

The following checked and counted signs were monitored over the subsequent 30-min period: diarrhea, lacrimation, ptosis, rhinorrhea, teeth chattering (each recorded as present/absent), salivation (4-point rating scale: 0 = absent, 1 = slight, 2 = moderate, 3 = marked), mouth movements, paw shakes, wet dog shakes, penile grooming (each recorded as total number of occurrences during session), startle (5-point rating scale; 0 = no response, 1 = mild with slight vocalization, 2 = moderate response with vocalization, 3 = marked response/jump with vocalization, 4 = intense with marked vocalization), weight loss (body weight change in the animal recorded immediately prior to, and 30 min after, naloxone injection).

### **Animal models of withdrawal include a number of characteristic somatic signs:**

Four rats from the morphine group that repeatedly exposed to morphine and then injected with naloxone, signs like Teeth Chattering, Sneeze and salivation, wet dog shakes, Grooming, and Diarrhea have been observed. Consequently, the objective symptoms observed in morphine plus naloxone-treated animals have been taken as markers of opioid withdrawal.

**Table S1. Number of withdrawal symptoms.**

	Teeth Chattering	Dog Shakes	Grooming	Diarrhea	Sneeze salivation
Rat 1	2	3	17	0	0
Rat 2	0	11	14	0	1
Rat 3	0	8	1	0	1
Rat 4	0	5	5	0	0