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The relationship of the audible pop to hypoalgesia associated with high velocity, low amplitude thrust manipulation: A secondary analysis of an experimental study in pain free participants

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Abstract

Objective—High velocity, low amplitude (HVLA) manipulation is an effective treatment for low back pain (LBP); however, the corresponding mechanisms are undetermined. Hypoalgesia is associated with HVLA manipulation and suggests specific mechanisms of action. An audible pop (AP) is also associated with HVLA manipulation; however, the influence of the AP on the hypoalgesia associated with HVLA manipulation is not established. The purpose of the current study was to observe the influence of the AP on hypoalgesia associated with HVLA manipulation.

Methods—The current study represents a secondary analysis of 40 participants. All participants underwent thermal pain sensitivity testing to their leg and low back using protocols specific to A δ fiber mediated pain and temporal summation. Next, participants received HVLA manipulation to their low back and the examiner recorded whether or not an AP was perceived. Finally, participants underwent immediate follow up thermal pain sensitivity testing using the same protocols. Separate repeated measure ANOVAs were used to observe changes in pain sensitivity prior to and immediately following HVLA manipulation.

Results—Hypoalgesia of A δ fiber mediated pain was observed in the low back following HVLA ($p < 0.05$) and this was independent of whether an AP was perceived ($p > 0.05$). Hypoalgesia of temporal summation was observed in the lower extremity following HVLA ($p < 0.05$) and this was

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Conflicts of Interest: No conflicts of interest were reported for this study.

Practical Applications

- An audible pop is associated with HVLA manipulation; however, the clinical and mechanistic relevance of the pop is not known.
- We observed HVLA manipulation related hypoalgesia to thermal pain sensitivity and this finding was not dependent upon the presence of a pop.

independent of whether an AP was perceived ($p=0.08$). However, a moderate effect size for temporal summation was observed favoring participants in whom an AP was perceived.

Conclusion—The current study suggests hypoalgesia is associated with HVLA manipulation and occurs independently of a perceived AP. Inhibition of lower extremity temporal summation may be larger in individuals in whom an AP is perceived, but further study is necessary to confirm this finding.

Introduction

High velocity, low amplitude (HVLA) thrust manipulation is suggested as an effective intervention in the treatment of low back pain.¹⁻⁴ An audible “pop” (AP) is characteristic of HVLA and may distinguish these interventions from other forms of manual therapy such as massage and mobilization. While the AP is associated with HVLA manipulation, a consensus is currently lacking as to the clinical relevance. For example, manuscripts have been published suggesting biomechanically efficient ways to achieve the AP,^{5, 6} research studies have used the AP as an indication of a successfully applied HVLA manipulation,^{7, 8} and sham HVLA manipulation techniques have been designed based on an avoidance of the AP.^{9, 10} In contrast, clinical studies¹¹⁻¹³ and a literature review¹⁴ have reported a lack of association between the AP and clinical outcomes.

Hypoalgesia, or a decrease in pain perception in response to an unchanging stimulus, is associated with HVLA.¹⁵⁻¹⁸ For example, HVLA corresponds to an increase in pain pressure threshold¹⁵ and a decrease in pain perception to unchanging thermal stimuli.¹⁶ Hypoalgesia following HVLA is hypothesized to indicate potential neurophysiological mechanisms of action.^{19, 20}

Central sensitization is an exaggerated pain response characterized by allodynia (pain perception to a previously non-painful stimulus) and hyperalgesia (heightened pain severity in response to a previously painful stimulus). HVLA is hypothesized to affect musculoskeletal pain through the alteration of changes associated with central sensitization¹⁹ and immediate hypoalgesia may be a clinical indicator of such an effect. Temporal summation is a clinical measure of central sensitization. Specifically, temporal summation is an increase in pain perception to an unchanging repetitive, painful stimulus applied at a frequency of ≤ 3 seconds and is observed in both healthy individuals and, to a greater extent, in those experiencing pain conditions.^{21, 22} We have previously observed hypoalgesia of temporal summation following HVLA manipulation to the lumbar spine which was not observed in comparison groups riding a stationary bike or performing lumbar extension range of motion exercises.¹⁶ In contrast, hypoalgesia for A-delta fiber mediated pain perception did not differ between the 3 groups.¹⁶ Subsequently, HVLA manipulation may produce a hypoalgesic response which differs from other common rehabilitation interventions due to a specific effect on temporal summation.

The influence of the AP on immediate hypoalgesia corresponding to HVLA manipulation is not clear. Hypoalgesia represents a potential neurophysiological mechanism behind the clinical effectiveness of HVLA manipulation. An association between hypoalgesia and an AP would suggest a greater neurophysiological response corresponding to the AP with implications for a potential mechanism of HVLA manipulation. Therefore, the purpose of the present study was to assess the role of the AP in HVLA manipulation associated thermal pain sensitivity to both A-delta fiber mediated pain perception and temporal summation following HVLA manipulation. We hypothesized that the AP would not be associated with greater hypoalgesia to thermal pain perception, similar to the findings of prior studies related to clinical pain.¹¹⁻¹⁴

Methods

The current study represented a planned secondary analysis. The protocol and results of the primary study are provided in detail elsewhere.²³ Briefly, in the primary study, we studied the association between expectation and changes in thermal pain sensitivity associated with HVLA manipulation in 60 healthy participants. The purpose of the primary study was to examine the influence of expectation on thermal pain sensitivity outcomes. Including the AP in our primary analysis would have required a larger sample size to ensure adequate power and we had no specific hypotheses about the interaction between the AP and expectation. Additionally, we would have had less control over balance of the groups due to the unpredictability of achieving an AP. Subsequently, we tracked the AP in the primary study for the express purpose of performing a secondary analysis. In the primary study, a negative treatment effect was observed in one of our intervention groups. Therefore, the current analysis only included participants in the two remaining intervention groups in whom a treatment effect was not observed ($n = 40$).

Participants

The University of Florida Institutional Review Board approved the current study. A sample of convenience was recruited from the University of Florida Health Science Center community by flyer and word of mouth. Potential participants were screened for appropriateness by a study representative and those wishing to participate signed an informed consent form. Inclusion criterion was age eighteen to sixty and exclusion criteria were non-English speaking, systemic medical conditions (e.g. diabetes, hypertension), current use of psychiatric medication, pregnancy, regular use of prescription medication for management of pain, presently experiencing low back pain, or history of surgery to the low back.

Measures

Demographic Questionnaire—Participants completed a demographic questionnaire regarding age, sex, race, education, and prior history of low back pain.

Psychological Questionnaires—Psychological questionnaires specific to pain catastrophizing, fear of pain, and anxiety were included due to a known influences on experimental pain.²⁴⁻²⁷ We chose to evaluate for baseline group differences in these factors to account for potential confounders that could affect reporting of thermal pain sensitivity.

Pain Catastrophizing Scale (PCS)—The PCS consists of 13 items specific to individual coping styles with pain which are each quantified with a five point ordinal scale. Higher scores indicate greater levels of catastrophizing. The score may be taken as a whole or as individual factors of rumination, helplessness, and magnification. Prior studies have validated the factor structure and found good internal consistency reliability and validity of the PCS.^{25, 28-30}

Fear of Pain Questionnaire-III (FPQ-III)—The FPQ-III³¹ consists of 30 items, each scored on a 5-point adjectival scale, which measures fear of normally painful situations. Higher scores indicate greater pain related fear. The FPQ has demonstrated sound psychometric properties in both experimental and clinical pain studies.^{26, 31, 32}

Anxiety Visual Analog Scale (VAS)—Anxiety was measured through a 10 cm VAS. Participants were asked to indicate along the VAS anchored with none and most severe anxiety imaginable the amount of anxiety they were currently feeling regarding the experimental pain task they were about to experience. VASs have been used to measure anxiety in other studies and have demonstrated sound psychometric properties³³⁻³⁶.

Thermal Pain Sensitivity—Thermal pain sensitivity testing was performed using the Medoc Neurosensory Analyzer (TSA-2001, Ramat Yishai, Israel) with hand-held peltier-element-based stimulator. We included previously established protocols biased towards A δ fiber mediated pathways and temporal summations.^{21, 37} Participants first underwent a practice session in order to familiarize themselves with the pain testing protocol immediately followed by the full QST.

Numeric Rating Scale (NRS)—NRSs were used as a measure of evoked thermal pain sensitivity. Participants were asked to quantify any evoked pain using a NRS anchored by “0” (no pain at all) and “100” (worst imaginable pain). The NRS is frequently used as a measure of both clinical and experimental pain and has demonstrated sound psychometric properties in previous studies³⁸⁻⁴¹.

A δ fiber mediated pain (first pain)—A δ fiber mediated pain was assessed in the non-dominant posterior calf and adjacent to the non-dominant posterior superior iliac spine through the application of heat pulses of 3 seconds duration. The baseline temperature of the thermode was 35°C and rose at a rate of 10°C/sec to 47 or 49°C. All participants received pulses of both 47 and 49°C in a random order. The research assistant recorded NRS ratings of pain intensity for each heat pulse. Participants were asked to rate their “first” pain intensity felt, believed to be primarily mediated by input from A-delta fibers.^{21, 37} Participants underwent the protocol two times at each anatomic site waiting 60 seconds between trials. Pain sensitivity scores in response to both the 47 and 49°C heat pulses were pooled and the average NRS rating of the combined temperatures in both the low back and the lower extremity served as the measure of pain sensitivity at each location.

Temporal summation—Temporal summation was assessed in the non-dominant plantar surface of the foot and the non-dominant posterior superior iliac spine following a previously established protocol.^{21, 37} A train of ten consecutive heat pulses of less than one second duration at an inter-stimulus frequently of .33 Hz (temporal summation) was applied with a baseline temperature of 35°C and peak temperature of 51°C. Participants were asked to rate their delayed (second) pain using a NRS and the average of the first 5 pulses served as the measure of pain perception.

HVLA Intervention

The HVLA technique has been shown to be effective in the treatment of low back pain in participants meeting a clinical prediction rule.^{7, 8} Similar to the protocol used in a prior study,¹⁶ we performed the technique (Fig 1) two times on each side, regardless, of whether an AP was perceived. Immediately following the HVLA manipulation, the researcher marked on an intake form whether or not an AP had occurred during any of the thrusts. The determination of an AP having occurred was based upon the researcher's perception of either having felt or heard an AP during the application of the technique. This method of identifying an AP has been reported as valid.⁴² Following the application of the HVLA manipulation, the same quantitative sensory testing protocol was performed.

Statistical Analysis

Descriptive statistics were generated for continuous and categorical measures. Univariate ANOVA was used to assess differences in continuous variables of demographic, psychological, and baseline thermal testing measures between participants in whom an AP was perceived and those in whom an AP was not perceived. Chi-square analysis was used to assess differences in categorical demographic variables between participants in whom an AP was perceived and those in whom an AP was not perceived. We assessed baseline measures to account for

differences in potential confounding variables between individuals in whom an AP was perceived and those in whom one was not.

In order to assess the influence of the AP on pain perception following HVLA manipulation, we performed separate 2×2 repeated measure ANOVAs for each of the pain protocols (A δ and temporal summation) at each anatomic location (lower extremity and low back). AP status (perceived or not perceived) served as the between subject factor and time of thermal pain sensitivity assessment (pre to post HVLA) as the within subject factor. Alpha levels were set at 0.05 and all analysis was performed using the SPSS statistical package version 16.0 (SPSS Inc, Chicago, IL).

Results

Forty participants were included in this analysis. Baseline demographic, thermal pain threshold and psychological variables did not differ by participants on AP status, with the exception of those in whom an AP was perceived having less education (Table 1).

A δ fiber mediated pain perception (Table 2, Fig 2)

Lower extremity—Neither a significant group (AP perceived versus AP not perceived) by time (pre to post HVLA) interaction ($F_{(1,38)} = 0.97$, $p = 0.33$, partial $\eta^2 = 0.03$) nor a main treatment effect for time ($F_{(1,38)} = 0.50$, $p = 0.48$, partial $\eta^2 = 0.01$) were observed in the lower extremity of participants for A δ fiber mediated pain perception.

Low back—No significant group (AP perceived versus AP not perceived) by time (pre to post HVLA) interaction was observed in the low back ($F_{(1,38)} = 0.07$, $p = 0.79$, partial $\eta^2 < 0.01$) for A δ fiber mediated pain perception. Conversely, a significant main treatment effect for time was present ($F_{(1,38)} = 10.67$, $p < 0.01$, partial $\eta^2 = 0.22$). These findings corresponded to a mean hypoalgesia of 6.2, Cohen's $d = 0.30$.

Temporal Summation (Table 3, Fig 3)

Lower extremity—A significant group (AP perceived versus AP not perceived) by time (pre to post HVLA) interaction was neared ($F_{(1,38)} = 3.35$, $p = 0.08$, partial $\eta^2 = 0.08$) favoring the participants in whom an AP was perceived. A significant main effect for time was observed suggesting hypoalgesia to temporal summation occurred regardless of whether or not an AP was perceived ($F_{(1,38)} = 15.12$, $p < 0.01$, partial $\eta^2 = 0.29$). This finding corresponded to a mean hypoalgesia of 6.2, Cohen's $d = 0.26$.

Low back—Neither a group (AP perceived versus AP not perceived) by time (pre to post HVLA) interaction ($F_{(1,38)} = 0.15$, $p = 0.70$, partial $\eta^2 < 0.01$) nor a main treatment effect for time were observed in the low back for the temporal summation pain protocol ($F_{(1,38)} = 2.43$, $p = 0.13$, partial $\eta^2 = 0.06$).

Discussion

Central sensitization is characterized by allodynia and hyperalgesia. Clinical signs of central sensitization have been observed in individuals experiencing LBP.⁴³⁻⁴⁵ For example, generalized hyperalgesia⁴⁴ and lower pain thresholds and greater cortical activation in response to evoked pain⁴⁵ have been observed in individuals with chronic LBP in comparison to healthy controls. Central sensitization is theorized as instrumental in the progression of acute pain to chronic pain and in the maintenance of chronic pain.⁴⁶⁻⁴⁸ Subsequently, interventions effective in altering central sensitization may be particularly beneficial in the treatment of LBP. Similar to prior studies,¹⁵⁻¹⁷ we observed hypoalgesia associated with HVLA manipulation suggestive

of a mechanism of action upon central sensitization of pain; however, this finding was independent of whether or not an AP was recorded by the practitioner. These findings are similar to prior studies observing the lack of an association between the AP and the clinical effectiveness¹¹⁻¹³ or mechanisms of HVLA manipulation.⁴⁹ Our findings suggest that HVLA manipulation is associated with hypoalgesia to A δ fiber mediated pain and temporal summation regardless of whether an AP is perceived.

Interestingly, a trend of moderate magnitude was observed suggesting greater hypoalgesia to temporal summation in the lower extremity in individuals in whom an AP was perceived. Prior mechanistic studies have not consistently supported a relationship between neurophysiological effects and the AP. For example, Herzog et al⁴⁹ observed EMG responses associated with high velocity spinal manipulative treatments that occurred independently of an AP. Conversely, Teodorczyk-Injeyan et al⁹ observed a reduction of proinflammatory cytokine secretion in participants receiving HVLA manipulation with an AP in comparison to those without an AP. In a separate study, Teodorczyk-Injeyan et al¹⁰ observed Staphylococcal protein A induced secretion of immunoregulatory cytokine interleukin 2 increased significantly following HVLA manipulation regardless of whether an AP was perceived. However, a trend was observed over 2 hours for a reduction of this finding in participants in whom an AP was not observed in comparison to those in whom AP was observed. Similar to Teodorczyk-Injeyan et al,^{9, 10} our findings suggest neurophysiological effects corresponding with HVLA manipulation may be of a greater magnitude when associated with an AP. We have previously observed greater hypoalgesia to temporal summation in healthy participants receiving HVLA manipulation in comparison to those performing lumbar extension exercises or riding a stationary bike.¹⁶ These findings suggest a mechanism of action related to hypoalgesia of temporal summation at the dorsal horn of the spinal cord and specific to HVLA manipulation. The present study suggests this specific potential mechanism of HVLA manipulation may be magnified in individuals in whom an AP is perceived.

Clinically, HVLA manipulation is frequently applied with a biomechanical emphasis. For example, a misaligned or hypomobile segment is identified through careful examination and then a specific HVLA is applied to correct the noted fault. A number of inconsistencies are related to this method of clinical practice. Specifically, the biomechanical examination is unreliable,^{50, 51} techniques are not specific to a targeted vertebral level,⁵²⁻⁵⁴ and lasting positional changes are not obvious following the interventions.⁵⁵ Despite these inconsistencies, HVLA manipulation is an effective intervention for certain types of musculoskeletal pain suggesting a mechanism of action not specific to a biomechanical effect. Neurophysiological mechanisms are suggested as pertinent in the mechanisms behind the clinical effectiveness of HVLA manipulation and may provide a more reasonable explanation than a strictly biomechanical effect. Our findings suggest that a neurophysiological mechanism, hypoalgesia is associated with HVLA manipulation and that this potential mechanism may be enhanced when HVLA manipulation is accompanied by an AP.

Limitations

The present study included only participants who were pain free and experience evoked pain of a relatively brief duration. We are uncertain if similar findings would have occurred in participants experiencing LBP since response to the AP may be different in a clinical sample of individual experiencing LBP. We used protocols that are currently considered to discriminate between A-delta fiber mediated pain processes and temporal summation, but do not directly measure these processes in human subjects. Therefore, our thermal pain sensitivity measures are not definitively directly linked to the development of chronic pain syndromes. Furthermore, expectation has been observed as influential in the outcomes associated with manual therapy.^{23, 56} We did not assess individual expectation specific to the AP and future

studies should consider this factor. We did not ask individual participants whether they perceived an AP and a prior study¹¹ using both researcher and participant perception reported higher rates of an AP occurrence than we observed in the present study. Subsequently, a greater number of participants may have experienced an AP undetected by the study representative. Finally, our relatively low p value and moderate effect size for hypoalgesia to temporal summation in the lower extremity favoring participants in whom an AP was perceived suggests we may have been underpowered to observe these differences. A subsequent power analysis indicated we would have required 35 participants in each group in order to observe significant group differences at $p < 0.05$ with $\beta > 0.80$ at a similar effect size. Subsequently, future studies should attempt to replicate our findings in a larger sample.

Conclusion

Hypoalgesia to thermal pain was observed in pain free participants regardless of whether or not an AP was perceived. A trend was observed for a greater magnitude of hypoalgesia to lower extremity temporal summation in participants in whom an AP was perceived, but future research is necessary to confirm this finding.

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Figure 1. High velocity, low amplitude thrust technique used in this study

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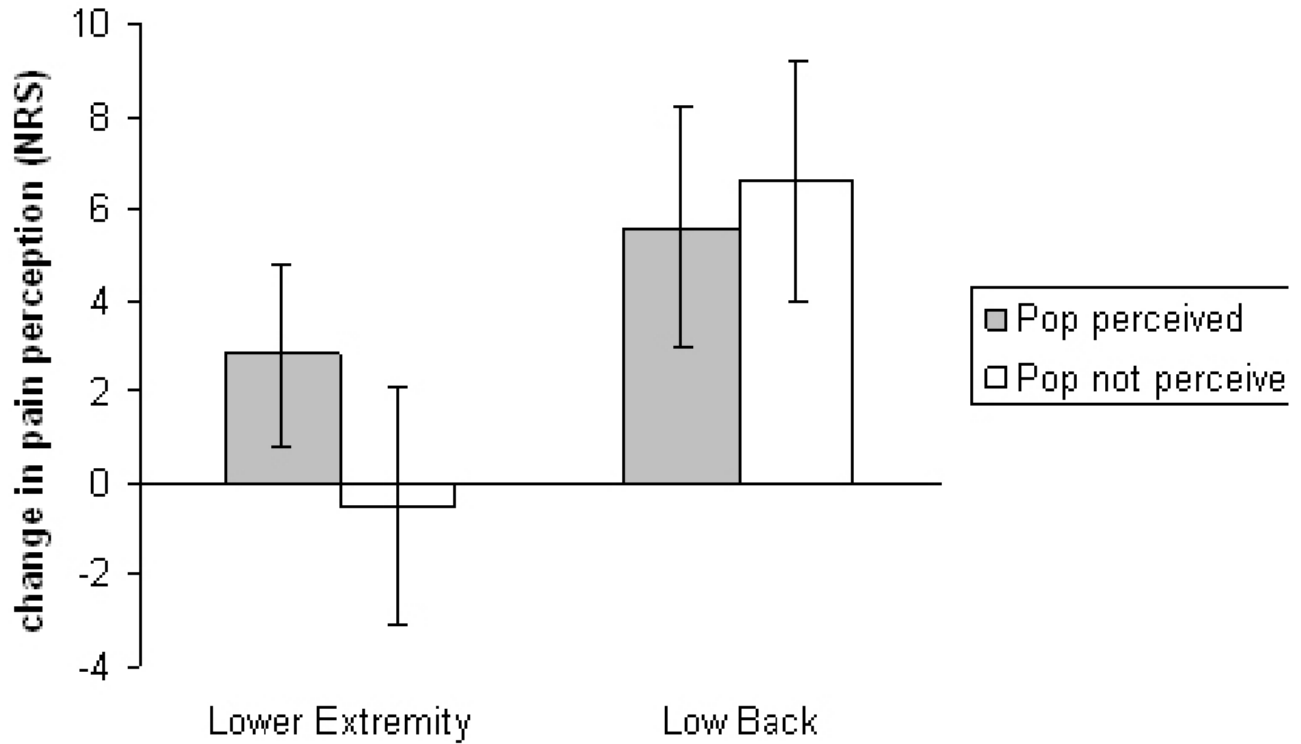


Figure 2. Pain perception to A δ fiber mediated pain

Key: Pre to post high velocity, low amplitude thrust manipulation change in self report of pain to standard thermal stimuli. Positive numbers on the Y axis indicate hypoalgesia while negative numbers indicate hyperalgesia. NRS= numeric rating scale anchored with 0= no pain at all and 100= worst pain imaginable. Error bars indicate one standard error of the mean.

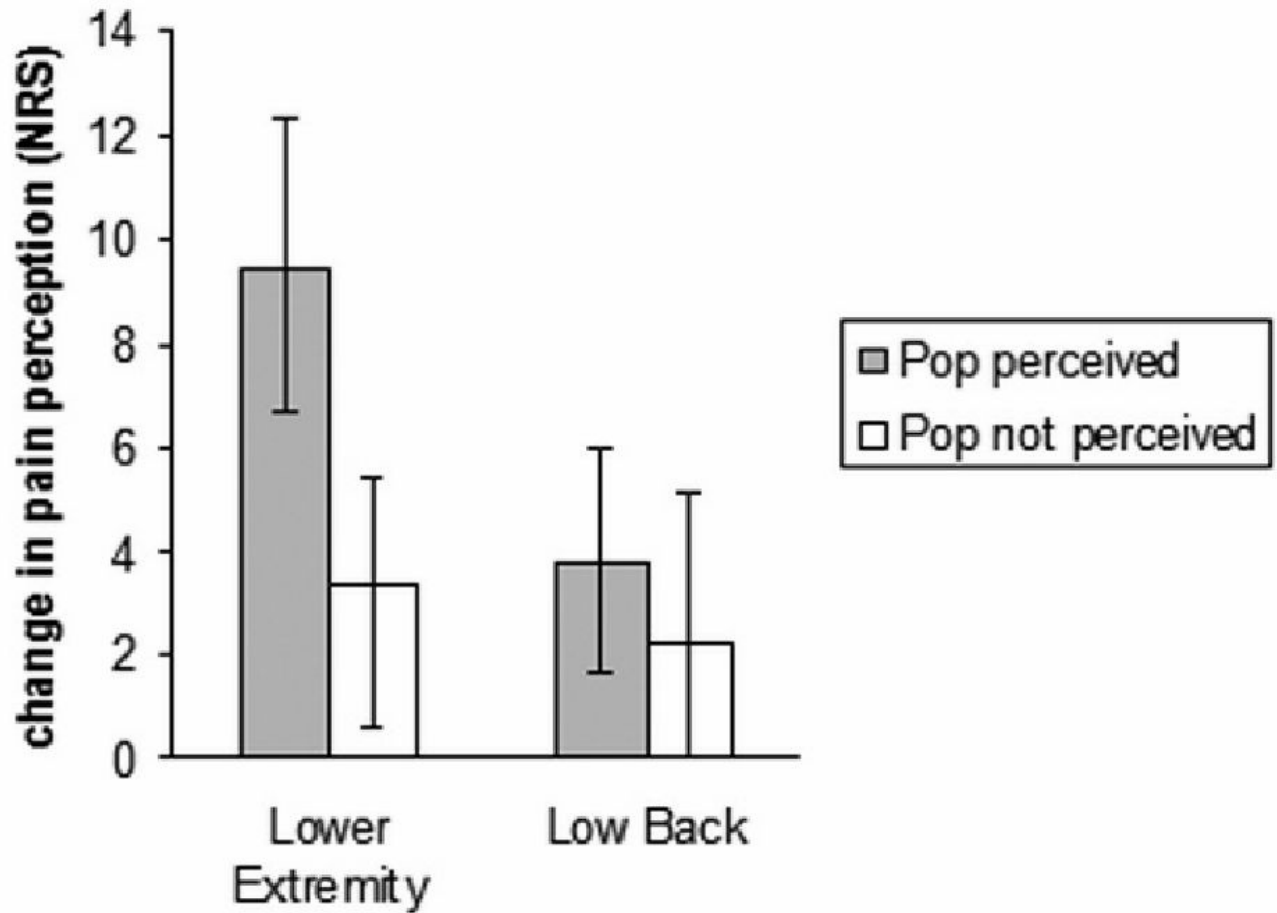


Figure 3. Change in temporal summation

Key: Pre to post high velocity, low amplitude thrust manipulation change in self report of pain to standard thermal stimuli. Positive numbers on the Y axis indicate hypoalgesia. NRS= numeric rating scale anchored with 0= no pain at all and 100= worst pain imaginable. Error bars indicate one standard error of the mean.

Table 1

Baseline measures of demographics, thermal pain threshold, and psychological variables comparing participants in whom an audible pop (AP) was perceived and not perceived.

	<u>AP</u>	<u>No- AP</u>	<u>Total Sample</u>	<u>p</u>
Sex: Male:	5	4	9	
Female:	13	18	31	0.47
Age (years (sd))	22.17 (1.72)	23.73 (3.37)	23.03 (2.83)	0.08
Race: Caucasian:	14	18	32	
African American:	2	0	2	
Other:	2	4	6	0.34
Education (years (sd))	15.67 (1.14)	16.67 (1.46)	16.21 (1.40)	0.02
History of LBP: Yes:	5	3	8	
No:	12	17	29	0.52
Threshold Pain Temperature (sd)	43.41 (2.53)	42.13 (5.17)	42.70 (4.20)	0.35
Threshold Pain Rating (NRS (sd))	15.1 (13.6)	18.1 (19.0)	16.8 (16.6)	0.57
<u>Psychological Questionnaires</u>				
PCS (sd)	16.44 (8.49)	14.05 (10.08)	16.22 (9.29)	0.90
FPQ (sd)	78.11 (19.07)	75.50 (15.66)	76.68 (17.10)	0.64
Anxiety VAS (sd)	19.11 (19.12)	25.52 (21.93)	22.56 (20.67)	0.34

Key: LBP= low back pain; NRS= numeric rating scale from 0= no pain at all to 100= the worst pain imaginable; PCS= Pain Catastrophizing Scale; FPQ= Fear of Pain Questionnaire; VAS= visual analog scale from 0= none at all to 100= worst imaginable

Table 2

Summary of comparison of within group and between group changes in A δ fiber mediated pain sensitivity.

	Pre	Post	Mean Difference	95% CI	Effect Size (Cohen's d)
WITHIN GROUP COMPARISONS					
<i>Low Back</i>					
AP	35.7(20.4)	30.1(17.0)	5.6(11.0)	0.1 – 11.1 *	0.30
No AP	36.5(20.4)	29.9(22.3)	6.6(12.3)	1.1 – 12.1 *	0.31
<i>Lower Extremity</i>					
AP	31.1(19.4)	28.3(17.0)	2.8(11.7)	-1.4 – 7.1	0.15
No AP	31.7(22.1)	32.2(26.1)	-0.5(12.0)	-5.8 – 4.8	-0.02
BETWEEN GROUP COMPARISONS (Change Scores)					
<i>Low Back</i>					
AP \times No AP			-1.0(11.3)	-6.5 – 8.6	-0.09
<i>Lower Extremity</i>					
AP \times No AP			3.3(10.3)	-10.1 – 3.5	0.32

Key: AP= audible pop, No AP= no audible pop; Pain sensitivity assessed with 101 point numeric rating scale anchored with 0= no pain and 100= worst pain sensation imaginable. All findings are presented in mean (standard deviation).

* = significant at $p < 0.05$.

Table 3

Summary of comparison of within group and between group changes in temporal summation.

	Pre	Post	Mean Difference	95% CI	Effect Size (Cohen's d)
WITHIN GROUP COMPARISONS					
<i>Low Back</i>					
AP	47.9(24.0)	44.1(22.1)	3.7(9.5)	-1.0 – 8.5	0.16
No AP	51.0(27.2)	48.8(25.9)	2.2(13.8)	-3.9 – 8.4	0.08
<i>Lower Extremity</i>					
AP	35.3(23.6)	25.8(19.4)	9.5(11.7)	3.6 – 15.3*	0.44
No AP	33.8(26.4)	30.4(26.9)	3.4(9.3)	-0.7 – 7.5	0.13
BETWEEN GROUP COMPARISONS (Change Scores)					
<i>Low Back</i>					
AP × No AP			1.5(11.8)	-9.2 – 6.3	0.13
<i>Lower Extremity</i>					
AP × No AP			6.1(10.2)	-12.8 – 0.6	0.60

Key: AP= audible pop, No AP= no audible pop; Pain sensitivity assessed with 101 point numeric rating scale anchored with 0= no pain and 100= worst pain sensation imaginable. All findings are presented in mean (standard deviation).

* = significant at $p < 0.05$.