Comparison Of Electrophysiological Properties Of Nociceptive Dorsal Root Ganglion (DRG) Neurons *in vivo* In Mouse And Rat

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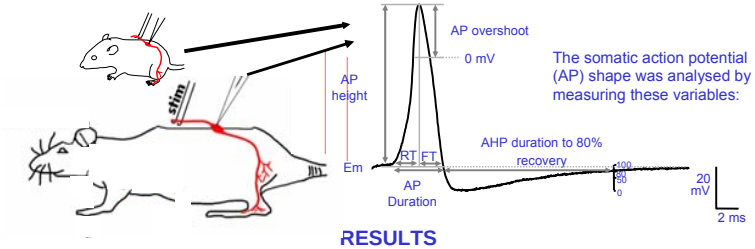
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INTRODUCTION

With the wide use of transgenic mice, mice are increasingly studied to determine the mechanisms underlying neuropathic pain. However, electrophysiological, especially *in vivo,* data is lacking from identified dorsal root ganglion (DRG) neurons in mouse. Therefore, we adapted techniques used for electrophysiological recordings from rat DRG neurons *in vivo*, to make similar recordings from L4/L5 DRG neurons in adult mouse. To examine whether differences of electrophysiological properties of DRG neurons exist between rat and mouse, we compare novel mouse data with published rat data (Fang et al 2005).

METHODS

All experiments were under the UK Animals (Scientific Procedure) Act of 1986. **Adult male C57Bl6 mice** (26-35g) were deeply anaesthetized with sodium pentobarbitone (80mg/kg, i.p.) with further doses (20-25mg/kg, i.v.) as required. Blood pressure was monitored throughout. Intracellular recordings in L4 or L5 DRG neuronal somata at ~30°C (28.5-32.5 °C) were made with sharp glass electrodes filled with 3M KCl. This enabled study of evoked somatic action potentials (APs), conduction velocity (CV) and sensory properties of C- and A-fiber nociceptors (responding to noxious mechanical and in some cases also noxious thermal stimuli) and of non-nociceptive low-threshold mechanoreceptors (LTMs). C-fiber units that did not respond to noxious or non-noxious stimuli were called unresponsive and are probably "silent nociceptive" units. At the end of experiments, animals were sacrificed with an anesthetic overdose. Comparison was made with of APs similarly recorded in L4-L6 DRGs of **young female Wistar rats** (150-180g), but with the muscle relaxant pancuronium (0.6mg/kg) during recording. Electrodes had either 3MKCl or 0.1M LiCl as the electrolyte (Fang et al 2005). AP variables were measured for overshooting APs in neurons with Em ≥-40mV: AP duration at base, AP rise time (RT), AP fall time (FT), afterhyperpolarization duration to 80% recovery (AHP); AP overshoot was measured in neurons with overshoot ≥-25mV.



The somatic action potential (AP) shape was analysed by measuring these variables:

RESULTS

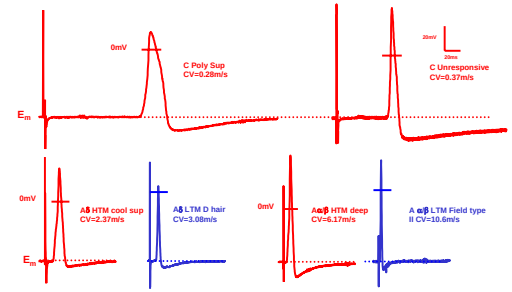


Fig. 1 Example of somatic action potentials (APs) recorded from physiologically identified DRG neurons of C57Bl6 mouse. Sup: superficial; HTM: high-threshold mechanoreceptor; LTM: low-threshold mechanoreceptor; CV: conduction velocity.

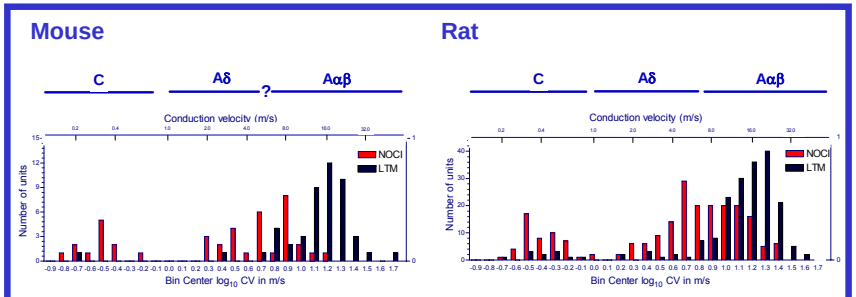


Fig. 2 Histograms of distributions of log10 conduction velocities (bins widths 0.1 log units) of identified DRG neurons recorded from adult male C57Bl6 mice (left) and young adult female Wistar rats (right). Distributions are similar in the two species.

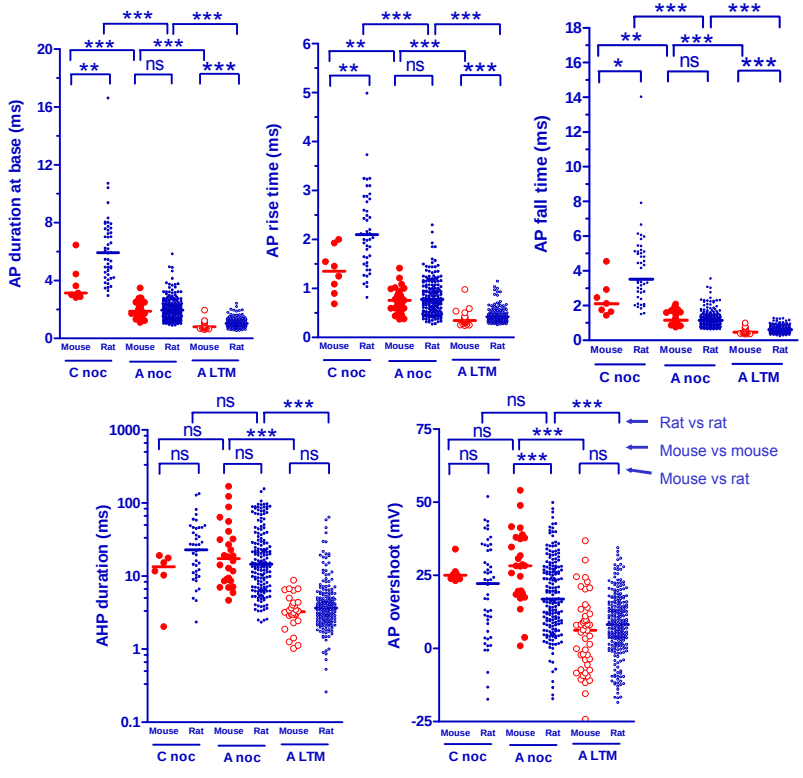


Fig. 3 Comparison of AP variables of DRG neuronal somata recorded from **adult male C57Bl6 (red)** and **young adult Wistar female rats (blue).** Mann-Whitney t-test was used. ns= P>0.05; *= P<0.05; **= P<0.01; ***= P<0.001.

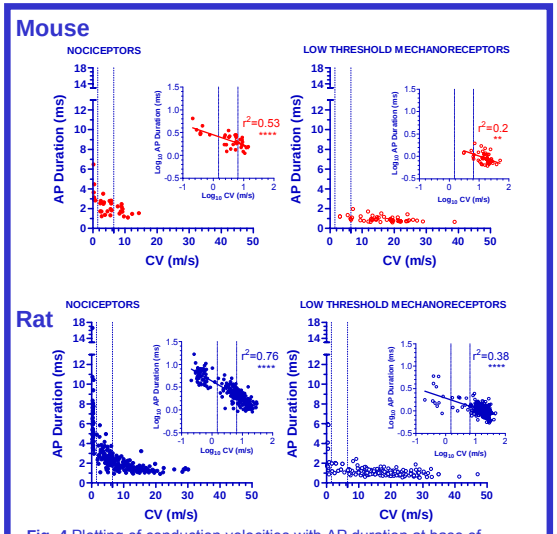


Fig. 4 Plotting of conduction velocities with AP duration at base of identified DRG neurones recorded from mouse (top) and rat (bottom). **, P<0.01; ****, P<0.0001. The plots show similar patterns except for a highly significantly (P<0.0001) steeper slope for the rat than the mouse nociceptors (double log plots).

SUMMARY OF RESULTS

Rat / Mouse	Noc Vs LTM C	Noc Vs LTM Ad	Noc Vs LTM Ab	Noc C Vs Noc Ad	Noc Ad Vs Noc Ab	Noc C Vs All Noc A
APdB	↑ -	↑ -	↑↑	↑↑	↑ ns	↑↑
APRT	↑ -	↑ -	↑↑	↑↑	↑ ns	↑↑
APFT	↑ -	↑ -	↑↑	↑ ns	↑ ns	↑↑
APos	↑ -	↑ -	↑↑	ns ns	ns ns	ns ns
AHP80	↑ -	↑ -	↑↑	ns ns	ns -	ns ns

SUMMARY

1. **Similarities in values between mice and rats:**
   i) C-fiber nociceptors: the AHPs and AP overshoots
   ii) A-fiber nociceptors: AP duration (both rise times and fall times) and AHPs
2. **Similarities in relationships between nociceptors and LTMs between rats and mice**
   i) As in rat, mouse A-fiber nociceptors had longer AP and AHP durations, and larger AP overshoots, than A-fiber LTMs
3. **Differences between mice and rats, mice have:**
   i) C-fiber nociceptors: shorter duration APs with faster rise and fall times
   ii) All nociceptors: different slope in relationship between AP duration and CV.
   iii) A-fiber nociceptors: greater overshoots in mouse than in rat

These results show many similarities and suggest possible differences in ion channel activities in mouse and rat nociceptors, although gender and greater mouse age may contribute.

Reference:
Fang X, McMullan S, Lawson SN, Djouhri L (2005). J Physiol 565: 927-943.

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