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Offset Analgesia is reduced in older adults

Kelly M. Naugle, Yenisel Cruz-Almeida, Roger B. Fillingim, and Joseph L. Riley III

University of Florida, College of Dentistry, and Pain Research and Intervention Center of Excellence, University of Florida

Abstract

Recent studies indicate that aging is associated with dysfunctional changes in pain modulatory capacity, potentially contributing to increased incidence of pain in older adults. However, age-related changes in offset analgesia (offset), a form of temporal pain inhibition, remain poorly characterized. The purpose of this study was to investigate age differences in offset analgesia of heat pain in healthy younger and older adults. To explore the peripheral mechanisms underlying offset, an additional aim of the study was to test offset at two anatomical sites with known differences in nociceptor innervation. Twenty-five younger adults and twenty older adults completed six offset trials in which the experimental heat stimulus was presented to the volar forearm and glabrous skin of the palm. Each trial consisted of three continuous phases: an initial 15s painful stimulus (T1), a slight increase in temperature from T1 for 5s (T2), and a slight decrease back to the initial testing temperature for 10s (T3). During each trial, subjects rated pain intensity continuously using an electronic visual analogue scale (0–100). Older subjects demonstrated reduced offset compared to younger adults when tested on the volar forearm. Interestingly, offset analgesia was nonexistent on the palm for all subjects. The reduced offset found in older adults may reflect an age-related decline in endogenous inhibitory systems. However, while the exact mechanisms underlying offset remain unknown, the absence of offset at the palm suggests that peripheral mechanisms may be involved in initiating this phenomenon.

Keywords

Pain modulation; aging; elderly; offset analgesia

1. Introduction

The burden of chronic pain among older adults is substantial, with up to 60% of adults over 65 years reporting chronic pain in large community-based samples [48]. Pain is modulated by complex endogenous systems that facilitate and inhibit pain, and an imbalance of these systems may underlie multiple chronic pain conditions [23,25,27,29,35,42]. Prior work also

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Corresponding Author: Kelly M. Naugle, College of Dentistry, University of Florida, 1329 SW 16th Street, Rm 5180, Gainesville, FL 32608, Phone: 352-273-5975, Fax: 352-273-5985, knaugle@dental.ufl.edu.

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Summary

Offset analgesia was reduced in older adults compared to younger adults when tested on the volar forearm and nonexistent for all subjects on the palm.

Disclosure Statement

There are not actual or potential conflicts of interest for any of the authors.

suggests that diminished pain inhibitory capacity contributes to the high prevalence of pain among older adults [9,40,47]. Most recently, Riley and colleagues observed decreased endogenous pain inhibition among older compared to younger adults using conditioned pain modulation (CPM). CPM is the central inhibition of pain in a local area by a second heterotopic pain stimulus [50].

Offset analgesia (offset) is another experimental model engaging endogenous pain inhibition [16], whose generation and neuroanatomical pathways are distinct from those of CPM [30,34]. Offset refers to a pronounced reduction in perceived pain intensity evoked by slight decreases in noxious temperatures compared to those of equal magnitude increases [16]. Investigators have suggested that offset acts as an inhibitory temporal sharpening mechanism that amplifies reductions in noxious stimulus intensities [51]. Niesters et al. showed that offset analgesia was present in over 100 healthy volunteers, regardless of sex and age [35]. However, these findings are limited because the oldest cohort (60–80 years) included only 7 subjects, and offset was assessed with only one trial and without individualized test temperatures. Thus, more research is needed to determine whether this inhibitory process changes with age.

In all studies investigating offset, thermal stimulation has been applied to the non-glabrous (“hairy”) skin of the forearm or leg. Myelinated A-fiber and unmyelinated C-fiber nociceptors are present in the primate hairy skin [1,44], transmitting qualitatively different neural information to the spinal cord. A-fiber nociceptors transmit discriminate aspects of pain perception (first pain), while C-fiber nociceptors transmit late burning pain sensations (second pain). Two types of A-fiber afferents have been identified in the primate hairy skin, A-fiber mechano-heat Type I (AMH-I) and Type II (AMH-II) nociceptors [44,45]. AMH-II fibers are activated in the 43°C–49°C range and appear to be absent in the glabrous skin of primates [1,33,45]. No studies have explored potential anatomical site differences and contribution of peripheral mechanisms in offset. Since age-related primary afferent dysfunction appears to be important in changes in pain sensitivity, the differential nociceptor innervation of the thenar eminence and forearm permits the exploration of potential peripheral factors involved in offset and its relation to chronological age [45].

The primary aim of this study was to test the hypothesis that healthy older adults will exhibit reduced offset analgesia compared to younger adults. Additionally, evidence is inconsistent regarding sex differences in experimental models of endogenous pain modulation [10]. Thus, a second aim of the study was to evaluate possible sex differences in offset, and whether sex and age interact. Finally, to explore the peripheral mechanisms underlying offset, a third aim of the study was to test whether offset exists on the glabrous skin of the palm in addition to the volar forearm.

2. Methods

2.1. Subjects

Twenty-five healthy younger adults (age range: 18–27 years) and twenty healthy older adults (age range: 58–77 years) participated in this study. Subject and age group descriptors are presented in Table 1. Subjects were excluded if they met any of the following criteria: 1) inability to reliably rate pain, 2) current use of narcotics or any tobacco products, chronic use of analgesics, 3) serious systemic disease (e.g., diabetes and thyroid problems, 4) uncontrolled hypertension, 5) cardiovascular or pulmonary disease, 6) neurological problems with significant changes in somatosensory and pain perception at the intended stimulation sites, 7) serious psychiatric conditions (e.g., schizophrenia and bipolar disorder), and 8) chronic pain or any ongoing pain problem (headaches, injury-related pain, etc.). Subjects refrained from the use of any pain medication or coffee on the day of testing.

2.2. Study procedures

2.2.1. Orientation and training session—Persons who expressed interest in the study were provided information about the procedures, informed about HIPPA regulations and reviewed and signed an Informed Consent Form. To determine eligibility, subjects completed a health history questionnaire, supplemented by interview and a blood pressure measurement. Subjects then completed a training session to ensure comfort during the testing protocol and to teach them the continuous pain rating system.

2.2.2. Testing session—Upon arriving to the laboratory, subjects were seated on a comfortable chair and asked to relax for several minutes. Next, they were asked about their health, any medication use, and shown a video that described the experimental procedures. Then, two blood pressure readings were taken separated by 5 minutes. A third blood pressure measurement was taken if there was a change of greater than 5% in the first two readings. The temperature of the thermode to be used in the offset trials was then determined for each subject. The goal was to determine temperatures at which subject's experienced mild to moderate pain for a 30-s heat stimulus. The thermode temperature was set at 42°C for the first trial and increased across trials so that a stimulus response curve could be calculated. The temperatures were increased to a maximum pain rating of 60 (on a scale of 0–100). Two male subjects in the older adult group failed to reach the target pain ratings were assigned 49°C for the offset trials. An individualized test temperature was determined for both the thenar eminence of the palm and volar forearm. Six 30-s trials were then administered in which the experimental stimulus was presented to either the thenar eminence of the right palm or the right volar forearm. Stimulus site was alternated between trials and a minimum of a 60 s interstimulus interval was maintained to reduce sensitization.

2.2.3. Experimental Stimulus—Focal thermal stimuli (44–49°C) were administered by a Peltier-based thermode (23 mm × 23 mm). For each 30 s trial, a three-temperature stimulus train (e.g., 48°C [15 s], 49°C [5 s], 48°C [10 s]; See Figure 1) was used to quantify the magnitude of offset analgesia [16]. The thermode was brought to a neutral temperature (32°C), and then brought into light skin contact with a solenoid. After a short period, the temperature was ramped (40°C/s) to the subject's testing temperature for 15 s (T1). While past offset research has commonly used a duration of 5 s for T1, we chose 15 s to allow perceived pain to stabilize and provide a more valid comparison with the last phase of the temperature train. Then the thermode was heated an additional 1°C (forearm trials) or 0.5°C (palm trials) for 5 seconds for a manipulation phase (T2) and then cooled back to the subjects testing temperature (40°C/s) for 10 s for the inhibition or offset phase (T3). Importantly, preliminary testing ($N=6$; data not shown) indicated that a 0.5°C increase at the palm evokes an increase in pain intensity ratings that are similar in magnitude to a 1.0°C increase at the forearm (approximately 20 points on a 100 point scale). Furthermore, the results of the preliminary testing suggested that the magnitude of offset (100%=greatest inhibition; 0%= no inhibition) at each site was not influenced by the magnitude of temperature increase/decrease: 1) magnitude of offset for forearm at $\pm 1^\circ\text{C} = 82\% \pm 26\%$, 2) magnitude of offset for forearm at $\pm .5^\circ\text{C} = 80\% \pm 27\%$, 3) magnitude of offset for palm at $\pm 1^\circ\text{C} = 34\% \pm 23\%$, 4) magnitude of offset for palm at $\pm .5^\circ\text{C} = 36\% \pm 28\%$. The results of this study supported this finding. Thus, given that we are most concerned with the magnitude of change in perceived pain, rather than the magnitude of change in temperature, we chose an increase of 0.5°C for the palm and 1.0°C for the forearm. Furthermore, preliminary testing showed that a 1.0°C increase from T1 to T2 at the palm significantly increased the likelihood that pain ratings would approach an intolerable level.

2.3. Assessment of pain intensity

During each trial, subjects rated pain intensity continuously using the electronic visual analogue scale (eVAS). The eVAS consisted of a low friction sliding potentiometer (100 mm travel) with the following two anchors: the left endpoint designated as “no pain” (0) and the right endpoint as “intolerable pain” (100). Subjects were instructed to move the slider in proportion to their pain intensity in real time. Continuous ratings of heat pain provided a temporal profile of pain intensity over the trial duration.

2.4. Data Analysis

Individualized test temperatures for the offset trials were analyzed with a three-way ANOVA with site as the within subjects factor and age and sex as the between subjects factors. Trials in which subjects did not report pain during T1 were removed from the data analysis, because these trials are susceptible to a floor effect which prevents a true detection of offset analgesia. Four trials out of 135 were removed from the analyses of offset at the forearm and twelve trials out of 135 were removed from the analyses of offset at the palm. Offset has typically been evaluated by two different methods: 1) a comparison of the magnitude of pain increase from T1 to T2 to the magnitude of pain decrease from T2 to T3 [7, 16], and 2) evaluation of the absolute or adjusted magnitude of decrease in perceived pain following the temperature decrease [30, 34, 35]. We analyzed our data using both methods.

We first wanted to determine whether the temperature decreases (T2-T3) produced larger changes in pain intensity ratings than the equal magnitude temperature increases (T1-T2) and whether these changes differed between age, sex, and testing site. Thus, pain intensity ratings from the real time data were extracted during T1 approximately 100 ms prior to the beginning of the temperature increase to T2 (~15 s), during T2 approximately 100 ms prior to the beginning of the temperature decrease to T3 (~20 s), and during T3 at 10 s after the start of T3 (30 s). The magnitude of change in pain intensity ratings was calculated from T1 to T2 and T2 to T3 at 30 s. Prior work has shown that the minimum VAS ratings during offset occur approximately 10 s following the temperature decrease [31]. Therefore we expected age differences to be most robust at this time point. All offset-related dependent variables were collapsed across the three offset trials for each testing site. The three changes scores were analyzed separately at the palm and forearm with a 3-way mixed model analysis of variance (ANOVA), with age and sex as the between subject factors and transition (T1-T2, T2-T3) as the within subjects factor. Thermode temperature was included as a covariate. If the sphericity assumption was violated, then Greenhouse-Geisser degrees of freedom corrections were applied. As subsequent encounters with the three-temperature stimulus train become more predictable, the expectation of relief following the more painful stimulus of T2 could interact with the offset effect and facilitate inhibition [7]. Thus, planned age $\times$ sex $\times$ transition comparisons were performed on the first trial. The first trial should represent true offset effects without the interference of expectations.

To quantify the magnitude of offset analgesia using the second method [30, 35], the maximum eVAS rating during T2 (maxT2) and the minimum eVAS rating from the beginning of the T2-T3 transition until the end of T3 (MinT3) were extracted from the real-time eVAS ratings. The magnitude of offset analgesia was calculated as the difference between maxT2 and minT3 (Δ eVAS), corrected for the value of the peak eVAS during T2 (Δ eVAS_C= Δ eVAS/maxT2). Preliminary analyses indicated that the magnitude of offset did not significantly vary between trials for the palm or forearm as a function of age or gender, thus Δ eVAS_C was averaged across the three trials for each site. For each site, offset magnitude was analyzed using a 2-way between subjects ANOVA, with age and sex included as factors. This model also included thermode temperature as a covariate. Post-hoc

comparisons were made with Tukey's HSD procedure. Planned age $\times$ sex comparisons were also performed on the first trial.

3. Results

3.1. Individualized Test Temperature

A three-way ANOVA with site as the within subjects factor and age and sex as the between subjects factors revealed that the individualized test temperatures used for the offset trials approached but did not reach significance between the two sites (*forearm*, 46.70°C, $SD = 1.54$; *palm*, 47.05 °C, $SD=1.68$; $p = .059$) and between males ($M=47.56$ °C, $SD=1.23$) and females ($M=46.69$ °C, $SD=1.87$; $p= .057$). Additionally, no significant effects were observed for the age group main effect ($p=.34$) or in any of the interactions (p 's $> .05$).

3.2. Change in Pain Intensity Ratings: Forearm

Figure 2 represents the real-time data averaged across the three 30 s trials for each age group. Inspection of the means indicated that subjects experienced an increase in pain intensity during the transition from T1-T2, and a decrease in pain intensity during the transition between T2-T3. The 3-way ANOVA revealed significant age $\times$ transition interaction term [$F(1,40) = 7.44$, $p = .009$]. Post-hoc comparisons indicated that the younger group exhibited a significantly greater change in pain ratings when transitioning from T2 to T3 compared to T1 to T2. However, no significant differences existed between the transitions for the older group. Additionally, the change in pain intensity was greater for the younger group compared to the older group for the T2-T3 transition (See Figure 3a). All other main effect and interaction terms were not significant (p 's $> .05$).

The planned age $\times$ sex $\times$ transition ANOVA conducted on the first trial revealed similar effects as the previous analysis. A significant age by transition effect [$F(1,40) = 9.96$, $p = .003$] confirmed that older adults exhibited smaller decreases in perceived pain following the 1oC decrease in temperature compared to younger adults. Specifically, the younger group exhibited a significantly greater change in pain ratings when transitioning from T2 to T3 ($M=41.67$, $SD=22.5$) compared to T1 to T2 ($M=19.45$, $SD=12.30$). No differences existed between the transitions for the older group (T1-T2: $M=24.80$, $SD=12.33$; T2-T3: $M=23.10$, $SD=25.08$). Furthermore, the change in pain intensity was significantly reduced for the older group compared to the younger group for the T2-T3 transition. No other effects were significant (p 's $> .05$).

3.3. Change in Pain Intensity Ratings: Palm

The 3-way ANOVA conducted on change in pain intensity ratings for the palm revealed no significant effects (all p 's $> .05$). See Figure 3b. Furthermore, no significant effects were found for the first trial.

3.4. Magnitude of Offset Analgesia Corrected: Forearm

The age main effect was statistically significant [$F(1,40) = 4.18$, $p = .048$], indicating that magnitude of offset analgesia differed as a function of age group (See Figure 4a). The older group exhibited reduced magnitude of offset analgesia compared to the younger group. The sex main effect and sex by age interaction were not significant (all p 's $> .05$). The planned age by sex comparison on the first trial revealed similar effects of age on offset magnitude as the previous analysis, $F(1,40) = 5.21$, $p = .03$. The older group ($M=53.3\%$, $SD = 33.32$) exhibited attenuated offset magnitude relative to the younger group ($M=76.4\%$, $SD = 33.00$). All other effects were not significant (all p 's $> .05$).

3.5. Magnitude of Offset Analgesia Corrected: Palm

The 2-way ANOVA conducted on the magnitude of offset analgesia on the palm revealed no significant effects (all p 's > .05). See Figure 4b. Furthermore, no significant effects were found for the first trial.

4. Discussion

We sought to determine age and sex differences in offset analgesia tested at the volar forearm and thenar eminence of the palm. Three important contributions emerged from this data. First, healthy older adults exhibited decreased offset analgesia compared to young controls when tested at the forearm. Second, within each age group, offset analgesia was similar between males and females. Third, offset was not observed when the three stimulus temperature trains were applied to the thenar eminence, regardless of age and sex.

4.1. Age differences in offset analgesia at the forearm

As hypothesized, young adults showed a disproportionate decrease in pain intensity ratings following a slight decrease in noxious temperatures compared to those of equal magnitude increases. However, despite similar increases in pain intensity ratings from T1 to T2 between older and younger adults, older adults perceived smaller decreases in pain following the temperature decrease from T2 to T3. Additionally, the younger group's pain intensity ratings descended approximately 80% from their maximum pain rating towards no pain, while the older group's pain ratings fell on average only 62%. Prior research has also showed diminished endogenous pain inhibition in older adults with experimental paradigms using CPM [9,40,47]. The mechanisms underlying offset are largely independent of NMDA and μ -opioid receptors, and consequently those underlying CPM [30,34]. Thus, the collective data suggest that multiple endogenous inhibitory systems may grow dysfunctional with age, potentially placing older adults at a greater risk to develop chronic pain. Indeed, several studies suggest that ineffective pain inhibition represents a predisposition for chronic pain [41].

Reduction of offset associated with age could be due to central and/or peripheral mechanisms. A wealth of evidence has shown that the central and peripheral nervous systems exhibit age-related functional, structural, and biochemical changes. Multiple studies have reported that serotonergic and noradrenergic fibers originating from the brainstem and terminating in the dorsal horn are components of descending modulatory systems [13,21,22]. In line with this, fMRI studies have revealed that offset engages an inhibitory system which originates in the ventrolateral periaqueductal grey of the brain stem and involves areas consistent with serotonergic and noradrenergic brainstem nuclei [8,51]. Importantly, animal studies report an age-related decline in serotonergic and noradrenergic neurons in the dorsal horn [11,12, 19,26], resulting in impaired descending inhibitory processes. At the cortical level, older adults are characterized by reduced gray and white matter brain volumes, particularly in the cingulate, insular, and prefrontal cortex [5,39]. Interestingly, these brain regions are thought to play a role in the generation or maintenance of offset [51].

Another possible explanation for the current findings is a selective age-related enhancement of central sensitization [17,52]. Riley and colleagues found that older adults reported increased lingering pain following a reduction of noxious temperatures compared to younger adults [40]. This lingering pain may reflect pain after-sensations; a phenomenon known to be a manifestation of central sensitization [14]. In the current study, increased lingering pain from the T2 stimulus may have attenuated the offset response in older adults. However,

potentially refuting this hypothesis, Martucci et al. revealed that offset is not altered during a state of experimentally-induced central sensitization in healthy humans [31].

Finally, the primary afferent fibers transmitting nociceptive information to the spinal cord may become dysfunctional with age. Both older animals and humans have shown selective loss of myelinated afferents [36,37,46] and diminished function of the remaining fibers [20,46]. Prior work also has reported that A δ fiber block has less effect on pain threshold on older compared to younger adults, supporting a diminished contribution of this fiber type to pain thresholds in the elderly [3,17]. In the present study, our stimulus parameters were well below the activation threshold for AMH-I fibers, thus activating selectively AMH-II and C-fibers present in the forearm [15]. The epicritic input of AMH-II afferents may be integral to the initial signaling of temperature change and thus initiating offset. Therefore, the diminished input of AMH-II fibers in older individuals may have contributed to the reduced offset in our older subjects. Nonetheless, these proposed explanations are clearly speculative and future research is needed to substantiate the mechanisms underlying an age-related decline in offset.

4.2. Sex differences in offset analgesia

The present study did not find sex differences in offset in healthy young or older adults. This finding is in contrast with Neisters et al. who found greater magnitude of offset in males compared to females in a sample of healthy volunteers [35]. However, the sex differences were small and likely clinically insignificant (i.e., 98% in men v. 94% in women). Dysfunctional endogenous pain modulatory systems characterize many chronic pain conditions which disproportionately affect women, including fibromyalgia syndrome, temporomandibular disorders, and irritable bowel syndrome [15,23,24,27,43,49]. Thus, it is often hypothesized that women have altered endogenous pain modulation compared to men. Indeed, a recent metaanalysis demonstrated that males show greater CPM than females [38]. In contrast, the current data suggest that the inhibitory system activating offset functions similarly between healthy men and women.

4.3. Offset analgesia at the thenar eminence

Offset analgesia was nonexistent in all subjects when the three stimulus temperature train was applied to the thenar eminence of the palm. Rather, the increase in noxious temperatures elicited a similar change in perceived pain compared to the equal magnitude decrease in temperature. Furthermore, the magnitude of offset was only approximately 30%. Several possibilities may explain our observed anatomical site-related differences in offset, which may implicate peripheral factors in this phenomenon. Evidence suggests that AMH-IIs, signaling first pain of heat stimuli, are not present in the primate glabrous skin [1,33,45]. Instead, the thenar eminence is highly innervated by C-fiber nociceptors [15], which are implicated in the transmission of late pain and burning sensations [2,4]. C-fiber, but not A-fiber activity is attenuated by morphine [6] and offset has shown to be a mu-opioid independent phenomenon [30]. Furthermore, anterior and posterior insula activation has been distinctly associated with excitation of A-delta heat nociceptors [32] and the insula has shown greater activation during offset than during pain [51]. Taken together, AMH-II nociceptors may be critical to this inhibitory temporal sharpening mechanism. Furthermore, the three stimulus temperature train may have evoked greater late pain sensations on the palm relative to the forearm, due to increased presence of C-fiber activity at the palm. The greater late pain sensations could have masked the offset response. Alternatively, Iannetti [18] has proposed that no differences in nociceptive afferents mediating first pain exist between the human glabrous and hairy skin. If this is the case, our findings are consistent with the previously reported thickness-dependent delay in temperature detection in the

human palm. Additional research is needed to investigate the precise role of primary afferent neurons involved in offset.

4.4. Methodological Issues

Several methodological issues should be considered when interpreting the results. First, we cannot exclude the possibility that the 0.5°C decrease in noxious temperatures during the palm trials was not large enough to evoke offset. However, the 0.5°C increase from T1 to T2 during the palm trials elicited an equal magnitude increase in pain ratings as the 1.0°C increase during the forearm trials. Furthermore, our preliminary testing indicated that a 0.5°C drop in temperature is sufficient to elicit offset at the forearm. Secondly, Derbyshire et al. recently showed that the magnitude of offset increases over repeated testing, as subsequent trials become predictable and non-threatening [7]. Thus, the reduced offset in older adults could have been driven by age-related differences in the learned expectations across trials. However, preliminary analysis revealed that differences in the magnitude of offset across trials did not differ as a function of age. Furthermore, we conducted planned analyses on the first offset trial at the forearm and palm, which should represent the offset response without the potential confound of expectations. These results indicate that differences in offset were not due differential expectations. Thirdly, Derbyshire et al. also revealed that a within trial adaptation to the painful stimulus may exaggerate the offset effect [7]. Thus, the greater offset magnitude observed in younger adults may have potentially been driven by greater within trial adaptation to the stimulus compared to older adults. Finally, inspection of confidence interval data, as recommended by Levine et al., [28] suggests that the current study may have been underpowered to detect an age by sex interaction.

4.4. Conclusion

In conclusion, the present data indicate that older adults exhibit reduced offset analgesia, potentially reflecting an age-related decline in either endogenous inhibitory systems or primary afferent fibers. Furthermore, while the exact mechanisms underlying offset remain unknown, the absence of offset at the palm and in older adults at the forearm suggest that peripheral mechanisms may be involved in initiating offset or that the inhibitory processes regulating offset are susceptible to disruption by peripheral factors. Additional research is needed to test these hypotheses and to determine the origin of age-related deficits in offset. Most importantly, however, future research needs to determine what size difference in offset might be considered clinically significant and evaluate whether deficient offset predicts incidence of clinical pain in older adults and in chronic pain populations.

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Figure 1.

Session timeline and calculation of offset analgesia dependent variables. For the baseline phase (T1), the thermode was heated to the subject's testing temperature for 15 s. The thermode was heated an additional 1°C (forearm) or 0.5°C (palm) for 5 s for a manipulation phase (T2) and then cooled back to subjects testing temperature for 10 s (T3). Magnitude of offset analgesia ($\Delta eVAS$) = peak eVAS during T2 (maxT2) – minimum eVAS during T3 (minT3). Magnitude of offset analgesia relative to peak effect ($\Delta eVASc$) = ($\Delta eVAS$ / Peak eVAS)100%. Pain intensity ratings were also taken at T1 just prior to temperature increase, T2 just prior to temperature decrease, and T3 at 30 s.

Figure 2.
Average real-time eVAS ratings for Younger and Older subjects at the forearm and palm.

Figure 3.

The magnitude of change in pain intensity ratings produced by increases and decreases in stimulus temperatures for younger and older adults at the (A) forearm and (B) palm. For younger subjects only, changes in pain intensity were greater at the T2-T3 temperature decrease compared to the temperature increase from T1-T2. The change in pain intensity was significantly reduced for the older group compared to the younger group for the T2-T3 transition. *= significant difference at $p < .05$.

Figure 4.

Differences in magnitude of offset analgesia relative to peak effect ($\Delta eVAS_c$) by age group at the (A) forearm and (B) palm. Older adults exhibited significantly reduced offset analgesia compared to young adults at the forearm, whereas no differences were found at the palm. *= significant difference at $p < .05$.

Table 1

Subject and age group characteristics.

	Younger group N=25		Older group N=20	
	Men N=10	Women N=15	Men N=9	Women N=11
Age (mean, SD)	22.40 (1.71)	21.87 (2.62)	67.33 (5.87)	69.64 (7.13)
Age (range)	20–25	18–27	63–73	58–77
Heat stimulus temperature – Forearm (mean, SD)	47.05 (0.79)	46.00 (1.58)	47.50 (1.72)	46.89 (1.61)
Heat stimulus temperature – Palm (mean, SD)	47.85 (0.43)	46.26 (1.95)	47.24 (1.73)	47.36 (1.74)
Baseline systolic blood pressure (mean, SD)	121.61 (14.17)	122.73 (14.72)	129.94 (10.22)	118.95 (17.85)
Baseline diastolic blood pressure (mean, SD)	64.28 (4.88)	67.50 (8.58)	72.55 (8.46)	68.59 (13.58)