**Supplementary Methods**

***3-Choice Serial Reaction Time Task in Mice***

Aluminum operant chambers measuring W22 × D26 × H18 cm (Med Associates Inc., St. Albans, VT, USA) were used for the 3-CSRTT. The curved rear wall of each chamber contained nine holes. Each hole had an infrared photocell beam for detection of nose poke responses, and a yellow LED light was located behind each hole. Every other hole was sealed so that only the three centrally positioned ports were accessible. A food magazine was located on the opposite wall of the chamber, and a house light was located at the top of this wall. The food magazine had a yellow LED light located on its ceiling. The apparatus was controlled by a computer program written in the MED-PC language (Med Associates Inc., St. Albans, VT, USA).

Training in the 3-CSRTT was conducted once daily, and each session began by illuminating the house and food magazine lights. The first trial began when a mouse entered the magazine, which turned off the house and magazine lights. After a 5-s delay, which was referred to as the inter-trial interval (ITI), one of three hole lights was briefly illuminated (stimulus duration) in a pseudo-random order, so that the mouse could not predict which hole would be illuminated. Nose poking during the ITI was recorded as a *premature response*, which is an index of impulsive action. Nose poking into the lit hole while it was illuminated or within 5 s of the limited hold was recorded as a correct response and resulted in illumination of the house and magazine lights and subsequent delivery of a palatable food pellet (20 mg each, dustless precision pellets, Bio-Serv, Frenchtown, NJ, USA). Once the mouse entered the magazine to receive his food reward, the magazine light was again turned off. After a 0.5-s delay, the magazine light and house light flashed for 0.5 s, and these lights were then illuminated continuously. Another nose poke into the magazine caused the magazine and house lights to turn off, indicating the start of a new trial. Nose poking into an unlit hole was recorded as an incorrect response. When the animal failed to nose poke within the limited hold (5 s), it was recorded as an omission. Additional nose poking into any of the three ports prior to food collection was recorded as a *perseverative response* and was regarded as an index of compulsive behavior. Premature responses, incorrect responses, omissions, and perseverative responses resulted in a 5-s time-out period during which the house light was illuminated. After the time-out period, the magazine light and house light flashed for 0.5 s, and these lights were then continuously illuminated. A nose poke into the magazine was required to start the next trial. Only in case of premature response, nosepoke into the magazine after the time-out period restart the same trial. The *correct response latency* (the mean time between stimulus onset and a nose poke into the correct hole) and *reward latency* (the mean time between reward delivery and a nose poke into the food magazine) were recorded and they were regarded as attentional/motor and motivation/appetite functions, respectively. The number of *total trials* was regarded as an index of motivation. *Accuracy* [correct responses / (correct and incorrect responses) ×100] was calculated and regarded as an index of attentional function; *%omission* [the number of omission / total trial ×100] was calculated and regarded as an index of motivation/attentional function. Each session lasted for either 60 min or until 100 trials were completed, whichever came first. At the beginning of the training schedule, the stimulus duration lasted 30 s. Depending on individual performances, the stimulus duration was progressively reduced to 1 s (30, 15, 10, 7, 5, 4, 3, 2, 1.5, and 1 s). After completion of the training, the stimulus duration was fixed at 1 s, regardless of performance. We used the following criteria for determining stable performance: the number of correct responses and %accuracy in the last two consecutive sessions as higher than 40 and 70%, respectively (Supplemental Figure S3A-C). During the testing phase of this study, the duration of the ITI was prolonged to 9 s because the mice made only a few (< 10) premature responses in the task procedures with a 5 s ITI. Each testing session was conducted for 70 min or until 100 trials were completed, whichever came first. Prior to the drug experiment, one session with a 9-s ITI was conducted to measure basal impulsivity (n = 14). Subsequently, eight mice received an acute administration of milnacipran (0, 3, 10, or 30 mg/kg., i.p.) 60 min prior to 3-CSRTT testing. Each drug session was conducted with more than a week interval from the previous drug session. The order of the drug injections was counterbalanced using a Latin square design. All 3-CSRTTs were performed between 9:00 a.m. to 11:00 a.m.

***Resident-intruder test (RIT)***

After the mice had been individually housed and had been subjected to 3-CSRTT training for 5-6 weeks, they were studied to measure their aggression toward an intruder (Figure 1). An intruder was introduced into the home cage (W24 × D17 × H13 cm) of the resident male. Their behaviors were recorded for 5 min after the first attack bite. The intruder was removed if no attack occurred within 5 min. This encounter occurred once every other day until animals showed a stable number of attack bites, and stability was reached within 6–12 encounters [the variability of attack bites in the last three confrontations was less than 20%, see Supplemental Figure 3D]. Aggressive intruders were excluded from the group of stimulus animals.

After the number of attack bites was stabilized, a further 3 days of encounters (5 min) were conducted to obtain basal aggression levels (n = 14). Subsequently, eight resident mice received an acute administration of milnacipran (0, 3, 10, or 30 mg/kg., i.p.) 60 min prior to an encounter with an intruder. Each drug session was conducted with more than a two-day interval from the previous drug session. The order of the drug injections was counterbalanced using a Latin square design. Encounters lasted 5 min and behaviors were video-recorded and later scored by an experimenter who was blind to the treatments. Behaviors were categorized as follows: attack bite, threat behavior (consisting of a sideways threat, tale rattle, pursuit, upright posture, and aggressive grooming), latency to first attack bite and threat behavior, and walking. Agonistic behavior [attack bite + threat behavior] and agonistic latency (latency to first attack bite or threat behavior, whichever came first) were calculated. All RITs were performed between 2:00 p.m. and 5:00 p.m.

We obtained pharmacological validity of the current RIT procedure using buspirone and clonidine administrations (Supplemental Figure S1).

***Forced swimming test (FST)***

Following the completion of the 3-CSRTT testing, 14 mice were subjected to the FST to measure trait helplessness (Figure 1). Thirty-two naïve mice were used for FST drug testing. They received an acute administration of milnacipran (0, 3, 10, or 30 mg/kg., i.p., n = 8 each) 60 min prior to being placed in the cylinder. Mice were placed in a cylinder glass (diameter, 23 cm; height, 30 cm; Iwaki, Japan) containing water at a temperature of 24°C ± 1°C and a depth of 12 cm; mice could not escape nor touch the bottom of the cylinder. The swimming test lasted 6 min and behaviors were video-recorded and scored later by an experimenter who was blind to the treatments. Only the last 4 min of behaviors were analyzed, and they were categorized as follows: floating, the mouse is completely still in the water, except for isolated movements to right itself; kicking, movement of both hind legs; swimming, movement of all four legs with the body aligned horizontally in the water; climbing, movement of all four legs with the body aligned vertically in the water; and immobility latency, latency to first floating or kicking, whichever came first. The sum of the durations of floating and kicking behaviors was used as an index of immobility. We used a between-subject design for the FST to avoid repeated exposure to severe stress. All FSTs were performed between 9:00 a.m. and 11:00 a.m.

We obtained pharmacological validity of the current FST procedure using bupropion administration (Supplemental Figure S2).