praise, punctuated by occasional handshakes, and pats on the head as rewards for good behavior. Parents judiciously ignored these prescriptions. However, orphanages across the world implemented them with disastrous and irreversible consequences. The ‘failure to thrive’ of institutionalized children has been attributed to emotional neglect and the absence of affective touch [2–4]. Indeed, the lack of affective touch during early development derails normal development of the social brain, leaving individuals unable to establish lasting emotional bonds later in life [5]. These changes appear to be irreversible because affectionate care and extra enrichment provided by the adoptive parents of children neglected and abused in the notorious Romanian orphanages in the 1980s did not reverse the brain abnormalities acquired early in life [6,7].

It appears, therefore, that physical contact with a caretaker through affective touch during early development lays down the neural foundation for normal emotional reactivity and regulation [8]. Adolescents who were institutionalized during infancy showed increased emotional reactivity associated with persistent hyperactivity of the amygdala and enhanced amygdala connectivity with the prefrontal cortex [9,10]. The amygdala itself plays a central role in emotional reactivity [11] by setting in register the perceived or expected emotional significance of stimuli with autonomic activation [12,13]. It is possible that affective touch modifies activity within the amygdala or modifies neural communication between the amygdala and other brain areas, leading to downregulation of emotional reactivity through vagal mechanisms [14].

Beyond its role in emotional development, the amygdala coordinates emotional behavior throughout adulthood.

Affective touch is fully integrated into our adult emotional vocabulary, allowing us to receive and understand a rich variety of emotional signals through our skin [15]. Adults can also experience the negative physical and emotional effects of touch deprivation. Social distancing during the Covid-19 pandemic brought to light our ‘touch hunger’ that shaped the negative experience across age groups [16,17]. Despite the significance of touch in shaping our social and emotional experiences, the specific neural processes in the amygdala that transform particular types of tactile inputs into a social and emotional experiences are just beginning to come to light.

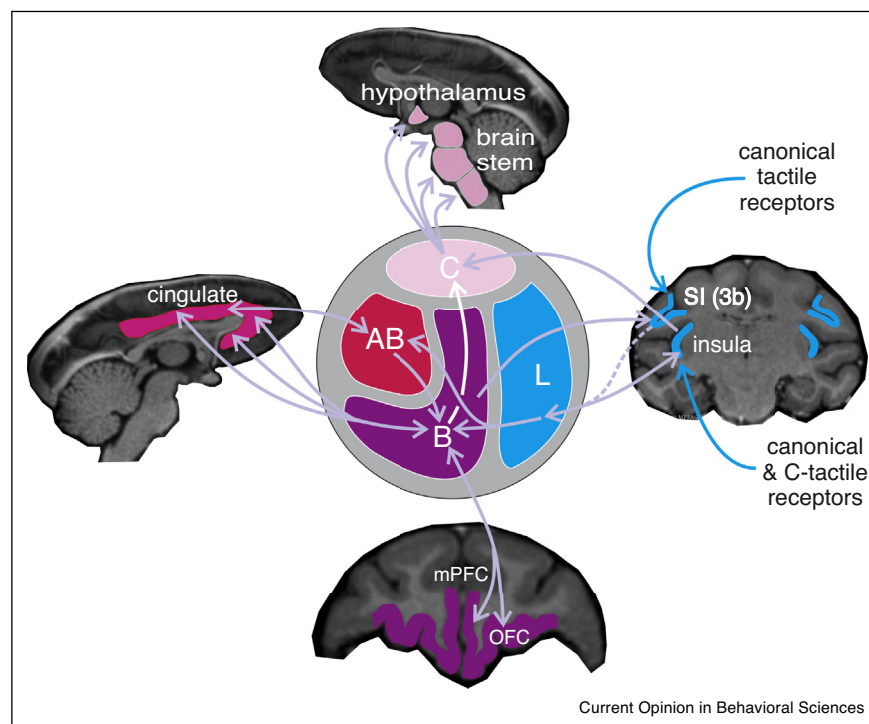
The amygdala processes multiple dimensions of touch

It is only recently that subsets of neurons in the non-human primate amygdala have been shown to clearly respond to tactile stimuli [18,19]. It remains unclear,

however, what aspects of tactile stimuli these neurons respond to and whether they respond to the positive valence associated with affective touch. Intracranial recordings and neuroimaging studies in humans and non-human animals have converged on the idea that the amygdala responds differentially to the positive or negative valence/value of both non-social and social stimuli [20,21]. However, neurons in amygdala also respond to neutral or ambiguous stimuli, to novelty, to alerting stimuli, and even to abstract constructs [reviewed in Ref. 22**].

Indeed, most neurons in the amygdala are tuned to multiple dimensions of a stimulus and/or of the ongoing behavior [22**,23**]. For example, neurons in the amygdala that respond to touch also respond to visual and auditory stimuli [19] and to the production of facial expressions [18,24] that activate the mechanoreceptors in

Figure 1



Bottom-up and top-down touch-related signals converge in the basal and accessory basal nuclei of the primate amygdala. Tactile stimuli detected by the canonical skin mechanoreceptors are processed by the tactile subdivision (3b) of the primary somatosensory cortex (SI). Inputs from C-tactile afferents are processed in the insula. The output of these two cortical areas projects to the lateral (L) nucleus of the amygdala, and after local processing, is forwarded to the basal (B) nucleus. In the basal nucleus these bottom-up inputs converge with top-down inputs from limbic cortical areas that include the cingulate cortex (with the dorsal, pregenual and subgenual subdivisions) and the orbitofrontal cortex (OFC). The basal nucleus also receives input from the medial segment of the prefrontal cortex (mPFC). The cingulate cortex, the OFC and the mPFC also target the accessory basal nuclei (connections not shown). The connections of the amygdala with limbic cortical areas are reciprocal. The output projections of the basal nucleus broadcast the outcome of the top-down and bottom-up evaluation of touch stimuli to multiple cortical areas. This output is also transferred to the central nucleus (C) that engages autonomic centers in the hypothalamus and brainstem. The insula also has reciprocal connections with the central nucleus. Autonomic centers at each level of brainstem regulate visceral responses to touch and coordinate the relative dominance of sympathetic and parasympathetic responses. Projections to the hypothalamus and brainstem also trigger the release of hormones (e.g. oxytocin) and endogenous opioids that may contribute the subjective experience and the social behaviors elicited by affective touch.

the facial skin. It is unclear, however, whether these neurons respond to the same viewed and produced facial expressions, as in the canonical mirror neuron system [25]. Furthermore, multidimensional neurons in the amygdala often respond to apparently random combinations of features [26]. For example, in monkeys, the same neurons respond to the magnitude of rewards received and to the social status of familiar conspecifics [27] or to combinations of task-related vigilance, face identity, and reward amount [28]. In humans, the same neurons have been shown to encode both novelty and the identity of visual stimuli [29].

It is also possible that tactile-responsive neurons in the amygdala signal the context in which social touch occurs, or some other aspects of ongoing behavior — a question that we are actively investigating. Based on more extensively explored sensory domains, it is expected that neurons in the amygdala signal the pleasantness/unpleasantness of touch as a function of the relationship between the receiver and the person who delivers the touch, the autonomic state of the receiver, and even the recipient's expectations. Indeed, Ellingsen *et al.* [30^{*}] argued that all these factors contribute to the hedonic value of social touch that emerges through the convergence of bottom up and top-down mechanisms.

The connectivity of the amygdala is ideally suited for processing multiple aspects of touch

The amygdala, by virtue of its nuclear organization and the connectivity of each nucleus, is ideally suited for convergent processing of the physical and the socio-emotional dimensions of tactile signals. The lateral nucleus of the amygdala receives highly processed sensory signals from secondary sensory and multisensory association areas of the temporal and parietal cortices (Figure 1) [31]. Affective touch that activates C-tactile afferents is processed primarily by the insula [32], which in turn is connected to the amygdala via multiple, bidirectional processing loops [33,34^{*}]. The output of the lateral nucleus projects to the basal nucleus of the amygdala (Figure 1) where it converges with inputs from the prefrontal cortex [35].

The medial prefrontal cortex and the orbitofrontal cortex (mPFC and OFC, Figure 1), in addition to responding to the interactive aspects of social stimuli [36,37], also signal social rules and norms [38]. In the tactile domain, strong cultural rules and taboos restrict the area of the body that can be touched by others [39]. Thus, in the basal and accessory basal nuclei (B and AB, Figure 1) of the amygdala, the physical features of tactile stimuli (processed initially in the lateral nucleus) can be combined with higher-level evaluations of touch in the prefrontal cortex. The outcome of this evaluation is likely broadcast from the amygdala to a large array of targets that include

primary and secondary sensory areas, association areas, limbic cortical areas (such as the anterior cingulate cortex, the insula, and the orbitofrontal cortex) and the autonomic centers in the brainstem and hypothalamus via the central nucleus (C, Figure 1) [40]. The amygdala regulates sympathetic, parasympathetic, and endocrine responses via the connections from the central nucleus to distinct hypothalamic nuclei and to autonomic centers in the brainstem. The projections to the brainstem also target the locus coeruleus, the dorsal raphe, and the ventral tegmental area, the main sources of monoamines in the brain.

There are two main types of cortical projections from the basal (and accessory basal) nucleus. One targets emotionally relevant cortical areas, establishing several parallel loops that carry out multiple functions [41]. The other projects to various stages (both association and primary cortices) of sensory processing. Such connectivity may explain the presence of valence-dependent modulation in even early stages of cortical sensory processing. This has been best demonstrated in the visual domain. For example, in macaques, multiple areas of the temporal visual cortex respond differentially to aggressive and friendly facial expressions [42]. Lesions of the amygdala, however, eliminate this valence effect, leaving face detection and face discrimination intact [42]. It is possible, therefore, that the responses in primary somatosensory cortex to the pleasantness of touch or the hedonic value of a caress from an attractive person of the opposite sex [43] are due to the activity of neurons in the basal nucleus that project to the primary sensory areas [40,44]. Such neural activity in the basal nucleus may not induce detectable hemodynamic changes in the amygdala itself. Indeed, focal, near-infrared stimulation restricted to a subnuclear region in the basal nucleus of anesthetized monkeys, causes significant increases in the BOLD signal in multiple sensory areas without an equally large activation in the amygdala itself [45^{*}].

The basal and accessory basal nuclei also project to the central nuclei of the amygdala either directly or via the intercalated nuclei [46]. The central nuclei are part of an autonomic network that coordinates bodily responses to stimuli of importance [47]. It is likely that the elevated vagal tone in response to affective touch in humans is initiated by the central nucleus of the amygdala [14]. This conjecture gathers momentum if we consider that through the central nuclei, the amygdala is looped into the interoceptive circuit of the brainstem and the insula [48^{**}] and may contribute to the coordinated mind-body states elicited by affective touch [49^{**}].

The anatomically favorable position of the amygdala for the convergence of pathways that transmit physical and affective dimensions of touch is borne out by empirical data. Despite the challenges of reliably detecting BOLD

signal in the amygdala [50,51], a few neuroimaging studies showed robust activation of the amygdala in response to affective touch. When the amygdala was activated by pleasant tactile stimuli, the BOLD signal was correlated with the perceived pleasantness of touch [52], likely because pleasurable tactile sensations activate the opioid system within the amygdala [53]. A subset of studies showed affective touch enhanced the functional connectivity between the amygdala and limbic cortical areas. For example, pleasant touch in humans elicited enhanced functional connectivity of the insula and amygdala with medial prefrontal areas [54]. Likewise, pleasant touch, but not painful stimuli, elicited coordinated activity between the anterior cingulate cortex and a region corresponding to the extended amygdala [55].

Context dependence of touch processing in the amygdala

The subjective value of social touch partially depends on the identity of the toucher. Indeed, the BOLD signal in the amygdala of human subjects differentiates between touch received from a bonded partner or a stranger of opposite sex [56**]. This confirms that top-down, higher-level social evaluation of touch is processed by the amygdala, in this case, the relationship between the toucher and the receiver [39]. The pleasantness of social touch also depends on social context. Support for this comes from studies that combine touch with other social signals such as facial expressions. Seeing smiling faces, for example, enhanced the perception of pleasant touch while seeing negative facial expressions potentiated the perception of unpleasant touch [57]. Faces and facial expressions are processed in the amygdala [58], so it is not surprising that patients with amygdala lesions failed to show enhanced detection of tactile stimulation when viewing images of faces being touched (a phenomenon reliably documented in healthy controls) [59*]. Such findings suggest a capacity of the amygdala to integrate social context into the processing of tactile information, likely due to the rich connectivity and multidimensionality of its component neurons [22**,23**,28,60].

Grooming in nonhuman primates is equivalent to affective touch in humans

Many species of non-human primates build and maintain social bonds through reciprocal grooming. Grooming is often traded for coalition support, infant handling, and for tolerance at feeding and drinking sites [61]. Macaque monkeys solicit grooming by ‘groom presenting’ (offering access to body parts) to a trusted social partner. They often lie in front of the groomer, adopt positions that expose vulnerable body parts to the groomer’s hands and teeth, close their eyes, and appear fully relaxed [62]. They may fall asleep, relinquishing attention and vigilance to the trusted groomer. Some species of macaques invest 15–20% of their daily activity in social grooming, which exceeds hygienic needs, but pays off during social conflict

when grooming partners support each other [63]. The hedonic value of grooming is illustrated by the observation that animals readily perform a monotonous and repetitive operant task in exchange for grooming [64]. Indeed, grooming received by macaques from trusted human trainers has comparable physiological effects to grooming from conspecifics, including decreased sympathetic and increased parasympathetic (vagal) activity, indexed by lower heart rate and increased heart rate variability [65*]. Many of the beneficial effects of grooming are related to the release of oxytocin that suppresses the effects of cortisol and reduces reactivity to psychosocial stressors [66,67].

The pleasantness of grooming may be related to the release of endorphins [68–71] perhaps triggered by activation of C-tactile fibers in the skin that respond to particular patterns of affective touch [72]. The physiological effects of grooming in macaques match the effects observed in humans: pleasant touch increases vagal tone, thereby reducing the negative effects of stress [14]. In addition to autonomic changes, stress-reducing effects manifest through measurable behaviors, such as the relaxation of the facial corrugator muscle that is typically contracted during negative affective states [73]. Neural recordings from the amygdala of macaque monkeys that receive social grooming, as we are presently carrying out, are expected to reveal some of the cellular underpinnings of affective touch. The amygdala is expected to signal valence (pleasant or unpleasant), social context, autonomic state, or other, more abstract variables. These expectations are justified by previous studies in the visual domain carried out in both our and other laboratories.

Affective touch links the amygdala to attention and vigilance

We have recorded neural activity simultaneously from the amygdala and somatosensory cortex of macaques in response to alternating blocks of non-social and social tactile stimuli (Martin *et al. Soc Neurosci Abstr*, 2021, P317.04). Social stimuli were grooming-like finger sweeps to the monkey’s face delivered by a trusted human. Gentle airflow delivered to multiple regions of the face that avoided the eyes, nostrils, and the ears served as innocuous non-social stimuli. Grooming induced significant decreases of heart rate confirming that being touched by a human groomer was pleasant. Indeed, the subjects often closed their eyes and appeared to fall asleep. During blocks of non-social tactile stimulation, heart rate was significantly elevated compared to the blocks of grooming. As expected, neurons in the somatosensory cortex responded to both non-social and social stimuli, differentiating between location and contact pressures. Consistent with our previous studies [18,19], approximately 30% of neurons in the amygdala responded to non-social tactile stimuli. Contrary to our expectations, however, <10% of those amygdala neurons that responded to the

non-social stimuli responded to social touch, even when the social touch was delivered with comparable pressure and to the same areas of the skin. Furthermore, virtually no amygdala neurons responded selectively to social touch.

The failure of neurons to respond to social touch, suggests a gating mechanism, possibly related to the vagal tone induced by grooming. Indeed, the small fraction of neurons that responded to both social and non-social touch were recorded in sessions when the heart rate remained high across the blocks. During these predictable periods of grooming, neurons in the amygdala did not respond to each grooming sweep. Rather, they appeared to signal a long-lasting (seconds to minutes) internal state induced by grooming. Taken together these findings suggest that neural activity in the amygdala may be decoupled from monitoring the external environment to monitoring an internal state that has clear autonomic correlates. This phenomenon of gating phasic responses of the amygdala may have not been reported previously because during typical experiments of neural recordings from the amygdala, animals remain vigilant and engage with stimuli that carry emotional or behavioral significance. In response to grooming, however, we observe the opposite, a temporary disengagement of the amygdala from discrete incoming stimuli. This new finding should not be interpreted as a failure of the amygdala to respond to affective touch. On contrary, these tonic signals associated with internal state seem more pervasive and robust than responses to brief visual, auditory, or innocuous tactile stimuli.

One explanation for the suppression of episodic neural responses to grooming may be that the animal's sensorium is no longer oriented outwardly, as the responsibility of monitoring the environment for potential danger is transferred to the groomer. Indeed, the amygdala plays a pivotal role in vigilance and attention [74] and shows enhanced, almost automatic facilitation of attention for threat-related stimuli [75,76]. Accordingly, vigilance and apprehension are correlated with high gamma oscillations in the amygdala that entrain and increase the spiking activity of the resident neurons [77**]. It may be that, during periods of positive social contact, the amygdala tonically signals to the rest of the brain the safety of this behavioral context while enhancing activity in the parasympathetic branch of the autonomic nervous system. While the amygdala is broadly known for the 'fight or flight' response, it may play an equally important role in coordinating vagal states. The significant and persistent elevation of heart rate in monkeys with bilateral amygdala lesions [78*] suggest the loss of vagal mechanisms that slows spontaneous heart rate. In light of these observations, it is not surprising that individuals deprived of affective touch have increased sympathetic reactivity to emotional stimuli and poor emotional regulation [6,7*,8*,9,10**].

Future directions

In a broader framework, the sustained (rather than phasic) changes in amygdala activity elicited by grooming, and probably affective touch in humans, can be interpreted as a shift of processing priority from exteroception to interoception. Affective touch activates the C-tactile afferents and this peripheral system seems aligned with interoceptive processing of pain, temperature, itch, and the general status of internal tissues [79]. As such, the affective motivational dimensions of touch may give rise to prolonged brain states, that do not show large moment-by-moment oscillations [80] as would be expected from discriminative touch. The amygdala is expected to be a key site for the integration of information processed by interoceptive and exteroceptive circuits as this is where interoceptive autonomic afferent activity intersects with the neural representations of positive and negative value/valence [81]. Indeed, the amygdala responds to interoceptive signals and to external sensory stimuli of all modalities and across the entire spectrum of valence [22**,23**]. Pain also activates the amygdala [82] as the ultimate stimulus that requires attention and conjures up strong affective responses. In primates, the amygdala also contributes to the evaluation of social information signaled by bodies, faces, facial expressions, gaze direction, eye contact, social status, and the observed or expected behaviors of social partners [22**]. The amygdala provides, therefore, a fertile ground to explore the cellular basis of the homeostatic integration of interoception with the multitude of other functions it performs.

A major challenge for future research will be to determine the cellular mechanisms by which affective touch alters the output of the amygdala to enable positive emotional states. If the mechanism for this change is a shift from exteroceptive to interoceptive processing, it will be important to explore the extension of sympathetic and vagal pathways beyond the brainstem, into areas such as the amygdala, insula, anterior cingulate, and medial prefrontal cortex. These structures are known to process the emotional significance of stimuli and to generate affective states that regulate and govern emotional and social behavior. It is highly likely that these region's evaluation of stimuli (and the ensuing behaviors) depends not only on the external features of stimuli but also on the internal state of the organism. Where and how the majority of interoceptive signals are processed and how they factor into cognitive and affective brain states remains to be brought to light.

Conclusion

In conclusion, the amygdala may play multiple, complementary roles in affective touch. When the subject is vigilant and engaged in a task, the amygdala may signal the sensory and affective dimensions of touch, including pleasantness and social variables. These signals are detectable during typical experimental settings wherein

the subjects are rarely fully relaxed. If, however, the receiver feels safe, and can relinquish vigilance and attention to the social partner, the amygdala may cease processing the exteroceptive touch stimuli and shifts processing toward interoceptive signals.

Conflict of interest statement

Nothing declared.

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