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Feature Review

The Neurobiology of Human Attachments

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Attachment bonds are a defining feature of mammals. A conceptual framework on human attachments is presented, integrating insights from animal research with neuroimaging studies. Four mammalian bonds are described, including parent–infant, pair–bonds, peers, and conspecifics, all built upon systems shaped by maternal provisions during sensitive periods, and evolution from rodents to humans is detailed. Bonding is underpinned by crosstalk of oxytocin and dopamine in striatum, combining motivation and vigor with social focus, and their time sensitivity/pulsatility enables reorganization of neural networks. Humans' representation-based attachments are characterized by biobehavioral synchrony and integrate subcortical with cortical networks implicated in reward/motivation, embodied simulation, and mentalization. The neurobiology of love may open perspectives on the 'situated' brain and initiate dialog between science and humanities, arts, and clinical wisdom.

The measure of the intensity of love
Is measure, also, of the verve of earth.
For me, the firefly's quick, electric stroke
Ticks tediously the time of one more year.
And you? Remember how the crickets came
Out of their mother grass, like little kin,
In the pale nights, when your first imagery
Found inklings of your bond to all that dust.
Wallace Stevens, *Harmonium*

Human Attachments throughout Life Share Underlying Neurobiology

Since the dawn of humanity, 'the intensity of love' has been depicted by modalities vastly different from scientific 'measurement': cave paintings, clay figures, story-telling, dance, music, and poetry. Over the last decades, studies in animal models, particularly rats and monogamous prairie voles, began to uncover the cellular, neural, and endocrine mechanisms implicated in maternal care and pair bonding. Those gave rise to a new field of inquiry – the neurobiology of human attachments – which integrates insights from other mammals with new tools available for human research – brain imaging, neuroendocrinology, genetics and epigenetics, and peptide administration – to test the biological basis of human attachments. This emerging field is generating a growing body of knowledge which requires a new conceptual framework, one that integrates cross-species comparability with the distinct features of human love [1,2].

The goal of this paper is to provide such a conceptual frame for the neurobiology of human attachments and address its tenets, parameters, and neural basis. While this conceptual

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framework is built upon empirical data in animals and humans, some of its details are speculative and may guide future research. I argue that the study of mammalian bonding must be conducted from a developmental perspective, both in relation to the life of an individual and in the context of animal evolution, and that this is especially the case in humans whose large associative cortex is wired, to a large extent, by early experiences within child-rearing contexts [3–5]. Later attachments, with romantic partners, close friends, mentors, or in-group members from sports teams to nations, repurpose the basic machinery established by the mother–offspring bond during early '**sensitive periods**' (see Glossary). I further suggest that the neurobiology of attachment rides on systems that maintain brain plasticity through time-sensitive pulsatility – dopamine (DA) and oxytocin (OT) – which, by forming tighter crosstalk during periods of bond formation [6], integrates reward salience with social focus to reorganize neural networks around the new attachment [7–9]. Studies in rodents have shown that the integration of OT and DA in **striatum** supports the formation of maternal–infant and pair bonds [10]. Yet, while similar mechanisms are thought to underpin bond formation in humans, attachment bonds acquired substantial complexity, duration, and flexibility across mammalian evolution, reaching their apex in humans' long-term exclusive attachments that integrate subcortical reward with higher-order representational components (Figure 1, Key Figure). Such flexibility affords not only the immense variability of human attachments across cultural contexts but also enables later reparation, and while early bonds shape the social brain and its underlying neurobiology, humans can repair, via top–down processing, commitment, and discipline, the effects of early maladaptive relationships by later benevolent ones. Key propositions of the model are summarized in Box 1.

Box 1. Key Propositions of the Neurobiology of Human Attachments Model

- Research on human attachments implicates a developmental perspective: Mammalian bonding is supported by neurobiological systems shaped by the mother–offspring relationship during early sensitive periods [36].
- Continuity in neurobiological systems underpins human bonds: Human attachments repurpose the basic machinery established by the parent–offspring bond in the formation of other attachments throughout life, such as romantic attachment or close friendships [1].
- Human bonds are selective and enduring: Bonds are specific to attachment target and last for extended periods, often a lifetime. Gradients of the selective and enduring components define the various human bonds (see Figure 1 in main text).
- Bonding is behavior based triggered by the expression of species-specific, person-specific, and culture-specific behavioral patterns: Bonding implicates bottom–up processes. Bonding-related brain and neuroendocrine systems are activated by attachment-related behavior [5,37].
- Biobehavioral synchrony is a key feature of human attachments: Human attachments are characterized by the coupling of coordinated nonverbal behavior with coordinated physiological response among partners during social contact [101] (see Figure 2 in main text).
- Central role of the oxytocin system and oxytocin–dopamine connectivity: OT is implicated in human mothering, fathering, coparenting, romantic attachment, and close friendship. Integration of OT and DA in striatum ignites bonding, imbuing attachments with motivation and vigor [9].
- Bond formation involves increased activity and tighter crosstalk among relevant systems: Activation and closer links among systems underpinning affiliation, reward, and stress management are observed during periods of attachment formation [6].
- Human attachments promote homeostasis, health, and well-being throughout life: Social attachments enhance health and happiness while social isolation increases stress, impaired health, and death [176].
- Patterns of attachment are transferred across generations: Behavioral patterns experienced in early life organize OT availability and receptor localization in the infant's brain, shaping the capacity to parent the next generation [66,129].
- The human brain is a situated organ, shaped by the mother–infant attachment and proximity to mother's body to function within the social ecology: The young mammal's immature brain at birth and need for close proximity to a nursing mother shape the brain as a 'situated' organ, constantly responding online to the social world [71]. Humans' protracted maturity sculpts the dialogical nature of the human brain and its constant need for social affiliations.
- Human bonds experienced throughout life are transformative and have the potential to repair early negative relationships by later benevolent ones: The great plasticity of the human social brain and its behavior-based nature enable later attachments to reorganize neural networks and repair, at least partly, negative early experiences. This highlights the translational potential of research on the neurobiology of human attachments [177].

Glossary

Activity-dependent facilitation: occurs when presynaptic spike activity is paired with activity of facilitatory interneurons, leading to enhanced neuronal activation [198].
Alloparenting: the care of infants by adults other than the biological mother. Alloparenting is common across primate species and enhances infant survival [84].
Biobehavioral synchrony: the coordination of biological and behavioral processes between attachment partners during social contact. It is a key feature of human attachments.
Heteromers: G protein-coupled receptors (GPCRs) consist of seven membrane-spanning alpha-helical segments that combine into a single receptor. However, GPCRs can form heteromers by combining two or more GPCR subunits. The oxytocin receptor belongs to the G protein-coupled receptor family. NA shell contains oxytocin receptors that may form heteromers with D2 receptors on medium spiny neuron. The ligand-binding properties and neural pathways of heteromers integrate aspects of both parent receptors.
Long-term depression: reduction in the efficacy of neuronal synapses following a long repeated stimulus.
Medium spiny neurons (MSNs): projection neurons that are GABAergic (inhibitory) and comprise over 90% of neurons in the human striatum. MSN come in two formats. The D1-type (D1 dopamine receptor-expressing neurons) functions in the 'direct pathway', that is, convey their information directly to the output nuclei of basal ganglia. The D2-type (D2 dopamine receptor-expressing neurons) functions in the 'indirect pathway', conveying information to basal ganglia indirectly via pallidal neurons. Some MSNs express for both D1-type and D2-type receptors.
Myoactivity: the stimulation of rhythmic tissue contraction. Myoactivity is the most conserved function of the oxytocin system, which has been integrated in mammals into the oxytocin-controlled uterine contractions and milk ejection [43,62].
Sensitive periods: specific time windows in early life when the brain must experience certain environmental inputs for proper maturation [2]. In the context of

The Neurobiology of Mammalian Affiliation: Crosstalk of DA and OT

Our proposed model suggests that the 'intensity of love', the quality of attachment, is measured in terms of the vigor [11] of DA action in striatum, particularly in the nucleus accumbens (NA). DA acts in the NA to organize goal-directed reward-related behavior characterized by initiation and vigor by inhibiting the inhibitory output of NA GABAergic (inhibitory) **medium spiny neurons,** which then release ventral pallidum (VP) neurons in the basal ganglia to enable motor action [12–15]. Disinhibition of the inhibitory control in the accumbens–pallidal indirect pathway, pathway from striatum to basal ganglia which is not direct but acts via pallidal neurons, renders the VP accessible to glutamate (excitatory neurons) inputs, leading to energetic behavior and marking the striatum as a limbic–motor interface where reward translates into action marked by vigor and goal directedness [16,17].

Yet, while DA neurons function as general-purpose stimulators to reward-related targets, it is their close links with OT receptors in striatum, where OT receptors abound [18,19], that imbue attachment bonds with incentive value and direct action toward affiliative goals, such as maternal care [9,20,21]. Actions of DA D1-type and D2-type neurons on OT receptors in NA shell establish maternal memory and form repetitive patterns of caregiving, as shown in rats [22]. OT stimulates the accumbens–pallidal indirect pathway, strengthening synaptic activity in VP and forming memories of the attachment context. NA shell contains OT receptors that may form **heteromers,** neurons expressing for multiple receptors, with DA D2-type receptors on medium spiny neurons, and OT binding to OT receptors increases affinity of DA to associated D2-type receptors [23]. Since D2 receptors depress activity of medium spiny neurons, OT can potentiate these inhibitory effects. The combination of DA D1-type and D2-type receptors and OT receptors in NA shell functions to depress the striatal inhibitory input to VP and enables supernormal excitation of basolateral amygdala projections to VP, which, through **activity-dependent facilitation,** creates the effects of mesolimbic DA on attachment-focused action [24,25]. The coactivation of D2-expressing neurons in the NA by OT enables neurons specifically suited to identify sensory–motor reward patterns to employ reward computations of D2 neurons to encode the temporal patterns of social reward, as shown in rhesus macaques [26,27]. This allows the brain to internalize the social partner and its preferences, encode relationship-specific patterns of social exchange, and draw reward from the matching of self and partner's actions (i.e., social synchrony), which lead to consolidation of the bond [13,26].

Overall, the tighter OT–DA crosstalk in the NA during bond formation enables plasticity of the brain reward system and its flexible adaptation to incorporate the new bond into the self [18,28,29]. Studies in prairie voles show that the NA receives OT receptors containing inputs from multiple cortical regions, including sensorimotor and associative cortices and these enable the formation of sensory and motor memories of attachment experiences [30]. Furthermore, OT receptor density in the NA in infancy was found to predict the time spent huddling with partner in female prairie voles [31], and bereavement-like behavior and activation of stress-related neurohormonal systems following partner loss in male prairie voles were associated with suppression of OT signaling in the NA [32]. These findings highlight the role of accumbens OT in forming continuity from parental to pair bonds and in buttressing the protective function of long-term attachments. Finally, research in rats describes the role of OT in **long-term depression** in amygdala, attenuating amygdalar response to aversive social stimuli [33,34]. Such long-term depression reduces fear and facilitates the approach orientation required for bonding [35]. Thus, while DA affords vigor and motivation, OT provides the soothing and tranquility necessary for bond formation via its regulatory effects on hypothalamic–pituitary–adrenal axis activity [36,37] and anxiolytic properties [38]. This creates a unique neurobiological state of 'immobility without fear' [39], a state specifically suited for the formation of new attachments.

bonding, these involve the species-typical parenting behaviors.

Striatum: a subcortical structure serving key role in the reward system. The striatum receives dopaminergic inputs from multiple brain areas and is the central input to basal ganglia. The ventral striatum contains the NA and the dorsal striatum includes the putamen and caudate. The 'corpus striatum' comprises the striatum and globus pallidus.

Trophallaxis: the exchange of sensory signals among members of a social group [199]. The term was extended to include social stimuli [103] and to denote the reciprocal multisensory stimulation of low intensity that elicits approach response. Parenting marks a prototypical form of trophallaxis [105].

Key Figure

Attachment Bonds across Mammalian Evolution

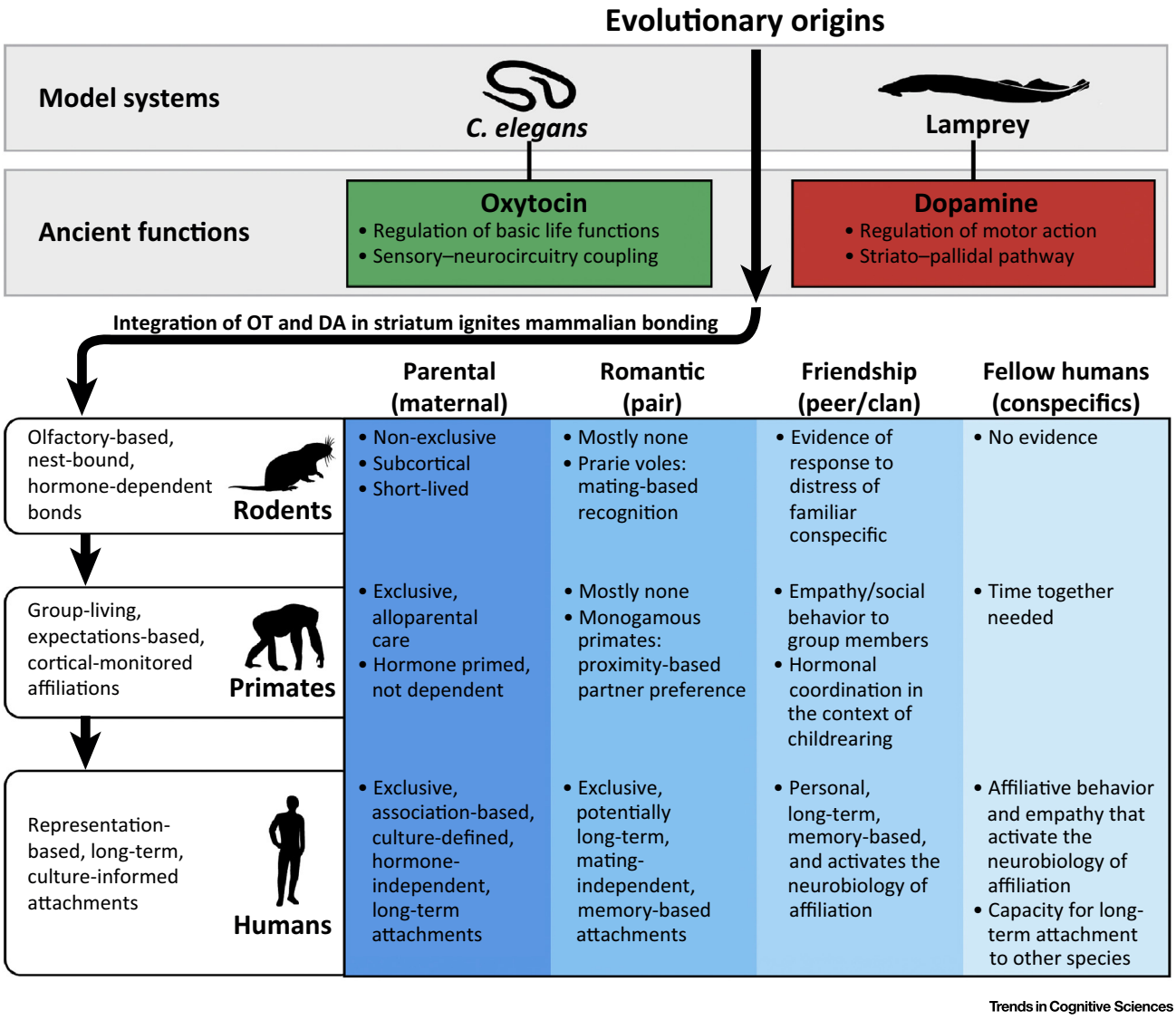


Figure 1. The figure describes the four bonds observed across mammalian species – parent–infant, pair bonds (romantic attachment), peers (close friendships), and conspecifics (fellow humans) – and charts their expression in rodents, primates, and humans. Attachment bonds in mammals are underpinned by functioning of two ancient systems, OT and DA, which maintained basic organization across vertebrate evolution and supported group living in harsh ecologies (OT) and motivational goal-directed action (DA) throughout animal evolution. *Caenorhabditis elegans* and lamprey are presented here to illustrate model systems used by research to study the ancient functions of OT and DA. The model proposes, on the basis of studies in rodents and primates, that the integration of OT and DA in striatum ignites mammalian bonding. In humans, attachment bonds are marked by two main features: selective (specific to attachment target) and enduring (long lasting). The figure describes how these two features undergo substantial reorganization across mammalian evolution. The decrease in color intensity from parental to pair to peer to conspecific indexes the gradual weakening of intensity in these selective and enduring features from the parent–infant attachment (most intense color) to humans interactions with strangers (least intense color). Abbreviations: DA, dopamine; OT, oxytocin.

Humans are wired for social affiliation via activity of this limbic circuit, comprising the OT-producing hypothalamus, extended amygdala network, and striatum [including the ventral tegmental area (VTA), which projects to striatum, and VP, which receives projections from it]. This limbic network regulates critical survival and motivation functions and redirects them in the service of social life [40]. Yet, while DA–OT links chart a mammalian-general mechanism of bonding, as observed in rat mothers, prairie voles, and primates, connectivity of this limbic system with cortical sites via multiple ascending and descending projections supports humans' long-term exclusive attachments [5,41,42]. Notably, striatal activity has been detected in nearly all imaging studies of human attachments; however, striatal/VTA activations are typically coupled with both subcortical (amygdala and hypothalamus) and cortical structures, particularly the anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC), and orbitofrontal cortex (OFC) of the reward system, in addition to structures supporting mentalizing, including the superior temporal sulcus (STS) and temporoparietal junction (TPJ), and those underpinning embodied simulation functions, such as anterior insula (AI), inferior parietal lobule (IPL), inferior frontal gyrus (IFG), and supplementary motor area (SMA). Aspects of OT system functionality have similarly been implicated in human maternal, paternal, romantic, and friendship attachments in research employing OT administration, peripheral measures, or allelic variability and methylation of the OT receptor gene (Box 2) [6,43–54]. Longitudinal studies following humans from infancy to adulthood describe OT involvement in the transfer of attachment from parents to friends and romantic partners [55,56]. Human studies indicate tighter connections between OT and DA in response to bonding-related cues as mediated by social synchrony; for instance, coactivation of OT- and DA-rich brain areas in response to infant stimuli [47,53], heightened VTA response to romantic partner following OT administration [7], or increased coupling of peripheral biomarkers during parental and romantic bonding [6]. This enables the subcortical system of motor 'vigor' to extract

Box 2. Time Sensitivity/Pulsatility of the Dopamine and Oxytocin Systems Enables Plasticity of Neural Networks to Incorporate the New Attachment

Dopamine

Phasic DA striatal neurons process the timing of reward and encode reward anticipation, which builds the internal sense of time in the brain [13]. Since DA neurons are sensitive to reward stemming from social interaction [26] and can link reward to attachment experiences, they ground reward in cycles of caregiving actions. DA is implicated in circadian timing and encoding the temporal component of experiences [60], which imbues attachments with sense of continuity over time. Computations in striatal DA neurons, while not uniquely social, can integrate social components into their temporal predictions, partly through OT's role in augmenting the salience of social stimuli [61]. This permits social signals to act upon a pre-established synaptic tract and associate it with specific reward outcome [24]. It also enables an initial brief, unselective, and broad increase in DA activity to become subjective and social, and function with accuracy, energy, and specificity [13].

Oxytocin

Pulsatility is a defining feature of OT functionality across evolution [43,62]. OT is released from both OT-producing hypothalamic neurons and dendrites, the branched projections of neurons, and this enables OT to operate at far locations from OT-producing sites [178]. Dendritic release primes vesicle (small fluid-consisting structure within a cell) stores for activity-dependent release and this enables a diffuse signal to maintain long half-life in the central nervous system and extracellular fluid to execute far-reaching behavioral goals [179]. OT signals cause dendrite release without increasing electrical activity, which, via peptidergic feedback, can become self-sustaining by creating autoregulated release primed by salient experiences [180–183]. OT functions at both presynapsis and postsynapsis to attenuate GABAergic inhibitory neurons, enlarging extracellular interactions among OT cells while reducing interactions with other stimuli, which leads to synchronization across multiple brain areas [184–187]. Once activated, release is repeated in time-sensitive bursts. Special primed signals, such as attachment-specific cues, can trigger dendrite release, relocating OT in vesicles from reserve to releasable stores [188,189] and future release is then shaped by the primed cue [190,191]. In addition, OT participates in modifying the excitation-to-inhibition balance by causing GABAergic signaling to change from excitatory to inhibitory around birth [192,193]. This opens a time window of increased neural sensitivity to specific attachment cues (i.e., sensitive periods). Such time-sensitive mechanisms chart the way by which attachment experiences impact the infant's OT release, the stimuli that will trigger it in future attachments, and its ultimate organization in specific sites in the brain [2]. This is also how OT transmission, which is not between neurons but between populations of neurons, can act across great distances and cause coherent, long-lasting, self-sustaining effects on behavior [113,129,194].

from repeated attachment experiences the representation of love and transfer it to other bonds throughout life, extending the neurobiology of maternal–infant bonding across human attachments and beyond.

Time-Keeping Pulsatility

Another important feature of the neurobiology of attachment is the time sensitivity of both DA and OT, which is critical for their role in neural plasticity. OT and (phasic) DA are characterized by pulsatile release that supports time-keeping mechanisms implicated in patterned action and seasonal rhythmicity. OT and DA are evolutionary-ancient systems involved in the regulation of basic life functions across vertebrate evolution [57–59] (Figure 1). The pulsatility/time sensitivity of OT and DA enabled their involvement in neural plasticity, which is required for selective recognition and long-term memory, the two key features of human attachments.

Dopamine

While phasic DA striatal neurons encode for general reward and reward anticipation, these neurons can incorporate social reward into their computations [13,26]. This lends support to the hypothesis that attachment experiences, which are repeated and predictable in nature, may become particularly salient targets for the reward computations of striatal DA neurons. The role of DA in circadian rhythmicity [60] facilitates the consolidation of attachments, imbuing them with a sense of regularity and stability. Studies in primates have shown that striatal DA neurons can differentiate reward stemming from self and partner, anticipate predictable social interactions, and draw reward from the matching of self and partner's actions [26]. It is thus assumed that the temporal sensitivity of DA neurons enables humans to draw reward from the experience of **biobehavioral synchrony,** which is built on familiarity with the partner's repeated social patterns. Since OT increases the salience of social stimuli [61], the integration of OT and DA in striatum enhances the experience of social synchrony, leading to cycles of coordinated moments within attachment bonds that become rewarding and therefore repetitive, receiving motivation and vigor from DA and social focus and tranquility from OT.

Oxytocin

Pulsatility is a defining feature of OT functionality across evolution, and **myoactivity** is OT's most conserved feature [43,62]. Pulsatility is critical for the unique dendritic release that supports OT's role in bonding (Box 2). This mode of functioning leads to autoregulated, feed-forward release that is triggered by primed attachment experiences, which, once activated, release repeated rhythmic bursts. Such time-sensitive mechanisms chart the way by which early attachment experiences shape the ultimate organization of OT in specific sites in the infant's brain, the stimuli that will trigger it in future attachments, and its cross-generational transfer via the expression of parenting behavior in the next generation [2].

The molecular underpinnings of the time sensitive mechanisms for the two systems are described in Box 2.

Mammalian Affiliative Bonds: Parents, Partners, and Peers

Attachment bonds are a defining feature of mammals. Pregnancy, birth, and lactation and their underlying neurobiology define class mammalia [1,2,58,63,64]. Life for a young mammal begins with two constraints; an immature brain at birth and the need for close proximity to a nursing mother. Consequently, provisions embedded in the mother's body and the species-typical maternal behaviors organize the immature brain, orienting it to social life via relationship with the mother [65]. Networks supporting mammalian sociality develop in the context of the mother–offspring bond and are shaped by variations in maternal care [4,66]. In the 3–5% of mammalian species that are biparental, the father's presence and parenting behaviors also play a role in infant brain development both directly and through their effect on reducing maternal stress [67].

The mother's body provides the first environment for the developing mammal. Maternal heart rhythms, smell, touch, movement patterns, arousal dynamics, social cues, and stress response mark the first environmental signals the brain encounters, programming it to live in close proximity with others, signaling to the developing central nervous system the amount of stress the environment contains [68,69], and tuning the brain to function as a 'situated' organ [70], constantly receiving information, updating predictions, and responding online to the social world [71–73]. It has been recently argued [74] that the brain's modus operandi is not solipsistic but situated and research on the 'situated' brain should become the focus of social neuroscience. This position resonates with the central hypothesis proposed here, that is, the social embeddedness of the immature mammalian brain at birth shapes it as a fundamentally dialectic organ and that elucidating the mechanisms by which early attachments program the brain may provide new understanding into the brain's basic mode of action.

Attachment bonds are marked by two key features; they are selective (specific to attachment target) and enduring (long-lasting) [37]. These two components underwent substantial reorganization across mammalian evolution and specific combinations of their gradients define the various human bonds (Figure 1). The human parent–offspring bond is selective and enduring. Romantic bonds are also selective – at least in most cultures and recent human history – and enduring, but more precarious; while humans rarely abandon their children, romantic attachments can terminate under normative conditions and this may account for the tighter crosstalk of the OT and reward systems during romantic bonding [6,75]. Close friendships are selective and enduring, but these appear in a weaker form, with humans nurturing numerous friendships simultaneously and long friendships dwindling with no overt breakup. Humans' relationship to conspecifics is neither selective nor enduring; yet humans are unique in their ability to activate the behavioral and neurobiological systems of affiliation toward unfamiliar fellow humans. For instance, humans express empathy or synchronize gaze with strangers and both activate the OT system [76,77].

The ancient OT and DA systems foreshadow the selective and enduring features of mammalian bonds. Across vertebrate evolution, the OT-family molecule has repurposed the basic life functions controlled by the ancient vasotocin molecule in the service of social life, adapting it to the social hierarchies, seasonality, and social organization of each species [59,78]. The sensory–neurocircuitry coupling among group members in lower species, modulated by OT's pulsatile release, transformed from group collaboration into the biobehavioral synchrony of nursing mother and young in mammals [43]. The ancient DA system integrated repetitive motor action with goal-directed reward via organization of the striatal–pallidal indirect network and the evolution of GABAergic (inhibitory) control over motor neurons. Motor inhibition, a critical component of any higher-order motor program [79], enabled the quiescence required for the formation of attachment bonds.

Yet, as seen in Figure 1, humans' selective and enduring bonds mark a long progress from their ancient origins. The mother–offspring bond in rodents is nonselective and short lived; rodent mothers care for any infant in their surrounding (bond to a generic infant) and bonds are bound to the nest, primed by hormones of pregnancy, and depend on olfactory cues [1,10,80]. Within these constraints, however, it is research in rodent mothers and monogamous prairie voles that uncovered the cellular and molecular basis of the selective and enduring components of attachment and charted commonalities between parental and pair bonds [10,81].

Primates' enlarged neocortex enables the formation of selective attachments that rely on complex social signals which are necessary for life in large groups [82,83]. The widespread practice of **alloparenting** highlights the primates' parental brain as an adaptive template that

can flexibly activate via bottom–up caregiving behavior [84,85]. Primates' bonding is hormone primed but not hormone dependent and olfactory cues are integrated into visually guided social bonds [86]. Most primates, like rodents, are not monogamous and across both primates and rodents, extended paternal care is observed only in monogamous species, indicating that male–female mating and physical proximity are required to trigger the neurobiology of fathering [87,88]. This is in contrast to humans, for whom the paternal and pair bonds are independent [48]. As to 'peers', rodents [89] and primates [90] show behavioral and hormonal contingencies to distress of a conspecific (member of the same species), such as elevation in cortisol or behavioral mimicking, and cooperative breeding marmosets also display OT synchrony among childrearing adults [91]. Peer-reared rhesus macaques, while exhibiting lifetime aberrations in social behavior, express bonding to peers [92,93], indicating that friendshiplike behavior is common across primate species.

Humans' cortical complexity enables integration of the subcortical limbic network and ancient OT and DA systems into love that is built on representations and memory, translates multisensory experiences into higher-order associations, adapts to cultural norms to carry bonds across generations and ground them in meaning systems, conceives both the overlapping and autonomy of self and other [94], incorporates sociocognitive abilities of empathy and trust to maintain long-term affiliations, and extends the here-and-now so that love can be felt in its absence (e.g., deceased parents) and transcend to abstract ideas (God, homeland), humankind, and other species (pets). Notably, all these forms of love activate the neurobiology of affiliation [95–97] and are built on early attachment experiences [2,98,99]. Humans, as Wilson recently noted [100], can create a feeling that life is meaningful by activating their affiliative biology toward continuum of experience, from Earth's biosphere of flora and fauna to highest levels of abstraction and the arts.

Biobehavioral Synchrony

Biobehavioral synchrony, the coordination of biological and behavioral processes between attachment partners during social contact, is a critical component of human attachments [1,2,25,101]. Biobehavioral synchrony evolved from the coordinated group activity of lower species where joint motor action (involving DA) is locked with coupled physiology to achieve survival-related collaborative goals (involving OT); for instance, ants carrying a grain of wheat to shelter, fish swimming to ward off a shark, or birds flocking toward warmer climates [1,2,37,102–104].

Life within social groups requires constant exchange of social signals among members and the term '**trophallaxis**' [95,105] has been coined by entomologists to denote the exchange of sensory and social signals among members of a social group. Three aspects of trophallaxis have been integrated into mammalian bonds: the low intensity and arousal-modulatory nature of attachments, the social reciprocity and online construction embedded in them, and the trophallaxic process as charting a line from parent–offspring bond to life within social groups [1]. Most importantly, humans' biobehavioral synchrony is straightforwardly built on trophallaxis in highly social invertebrate species, such as ants.

Biobehavioral synchrony is observed across human attachments, in parental, romantic, friendship, and fellow–human interactions, and employs great flexibility so that human synchrony is not metronome precise but unfolds a stochastic process, follows dynamic systems' principles, and integrates patterned order and local variability [106,107]. The basic characteristics of biobehavioral synchrony, however, are maintained across evolution; it involves the coordination of biological processes and species-typical behaviors expressed during social contact, it initiates young to life in social groups, it assembles online from the inputs of multiple parties, and it relies on the ancient OT system [37,101].

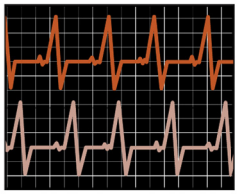
During or immediately following social contact, human synchrony is evident in four systems: behavior, autonomic, hormones, and brain, and, to varying degrees, this coupling is found across the four human attachment constellations (Figure 2). Synchrony between partners' nonverbal behaviors in the gaze, affect, vocal, and touch modalities has been observed in mother–infant interactions since the 1950s and thought to entrain the neonate's physiological periodicities of sucking, crying, and circadian rhythmicity [108,109]. Fathers similarly engage in behavioral synchrony, but utilize a quick-paced, high-arousal temporal pattern [110]. Synchronous parent–infant interactions are accompanied by physiological coordination [2,5,101,111]; parent and infant's heart rhythms are coupled during episodes of behavioral synchrony, but not during nonsynchronous moments [112]; and following synchronous interactions, OT release is coordinated between parent and child [113]. Synchronous moments induce brain-to-brain coupling between mother and child in key nodes of the social brain.

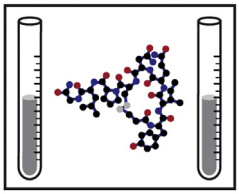
Synchronous interactions experienced during early sensitive periods are expressed in later attachments throughout life. Matched interactions are observed between romantic partners and show similar second-by-second coordination of gaze and affect [6,114]. Heart-rate coordination [115], OT coupling [116], and brain-to-brain synchrony have been described among couples. Mother and father show a coordinated brain response in structures of the embodied simulation and mentalizing networks (STS, IPL, and AI) when viewing a video of their own infant [117]. Interactions among close friends show behavioral reciprocity; however, interactions among friends are not as tightly coupled as those observed in parental or romantic attachment [55,118]. Evidence suggests that OT increases following contact with friends, albeit the increase is not coupled [55]. Finally, teams trained for coordinated action and group cohesion, such as military units, exhibit wide response across the social brain in the alpha band to vignettes depicting synchronous group activities, particularly coordinated unit in battle [119].

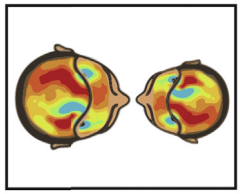
Unlike other mammals which require familiarity with conspecific for biobehavioral coordination, humans display behavioral synchrony toward strangers; humans coordinate gaze and vocal turn-taking during conversations with strangers while touch synchrony is preserved for intimate bonds [1]. When strangers sit in close proximity and execute joint tasks, they also display heart-rate coupling, brain-to-brain synchrony of alpha rhythms, and coordinated brain response in temporoparietal structures, such as STS and IPL [120–122]. Empathy to strangers in distress is impacted by OT administration and observing groups in collaborative action elicits OT response [119]. Furthermore, the brain responds to 'similar to me' synchronous action; mothers observing synchronous interactions of unfamiliar mothers and their infants activate areas of the reward system (NA, dorsal ACC), and the degree of activation parallels their own behavioral synchrony [123]. Finally, evidence highlights humans' preference for synchrony in large crowds in walking, marching, or rowing [124]. Such group-maintaining mechanisms are rooted in earliest mammalian experiences – the matching of physiology and behavior between mother and young generalized by humans' large associative cortex across time, place, and person.

Longitudinal studies show long-term associations between the degree of parent–infant synchrony and the quality of later attachments with close friends and romantic partners and with abilities that support participation in human social life, including empathy, moral orientation, theory-of-mind, and culture-specific modes of self-regulation [125–127]. Early synchronous interactions also shape children's social brain. For instance, parent–infant synchrony longitudinally predicts intactness of the brain basis of empathy in adolescence [128]. Similarly, parents' brain response to infant cues is combined with behavioral synchrony to predict preschoolers' emotion regulation and socialization [129], and parental OT integrates with parent–infant synchrony to shape children's social reciprocity toward best friends [55]. These studies demonstrate that the parent's affiliative neurobiology and synchronous behavior shape human children's attachments to nonparental figures and buttress human-specific social

Biobehavioral synchrony in human attachments







	Behavioral synchrony	Heart rate coupling	Endocrine fit	Brain-to-brain synchrony
 Parents	• Synchronized behavior in gaze, affect, vocal, and touch • Mother-specific father-specific	• Synchronized HR during synchronized interactions	• Coordinated OT response following contact • Coordinated cortisol response to stress	• Coordinated brain oscillations in alpha and gamma rythms
 Romantic partners	• Synchronized nonverbal patterns • Coordinated self-disclosure + empathy	• HR coordination during or following interaction	• Coordination of OT and cortisol among parents • Coordination of OT among lovers	• Coordination of brain response in mentalizing network in parents • Coordination of gamma oscillations in temporal cortex in lovers
 Friends	• Patterns of social reciprocity	• Teams coordinate heart rythms during joint action	• OT is released during interactions with friends • No evidence for coupling	• Alpha response to behavioral synchrony among teams in social brain • Coordination among teams in mirror network
 Strangers	• Coordination of culture-spcific display rules (e.g., eye gaze)	• Evidence for some coordination during joint action in close proximity	• OT is implicated in acts of empathy • No evidence for coupling	• Evidence for coordinated activation in mentalizing areas during interaction

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Figure 2. Biobehavioral Synchrony in Human Attachments. Human attachments are characterized by the coupling of the partners' physiological and behavioral processes during moments of social contact. Such coupling is observed across four systems: matching of nonverbal behavior, coupling of heart rhythms and autonomic functioning, coordination of hormonal release, and brain-to-brain synchrony. In humans, biobehavioral synchrony is observed in the four affiliative bond constellations: parental, romantic, friendship, and strangers. Abbreviations: HR, heart rate; OT, oxytocin.

competencies, highlighting the lifetime effects of the neurobiology of human attachment and its cross-generational nature.

Notably, our focus on the OT system stems from its critical role in the formation and maintenance of attachment bonds in humans and other mammals. Other hormones, including cortisol, testosterone, prolactin, progesterone, vasopressin, beta-endorphin, and estradiol, have been studied in relation to human attachments. Our hypothesis, supported by studies from our laboratory [1], suggests that OT serves a key integrative function by providing a neuroendocrine milieu for the effects of multiple hormones on the development of human attachments.

The various measures used in research on human attachments are described in Box 3.

Human Attachments and the Brain

Humans' rootedness in mammalian affiliative biology renders the integration of OT and DA in striatum an important foundation for human attachment, albeit the role of other neurohormonal and neurotransmitter systems has been described [9,10,81]. Recently, fMRI studies began to test the neural basis of humans' multiple attachments by assessing brain responses to auditory,

Box 3. The 'Measurement of Love'

Neuroscience research has utilized the following tools to measure human attachments:

Micro/macroanalysis of social behavior and behavioral synchrony: Observation of interactions between mothers and infants and among couples has been conducted for nearly a century. Studies use either global rating scales addressing the quality of the partners' behaviors (e.g., 'responsive', 'intrusive') or focus on micro-level detection of bonding-related behaviors (e.g., 'motherese' vocalizations, social gazing) and their coordination among partners [98]. Studies employed similar micro- and macro-level analysis in other attachments, including romantic/marital relationships and friendships.

Autonomic response: Parenting and couple studies employed measures of heart period and respiratory sinus arrhythmia as indices of parasympathetic functioning during social interactions, evaluating changes from baseline and during various dyadic stressors (e.g., parent–infant 'still-face', couples 'conflict dialog'). Skin conductance has been used to index sympathetic activity and multiple autonomic measures have been integrated into a single index of autonomic arousal [195,196].

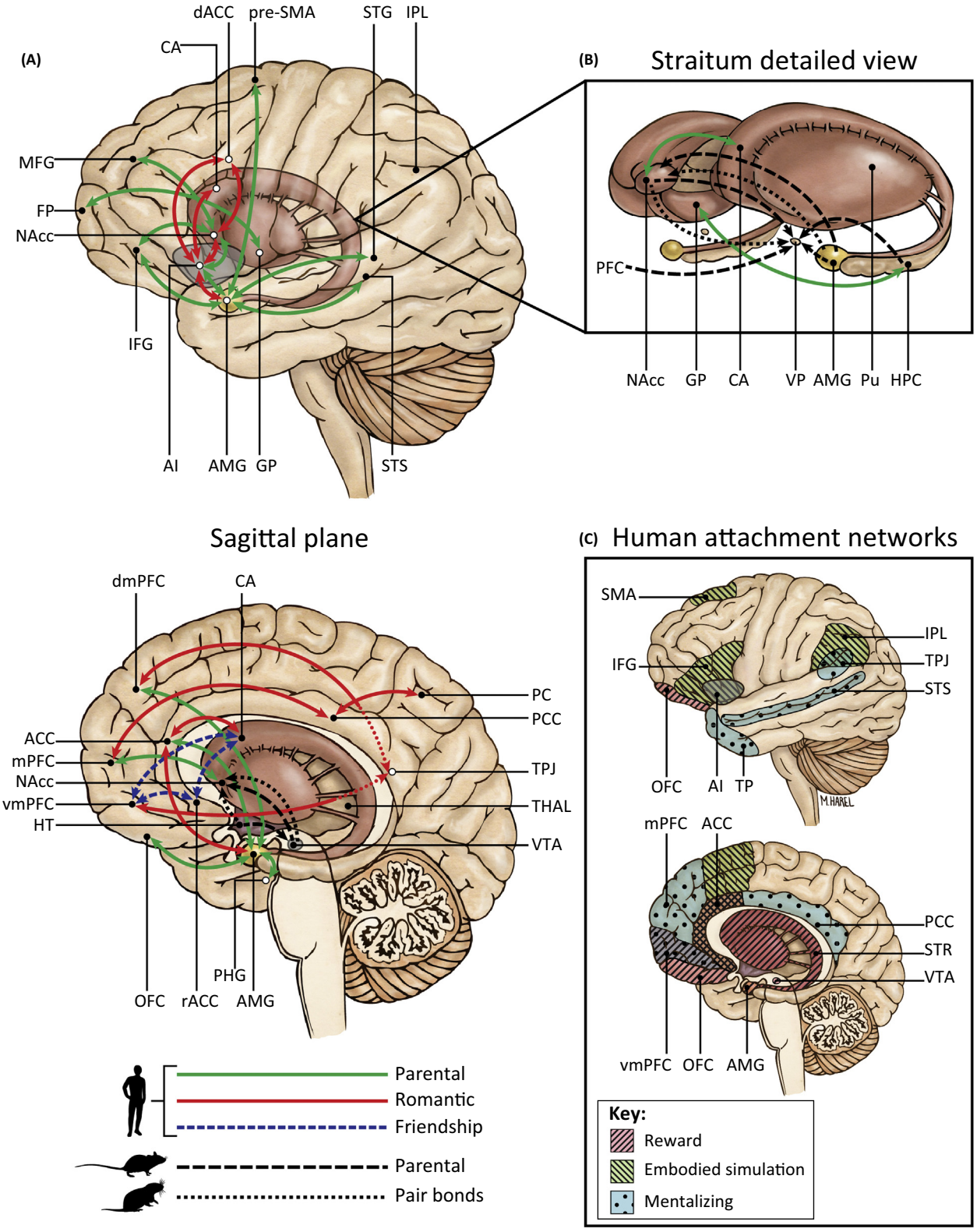
Hormones: Peripheral measures of hormones from plasma, saliva, urine, and, less commonly, from cerebrospinal fluid, have been tested as correlates of human attachment bonds. Hormones studied in attachment contexts mainly include cortisol, testosterone, oxytocin, vasopressin, prolactin, progesterone, estradiol, salivary alpha amylase, and beta endorphin.

Peptide administration: Nasal administration of OT and, to a lesser extent, vasopressin has been used to address the effects of neuropeptides on affiliative response and the brain networks supporting human social abilities. Studies typically employ a double-blind design where peptide administration is compared with placebo in a within-subject or between-subject design [197].

Brain oscillations: Electroencephalogram and emerging studies in MEG have been used to examine questions related to bond formation and social affiliation, in addition to understanding the role of brain oscillations in human social functions [119,128,174]. Research on brain oscillations and their cortical generators afforded by MEG can open new vistas on the neurobiology of attachment.

Brain imaging: fMRI has been recently used to address various aspects of human attachments and these studies are summarized in the Supplemental Information online. Studies often use auditory, visual, or multimodal stimuli of the attachment partner (infant, romantic partner) as fMRI stimuli.

Genetics/Epigenetics: Individual differences related to allelic variability on genes related to the oxytocin–vasopressin pathway (*OXTR*, *AVPR1a*), dopamine (DRD4, DRD2, DAT1, COMT), or serotonin (5-HTT) have been used to examine genetic markers associated with individual differences in attachment behavior or the effects of various early attachment experiences on later functioning. Recent studies have also tested methylation on the *OXTR* gene in relation to attachment-related outcomes [43].



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visual, or multimodal stimuli of the attachment target; for example, infants to their parents, romantic partners, or friends. Overall, various findings indicate that while the VTA/ventral striatum ignites the brain's experience of attachment and imbues it with reward and vigor, human attachments integrate subcortical with multiple cortical reward- and sociocognitive-related networks (Figure 3).

A survey of published studies using fMRI to investigate humans' various social attachments (see the Supplemental Information online for more details) provides evidence for three main interconnected neural systems that integrate to establish, maintain, and enhance our affiliative bonds with others. Some brain areas participate in more than one system.

The first is the 'reward-motivation' system, including the striatum (NA, caudate, putamen), amygdala, VTA, OFC, ventromedial prefrontal cortex (vmPFC), and ACC, employing DA- and OT-rich pathways [12,130,131], and supporting multiple attachment-related motivational behaviors, such as social orienting, social seeking, and maintaining contact across extended periods [132,133]. Attachments have intrinsic motivational value that combines immediate hedonic response with approach motivation, goal-directed behavior, and learning [134]. The striatum and its massive projections from both frontal cortex and amygdala [130,135,136] are implicated in detecting attachment-relevant cues, appraising their valence, and guiding action by coding the affective properties of stimuli [137–139]. Notably, even within the striatum there is a shift from ventral (NA) to dorsal striatum (caudate) in corticostriatal connectivity with the stabilization of the bond [140,141], reflecting a shift from reward-related drive and novelty seeking to familiarity processing and predictability [142,143]. Caudate–cortical connectivity is associated less with passion, sexual desire, or parental response to vulnerable infants but with long-term relationships, habit formation, and companionship among couples [141], and social cooperation and trust among friends [144]. The caudate is involved in reinforcement learning, goal-directed action, and weighing the relative values of outcomes [135,145] and authors suggest that the shift from ventral to dorsal striatal functioning accompanies attachments as they settle into joint goals, mutual habitat, and reciprocity, and is mediated by OT [140]. The existence of convergent projections from the cortex to striatum, along with hippocampal and amygdala-striatal projections, places the striatum as a central entry port for processing emotional/motivational information supporting human attachments.

The amygdala and its associated network play a critical role in human attachment, particularly mothering [5,10,146] and romantic attachment [88]. Maternal bonding requires vigilance for infant safety and romantic attachment involves heightened emotionality and interoceptive sensitivity to signs of safety and danger. Amygdala activations have been detected in 'all' imaging studies of mothers [5] and in most studies of fathers, romantic partners, and close

Figure 3. The Brain Basis of Human Attachments. (A) Connections among subcortical and cortical structures supporting attachment in the human brain are indicated by solid green lines for parent–infant bonds, red lines for romantic bonds, and broken blue lines for suggested connections in friendship bonds (taken from 86 fMRI papers on humans' various social attachments, see the Supplemental Information online for details of each study). Neural models for parental care in rats are indicated by broken black lines and for pair bonding formation in prairie voles by dotted black lines [10,19,80]. (B) The basal ganglia intraconnections (striatum: NA, Pu, CA; VP; and GP) and interconnections with cortical structures (PFC) and subcortical structures (AMG and HPC). (C) The human affiliation networks. Three main interconnected neural systems underpinning human attachments (some areas participate in more than one system). The reward network (broken lines/pink colored), supporting approach motivation, social orienting and seeking, goal-directed behavior, social learning, and the incentive value of attachment cues [134], includes the striatum, OFC, ACC, vmPFC, VTA, and AMG. The embodied simulation network (broken lines/green colored) enables individuals to resonate with other's mental state and emotion via embodiment mechanisms and grounds experience in the present moment [94] and includes the AI, ACC, IFG, IPL, and SMA. The mentalizing network (dotted/bright blue colored), supporting social cognition, mental-state understanding, and social goal interpretation [164], comprises frontotemporal–parietal regions including the STS, PCC, TPJ, TP, and mPFC. Abbreviations: ACC, anterior cingulated cortex; AI, anterior insula; AMG, amygdala; CA, caudate; CT, cortisol; dACC, dorsal anterior cingulated cortex; GP, globus pallidus; HPC, hippocampus; HT, hypothalamus; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; MFG, middle frontal gyrus; NA, nucleus accumbens; OFC, orbitofrontal cortex; PC, precuneus; PCC, posterior cingulated cortex; PFC, prefrontal cortex; PHG, parahippocampal gyrus; Pu, putamen; rACC, rostral anterior cingulated cortex; SMA, supplementary motor area; STG, superior temporal gyrus; STS, superior temporal sulcus; TP, temporal pole; TPJ, temporoparietal junction; THAL, thalamus; vmPFC, ventromedial PFC; VP, ventral pallidum; VTA, ventral tegmental area.

friends. The amygdala guides attention to biologically relevant stimuli, adjusts social orienting, codes the intensity of reward, and computes the salience of social information [147,148]. Interestingly, amygdala activation in human attachments is typically coupled with other areas of the subcortical limbic circuit (hypothalamus, VTA, VP), insular–cingulate cortices, and temporal–frontal areas [STS, superior temporal gyrus, prefrontal cortex (PFC)] [47,129,149].

Human attachments require complex higher-order processes that involve learning, memory, planning, and predictions and depend on frontostriatal connections of the reward circuit, particularly vmPFC, OFC, and ACC. These connections enable the encoding of reward-related expectations, associations, and representations; evaluation of the affective valence of attachment stimuli; and maintenance of flexible representations to guide action [150,151]. Such corticostriatal connections provide the foundation for the human capacity to combine reward, passion, proximity seeking, 'vigor', and unconscious motivation with higher-order abilities that mark the top–down control, trust, empathy, and commitment of human attachments and enable humans to tend and maintain them. The OFC, the latest evolving structure of the human brain and the end point of the reward pathway [152], implicates in the representation of 'pleasantness' and in effortful, goal-directed actions to tend long-term relationships [153]. The OFC selects among rewards, enables the resistance of immediate rewards toward long-term attachment goals, and shapes affiliations in the color of culture, ritual, and personal preferences with stability and far-sightedness [154]. The vmPFC enables representation of love and its entire 'ripples' of associations, sense of 'yearning' that is critical for human love (maintaining love in its absence), the appraisal of safety, and the sense of self as both overlapping and separate from attachment partner, an overlap that defines the experience of intersubjectivity [155,156]. The vmPFC exerts inhibitory control over limbic regions, reducing anxiety/avoidance in safe environments and long-term attachments [157].

The second system underpinning human attachment is the 'embodied simulation/empathy network', including the insula, ACC, IFG, IPL, and SMA. Embodied simulation is an evolutionary-ancient mechanism, which, via automatic interoception and internal representations, recreates other's state in one's brain. Embodied simulation is critical for grounding a 'shared world' in the brain and underpins the human capacity to build and maintain attachments [94,158]. This form of interpersonal 'matching' relies on neural pathways that involve both the experience of internal body formats and the perception of similar states in others via perceptual–motor coupling [120,159]. This network enables the parent/partner to integrate interoceptive and affective information, resonate with mental states and emotions, and ground experience in the present moment thus giving it color, immediacy, and 'situatedness' [160,161]. von Economo neurons, projection neurons located in layer V of the anterior cingulate and frontoinsular cortices, are implicated in the conscious perception of bodily states and afford the integrated representations of social moments as they are lived [162,163].

Finally, interoceptive mechanisms are insufficient to support representation-based human attachments. Human bonds rely on 'mentalizing' processes – higher-order cognitive processes involving complex top–down inferences of others' mental states by attributing beliefs, thoughts, and intentions to others to create a full sense of 'togetherness' [164,165]. Mentalizing processes underpin attachment formation by building on the individual's ability to appreciate multiple perspectives, understand partner's goals and motives, and keep in mind his/her values and concerns [74,166]. Frontotemporal–parietal structures, particularly the STS, posterior cingulated cortex, TPJ, temporal pole, and mPFC, are components of the 'mentalizing system', the third network of the 'global human attachment network' (Figure 3). The STS and TPJ are central regions of this network [167] and play a vital role in social cognition [164], evaluation of others' state, social goal interpretation, and prediction making and their online updating [168–170]. The STS combines embodied simulation (mirror) and mentalizing properties [171], integrates fast

bottom–up simulations (biological motion) with slower top–down understanding (theory-of-mind), and provides critical support for the process of attachment formation [172]. Interestingly, the STS has been shown as particularly relevant to the development of fathering, a bond built more on top–down understanding of infant signals than on the ancient limbic structures that support mothering [48].

Finally, research is beginning to use magnetoencephalography (MEG) to study the participation of neural oscillations and their cortical generators in human attachments. Overall, it has been suggested [70,74] that brain oscillations underpin brain-to-brain synchrony among attachment partners or between humans during social interactions and participate in binding members into a social group. In several recent studies, my colleagues and I detected the involvement of alpha (8–14 Hz) and gamma (30–60 Hz) rhythms in human bonding, the two frequencies defining top–down control mechanisms and bottom–up rapid processing, respectively, with gamma rhythms often integrating into alpha to create the interplay of automaticity and control needed for bond formation [173]. We found that empathy to others' pain is supported by alpha rhythms in mentalizing structures [174]; that adolescents exposed to maternal depression across the first years of life terminate alpha response in posterior STS at a late time window (900–1100 s poststimulus), suggesting aborted top–down processing of empathic resonance [128]; and that brain-to-brain synchrony of alpha rhythms in SMA (embodied simulation) binds members of a group and differentiates them from the outgroup [167]. Importantly, MEG studies of human attachment are rare and may provide valuable information on the temporal course of the brain response to attachment-related cues.

Concluding Remarks and Future Directions

Can the scientific measurement of love and research on the 'affiliative brain' (Box 3; see Outstanding Questions) open new vistas not only for understanding human attachments but also for neuroscience in general? I submit that the answer is affirmative for three reasons.

First, when humans are asked about the most important aspect of their life, they often describe their affiliations. The capacity to give and receive love and maintain long-term bonds is increasingly recognized as key to human thriving, impacting well-being, positive outlook in the face of adversity, physical health, and better aging [175]. Yet, we still know relatively little about the mechanisms by which social bonds impact our immune system, express throughout the life span, predict better aging, or transmit from parent to offspring. Knowledge is also limited as to how two humans coordinate their brain response online during social interactions and how early experiences longitudinally tune the brain to social life. A better understanding of the neurobiology of affiliation can shed light on how to live a personally meaningful life, as well as how we might repair developmental and affiliative disruptions, as can occur in cases of maternal postpartum depression, premature birth, or impoverished or dangerous environments where the social envelop provides no safe haven for proper bonding.

Second, the flip side of the neurobiology of affiliation is the neurobiology of intergroup conflict, racial bias, and tribal hatred, both activating the same ancient systems, which evolved to help organisms rapidly distinguish friend from foe [77]. It is critical we understand how the brain shuts down its empathic response when the inflicted is a member of the 'outgroup', particularly outgroup perceived as potentially threatening. We recently found that shutting down the brain's empathy centers is accomplished by tightening brain-to-brain synchrony among ingroup members, increasing OT production, and imposing top–down attenuating processes on bottom–up automatic response to the distress of outgroup [77,167].

Finally, the neurobiology of affiliation stands at the crossroad between science and humanities, with the potential to provide deeper integration of the two after centuries of separation into

Outstanding Questions

Can the neurobiology of attachment provide insights into the mechanisms that support brain-to-brain coordination among humans during social contact and foster the transition from a 'solipsistic' to a 'situated' model of the human brain?

Can knowledge on the neurobiology of attachment help understand the 'neurobiology of reparation': what processes enable humans to thrive after disrupted early attachments? Which individuals are better disposed to reparation following deficits in early bonding? And what components must still exist in the early environment to make reparation possible?

Can the 'measurement of love' integrate as a valid area of scientific inquiry? Can we develop novel tools and formulate new models?

How do cultural ecologies and meaning systems shape the neurobiology of attachment? Can conditions such as nuclear versus extended family living, traditional versus modern mate selection, or monogamous versus open partner relationships impact brain and endocrine systems implicated in bonding?

What are the lifetime effects of human attachments on health, well-being, and happiness? What are the processes by which attachment bonds exert their impact on health and longevity?

Can the neurobiology of attachment provide a unique entry point for the integration of science with the humanities, arts, ethics, and clinical wisdom?

distinct branches of knowledge. While Aristotle and Leonardo De Vinci were well-versed in both the sciences and arts of their period, such integration is no longer available or encouraged. The neurobiology of human affiliation requires that a biologically based evolutionary perspective, which provides mechanistic understanding but pays little attention to the individual, is supplemented by perspectives that focus precisely on the individual with his or her experiences, expressions, and aspirations, and are committed to the individual's well-being, health, and thriving. To study the neurobiology of human attachment, one must season the objectivity of science with the wisdom of the clinician, foresight of the philosopher, and creativity of the artist into a unified endeavor that can shed new light on the loftiest – and oldest – of human experiences: 'love'

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Supplemental Information

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