Altered endogenous pain inhibitory function in older adults with chronic pain: an fMRI study.

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IBRO 2023
11th IBRO World Congress of Neuroscience
GRANADA SPAIN · 9-13 September · 2023

Introduction

Chronic pain results in a vast global clinical burden being highly prevalent in the aged population, affecting about 50% of people over 65 years old (Dahlhamer et al., 2018). Increasing research points to a decline in the ability to internally regulate pain as a main contributing factor to this higher pain susceptibility in aging (Hackett et al., 2020). Therefore, the present study aimed to compare the resting state functional connectivity (rsFC) between pain-related brain structures in a group of older adults with chronic musculoskeletal pain with a group of pain-free older adults and young individuals. Moreover, we explored the association between alterations in rsFC in older adults with chronic pain and their pain inhibitory and facilitatory capability, measured using Conditioned Pain Modulation (CPM) and Temporal Summation (TS) paradigms, respectively.

To examine the rsFC in older adults with chronic pain and its association with their pain modulation capabilities, to better understand how chronic pain and aging combine.

Materials and Methods

Participants. 30 older adults with musculoskeletal chronic pain (69,5±6.58 years; 14 males), 29 pain-free older adults (70.483±4.60 years; 15 males), and 30 pain-free younger adults (20.0 ±1.58 years; 15 males).

Temporal summation (see Figure 1)**:** Electrical stimulation (trains of 3 stimuli of 1ms duration, separated by 5ms) was applied to the dorsum of the non-dominant hand (left). The TS was calculated comparing the pain sensation, measured with a VAS (0-100), evoked by a single pulse and the pain sensation of 5 individual stimuli applied with an ISI of 500 ms.

Conditioned pain modultation (see Figure 2)**:** Pressure-pain algometry was applied three times as the test stimulus before and after the application of the conditioning stimulus, which consisted of 90 seconds of tonic interdigital web pinching adjusted to elicit a pain intensity of 5 on a (0-10) VAS.

Data analysis. 1. CPM and TS measures were analyzed with a univariate ANOVA (young vs. older vs. older with pain). **2.** ROI to ROI rsFC anylisis between pain related structures was performed. **3.** Pearson's correlations were computed between rsFC showing significant differences between groups and the CPM and TS measures.

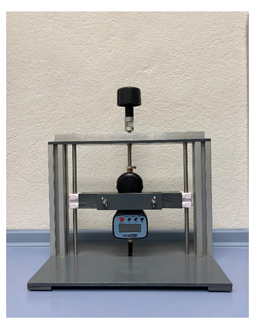


Fig. 1. Temporal summation (TS)

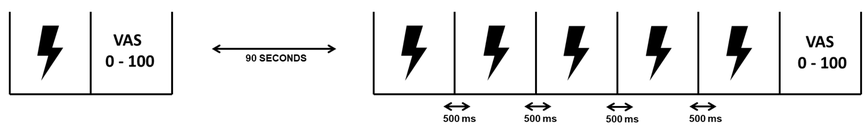
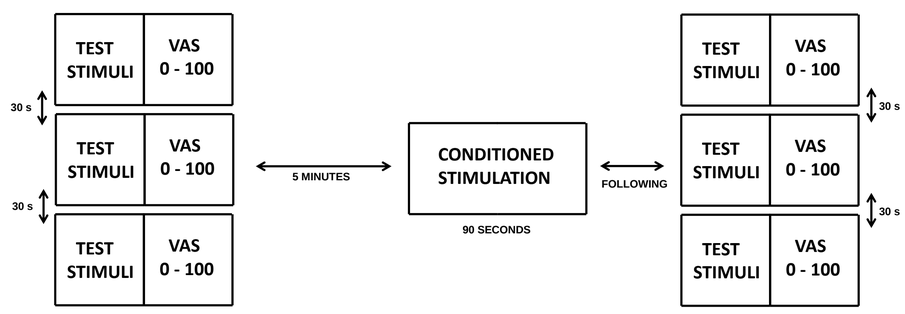


Fig. 2. Conditioned Pain Modulation (CPM)



Results

1. **CPM and TS measures.** Older adults with chronic pain showed reduced CPM in comparison to healthy older adults ($p = 0.022$) and younger adults ($p < 0.001$), while no differences were found between healthy older adults and younger adults ($p = 0.185$). No significant differences between groups were found in TS ($p = 0.625$) (see Figure 3).

2. **rsFC comparison.** Older adults with chronic pain displayed higher connectivity between SI and nucleus accumbens (NAc) (bilateral) (all $p < 0.025$) in comparison to pain-free older adults, and between dlPFC (R) and AMY (L) ($p = 0.0026$) in comparison to younger ones (see Figure 4)). Finally, both groups of older adults showed a decreased rsFC between pain-related structures (INS, AMY, THA, PAG) in comparison to younger participants (all $p < 0.05$).

3. **Pearson correlations.** Correlational analyses showed that functional connectivity between dlPFC (R) and AMY (L) was negatively associated with the CPM index in the older with chronic pain group ($p = 0.008$) (see Figure 5). No significant correlation with electrical TS was found.

Fig. 3. CPM and TS measures.

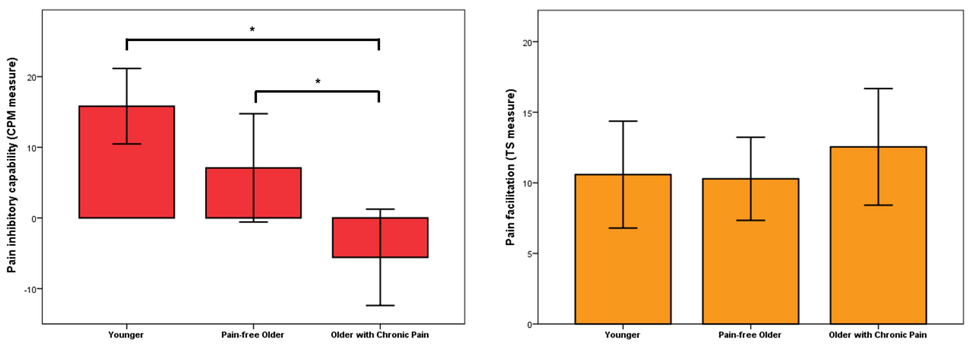


Fig. 4. rsFC comparison between groups.

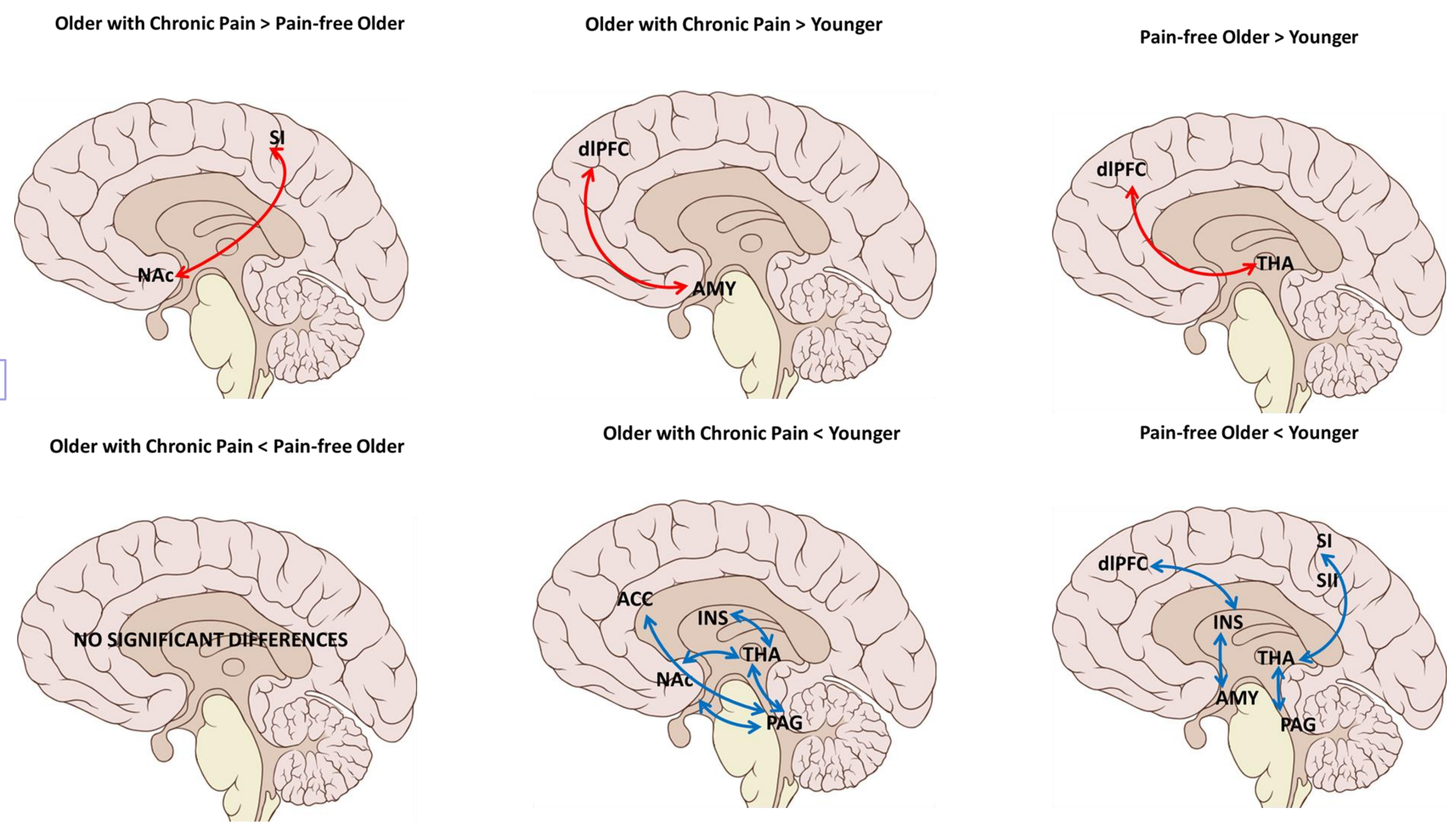
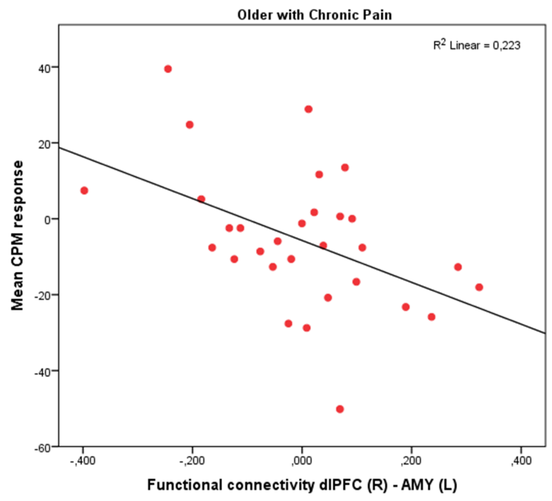


Fig. 5. Pearson correlation between rsFC and CPM measure.



Conclusions

Older participants with chronic pain displayed reduced endogenous pain inhibitory function which was related to increased connectivity between dlPFC and amygdala, suggesting that enhanced projections from the amygdala could be implicated in a pain-related cortical deactivation disfunction. Moreover, suffering from chronic pain in aging leaded to increased connectivity on brain structures linked to evaluative and motivational dimensions of pain experience (SI - NAc). Finally, both older adults' groups showed a decreased rsFC between structures related to pain inhibition. Altogether our results suggest that suffering from pain in older adults leads to different alterations in brain functioning and a dysfunction of pain inhibitory processes which significantly surpass those produced by normal aging.

References

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This study was supported by the Spanish Ministry of Economy, Industry and Competitiveness (PID2019-110096GB-I00 / AEI /10.13039/501100011033).

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