Differential sensitization of lamina I and lamina III-V neurons projecting to and/or through the parabrachial area in chronic inflammatory condition in anaesthetized mice

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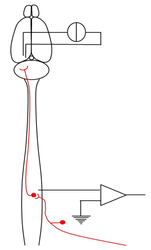
Aim

- Lamina I spinoparabrachial (SPB) neurons form the major ascending pain-related pathway in rodents, and contribute to both acute and chronic pain.
- Current research on lamina I SPB neurons in mice is exclusively based on recording from spinal cord slice, with all limitations attached.
- The aim of the present study was to evaluate the sensitization of lamina I and lamina III-V neurons projecting to and/or through the PB area in vivo using a simple model of chronic inflammation.

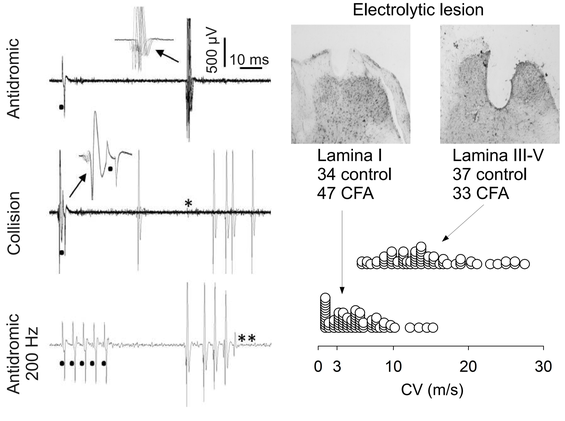
Set up and method



- Induction of chronic inflammation with s.c. injection of 25 µl complete Freund's adjuvant (CFA) in the plantar surface of the hind paw.
- Extracellular recording of lamina I and III-V projection neurons under deep anaesthesia in controlled physiological conditions 24 or 48 h after injection.
- Search of projection neurons based exclusively on antidromic stimulations from the PB area.

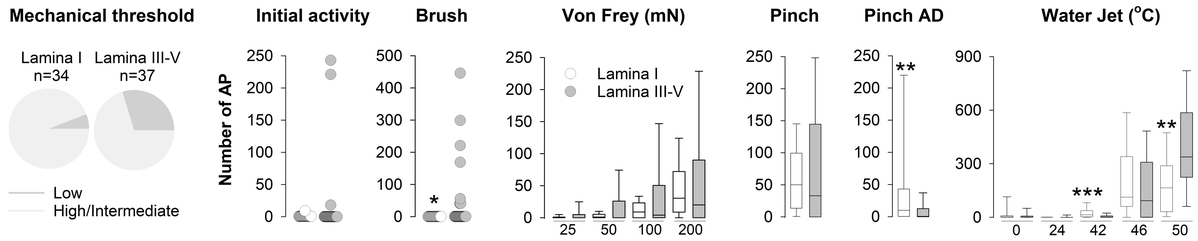
Results

1 Slower conduction velocity (CV) of lamina I compared to lamina III-V projection neurons



- "Antidromic" and "Collision": overlay of 10 successive responses.
- Missing action potential (**AP**): *, collided; **, axon to soma conduction failure.

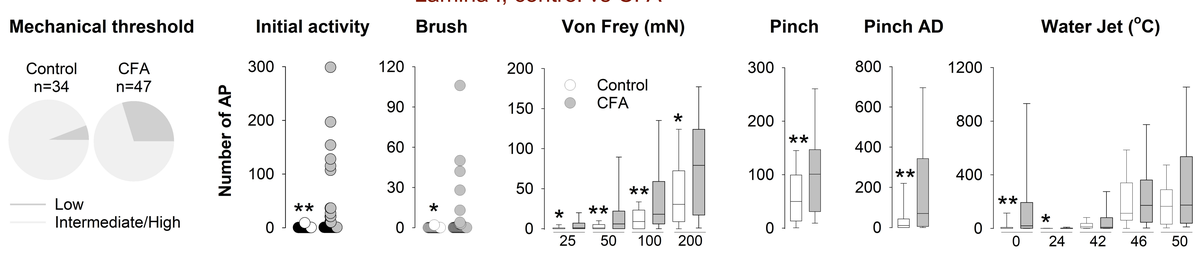
2 Exclusive presence of COLD and WDR projection neurons in lamina I and lamina III-V, respectively



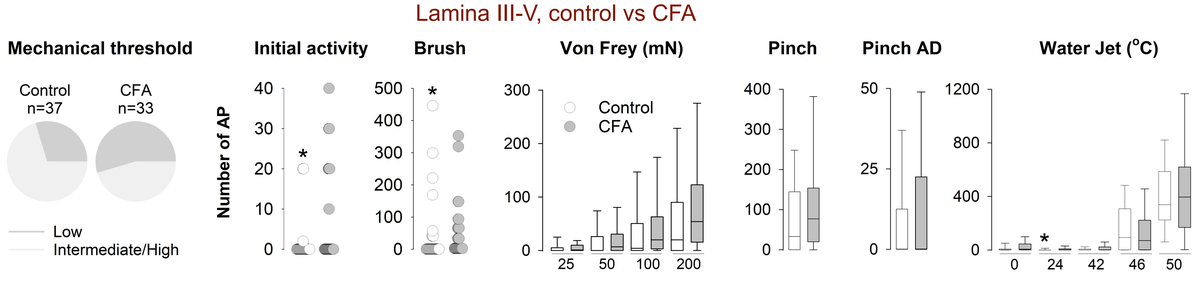
- Included in the 34 lamina I units, 3 COLD and 2 HEAT; in the 37 lamina III-V units, 3 TOUCH and 8 HEAT (5/8 responding with 2-3 s delay to water jet).
- COLD and wide dynamic range (WDR) projection neurons were only found in lamina I and lamina III-V, respectively. Nociceptive specific (NS) projection neurons were not restricted to lamina I.

3 Marked sensitization of lamina I compared to lamina III-V projection neurons after CFA injection

Lamina I, control vs CFA



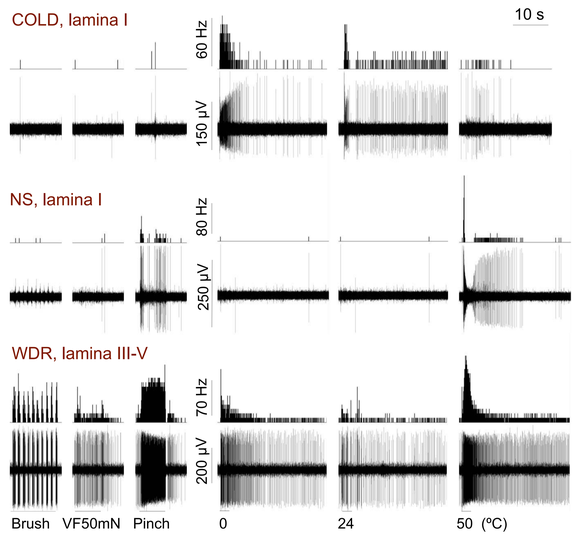
Lamina III-V, control vs CFA



- Note the mechanical and thermal (cold) sensitization of lamina I compared to lamina III-V projection neurons.
- Responses to WJ 50 ºC could not be measured in 37/81 lamina I neurons because of drop in action potential amplitude (see Results 4, NS response).

- *For the above graphs:*
- Low mechanical threshold, >5 AP in response to Von Frey 25 mN or/and brush.
- Initial activity: "spontaneous activity" over 1 min; Brush: sum of AP for 10 successive brushes; Von Frey and pinch: measured for 5 s; **Pinch AD**: pinch after discharge.
- Boxes: 10th, 25th, 50th, 75th and 90th percentile. *, p<0.05; **, p<0.01; ***, p<0.001. Mann-Whitney rank sum test.

4 Recording illustrations



Discussion

- The "abundance" of lamina III-V projection neurons obtained in the present study contrasts with the scarcity of lamina III-V SPB neurons identified on anatomical basis. It is likely that many (most?) lamina III-V neurons characterized herein were spino(hypo)thalamic (ST) neurons.
- The present data support that lamina I SPB neurons plays a role in the generation of allodynia and hyperalgesia upon chronic injury, but it does not rule out a significant contribution of lamina III-V projection neurons.
- The determination of the exact projection site of the different projection neurons is required for a better understanding of the function of the lamina I SPB and lamina III-V SPB or ST pathways.

References

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