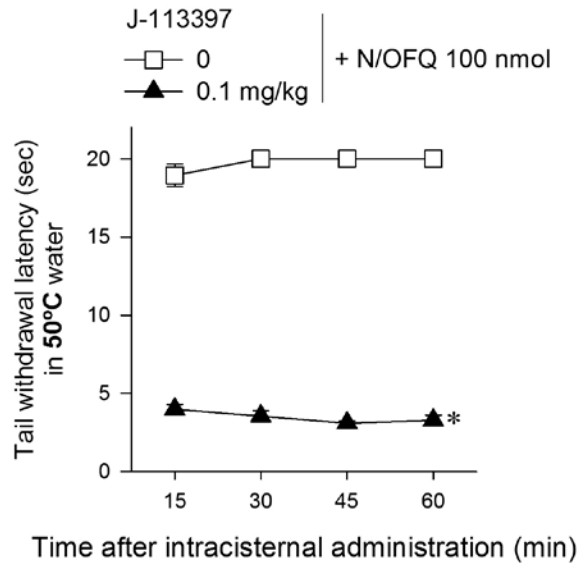


**Supplementary Information**

**2014-BJP-1336-RP**

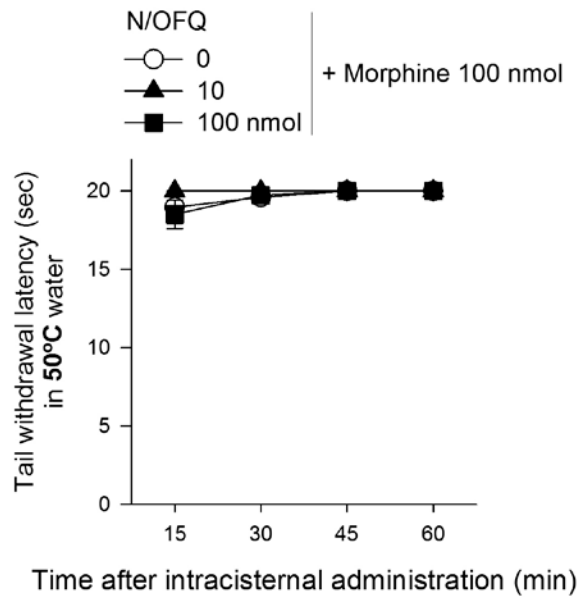
**Supraspinal actions of N/OFQ, morphine and substance P in regulating pain and itch in nonhuman primates**

**H Ding, K Hayashida, T Suto, D D Sukhtankar, M Kimura, V Mendenhall and M C Ko**



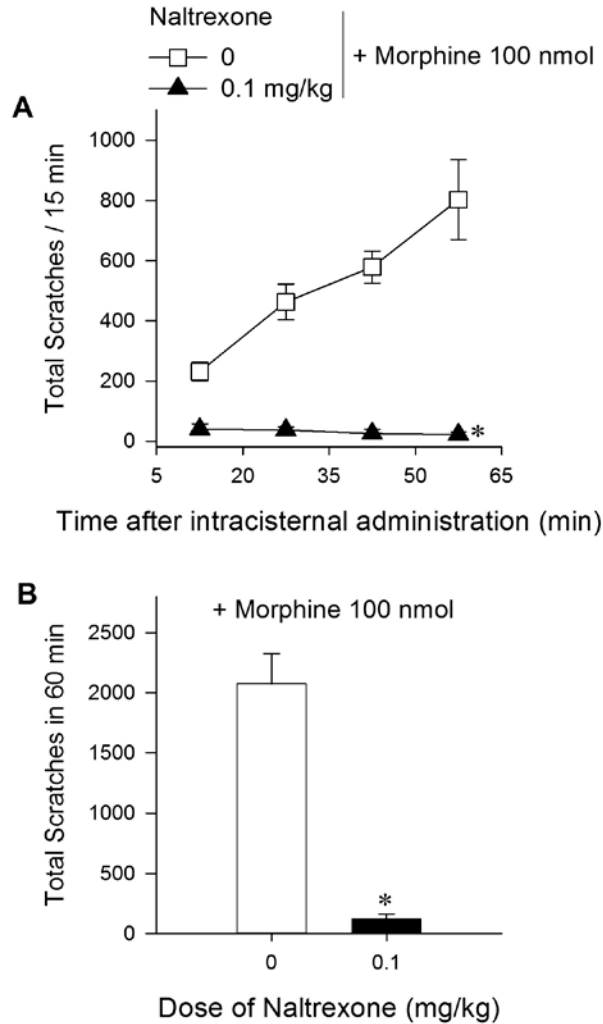
### Supplemental Figure 1.

Effects of the NOP receptor antagonist J-113397 on intracisternal N/OFQ-induced antinociception in rhesus monkeys. J-113397 (0.1 mg/kg) or vehicle (0.1 mL/kg) was administered subcutaneously 15 min before administration of intracisternal N/OFQ 100 nmol. Tail-withdrawal latencies in 50°C water were measured 15, 30, 45, and 60 minutes after intracisternal administration. Each data point represents mean  $\pm$  SEM (n = 4). Symbols represent different dosing conditions for the same monkeys. Asterisk (\*) denotes significant difference from the vehicle condition for all time points ( $p < 0.05$ ).



**Supplemental Figure 2.**

Comparison of thermal nociceptive responses of intracisternal morphine (100 nmol) in combination of N/OFQ at doses of 0, 10, and 100 nmol. Tail-withdrawal latencies in 50°C water were measured 15, 30, 45, and 60 minutes after intracisternal administration. Each data point represents mean  $\pm$  SEM (n = 4). Symbols represent different dosing conditions for the same monkeys.



### Supplemental Figure 3.

Effects of the  $\mu$  receptor antagonist naltrexone on intracisternal morphine-elicited itchy scratching responses in rhesus monkeys. Naltrexone (0.1 mg/kg) or vehicle (0.1 mL/kg) was administered subcutaneously 15 min before administration of intracisternal morphine 100 nmol.

A, time course of total scratches in each 15-minute time block. B, total scratches in the entire 60-minute observation period. Behavioral responses were recorded for a total of 60 minutes starting at 5 minutes after intracisternal administration. Each data point represents mean  $\pm$  SEM ( $n = 4$ ). Symbols represent different dosing conditions for the same monkeys. Asterisk (\*) denotes a significant difference from the vehicle condition for all time points (A) or as total responses (B) ( $p < 0.05$ ).