# Apparent lack of effect of oxaliplatin systemic treatment on the activity of unmyelinated nociceptors

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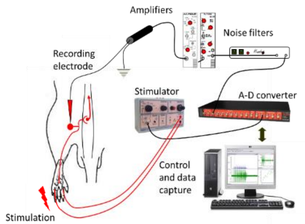
## Aim

To characterize the effects of systemic oxaliplatin on the activity of dorsal root ganglia (DRG) neurons with unmyelinated distal axons in C57BL/6 mice.

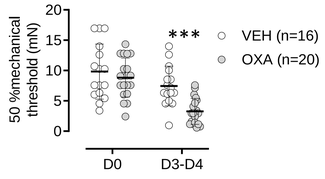
## Set up and method




Single i.p. injection of 6 mg/kg oxaliplatin or corresponding vehicle (5% glucose) in C57BL/6 mice.
Behavioural mechanical sensitivity assessed before oxaliplatin and 3-4 days after injection the day of DRG neurons recording.
L4 DRG neurons activity measured under isoflurane anaesthesia using a conventional rig for single-unit extracellular recording.

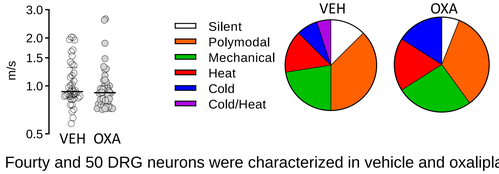
## Results

### 1 Oxaliplatin-treated mice displayed mechanical allodynia



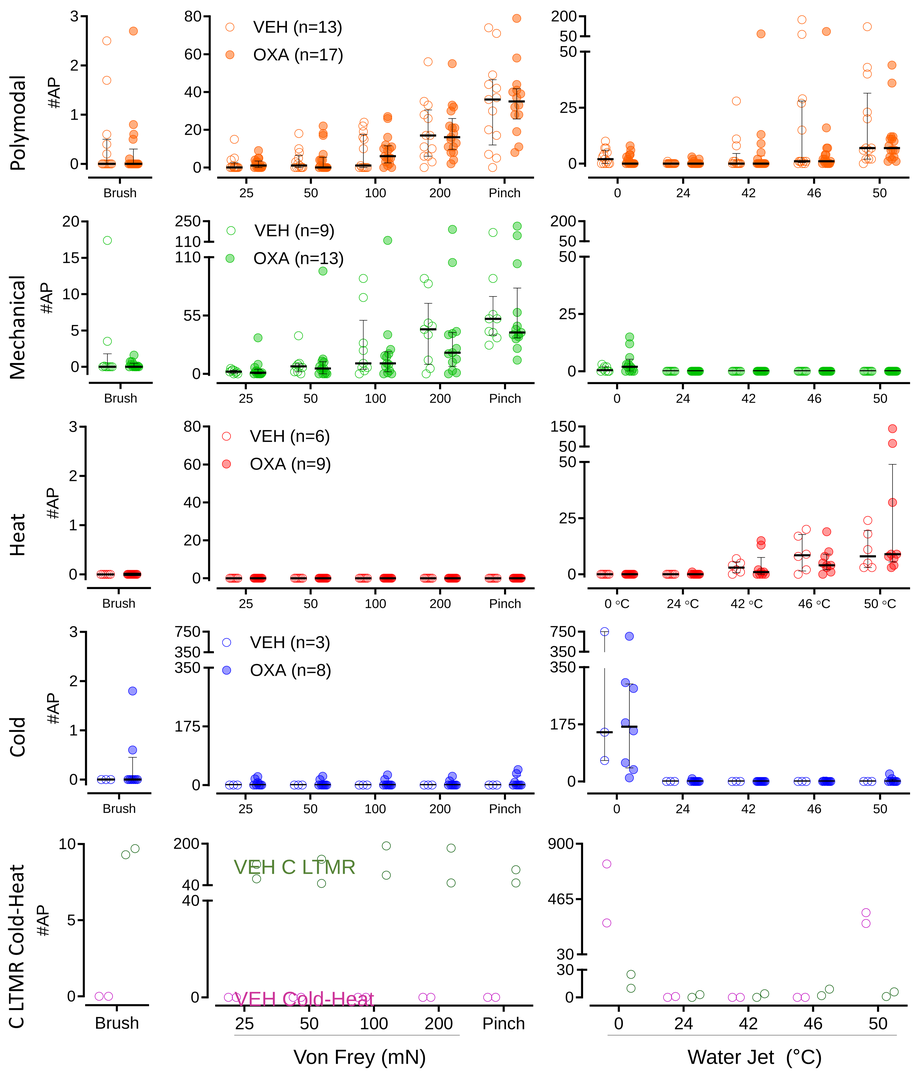

Mechanical threshold determined using the method of Chaplan et al., J Neurosci Methods, 1994, 53, 55-56.
***: p<0.001, Bonferoni multiple comparisons after 2 way ANOVA with RM.

### 2 Conduction velocities and modality distribution were similar between treatments



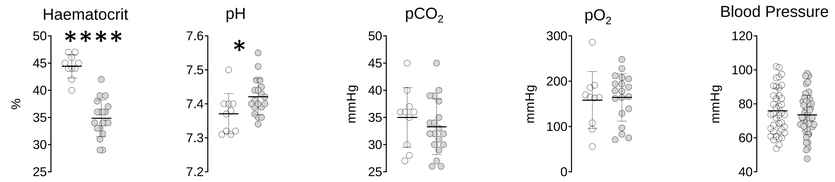

Fourty and 50 DRG neurons were characterized in vehicle and oxaliplatin-treated mice.
All, but 2 C low threshold mechanical receptors (C LTMR) and 8 silent receptors, were nociceptors.

### 3 Evoked responses were similar between treatments



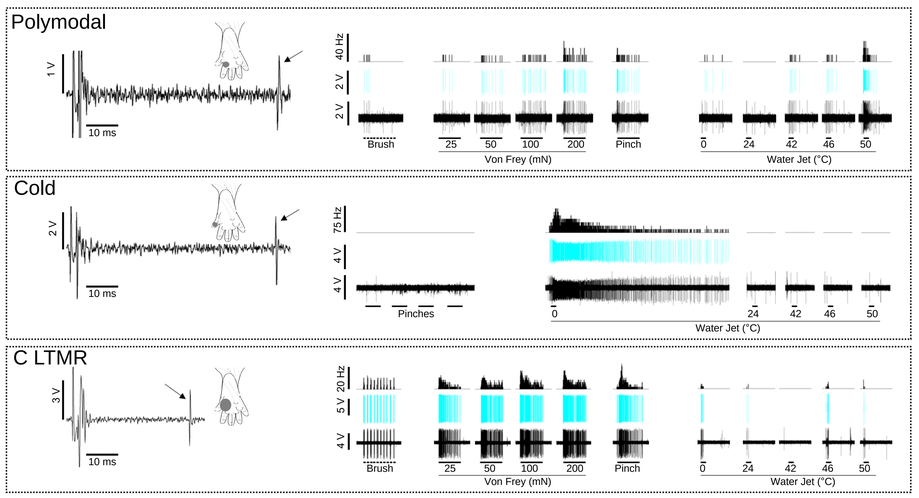

Evoked responses expressed as number of action potentials (AP); initial activity measured for 60 s; brush, mean of 10 successive sweeps; Von Frey and pinch applied for 6 s, measured for 5 s; thermal stimuli applied with water jet (10 ml, 2-3 s duration), measured for the entire duration of the response (3-30 s).
Cold-heat and C LTMR were only observed in the vehicle group (corresponding responses shown in purple and green on the lower graphs).
Data shown as individual values and median±interquartile range.

### 4 Oxaliplatin significantly decreased haematocrit




Blood biochemistry was measured in 10 VEH and 16 OXA mice at completion of the experiment. Blood pressure was measured during each individual DRG neuron recording (40 and 50 VEH and OXA measures, respectively). *, p<0.05; ****, p<0.0001; t-test.
Note the inverse correlation between pH and $pCO_2$, suggesting that the difference in ventilation might be at the origin of the difference in pH.
Data shown as individual values and mean±standard deviation.

### 5 Examples of recordings




Left hand side: response to electrical stimulation delivered as square wave pulse, 2 ms, 1 to 10 mA, using needles placed on each side of the receptive field. Arrow: nociceptor action potential (note the long latency).
Right hand side: responses to mechanical and thermal stimuli, showing the raw recording (lower line), the filtered action potentials (middle line), and the corresponding peristimulus histogram (upper line, number of AP/0.1 s bin).
Amplitude after 20 k gain.

## Conclusion

We did not observe mechanical-sensitization or cold-sensitization of “C fibre nociceptors” after a single dose of 6 mg/kg oxaliplatin. Yet, this treatment induced mechanical allodynia and anaemia.
The present result is in line with the induction of cold-response/cold-sensitization of myelinated, but not unmyelinated, DRG neurons by oxaliplatin. It also suggests that mechanical allodynia is not caused by changes in mechanical responsiveness of “C fibre nociceptors”.

Descoeur et al, EMBO Mol Med 2011, 3:266-278.
Sittl et al, PNAS 2012, 109:6704-6709.
MacDonald et al, Brain 2021, 144:1711-1726.