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Age-Related Decline in Cognitive Pain Modulation Induced by Distraction: Evidence From Event-Related Potentials

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Abstract: Distraction is known to reduce perceived pain but not always efficiently. Overlapping cognitive resources play a role in both pain processing and executive functions. We hypothesized that with aging, the analgesic effects of cognitive modulation induced by distraction would be reduced as a result of functional decline of frontal networks. Twenty-eight elderly and 28 young participants performed a tonic heat pain test with and without distraction (P + D vs P condition), and 2 executive tasks involving the frontal network (1-back [working memory] and go/no-go [response inhibition]), during which event-related potentials were recorded. A significant age-related difference in modulatory effect was observed during the pain-distraction test, with the older group reporting higher pain perception than the younger group during the P + D than during the P condition. Greater brain activity of early processes (P2 component) in both go/no-go and 1-back tasks correlated with less perceived pain during distraction in younger participants. For later processes, more cognitive control and attentional resources (increased N2 and P3 amplitude) needed for working memory processes were associated with greater pain perception in the older group. Inhibition processes were related to conscious distraction estimation in both groups. These findings indicate that cognitive processes subtended by resources in the frontal network, particularly working memory processes, are elicited more in elderly than in younger individuals for pain tolerance when an irrelevant task is performed simultaneously.

***Perspective:** This study suggests that age-related declines in pain modulation are caused by functional degeneration of frontal cerebral networks, which may contribute to a higher prevalence of chronic pain. Analyzing the impact of frontal network function on pain modulation may assist in the development of more effective targeted treatment plans.*

***Key words:** Tonic heat pain, distraction, aging, frontal network, pain modulation.*

Pain symptoms are reported by about 50% of older adults and are strongly associated with decreased quality of life.[33] Impaired pain modulation is a risk factor in the development of chronic pain[1,52] and therefore may contribute to the frequency of chronic pain in the elderly.

Pain modulation can be assessed using a bottom-up protocol, such as diffuse noxious inhibitory control (DNIC), in which ascending information (ie, tolerating tonic pain) induces descending inhibitory modulation of pain perception (ie, pain inhibits pain effect) and involves a spinal-medullary-spinal pathway.[46] One potential indicator of descending inhibition is resistance to pain, which can be assessed experimentally. Using this method, the efficacy of DNIC-induced analgesia was shown to be reduced in older adults.[14,22,40,49] Cognitive inhibition was recently found to correlate positively with tonic pain tolerance[53] and DNIC effect[28] in healthy elderly individuals, suggesting that functional declines in the frontal network may contribute to less efficient descending inhibition during normal aging. However, using these methods, the potential cognitive-emotional effects on modulation processes cannot be monitored experimentally, preventing the complete measurement of endogenous pain modulation.

Top-down pain modulation engages mainly the frontal cortex network,[21,42] one of the most vulnerable brain

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regions in aging.[36,38] Specifically, the prefrontal cortex (PFC) shows the greatest degree of atrophy with age. Executive functions, which are underpinned by the frontal lobes, were found to be affected in elderly individuals,[50] with their performance on executive tests correlating with structural and metabolic modifications in the frontal network.[37,43] Executive control of pain is related to the strategy by which an individual copes with pain, both cognitively (how the individual feels) and behaviorally (what the individual does).[51] In experimental pain studies, distraction is frequently used to induce a cognitive top-down modulation.[10] The effectiveness of distraction was shown to be related to the outcome of the competition between pain and distractors subtended by overlapping cognitive resources in the frontal networks.[9] Thus, distraction is considered a conscious pain control model involving frontal networks. Because functional decreases in the frontal cortex are more pronounced in elderly adults than in younger adults,[36,38,43] we hypothesized that with aging, the analgesic effect of distraction would be reduced as a result of diminished frontal functioning.

To assess the role of age-related functional decreases of the frontal networks in pain modulation, participants also performed the N-back test to evaluate working memory[12] and the go/no-go test to determine response inhibition.[15] These 2 processes are important for successful control of pain and are subtended by frontal networks. Working memory guides the orientation of attention by maintaining goal priorities active during the achievement of a task. Inasmuch as tolerating pain is highly demanding, the reduction of working memory resources in the elderly may limit their capacity to allocate resources toward distractions, thus reducing the analgesic effect of distraction. Inhibition refers to intentional control over goal-irrelevant mental processes and motor responses. Performances on inhibition tasks have been associated with both perceived intensity and behavior (duration of tolerance) on pain tolerance tests.[31,53] Because many studies have shown age-related reductions in inhibition performance,[28,47] we hypothesized that older individuals would be less efficient in inhibiting the avoidance impulse induced by pain. During these tasks, we also measured different components of event-related potential (ERP) recording, which can provide information on the brain activity of subprocesses. We particularly focused on cognitive control processes at early (P2) and late (N2) stages, inhibition processes (no-go P3), and attentional allocation in working memory processes (N-back P3). The correlations between distraction effects and these cognitive processes may help to reveal which processes are most affected by aging.

Methods

The present study is composed of 2 parts: a pain-distraction test and 2 executive function tasks with ERP recordings. Pain-distraction tests were used to investigate age-related differences in pain modulation function. Subsequently, distraction effects were correlated with the performance of executive tasks and brain activities to assess the effect of aging on cerebral mechanisms during pain modulation processes. All procedures were in accordance with the guidelines of the local ethics committee, which approved the study. The study was in line with the Declaration of Helsinki protocols.

Participants

All participants were paid and all provided written informed consent before participation. Participants were recruited by means of advertisements. Before inclusion, all participants were screened to exclude conditions that could alter pain perception, including peripheral neuropathy, multiple sclerosis, diabetes, stroke, hypertension, and psychiatric disorders. Normal or corrected visual and auditory abilities were also investigated (using audiogram and visual tests) to exclude perceptual disabilities. All older participants were assessed using the Mini Mental State Examination (MMSE) to exclude cognitive impairment (total score >27). Participants with chronic pain were excluded by asking if they had experienced pain every day for 3 months during the 6 months before the interview. Each participant completed the French version[29] of the Dallas Pain Questionnaire,[23] which assesses the severity of pain conditions (if applicable) on daily life in multidimensional aspects. Participants with severe clinical pain, who may have cerebral modifications as in chronic pain, were also excluded.

Sixty-five participants, 35 older adults and 30 younger adults, were recruited. All the older participants had total scores >27 on the MMSE (mean = 29.03, standard deviation [SD] = .96). Seven of the 35 older participants reported occasional and mild pain conditions, mostly caused by low back pain and joint pain. These participants had Dallas scores of class 1 or 2, confirming that their pain condition had minor to moderate impact on daily life.[32] These older participants were therefore included. No participant was taking any analgesic medications at the time of testing. One younger participant and 7 older participants were excluded because they could not tolerate the experimental procedures (ie, failed to achieve the target time of exposure [ET] in the second session of the pain test). One younger participant reported no pain and was also excluded. The study cohort thus consisted of 28 younger adults (14 men, 14 women; mean age = 24.8 $\pm$ 2.6 years) and 28 older adults (14 men, 14 women; mean age = 67.5 $\pm$ 4.7 years) (Table 1).

A comparison of demographic data showed that the 2 groups were comparable except that the younger group had between 1 and 2 more educational years than the older group (level 4.6 vs 3.8, $F_{(1,55)} = 11.71$, $P = .001$), and the older group had higher scores on the Pain Catastrophizing Scale (PCS)[17] than the younger group (22.4 vs 16.0, $F_{(1,55)} = 4.95$, $P = .030$). Thus, education and catastrophizing scores were included as between-group covariants and statistically controlled in all subsequent analyses.