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NEURAL CIRCUITS

Grooming's innate, innit?

> photo-stimulation of glutamatergic MeApd neurons in a male mouse that was engaged in an ongoing social behaviour ... interrupted this behaviour and subsequently triggered self-grooming

Innate behaviours, such as feeding, grooming and certain types of fear, are essential for survival. Much remains unknown about the mechanisms that trigger and regulate these behaviours, but a new study by Anderson and colleagues shows that inhibitory and excitatory neuron populations in the posterior dorsal part of the medial amygdala (MeApd) antagonistically regulate social behaviour and self-grooming (a non-social behaviour) in mice.

Previous studies have shown induction of *c-fos* (indicating neural activation) in the MeApd of mice that had just attacked an intruder mouse. The authors therefore first assessed whether activation of MeApd neurons actually promotes attack behaviour. Optogenetic stimulation of MeApd neurons in resident mice induced aggression towards intruder mice, including castrated males and females (which they would normally not attack), and the behaviour ceased as soon as the photostimulation was stopped. This showed that MeApd neurons indeed promote aggression.

The MeApd consists of GABAergic and glutamatergic neurons, and the authors next investigated whether one or both of these populations regulate the promotion of aggression. Labelling studies revealed that after an attack, more than 90% of activated (*c-fos*-expressing) cells in the MeApd were GABAergic and less than 10% of activated cells were glutamatergic. Moreover, optogenetic activation of GABAergic MeApd cells in male mice triggered aggressive behaviour towards normal and castrated male intruders, as well as female intruders. Conversely, optogenetic inhibition of these neurons three seconds after the onset of an attack halted the aggressive behaviour. These findings indicated that GABAergic MeApd neurons are both necessary and sufficient for promoting aggressive behaviour.

Could these neurons also regulate other social behaviours? Low-intensity optogenetic stimulation of GABAergic MeApd cells induced mounting behaviour towards intruders in some male mice and grooming of intruders in other males. These pro-social behaviours changed to aggression as the authors increased the stimulation intensity. Thus, GABAergic MeApd neurons promote different forms of social behaviour, depending on their level of activity.

The authors then investigated the role of glutamatergic MeApd cells in social behaviour. Optogenetic stimulation of these cells in male mice did not induce aggression, mounting or social grooming of intruder mice, but triggered self-grooming. The stimulation had this effect even in mice that were not exposed to an intruder. Moreover, photostimulation of glutamatergic MeApd neurons in a male mouse that was engaged in an ongoing social behaviour (attacking a male mouse or mounting a female) interrupted this behaviour and subsequently triggered self-grooming. Thus, glutamatergic MeApd neurons inhibit social behaviour and promote (non-social) self-grooming.

Interestingly, long-lasting pharmacological activation of glutamatergic MeApd neurons greatly reduced social behaviour but only rarely triggered self-grooming, indicating that the effects of these cells on social behaviour and self-grooming, respectively, are independent. Conversely, optogenetic activation of GABAergic MeApd neurons in self-grooming mice interrupted this non-social behaviour, both in mice exposed to an intruder and in solitary mice. As, by definition, the latter cannot engage in social behaviour, this finding suggests that GABAergic MeApd cells have an inhibitory effect on self-grooming that is independent of their effect on social behaviour.

This study has shown that distinct populations of MeApd neurons antagonistically regulate social behaviour and a non-social behaviour. The identification of neural circuits underlying innate behaviours may prove useful in understanding how these behaviours — both social and non-social — are altered in, for example, autism.

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ORIGINAL RESEARCH PAPER Hong, W., Kim, D.-W. & Anderson, D. J. Antagonistic control of social versus repetitive self-grooming behaviors by separable amygdala neuronal subsets. *Cell* **158**, 1348–1361 (2014)