The effect of treatment expectation on drug efficacy: imaging the analgesic benefit of the opioid remifentanil.

Abstract:
Evidence from behavioral and self-reported data suggests that the patients' beliefs and expectations can shape both therapeutic and adverse effects of any given drug. We investigated how divergent expectancies alter the analgesic efficacy of a potent opioid in healthy volunteers by using brain imaging. The effect of a fixed concentration of the ?-opioid agonist remifentanil on constant heat pain was assessed under three experimental conditions using a within-subject design: with no expectation of analgesia, with expectancy of a positive analgesic effect, and with negative expectancy of analgesia (that is, expectation of hyperalgesia or exacerbation of pain). We used functional magnetic resonance imaging to record brain activity to corroborate the effects of expectations on the analgesic efficacy of the opioid and to elucidate the underlying neural mechanisms. Positive treatment expectancy substantially enhanced (doubled) the analgesic benefit of remifentanil. In contrast, negative treatment expectancy abolished remifentanil analgesia. These subjective effects were substantiated by significant changes in the neural activity in brain regions involved with the coding of pain intensity. The positive expectancy effects were associated with activity in the endogenous pain modulatory system, and the negative expectancy effects with activity in the hippocampus. On the basis of
subjective and objective evidence, we contend that an individual's expectation of a drug's effect critically influences its therapeutic efficacy and that regulatory brain mechanisms differ as a function of expectancy. We propose that it may be necessary to integrate patients' beliefs and expectations into drug treatment regimes alongside traditional considerations in order to optimize treatment outcomes.