This Week in The Journal

Sex-Dependent Microglial Role in Reincision Hyperalgesia

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(see pages 3081–3093)

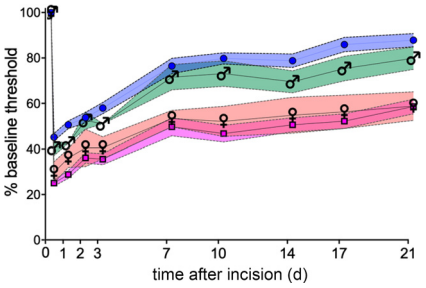
Babies born before term often require repeated medical interventions, ranging in severity from needle pricks to major surgery. These procedures activate still-developing pain pathways and can permanently alter sensory processing. Indeed, adolescents who were born prematurely and/or underwent multiple surgical interventions as newborns tend to have higher thermal and mechanical sensory thresholds than their peers, yet they experience greater and more prolonged pain (hyperalgesia) when undergoing surgery later in life.

Rodents subjected to hindpaw incision as pups also develop generalized hyposensitivity along with reincision hyperalgesia in adulthood. Because the hyposensitivity is widespread, it is thought to stem from plasticity in brainstem areas that exert inhibitory control over spinal pain circuits. In contrast, hyperalgesia occurs only when the same paw is reinjured, suggesting it results from local plasticity. Notably, reincision hyperalgesia is attenuated if the microglial inhibitor minocycline is administered at the time of the second incision, suggesting neonatal incision primes microglia to induce hyperalgesic responses in the future (Schwaller and Fitzgerald, 2014, Eur J Neurosci 39:344).

Moriarty et al. asked whether administering minocycline at the time of neonatal incision also attenuates hyperalgesia in adults. Additionally, because previous work has shown that microglia contribute to persistent pain only in males (in females, T cells are responsible), they asked whether reincision hyperalgesia occurs in females, and if so, whether it is prevented by minocycline treatment.

Hindpaw incision produced larger withdrawal responses to thermal or mechanical stimuli in adult rats that had undergone hindpaw incision as neonates than in previously uninjured rats. Importantly, reincision hyperalgesia was similar in males and females. Furthermore, incision increased proliferation and activation of spinal cord microglia in adults of both sexes. Nonetheless, treating neonates with minocycline at the time of incision reduced microglial activation and reincision hyperalgesia only in males.

These results show that sex differences in pain mechanisms extend to priming of microglia after neonatal incision. Because microglia have essential roles in the normal development of neural circuits, future work should determine whether neonatal minocycline impairs sensory development and whether any such effects differ between the sexes. Whether reincision hyperalgesia in females stems from T-cell priming should also be investigated.



Incision reduces pain threshold more in adult rats that had undergone incision as neonates (purple) than those that had not (blue). Treating neonates with minocycline prevented reincision hyperalgesia in males (green), but not in females (pink). For details, see Moriarty et al.

Activity Patterns Linked to Positive and Negative Memory Bias

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(see pages 3130–3143)

Positive and negative experiences are typically remembered better than neutral ones. This enhanced memory for emotional events depends on the amygdala, which is activated by both positive and negative emotions and is thought to facilitate memory formation through its interactions with other brain areas. Such interactions have been shown to occur during memory encoding in humans, and items that are subsequently remembered induce stronger activation than those that are forgotten. Differences in the strength of coupling between the amygdala and other brain areas might therefore explain why some people have stronger memories for positive events while others have better memories for negative events.

Although previous work has suggested that amygdala activity promotes memory encoding, whether interactions between amygdala and other areas facilitates consolidation remained unknown. To address this question, Kark and Kensinger measured coordinated activity (functional connectivity) between the amygdala and cortical areas during rest periods immediately before and after people viewed images having positive, negative, or neutral valence. They tested memory for the items in a surprise test the next day, and then asked whether changes in resting-state functional connectivity were related to memory for positive and negative images.

Approximately half of participants showed a bias for remembering negative images, while the other half showed a positive memory bias. Memory for negative images (and a bias for remembering these items) was associated with stronger coupling between the amygdala and early visual cortical areas during the postencoding rest period than during the preencoding period. In contrast, memory for positive images and positive memory bias were associated with increased coupling between the amygdala and prefrontal cortical areas.

These results suggest that the amygdala enhances memory for positive and negative emotional stimuli through interactions with different areas (frontal and visual cortex, respectively) in periods of rest that immediately follow the experience. These interactions might contribute to valence-dependent memory consolidation. Thus, differences in the strength of amygdala connections with sensory and prefrontal cortical areas might contribute to interindividual differences in positive and negative memory bias. Future work should determine whether instructing people to remember only positive or negative stimuli influences network interactions while shifting memory bias.

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