The Effect of Chewing Gum on Modulating Pain Responses

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Abstract

The purpose of this study was to examine how chewing gum modulates pain response by observing physiological changes associated with pain. Measures of heart rate (HR), mean arterial blood pressure (MABP), and respiratory rate (RR) were recorded while undergoing a cold pressor test (CPT), a standard procedure used for measuring pain responses. Based on the suggested ability to induce anti-nociceptive response, gum chewing was tested as a tool for modulating pain in twenty subjects between the ages of 20-25. We hypothesized that chewing gum while undergoing the CPT would minimize typical increases in HR, RR, and MABP associated with pain perception and yield higher pain thresholds and tolerances in subjects undergoing the test. Physiological responses were measured under four conditions: 1. -CG/-CPT, 2. -CG/+CPT, 3. +CG/-CPT, and 4. +CG/+CPT. A statistically significant difference in heart rate ($p= 0.005$) was measured between positive control condition 2 and experimental condition 4. Although chewing gum did not show statistically significant improvements in pain threshold or tolerance in this study, overall trends in improvement of tolerance provide motivation for further study.

Introduction

Pain is defined by Medilexicon's Medical Dictionary as a variably unpleasant sensation associated with actual or potential tissue damage and mediated by specific nerve fibers to the brain where its conscious appreciation may be modified by various factors. When we feel pain, peripheral nerves called nociceptors relay pain messages through electrical impulses to the spinal cord (Scott 1959). The information received by nociceptors enter the spinal cord at the dorsal horn. Dorsal horn neurons then release neurotransmitters to convey the message to the brain. The neurotransmitters arrive at the thalamus through which the signal is sent to the somatosensory cortex (physical sensation region that identifies and localizes pain), the limbic system (emotional feeling region that experiences suffering), and the frontal cortex (thinking region that assigns meaning to the pain) (Raff & Levitzky 2011). Physiological responses associated with pain perception include an increase in RR, increase in HR, and an increase in MABP (Seiger et al. 2012; Moltner, Holzl, & Strian 1990; Chawla & Kochar 1999).

Pain is a significant national health problem. It is the most common reason individuals seek medical care, with millions of medical visits annually, and some studies suggest that more than a third of the American population suffers from a chronic pain condition at some point in their life (New Directions in Pain Research, NIH). The American Academy of Pain Medicine estimates that pain costs our society between $560-$650 billion annually between the cost of healthcare to treat and the amount of productivity lost when unable to work (Institute of Medicine of the National Academies 2011). Both physical and monetary burdens of pain from an individual to a national scale present motivation for researching effective, low-cost pain relief that will improve quality of life.

The body employs various methods to modulate pain. One mechanism of pain reduction implicates neural pathways that activate low threshold mechanoreceptors (Purves et al. 2001). Studies have found that several supraspinal sites control sensory input by administering inhibitory control over neurons in the spinal dorsal horn. Complementary studies have found that there are several defined and organized supraspinal pathways that modulate transmission of sensory input by inhibiting the release of neurotransmitters from the presynaptic sensory neuron or by blocking neurotransmitter

receptors on the postsynaptic sensory neuron (Hagbarth & Kerr 1954; Renn & Dorsey 2005).

Previous research suggests that gum chewing can modulate pain by inducing the anti-nociceptive response. A group of physiologists in Tokyo Medical and Dental University and Toho University School of Medicine has found that rhythmic movement such as gum chewing can suppress the pain responses by enhancing the activity of serotonergic (5-HT) neurons in brain (Mohri et al. 2005). In their study, the researchers had experimental subjects chew mint flavored gum in order to generate rhythmic movement and measured the changes in 5-HT level with different levels of pain stimuli. Another study also suggests that chewing can help modulate pain. Ogawa et al. (2003) reported that masticating hard food suppressed chronic pain in rats, and the opioid system is suggested to be at least partially involved in the anti-nociceptive response.

A commonly used procedure to measure the physiological responses of pain is the CPT, a stimulus that produces a slowly mounting pain of mild to moderate intensity. The CPT has been used in many studies of pain, autonomic reactivity, and hormonal stress responses. An individual places his or her hand in ice water and that individual's heart rate and blood pressure are measured (Lowery 2003). The cold pressor test can also be used to indicate an individual's pain threshold (when pain starts occurring) and pain tolerance level (how long the individual can withstand the pain) with respect to time.

In this study we examine the effects of chewing gum on the physiological responses of pain as measured by the Cold Pressor Test. We hypothesize that an individual chewing gum undergoing the CPT will show a higher pain threshold and tolerance, as well as smaller increases in heart rate, blood pressure, and respiratory rate compared to when undergoing the CPT without chewing gum.

Materials and Methods

The resting HR, MABP, and RR were recorded using a Life Source Automatic Wrist Blood Pressure Monitor, BIOPOAC Systems simple sensor respiration transducer, and BIOPAC Student Lab software for four experimental conditions. Condition 1 served as a negative control: the subject did not chew gum (CG) and did not undergo the CPT (-CG/-CPT) in order to establish baseline HR, MABP, and RR values for later comparison. Conditions 2 and 3 served as positive controls (PC) for each variable. For condition 2, the subject underwent the CPT without chewing gum (-CG/+CPT). For condition 3, the subject chewed gum but did not undergo the CPT (+CG/-CPT). In condition 4, the subject chewed gum while undergoing the CPT (+CG/+CPT). All subjects were exposed to each of these conditions. Between the conditions with cold pressor tests and without cold pressor tests, subjects were given at least 20 minutes to rest in order to ensure proper recovery of the subject's physiological resting rates. The order of the conditions each subject was placed in was randomized in order to minimize the systematic error.

Test administrators placed the BIOPAC respiration sensor belt around subjects' chests and attached the blood pressure monitor to subjects' wrists to record baseline measures for HR, MABP, and RR. Subjects were informed of the test logistics according to the procedure below and requested to avoid speaking while undergoing the CPT to avoid discrepancies in data collection. The subject then placed his/her hand into an ice water bath maintained at 4^{o} C to undergo the CPT. The subject indicated the first onset of pain after submersion, by tapping his or her finger, and this threshold time was recorded. When the subject could no longer tolerate the cold, he/she removed the hand from the water bath, and time at indication of maximum pain tolerance was recorded. HR, MABP, and RR were recorded immediately after the subject

completed the CPT. The systolic and diastolic blood pressure values were converted to MABP values in order to describe the blood pressure in an individual for each condition. For each subject, MABP, HR and RR data were compared across conditions. 20 subjects (consisting of 12 males and 8 females) from Physiology 435 were assessed. Subject ages were 20-25 years. All gum administered in the experiment did not contain sugar.

Procedure

Preparation:

1. Prepare ice bath of 4º C by adding ice to bucket of cool water and measuring temperature with thermometer.
2. Attach blood pressure and heart rate monitor to subject's wrist (on the opposite hand of that to be placed in water).
3. Attach respiratory rate monitor around subject's chest and connect to BIOPAC Systems monitor and computer.
4. Record data for resting baseline of subject's respiratory rate, heart rate, and blood pressure for 1 minute while subject is seated.

Testing:

(to avoid distraction and limit data discrepancies, subject should undergo test without speaking)

1. Immediately, after baseline values are determined, subject places hand into ice water bath.
    a. Ice water bath is placed at a height below the subject's seated level so that the hand can be comfortably submerged in a upright, relaxed seated position.
    b. Hand is submerged up to the wrist
    c. Subject is instructed to keep palm open (do not make a fist)
2. Subject is timed while hand is submerged in the ice water bath to determine pain threshold (onset) and tolerance.
    a. Subject is instructed to indicate onset of pain by tapping finger of hand.
    b. When pain becomes intolerable subject removes hand.
    c. Maximum tolerance time is limited to 5 minutes, at which point subjects are asked to remove the hand from the ice bath.

Data Measurements:

1. Respiratory rate is measured continuously by BIOPAC systems software.
2. Heart rate is measured at rest and after the subject removes their hand from the ice water bath.
3. Blood pressure is measured at rest and when subject removes hand from ice water bath.

Recovery:

1. The subject was allowed to dry their hand off with paper towel after the cold pressor test was conducted.
2. Subjects were instructed to wait at least 20 minutes until returning for another cold pressor condition. After 20 minutes subjects were allowed to come back at their leisure.

Statistical Analysis

Collected data were analyzed by the Wilcoxon signed-rank test to determine statistical significance using the Rstudio (2012). Each subject's data from condition 2 (-CG/+CPT) and from condition 4 (+CG/+CPT) were paired to test whether their population means are different. We accepted the result to be significant if a p-value less than 0.05 was obtained.

Results

Mean Arterial Blood Pressure:

The median MABP among subjects did not show much variation across different experimental conditions (Table 1). In condition 1 (-CG/-CPT), it was 121.5 mmHg. In condition 2 (-CG/+CPT), the median value was 122.2 mmHg, and it was 124 mmHg in condition 3 (+CG/-CPT). Finally, the median MABP during condition 4 (+CG/+CPT) was 121.2 mmHg. Both direction and increment of the net change in MABP between condition 2 and condition 4 varied among subjects (Table 2, Figure 1). Subject number 16 had the largest increase (23.0 mmHg) in MABP in condition 4 compared to that in condition 2. On the other hand, subject number 8 had the largest decrease (-16.3 mmHg). Overall, the median net change in MABP was -0.5. The net change is statistically analyzed to be insignificant with a p-value of 0.823 (Table 3).

Heart Rate:

The median HR for subjects in condition 1 (-CG/-CPT) was 74.5 beats per minute (Table 1). While undergoing the Cold Pressor Test (CPT), median HR decreased to 69.0 bpm in condition 2 (-CG/+CPT). The positive control group for chewing gum (+CG/-CPT) produced a decrease in median HR of 72.5 bpm. Undergoing the CPT while chewing gum (+CG/+CPT) yielded a median HR of 72.0 bpm, which showed a decrease from baseline measures, but a median net increase of 5.5 bpm from condition 2 (Table 2). A Wilcoxon statistical analysis was conducted to obtain a p-value of 0.005 (Table 3). This net increase is significant, and the treatment of chewing gum, while undergoing the CPT, suggests a statistically significant impact on HR. Seventeen out of twenty participants showed an increase in HR, with an average increase of 6.25 beats per minute (Figure 2).

Respiratory Rate:

The median respiratory rates among subjects showed slight variation across different experimental conditions. The values were 17.0, 17.5, 18.0, and 19.0 breaths/min for conditions 1 to 4 respectively (Table 1). Similar to the MABP measures, both direction and increment of the net change in RR between condition 2 and condition 4 varied among subjects (Table 2). Subject number 7 had the largest increase (9 breaths/min) in RR when comparing the difference in condition 2 and 4. However, subject number 1 had a decrease (-5 breaths/min) in RR. The median net change in RR was 1.0. Overall, twelve out of twenty subjects showed an increase in RR going from condition 2 to condition 4 (Figure 3). The statistical analysis was concluded insignificant with a p-value of 0.903 (Table 3).

Pain Tolerance and Threshold:

The most noticeable characteristic of pain tolerance and threshold data was that it varied greatly by individual (Table 1). In the positive control condition 2 (-CG/+CPT), pain threshold ranged over 149 seconds and tolerance ranged over 275 seconds. Several subjects showed extremely high initial pain tolerance in comparison to others, and subjects 6, 10, and 15 reached the maximum time limit of 300 seconds for submersion in the ice water for condition 2 (Figure 4). Subject 11 also showed exceptionally high tolerance at 270 seconds. In condition 4 (+CG/+CPT), pain threshold and tolerance again covered wide ranges of 131 seconds and 282 seconds respectively. The same three subjects who were outliers in condition 2 again reached the maximum time limit, with the addition of Subject 11.

From Table 2, the net average change in pain threshold was an improvement of 2.40 seconds, but standard deviation was high at ± 29.43. Ten of twenty subjects showed increased pain threshold times, and subject 9 was an

outlier with improvement of 116 seconds from positive control condition 2 to experimental condition 4. Alternately, four out of twenty subjects showed declines of 19 seconds or more (Figure 4). The median threshold improvement of 0.5 seconds therefore presents a more accurate representation of change in pain threshold, but the statistical p-value 0.911 (Table 3) is too high to be considered significant, and from these results the null hypothesis cannot be rejected. Similarly, the net average change in pain tolerance was 29.20 seconds across twenty test subjects, but the standard deviation was again high at ±58.37 (Table 2). This can be attributed to several outliers who showed improvement in tolerance upwards of 75 seconds (Figure 5). The median improvement in tolerance was 0.5 seconds, and the statistical p-value 0.072, (Table 3) is again above the significance level, meaning that there is no evidence to reject the null hypothesis. However, it is clear that the overall trend in the net change in pain tolerance from condition 2 to condition 4 is positive (Figure 5).

Discussion

Mean Arterial Blood Pressure:

Literature suggests an expected increase in blood pressure for an individual undergoing CPT. According to Gagnon et. al. (2013), immersing the face into cold water produced an increase in systolic blood pressure by nine percent and in diastolic blood pressure by five percent. This increase is caused by a constriction of the arteries in order to preferentially direct blood to vital organs. Nagaoka et. al. (2002) demonstrated that the increase in MABP during a CPT was significantly correlated to the decreased diameter in the retinal artery.

In our study, a Wilcoxon statistical analysis using the data from condition 2 and 4 found a p-value of 0.823 (Table 3), showing no significance. However, nine of twenty subjects did exhibit the expected increase in MABP, which is consistent with Ferrari et al. (1987) characterization of blood pressure in having large spontaneous variability. Additionally, BP cuffs may give highly varied readings without any external influences present. Instances of significant prolonged or chronic pain have been demonstrated to cause an increase in MABP (Chawla & Kochar 1999), which contrasts with the short, timely manner of our experimental design. The combination of highly variable MABP readings and the relatively short exposure to pain in our study are likely the reasons that a significant change in MABP was not observed.

Heart Rate:

From an initial review of literature pertaining to chewing gum as a method to modulate pain response, we inferred that our experimental condition would result in manifestation of pain responses to a lesser degree: that a CPT conducted while chewing gum would produce a smaller increase in HR than the CPT alone. We predicted that the CPT would produce elevated HR due to induction of a general sympathetic response of the autonomic nervous system.

Further review of scientific literature indicates that the HR response to the CPT is not well defined and may be largely variable on an individual basis, and our results are consistent with this variability. One CPT study found that nineteen of thirty participants had a decrease in HR after an initial increase (Mouret et al. 2009). Similarly, in our study, eleven of twenty participants showed decreases in HR under the positive control conditions of the CPT, with an overall decrease in median for all twenty subjects. Upon obtaining decreased HR as a response to the positive control, rather than the expected increase, it is important to consider possible causes of reduced heart rate as a result of the cold pressor test. According to Tulppo et al. (2005), in healthy subjects, the result of

cardiac autonomic co-activation can be a decreased HR due to simultaneous sympathetic and vagal outflow that may lead to marked changes in beat-to-beat interval dynamics, an increase in blood pressure, and a breakdown of fractal organization of heart rate (Tulppo et al. 2005), which provides a possible explanation for decreases in HR that were observed in the CPT positive control condition 2. However, In analyzing the change in HR from positive control to experimental condition 4 (+CG/+CPT), subjects showed a median net increase of 5.5 bpm with a significant p-value of 0.005 (Table 3), which indicates that chewing gum while undergoing the CPT does have a significant impact on HR.

Owing to the fact that the positive control condition did not produce the anticipated increases in HR and produced a decrease in HR, it is difficult to compare data between conditions 2 (-CG/+CPT) and condition 4 (+CG/+CPT) in the way that our study initially intended. Literature on the effects of mastication on heart rate variability reveals that chewing also plays a role in the sympatho-vagal balance of the regulation of the heart by enhancing the sympathetic nervous activity and resulting in an increased heart rate (Shiba et al., 2002), which is consistent with the median net increase in HR produced by experimental condition 4. While we were unable to prove or disprove our hypothesis that chewing gum minimizes variation in HR caused by CPT pain due to unexpected results from the positive control CPT, our results do support that chewing gum produces statistically significant increases in HR. These results provide motivation to conduct further study of the CPT to determine whether a more predictable and consistent pain response in pertaining to HR can be produced.

Respiratory Rate:

Physiological measures under the positive controls for ice and gum chewing showed changes, compare to the baselines, in the direction we expected based on the literatures. After administration of a pain stimulus, there was a slight increase in RR as the median RR increased from 17.0 breaths per minute in condition 1 to 17.5 breaths per minute in condition 2. This is in accordance with Seiger et al. (2012) who suggest that RR will increase significantly in the presence of any pain stimuli. Additional studies suggest that there are more factors at play affecting RR aside from the pain stimuli. In a study conducted by MacFarland and Lund (1995), mastication influenced respiratory rhythms as shown by an increase in respiratory rate for most subjects. Our data also shows that there was an increase in RR in gum chewing condition compare to the baseline. The median RR increased by 1 breaths per minute in condition 3 compare to the RR in condition 1.

Despite the appropriate changes in positive controls, our experimental data did not yield any statistically significant result. The Wilcoxon analysis of the difference in RRs in conditions 2 and 4 found p-value of 0.903 (Table 3), and this is highly above the significant level. The failure to prove significance may be explained by having large individual variations with eight out of twenty individuals have decreases in RRs in condition 4 (Figure 3).

Pain Tolerance and Pain Threshold:

The experimental data showed no significant difference in pain threshold between the chewing and no chewing CPTs (p= 0.911). As seen in Table 2, subjects showed both small increases and decreases in threshold time between conditions resulting in a net median change of 0.5 seconds. We expected to see an increase in threshold time in the chew condition based on the pain modulation mechanisms described in Mohri et al. (2005) and Ogawa et al. (2003). The Mohri et al. (2005) study is based on the theory that the rhythmic movement of chewing increases the 5-HT neural activity

which in turn suppresses nociceptive responses and decreases pain. The study successfully measured an increase in 5-HT levels after 20 minutes and nociceptive suppression after five minutes of chewing gum. As participants in our study started chewing gum approximately one minute before the CPT this may not have been sufficient time for 5-HT levels to rise and begin to suppress pain. The general trend towards an increase in pain tolerance could be due to gradually increasing 5-HT action with time. Future studies could increase chewing time before pain is induced by the CPT to see if there is a greater difference in time to threshold and tolerance.

Another possible cause of the insignificant change in time to threshold may be the subjectivity of asking each subject to indicate "when they first feel pain". Though pain itself is subjective and can vary between people, we did not expect the subjectivity to be a factor in time to threshold or tolerance as each participant would judge pain similarly in both conditions. However, these instructions may have been too loose to get meaningful data. Future studies could ask participants to indicate when specific sensations such as tingling or numbness occur to obtain more concrete comparisons.

Limitations:

One area that could potentially be improved in our procedure was the method of inducing pain. Subjects may not have experienced sufficient pain to show a significant change in heart rate, blood pressure and respiratory rate. Fifteen percent of the subjects were so tolerant of pain that they exceeded the maximum time limits designed for the CPT. This made it impossible to measure their change in pain threshold because subjects were required to take their hand out at 300 seconds regardless of how comfortable they felt with their hand in the ice water.

When conducting our experiment it was also observed that, regardless of whether the subjects were chewing gum, subjects tended to keep their hand in the bucket longer the first time compared to the second time. This was most likely because the subject had already developed a negative association with putting his or her hand in the bucket after the first cold pressor test. Randomization of the order in which conditions were tested should have reduced the effects of this negative association; however, this effect might be further minimized by conducting each CPT condition on different lab days.

Lastly, the way in which we measured the amount of pain the subject experienced should be considered. There may have been other, more useful ways to record how much pain the subject experienced. Another possible physiological measure of pain response is electrodermal activity. According to a study by Romano et. al. (2014) upon anticipation of pain the Skin Conductance Response (SCR) increases. Though this measures anticipation of pain and not pain actually experienced, it might offer another measurement of biological pain response. As subjects were well informed of the pain they would be subjected to, it would be reasonable to say that measuring the electrodermal activity would have been a useful comparison of how pain affects the body under chewing and non-chewing conditions.

Conclusion:

In our study we predicted that subjects would have a higher pain tolerance when undergoing a CPT while chewing gum associated with smaller increases in heart rate, blood pressure, and respiratory rate than when not chewing gum. However, our result shows that only the change in heart rate is statistically significant and in accordance with our prediction. Due to our inconclusive data, we can neither accept nor reject our hypothesis. Though

we only saw significant results in the change in heart rate in this study, we still believe that with refinement of the procedure, our hypothesis may still be proven correct. This study provides future groups with baseline data and ideas to improve upon. The burden of pain on our society, both physical and monetary, demands that the research communities continue to investigate mechanisms by which pain is managed and eliminated. Studies looking at tools for immediate reduction in pain response by altering hormone levels and nociceptor activity pave the way for chronic pain modulation. Should chewing gum be proven to be an effective modulator of pain response, it would provide an extremely low-cost, accessible option for millions of people suffering worldwide.

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Table 1. MABP, HR, and RR values obtained for subjects in -CG/-CPT, -CG/+CPT, +CG/-CPT, and +CG/+CPT conditions. Average,median, and standard deviation values MABP, HR, and RR were obtained for each condition.

	Base			Positive Ctrl Ice			Positive Ctrl Chew			Experimental			No Chew		Chew	
subject	MABP	HR	RR	MABP	HR	RR	MABP	HR	RR	MABP	HR	RR	Pain Toler	Pain Thresh	Pain Toler	Pain Thresh
1	75.0	85	17	94.3	82	23	97.7	83	15	93.0	78	18	49	10	38	9
2	121.3	75	20	120.0	69	20	117.0	80	18	112.7	76	22	63	7	51	14
3	117.7	74	15	132.7	63	19	109.3	64	16	136.7	64	17	85	52	86	25
4	111.7	76	14	106.3	66	18	111.3	80	18	107.0	75	19	76	69	105	60
5	124.0	91	15	130.0	86	18	132.3	97	20	130.3	92	20	38	33	32	26
6	120.7	62	19	133.7	69	17	131.3	69	20	120.7	72	20	300	11	300	13
7	100.7	56	18	89.3	58	15	108.7	61	20	103.3	62	24	60	18	47	26
8	121.7	67	16	136.0	58	21	128.0	71	18	119.7	68	19	26	23	35	33
9	116.7	60	18	112.3	64	17	133.3	75	19	130.3	71	18	41	24	145	140
10	138.7	76	16	147.3	74	15	126.0	79	19	136.0	107	18	300	54	300	35
11	130.0	52	14	121.3	50	17	131.3	51	18	115.0	62	14	270	56	300	66
12	126.7	80	17	125.3	75	17	124.0	86	18	123.7	84	19	38	9	70	15
13	145.3	61	22	111.0	66	23	116.0	72	16	107.0	67	20	103	11	300	19
14	135.0	85	17	128.7	69	14	127.0	99	14	140.7	93	20	35	14	28	10
15	133.7	77	14	126.0	80	15	129.7	63	18	132.0	83	17	300	156	300	126
16	114.0	75	17	111.3	79	24	122.7	90	15	134.3	89	21	76	45	93	48
17	130.0	66	16	123.0	71	17	140.3	72	18	127.3	71	17	73	55	150	33
18	100.7	58	16	115.0	61	14	106.0	70	18	112.7	66	16	90	9	240	14
19	133.3	75	19	132.7	69	18	124.0	59	17	121.3	55	16	43	18	37	16
20	114.0	73	24	108.0	73	23	120.7	73	16	120.7	72	19	25	22	18	16
Average	120.5	71.2	17.2	120.2	69.1	18.3	121.8	74.7	17.6	121.2	75.4	18.7	104.6	34.8	133.8	37.2
Median	121.5	74.5	17.0	122.2	69.0	17.5	124.0	72.5	18.0	121.0	72.0	19.0	68.0	22.5	89.5	25.5
Stdev	15.8	10.6	2.6	14.4	8.9	3.1	10.9	12.4	1.7	12.7	12.7	2.3	98.9	34.6	111.5	36.5

*Units are MABP (mean arterial blood pressure) in mmHg, HR (heart rate) in beat/min, RR (respiratory rate) in breath/min, and pain tolerance and threshold in seconds

Table 2. Individual net change between +CG/+CPT and -CG/+CPT conditions. Individual net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable.

Subject	MABP (mmHg)	HR (beats/min)	RR (breaths/min)	Tolerance (seconds)	Threshold (seconds)
1	-1.3	-4.0	-5.0	-11.0	-1.0
2	-7.3	7.0	2.0	-12.0	7.0
3	4.0	1.0	-2.0	1.0	-27.0
4	0.7	9.0	1.0	29.0	-9.0
5	0.3	6.0	2.0	-6.0	-7.0
6	-13.0	3.0	3.0	0.0	2.0
7	14.0	4.0	9.0	-13.0	8.0
8	-16.3	10.0	-2.0	9.0	10.0
9	18.0	7.0	1.0	104.0	116.0
10	-11.3	33.0	3.0	0.0	-19.0
11	-6.3	12.0	-3.0	30.0	10.0
12	-1.6	9.0	2.0	32.0	6.0
13	-4.0	1.0	-3.0	197.0	8.0
14	12.0	24.0	6.0	-7.0	-4.0
15	6.0	3.0	2.0	0.0	-30.0
16	23.0	10.0	-3.0	17.0	3.0
17	4.3	0.0	0.0	77.0	-22.0
18	-2.3	5.0	2.0	150.0	5.0
19	-11.4	-14.0	-2.0	-6.0	-2.0
20	12.7	-1.0	-4.0	-7.0	-6.0
Average	1.01	6.25	0.45	29.20	2.40
Median	-0.5	5.5	1.0	0.5	0.5
Stdev	10.80	9.73	3.50	58.37	29.43

Table 3. Wilcoxon statistical analysis of variation between -CG/+CPT and +CG/+CPT conditions. There was no significant difference in MABP, RR, Pain Tolerance, and Pain Threshold between -CG/+CPT and +CG/+CPT conditions. A significant difference was found in HR between -CG/+CPT and +CG/+CPT conditions.

	P-value
MABP	0.823
HR	0.005
RR	0.903
Pain Tolerance	0.072
Pain Threshold	0.911

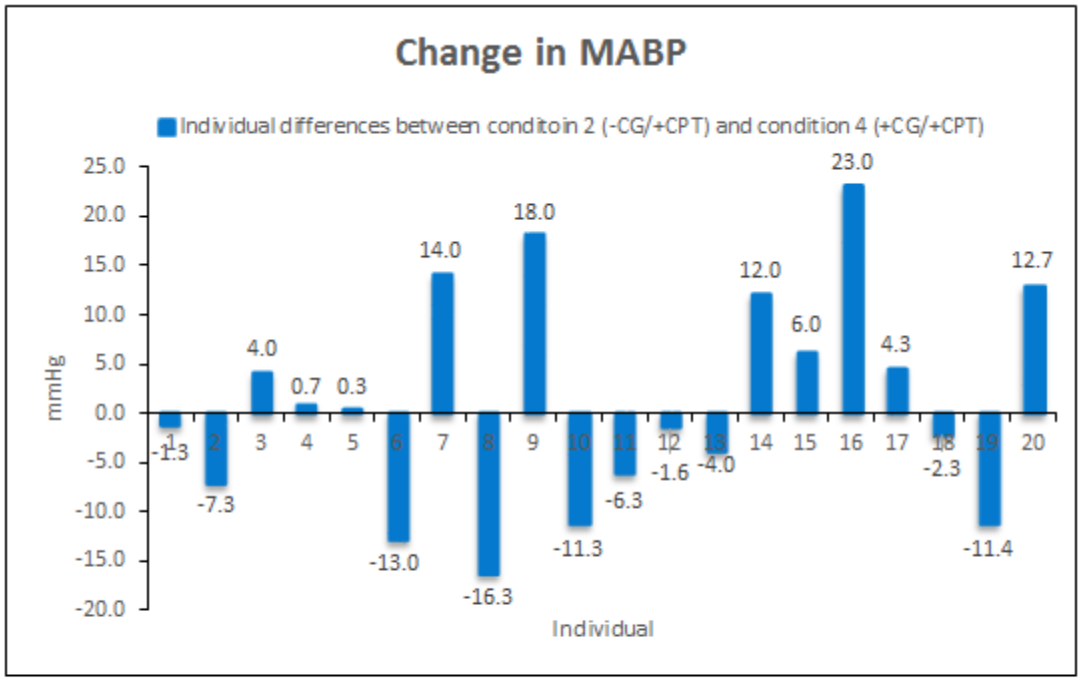

Figure 1. Individual differences between MABP in condition 2 and in condition 4. The net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable. Results show large variation in differences.

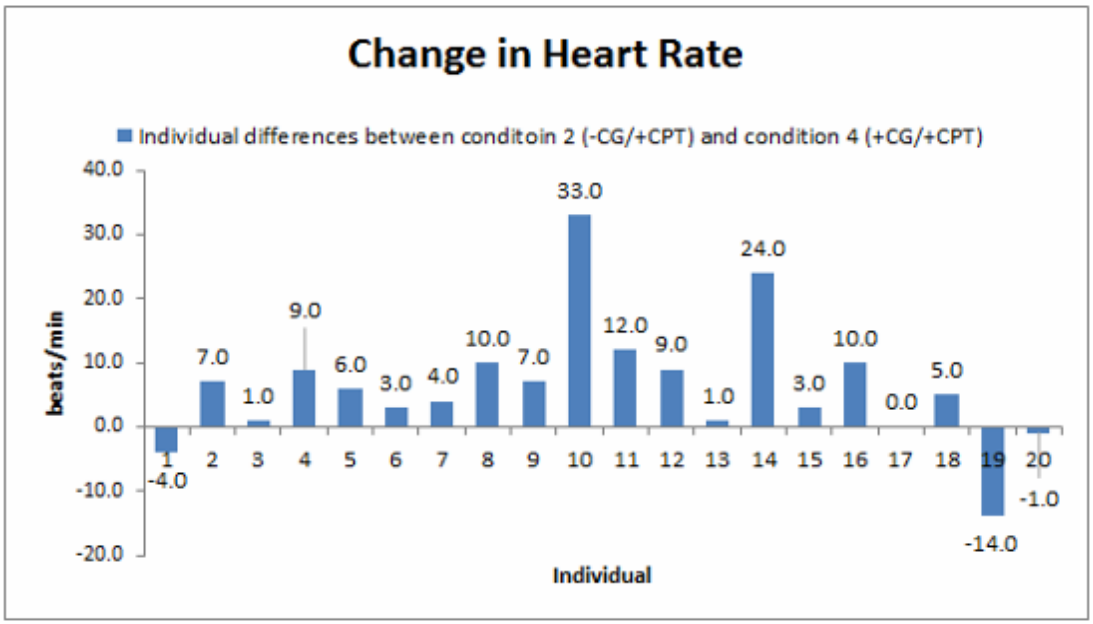

Figure 2. Individual differences between HR in condition 2 and in condition 4. Individual net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable. Overall results show significant increase in HR.

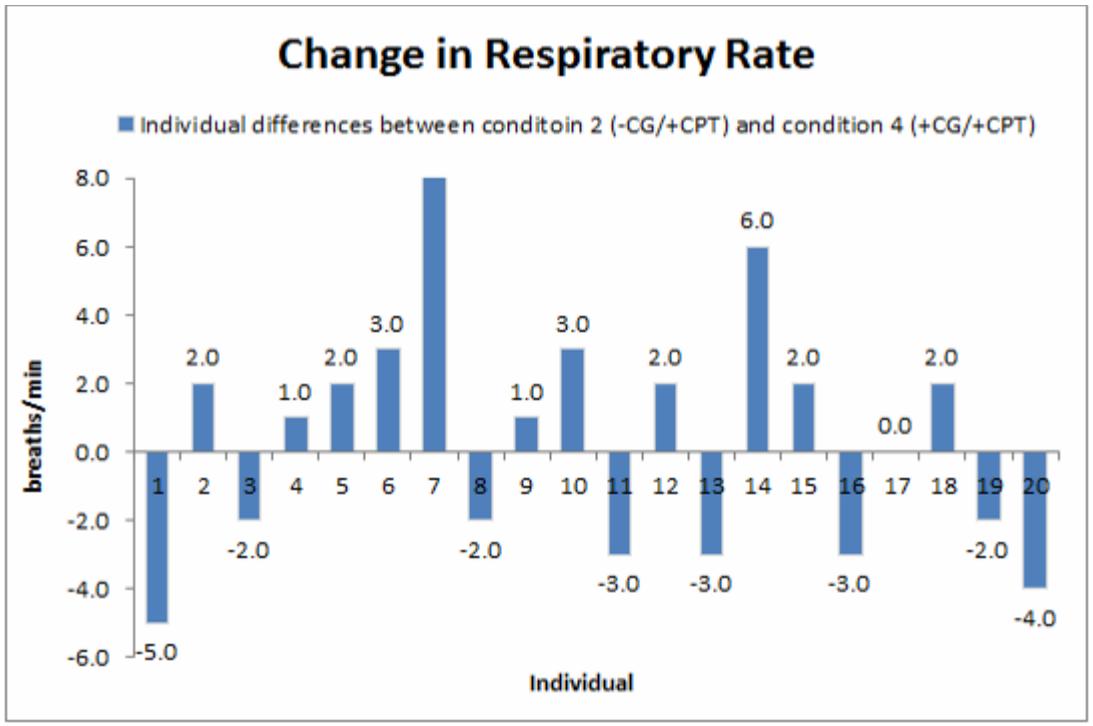

Figure 3. Individual differences between RR in condition 2 and in condition 4. Individual net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable. Results show large variation in differences.

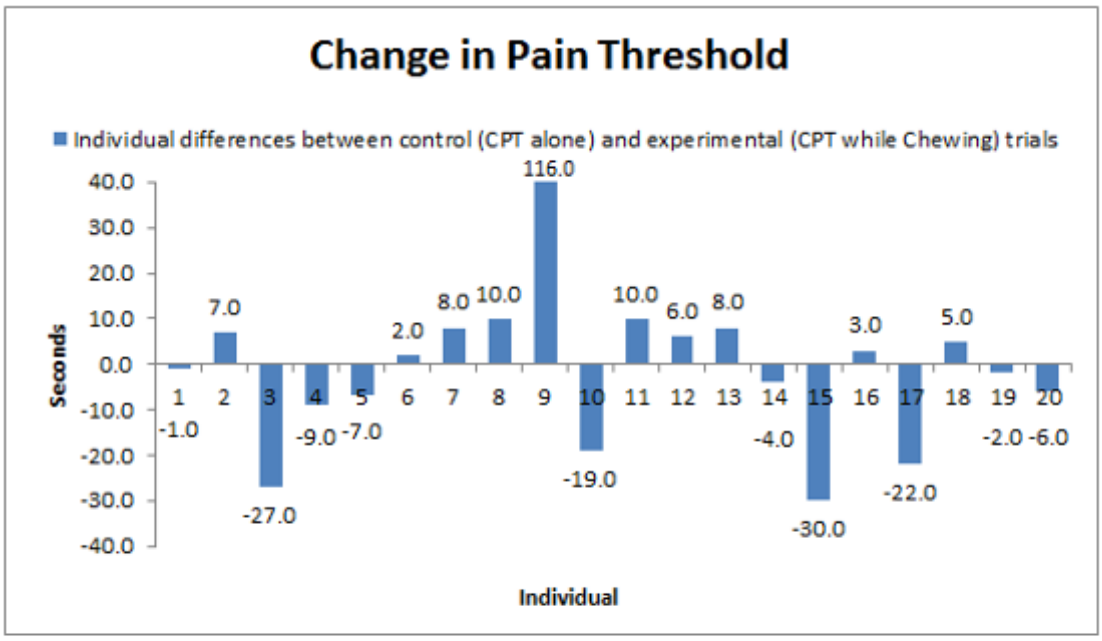

Figure 4. Individual differences between pain threshold in condition 2 and in condition 4. Individual net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable. Results show large variation in differences.

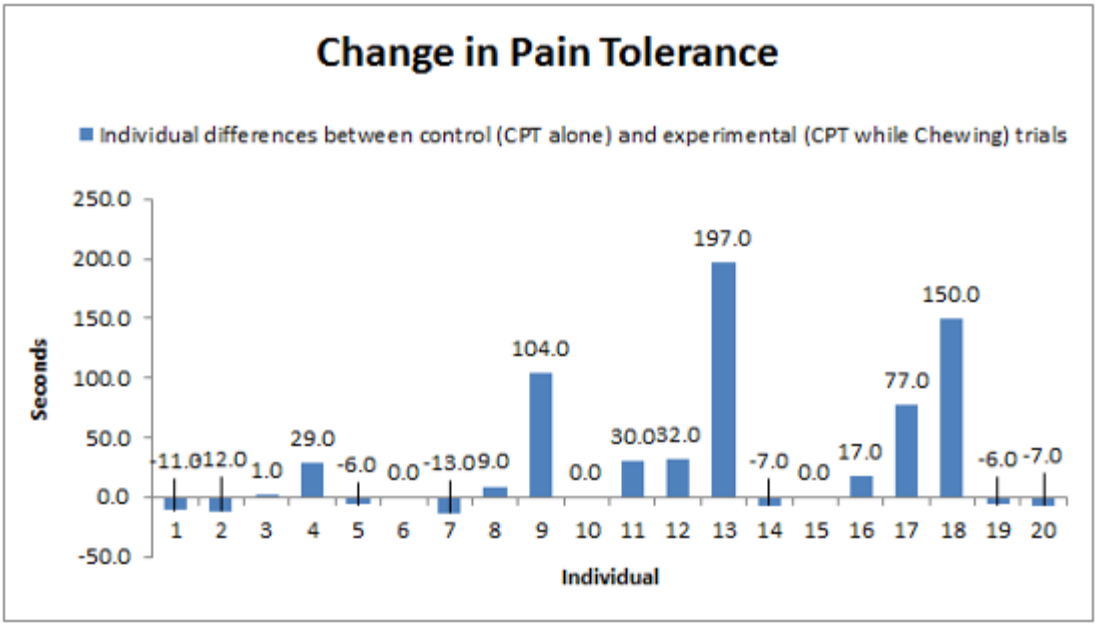

Figure 5. Individual differences between pain tolerance in condition 2 and in condition 4. Individual net change was calculated by subtracting values from +CG/+CPT conditions by values obtained from -CG/+CPT conditions. A positive net change indicated an increase in value for variable while a negative net change indicated a decrease in value for specified variable. Overall, little differences are observed, but there are four outliers in the direction of positive change.