Brain Circuitry Linked to Social Connection and the Desire to Cuddle Discovered

By Amielle Moreno

Why do scientists know more about the brain during fear than love? Behaviors such as startling and freezing in response to a fearful stimulus are rapid, vary little between subjects, and are easy to interpret. Things get messy when individuals show variability. Social behavior, like intimate partner selection and mating, has a lot of variability. To researchers willing to explore the neuroscience of love and mating the stage is set for major discoveries.

A recent research study published in Nature out of the Liu and Young laboratories at Emory University uncovered a dynamic conversation between two brain regions during intimate behavior. The new findings in prairie voles explores the brain connections behind social connections.

Scientists rely on the similarities between humans and laboratory animals to examine the mechanisms that control behavior. Just like humans, prairie voles are capable of consistently forming social bonds with mating partners, a rare trait in the animal kingdom. Scientists in this study used vole's as a model for interpersonal connection or *social bonding*, a connection between individuals strengthened by sex and measured by a desire to be close to one's partner. Growing from a rich literature on negative valence, the use of this monogamous animal system allows scientists to examine the neuro circuitry of complex positive social interactions.

"In our study, we were interested in how mating, a rewarding social experience, affects the communication between two brain areas," says lead author Dr. Elizabeth-Ann Amadei, "the medial prefrontal cortex (mPFC) and nucleus accumbens (NAcc)." These areas are both part of the brain's reward system. The NAcc is active when we respond to both aversive and rewarding stimuli in our environment. The frontal cortex is responsible for higher level processing, with the medial area (mPFC) specializing in social information. By examining the circuitry between the NAcc and mPFC, Dr. Amadei and her co-authors uncovered active changes in the brain during prairie vole match-making.

The brain is a mess of connections which has kept neuroscientists busy picking apart how and when brain regions communicate. Imagine a hall filed with people clapping. People are clapping at different times (phase/frequency) and loudness (amplitude). The clattering of noise seems incoherent at first, until you notice groups that sound like they're clapping in time (in coherence). You deduce this isn't random. These groups of clappers share a connection. The clapping people in this analogy represent neurons and their activity in the brain. Neuroscientists have come to appreciate that similar activity between regions of the brain suggests a special relationship; a circuit.

We clap in patterns! We're neurons!

Scientists have studied circuits by physically cutting between brain regions, injecting dye in a group of neurons to see how it spreads or by stimulating one region while recording activity of another. Here, researchers recorded activity in two brain regions with the belief that synchronized activity is compelling evidence of brain regions working together to process one's experiences.

And the social experience being studied is essentially a blind date. For the first time, female voles were matched with males while their behavior and brain activity were closely examined. The researchers recorded when females were performing non-social behavior, such as grooming themselves, or social behavior, such as sex/mating and huddling. Mating is known to strengthen the bond between prairie voles and huddling, or what humans would call cuddling, is an easy way to tell how much voles like each other. While the females were behaving with their new partners, the brain activity of both the NAcc and mPFC were recorded using implanted electrodes. Lo and behold, they found when animals were mating there was matching low frequency activity in both the NAcc and the mPFC. This coherence hint that there is an active connection between these areas.

Let's return to the metaphor of the hall filled with clappers, representing brain region activity. You've identified a special relationship between members of the mPFC and NAcc groups. They're connected but who's giving the direction? Is the mPFC the metronome to the NAcc, or vice versa?

Here's where the complexity of the brain thwarts the best attempts at analogy. Using modeling, the researchers weighted all the various combinations of who could be directing whom during the three behaviors. During mating, they determined that of all the signals produced by the mPFC, the low frequency acted as a metronome to drive high-frequency activity in the NAcc. In our analogy, for each clap from the mPFC, the

NAcc group claps like crazy. In that way, they're clapping in coherence, *and* at different frequencies. This drive by the mPFC on the NAcc is called *net modulation*.

But net modulation was almost completely absent during huddling. Why would this drive be high during one positive social behavior and low during another? "It was somewhat surprising that huddling, an expression of affiliative behavior, did not strongly activate the mPFC-NAcc connection" says Dr. Amadei.

During huddle sessions, the net modulation dropped. But even though circuit activity was low when prairie voles were huddling, net modulation still had a powerful effect on the huddling behavior. The researchers looked at the time when animals were not huddling and found the more net modulation, the more time they ended up huddling. Dr. Amadei suggests net modulation "might be more important for the switch toward (rather than expression of) affiliative behavior." In other words, the more connected the mPFC and NAcc, the less time it took before animals started to snuggle and kept snuggling.

All of this net modulation was triggered by the females mating. While individuals showed variability in net modulation before mating, sex strengthened this circuitry to a point where predisposition couldn't predict behavior. This is evidence of how powerful the mating behavior is for brain rewiring.

But it just doesn't seem like fun neuroscience unless we can manipulate something. Dr. Amadei sparked connections between would-be mates. She designed an enclosure that had a smaller cage inside for the male. This smaller cage prevented the females from mating. Seeing and sniffing another prairie vole isn't enough for a strong bond to form. Dr. Amadei and colleagues used optogenetics to electrically stimulating mPFC neurons connected to the NAcc at the special low frequency. When exploring a male was paired with the activation of the mPFC-NAcc circuit, the female later preferred spending time with that male. This strengthens their argument that low-frequency oscillatory drive from the mPFC to NAcc increases affiliative behavior and helps form social bonds.

Dr. Amadei says that this study found a "new biological correlate in the strength of connectivity between the mPFC and NAcc." If this translates to humans, we have a new way of understanding how intimate connections are formed. By exploring the individual variety of loving bonds, this research sets the bar higher for the study of complex social learning and behavior.