Characterisation of pain sensitivity in ageing mice

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Chronic pain is reported to increase with ageing and the increased life expectancy together with the current lack of effective and safe drugs tailored for this specific patient population makes pain management in the elderly a clear challenge for future years (Arneric et al., 2013). The effect of ageing on pain sensitivity and threshold is currently not well defined and research, focused on how ageing impacts on pain processing, has so far yielded mixed results both in humans and in experimental pre-clinical models (Cole et al., 2010; Yezierski, 2012).

This study aimed at examining the effects of ageing on pain processing at behavioural and molecular level. Pain behaviour was assessed in 2 month-old C57BL/6 mice and in ageing (6, 12, 18 months) C57BL/6 mice; molecular changes were investigated at spinal cord level in different age groups (2, 6, 12 month-old C57BL/6 mice).

Sensitivity to mechanical and thermal stimuli measured by Von Frey's, pinprick, Hargreaves and acetone tests progressively increased with ageing. At molecular level, the expression of some markers of autophagy, an intracellular homeostatic process implicated in ageing (Cuervo et al., 2005) and more recently in pain mechanisms (Berliocchi et al. 2011, 2015), was investigated in the dorsal spinal cord. No relevant age-related changes were detected in basal levels of the autophagic markers LC3 and p62, but a progressive decrease in Beclin-1 expression was observed.

Also the analysis of the Ca^{2+}-channel subunit $\alpha_2\delta$-1 revealed age-related changes in spinal cord expression of this biochemical marker, suggesting the possibility of a different response to drugs like gabapentinoids, that target this subunit and are commonly used for pain management in the elderly. To verify this, the formalin test (Dubuisson & Dennis, 1977) was used to evaluate pain behaviour in 2 month-old C57BL/6 mice and in 6 month-old C57BL/6 mice and the effect of the intraperitoneal (i.p.) administration gabapentin (10 mg/Kg and 100 mg/Kg) on the formalin-evoked nocifensive behavior was investigated and compared with the treatment with vehicle. Results showed different pain sensitivity following formalin injection and relevant differences in the pharmacological response between different age groups.