Chronic pain threshold changes in a new complex schizophrenia model

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Introduction: The decrease in pain sensitivity is a well-known symptom of schizophrenia. We induced schizophrenia-related alterations by selective breeding and subchronic ketamine treatment with social isolation in rats. The aim of the present study was to determine the pain sensitivity in acute and chronic pain tests.

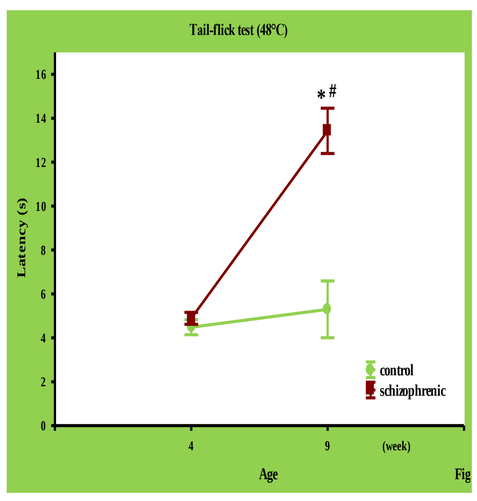
Methods: Twelfth generation of male Wistar rats after weaning (day 21 of age) was both housed individually for 4 weeks and treated with ketamine (30 mg/kg subcutaneously, s.c.) for 3 weeks, then followed 1 week resocialization. The control group did not receive any treatment.

Acute nociceptive threshold was assessed by the Tail-flick test at 4 and 9 weeks of age. The reaction time was determined by immersing the distal 5 cm portion of the tail in hot water (48 °C) until a tail-withdrawal response was observed.

Chronic mechanical allodynia was determined using a dynamic plantar aesthesiometer (Ugo Basile). Measurements were done with a straight metal filament that exerts an increasing upward force at a constant rate (6.25 g/s) with a maximum cut-off force of 50 g. At the age of 14 week 2 x 1 mg monosodium iodoacetate (MIA) was injected, on two consecutive days, into the right hind ankle joint of animals to induce osteoarthritis leading to mechanical allodynia. The mechanical pain threshold was detected before the inflammation and one and two weeks thereafter. Additionally, the antinociceptive effect of 1mg/kg (s.c.) morphine was also assessed in every 15 minutes for 120 minutes. The degree of edema was also measured by a digital caliper.

Results: The tail-flick latency at the age of four weeks was similar in the two groups. In contrast, the new substrain showed enhanced tail-flick latency at the age of 9 weeks compared to the control animals (Fig.1.).
Regarding the mechanical sensitivity before MIA injection, a significant decrease was observed in the new substrain (Fig.2.). After injection of MIA the pain threshold significantly decreased in the inflamed side in both groups, but a higher degree of allodynia was observed in the control group. Morphine produced significant decrease in allodynia in both groups (Fig.3.), but its effect did not differ in the two groups. Regarding the ankle cross section area, the injection of MIA caused a prolonged, significant edema, without significant difference between the groups (Fig. 4A, B).

* Indicate significant difference from control groups.
\# Indicate significant difference from 4 week.



Fig

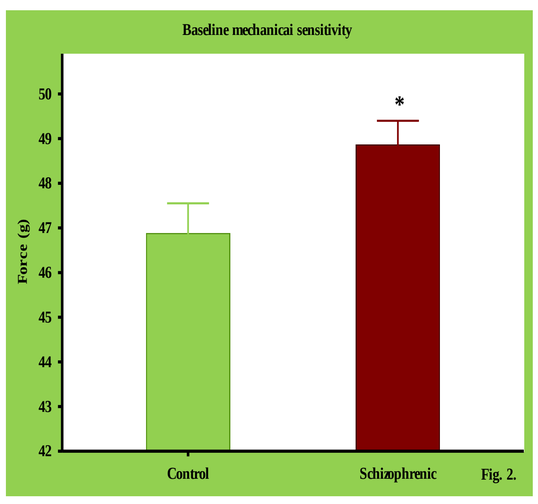


Fig. 2.

* Indicate significansy between the two groups

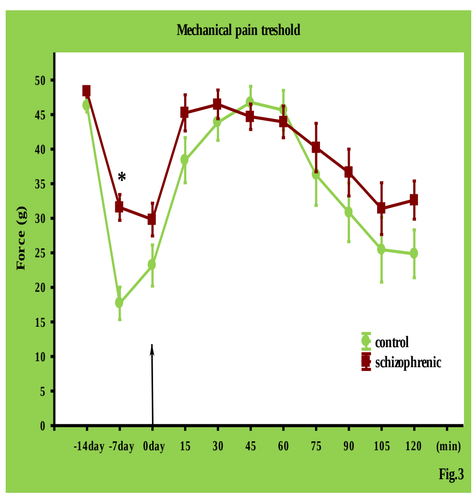


Fig.3

\# Indicate significant difference from 0 week

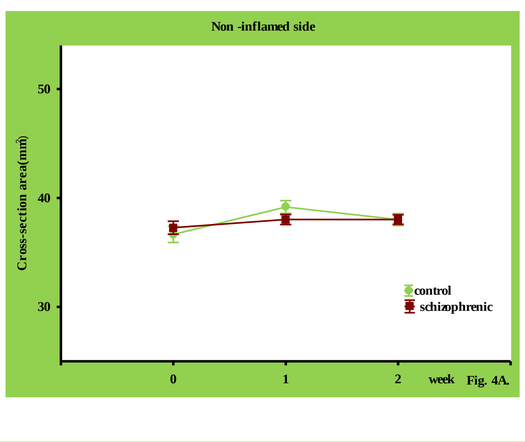


Fig. 4A.

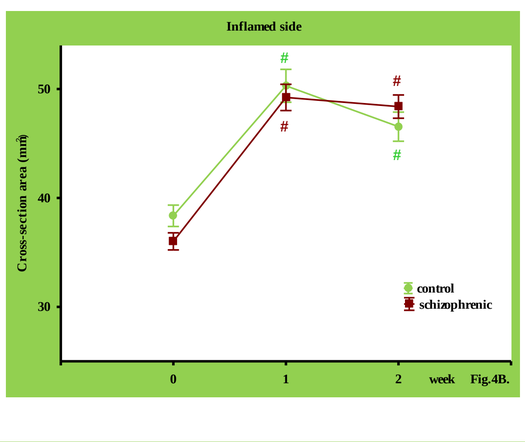


Fig.4B.

Conclusion: Our study proved that the selective breeding after juvenile isolation and ketamine treatment led to decreased thermal and mechanical pain sensitivity in both acute and chronic pain models, suggesting that this new substrain can simulate the hypoalgesic phenomenon of schizophrenia.

NEW SZÉCHENYI PLAN

HUNGARY'S RENEWAL

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