LETTERS TO THE EDITOR

Rewards of beauty: the opioid system mediates social motivation in humans

Facial attractiveness is a powerful cue that affects social communication and motivates sexual behavior.[1–3] Attractive people are both judged[4] and treated[5] more positively, reflecting the biased stereotypical notion that 'beautiful is good'. Indeed, beautiful faces are processed by the limbic reward system[6] and according to the same economic principles as non-social rewards.[7] The human reward system has a high density of μ-opioid receptors,[8] which have an important role in affiliation and attachment.[9–11] Here, we causally test whether the healthy human opioid system mediates facial attractiveness preference.

In rodents, μ-opioid (MOR) neurotransmission can increase both hedonic value ('liking') and motivational salience ('wanting') of rewards.[12] When several rewards are available, MOR agonism increases and antagonism decreases preference specifically for the most valuable option. For instance, rats ate fewer palatable cookies but not less standard chow after MOR antagonism,[13] while MOR stimulation enhanced sexual 'wanting' of only estrous, but not nonestrous, females.[14] We predicted that antagonism of the human opioid system would decrease, while MOR agonism would increase 'liking' and 'wanting'[6] specifically for the evolutionarily most valuable option, namely attractive opposite-sex faces.

In this double-blind, placebo-controlled cross-over study, 30 healthy males (see Figure 1 and Supplementary Information) viewed photographs of faces of varying attractiveness levels. In each session, participants received a μ-opioid receptor agonist (morphine 10 mg), a nonselective opioid receptor antagonist (naltrexone 50 mg) or placebo, and performed one 'liking' and one 'wanting' task (see Parsons et al.[15]). In the 'liking' task, participants viewed each face for 5 s before rating attractiveness on a visual analog scale with anchors 'very unattractive' to 'very attractive'. In a 'wanting' task of fixed duration (3.65 min), participants increased or decreased the preset viewing time of each face (5 s) by pressing
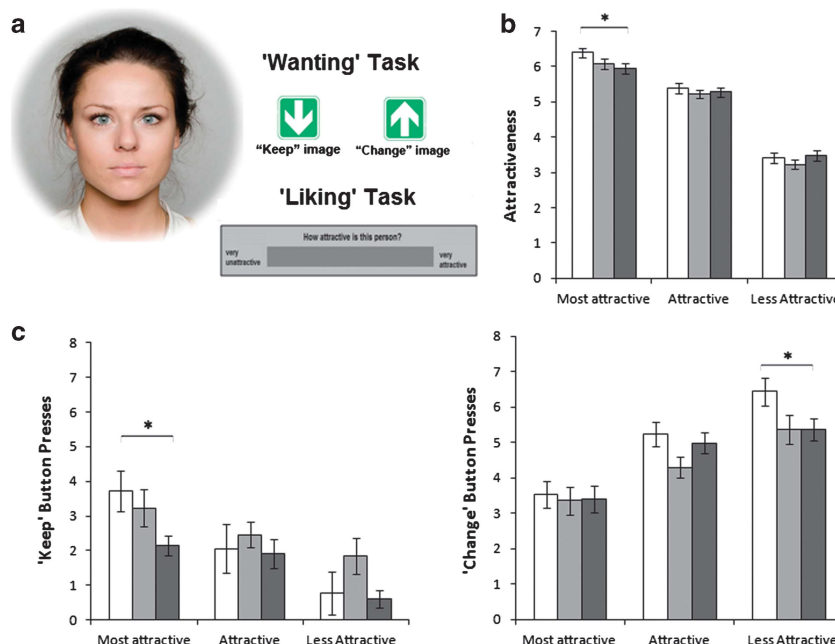

Figure 1. (**a**) In both the 'wanting' and 'liking' tasks, participants viewed faces from a purposely developed Oslo Face Database. The attractiveness categories were calculated based on the ratings from an independent group of 20 male participants (the depicted female face is from the 'Most Attractive' category). Thirty healthy males received a μ-opioid agonist (morphine 10 mg), a nonselective opioid antagonist (naltrexone 50 mg) or placebo (per-oral) on three separate days. In the 'wanting' task, participants could press one of two arrow keys to view the image for longer ('keep') or shorter ('change') time than the preset 5 s, without altering total task duration. To account for the data loss due to technical error of the 'liking' task, seven more participants were tested using the same paradigm. In the 'liking' task, participants rated attractiveness of each face using a VAS scale. (**b**) Morphine treatment enhanced and naltrexone treatment decreased men's 'liking' of the most beautiful female faces (ratings on the VAS scale from 0 to 10). (**c**) 'Wanting' of attractive females, as measured by the total of 'keep' button presses, was similarly affected by opioid manipulations. However, morphine also increased motivation to avoid viewing the least attractive female faces, as measured by the total of 'change' button presses. *$P < 0.05$.

buttons to keep looking at the same face or change by proceeding to the next face.[15]

Linear multilevel (mixed models) regression analysis was employed to assess viewing times and 2.5-SD-trimmed 'keep' or 'change' button-press data from the 'wanting' task, and attractiveness ratings from the 'liking' task. Main factors were drug, attractiveness and gaze direction. Control variables were session number, stimulus order, image set and OPRM1 group (AA or GA; see Supplementary Information).

'WANTING' TASK

Both morphine and naltrexone decreased the average viewing time by ~200 ms compared with placebo (main effect of drug, $F_{(2,1208)} = 3.6$, $P = 0.026$). However, a planned contrast of *keep* button-press data revealed the expected pattern of 'wanting' increases with morphine and decreases with naltrexone for the most attractive female faces (M > N, $t = 2.56$, $P = 0.011$, Cohen's $d = 0.95$, Figure 1b). Yet, for the least attractive females, morphine increased 'wanting' to *change* the photo, relative to placebo and naltrexone treatment (M > N, $t = 2.52$, $P = 0.012$, Cohen's $d = 0.94$). Analysis of total key-presses per image revealed a significant increase in 'wanting' behavior after morphine relative to naltrexone treatment ($F_{(2,1206)} = 5.2$, $P = 0.006$, M > N, $t = 3.18$, $P = 0.001$, Cohen's $d = 1.18$), consistent with opioid mediation of human motivational preference for faces.

'LIKING' TASK

In line with our prediction that the opioid system mediates 'liking' for the evolutionarily most valuable option, attractiveness ratings were significantly higher after morphine compared with naltrexone treatment only for the most attractive female faces (M > N, $t = 2.13$, $P = 0.034$, Cohen's $d = 0.91$, Figure 1b, data from 23 participants, see Supplementary Information). The main effect of drug did not reach significance ($F_{(2,1314)} = 1.8$, $P = 0.16$).

Our results offer the first evidence that pharmacological manipulation of the human MOR system affects both aesthetic evaluation of and motivation for viewing opposite-sex faces. In line with findings from rodent literature,[13,14] the effects of the MOR manipulations were strongest for the most valuable stimuli, that is, the most beautiful women. Morphine increased and naltrexone decreased men's 'liking' of these faces. We also observed an increase in 'wanting' behavior after morphine relative to naltrexone treatment, indicating that manipulation of the opioid system affected participants' motivation to expend effort. Specifically, activation of the opioid reward system with morphine not only increased 'wanting' key-press behavior to keep viewing the beautiful faces but also increased motivation to avoid viewing the least attractive faces.

The two components of reward, hedonic evaluation ('liking') and motivational salience ('wanting') were previously shown to partially dissociate when men viewed female faces of varying attractiveness levels,[6] and when males and females viewed images of infants.[15] The current study revealed an opioid-related increase in motivation to avoid the least attractive female faces, which was not mirrored by changes in reported attractiveness of these faces. For the most beautiful faces, however, the MOR manipulations affected 'liking' and 'wanting' similarly and in the expected directions.[11] Together, these findings suggest that the human opioid system may mediate social motivation by enhancing the salience and reward appraisal of the most valuable stimuli, while inhibiting 'wanting' of less valuable social cues.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

O Chelnokova[1], B Laeng[1], M Eikemo[1], J Riegels[1], G Løseth[1], H Maurud[1], F Willoch[2] and S Leknes[1,2]
[1]Department of Psychology, University of Oslo, Oslo, Norway and [2]Department of Medicine, University of Oslo, Oslo, Norway
E-mail: o.v.chelnokova@psykologi.uio.no or s.g.leknes@psykologi.uio.no

REFERENCES

1 Perrett DI, Lee KJ, Penton-Voak I, Rowland D, Yoshikawa S, Burt DM et al. Nature 1998; 394: 884–887.
2 Rhodes G, Simmons LW, Peters M. Evol Hum Behav 2005; 26: 186–201.
3 Parsons CE, Young KS, Mohseni H, Woolrich MW, Thomsen KR, Joensson M et al. Soc Neurosci-Uk 2013; 8: 268–274.
4 Dion K, Walster E, Berschei. E. J Pers Soc Psychol 1972; 24: 285–289.
5 Langlois JH, Kalakanis L, Rubenstein AJ, Larson A, Hallam M, Smoot M. Psychol Bull 2000; 126: 390–423.
6 Aharon I, Etcoff N, Ariely D, Chabris CF, O'Connor E, Breiter HC. Neuron 2001; 32: 537–551.
7 Hayden BY, Parikh PC, Deaner RO, Platt ML. Proc Biol Sci 2007; 274: 1751–1756.
8 Biederman I, Vessel EA. Am Sci 2006; 94: 247–253.
9 Nelson EE, Panksepp J. Neurosci Biobehav Rev 1998; 22: 437–452.
10 Machin AJ, Dunbar RIM. Behaviour 2011; 148: 985–1025.
11 Hsu DT, Sanford BJ, Meyers KK, Love TM, Hazlett KE, Wang H et al. Mol psychiatry 2013; 18: 1211–1217.
12 Berridge KC, Kringelbach ML. Psychopharmacology 2008; 199: 457–480.
13 Cooper SJ, Turkish S. Pharmacol Biochem Be 1989; 33: 17–20.
14 Mahler SV, Berridge KC. Psychopharmacology 2012; 221: 407–426.
15 Parsons CE, Young KS, Kumari N, Stein A, Kringelbach ML. Plos ONE 2011; 6: e20632.

Supplementary Information accompanies the paper on the Molecular Psychiatry website (http://www.nature.com/mp)

Metamoodics: meta-analysis and bioinformatics resource for mood disorders

Mood disorders, including major depression (MD) and bipolar disorder (BP), are among the most common psychiatric disorders.[1] Although genetic factors have an important role in their etiology,[2,3] the heritability of these disorders remains largely unexplained. Owing to advances in high-throughput genomic technologies, it is becoming increasingly feasible to investigate the genetic architecture of these disorders at an unprecedented resolution. The challenge is how to make sense of the enormous flood of data generated by the diverse genomic studies that use these new