Neuropsychopharmacology (2017), 1–2

Opioidergic regulation of pain and pleasure in human social relationships

Affiliative bonds are the hallmark of human sociability, having evolved to support survival, reproduction, and nurturing of the offspring. Social relationships are associated with security and comfort. Such feelings could serve as safety signals, promoting incentive motivation towards social bonding. Building up on the seminal work by Jaak Panksepp and colleagues, recent genetic studies suggest that different neurochemicals including dopamine, oxytocin, and particularly opioid peptides regulate different aspects of sociability (Pearce *et al*, 2017). Indeed, human positron emission tomography (PET) studies have shown that the endogenous opioid system, best known for its role in pain and reward, supports also social bonding in humans. Prosocial behavior, such as social laughter, triggers endogenous opioid release in thalamus and insular cortex concomitantly with increased calmness and amusement (Manninen *et al*, 2017). Such group-level opioid release via contagious laughter, rather than time-consuming dyadic bonding, may have allowed humans to significantly extend their social sphere. Conversely, also social rejections or losses may trigger similar endogenous opioid activation as social bonding (Hsu *et al*, 2013), paralleling the contribution of the opioid system to processing of purely sensory pleasure and pain in humans. Thus, the opioid system seems to modulate both motivation towards social contacts and support, and away from solitude.

Capacity for vicarious experience is a key feature of human sociability: feeling others' pain in our own mind may create a strong urge to help others in distress. Fusion imaging work combining PET with functional magnetic resonance imaging shows that the more opioid receptors humans have in their brain, the more strongly their frontocortical areas respond to seeing others' distress (Karjalainen *et al*, 2017). Similarly, placebo analgesia (modulated by the opioid system) also reduces empathy-related brain responses towards others' distress (Rutgen *et al*, 2015). Accordingly, the physical and vicarious pain share the same neuromolecular basis, and opioidergic neurotransmission may facilitate more complex prosocial motivation than just social bonding.

Molecular imaging studies have also established that individual differences in endogenous opioid system explains individual differences in sociability. In particular, opioid receptor availability in the frontal cortex—a region involved in variety of socioemotional processes—predicts both the security of romantic attachment bonds (Nummenmaa *et al*, 2015) as well as the tendency for prosocial expressions such as laughter in social settings (Manninen *et al*, 2017). Genetic as well as experience-dependent plasticity of the endogenous opioid system might thus constitute an important precursor for trait-like differences in social behavior, including prosociality and helping behavior.

All in all, these results extend pharmacological work in non-human primates showing that opioid agonists decrease and antagonists increase social grooming (analogous prosocial behavior to human social laughter), suggesting a shared opioidergic bonding mechanism across humans and other primates. Furthermore, the recent data show that in humans the opioid system has evolved to serve not only reproductive or maternal dyadic bonding, but also large-scale affiliative bonding and altruistic behaviour such as helping triggered by seeing others—even unfamiliar individuals—in distress.

Most humans strive for social contacts throughout their lifespan, and lack of social contacts has significant negative consequences for both psychological and somatic health. Accordingly, properly functioning endogenous opioid system might be an important precursor for psychological resiliency and well-being in general. This may explain why disruption of the endogenous opioid system by, for example, heroin abuse may lead to antisocial behavior. However, the specific role of the opioid system in different types of social relationships (such as romantic versus affiliative) needs to be resolved in future studies.

FUNDING AND DISCLOSURE

This work was supported by the Academy of Finland grants #265915 and #294897 to LN, and personal grant from Päivikki and Sakari Sohlberg Foundation to TK. The authors declare no conflict of interest.

Lauri Nummenmaa[1,2] and Tomi Karjalainen[1]

[1]Turku PET Centre, University of Turku, Turku, Finland; [2]Department of Psychology, University of Turku, Turku, Finland
E-mail: lauri.nummenmaa@utu.fi

Hsu DT, Sanford BJ, Meyers KK, Love TM, Hazlett KE, Wang H *et al* (2013). Response of the mu-opioid system to social rejection and acceptance. *Mol Psychiatry* **18**: 1211–1217.

Karjalainen T, Karlsson HK, Lahnakoski JM, Glerean E, Nuutila P, Jaaskelainen IP *et al* (2017). Dissociable roles of cerebral mu-opioid and type 2 dopamine receptors in vicarious pain: a combined PET-fMRI study. *Cereb Cortex* 1–10.

Manninen S, Tuominen L, Dunbar RIM, Karjalainen T, Hirvonen J, Arponen E *et al* (2017). Social laughter triggers endogenous opioid release in humans. *J Neurosci* **37**: 6125–6131.

Nummenmaa L, Manninen S, Tuominen L, Hirvonen J, Kalliokoski KK, Nuutila P *et al* (2015). Adult attachment style is associated with cerebral μ-opioid receptor availability in humans. *Hum Brain Mapp* **36**: 3621–3628.

Pearce E, Wlodarski R, Machin A, Dunbar RIM (2017). Variation in the β-endorphin, oxytocin, and dopamine receptor genes is associated with different dimensions of human sociality. *Proc Natl Acad Sci USA* **114**: 5300–5305.

Rutgen M, Seidel EM, Silani G, Riecansky I, Hummer A, Windischberger C *et al* (2015). Placebo analgesia and its opioidergic regulation suggest that empathy for pain is grounded in self pain. *Proc Natl Acad Sci USA* **112**: 5638–5646.

Neuropsychopharmacology Reviews (2017) **00,** 1. doi:10.1038/npp.2017.200