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Anterior Cingulate inputs to nucleus accumbens control the social transfer of pain and analgesia

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Empathy plays a critical role in social interactions, and many species, including rodents, display evolutionarily conserved behavioral antecedents of empathy. In both humans and rodents, the anterior cingulate cortex (ACC) encodes information about the affective state of others. However, little is known about which downstream targets of the ACC contribute to empathy behaviors. We optimized a protocol for the social transfer of pain behavior in mice and compared the ACC-dependent neural circuitry responsible for this behavior with the neural circuitry required for the social transfer of two related states: analgesia and fear. We found that a 1-hour social interaction between a bystander mouse and a cagemate experiencing inflammatory pain led to congruent mechanical hyperalgesia in the bystander. This social transfer led to activation of neurons in the ACC and several downstream targets, including the nucleus accumbens (NAc), which was revealed by monosynaptic rabies virus tracing to be directly connected to the ACC. Bidirectional manipulation of activity in ACC-to-NAc inputs influenced the acquisition of socially transferred pain. Further, the social transfer of analgesia also depended upon ACC-NAc inputs. By contrast, the social transfer of fear instead required activity in ACC projections to the basolateral amygdala. This shows that mice rapidly adopt the sensory-affective state of a social partner, regardless of the valance of the information (pain, fear, or pain relief). We find that the ACC generates specific and appropriate empathic behavioral responses through distinct downstream targets. More sophisticated understanding of evolutionarily conserved brain mechanisms of empathy will also expedite the development of new therapies for the empathy-related deficits associated with a broad range of neuropsychiatric disorders.

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