Supplemental Digital Content 1



Subjective aversive effects were assessed on 100mm visual analog scales (VAS) during the infusion of saline placebo and alfentanil. The impact of the placebo infusion on ratings of subjective aversive effects was assessed in participants who were exposed to saline placebo before alfentanil. The impact of the placebo infusion could not be assessed in participants who received alfentanil before saline placebo because residual alfentanil concentrations were still present during the infusion of saline placebo. VAS scores for pruritus, nausea, dizziness and sedation are depicted for participants who received saline placebo before alfentanil. The incidence of pruritus, nausea, and dizziness was low and the magnitude of such effects was modest during the saline placebo infusion. While ratings for sedative drug effects were also of moderate magnitude, the incidence of this drug effect was quite high during the saline placebo infusion.

Supplemental Digital Content 2



Subjective reinforcing effects were assessed on a 100mm visual analog scale (VAS) during the infusion of saline placebo and alfentanil. The impact of the placebo infusion on ratings of reinforcing drug effects was assessed in participants who were exposed to saline placebo before alfentanil. The impact of the placebo infusion could not be assessed in participants who received alfentanil before saline placebo because residual alfentanil concentrations were still present during the infusion of saline placebo. VAS scores for average and maximum drug liking, and maximum drug disliking are depicted for participants who received saline placebo before alfentanil. The incidence of drug liking and disliking was low during the saline placebo infusion.