TH460

Impact of expectation of analgesia on conditioned pain modulation in inhibitors and non-inhibitors

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Background and aims

The **conditioned pain modulation** (CPM) test can be **influenced** by supraspinal mechanisms, such as **expectation**. Examining such impact in individuals with **distinct profiles** of CPM efficiency could enhance our understanding of the **mechanisms underlying** endogenous pain modulation and its **clinical implications**. This study assessed the effect of expectation of analgesia on CPM in healthy participants with inhibitory and non-inhibitory modulation.

Methodology

43 healthy participants
22 men and 21 women
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CPM protocol

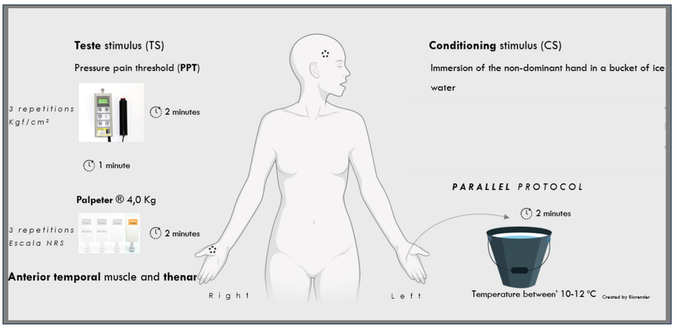


Figure 1. Parallel protocol of the conditioned pain modulation (CPM) test using the digital algometer in the trigeminal and spinal regions. After 30 seconds of immersing the non-dominant forearm in ice water, 3 measurements of the test stimulus (TS) under the influence of the conditioning stimulus (CS) were obtained at the two evaluation sites consecutively, totaling approximately 2 minutes. After a 1-minute interval, the CPM evaluation was performed with another TS

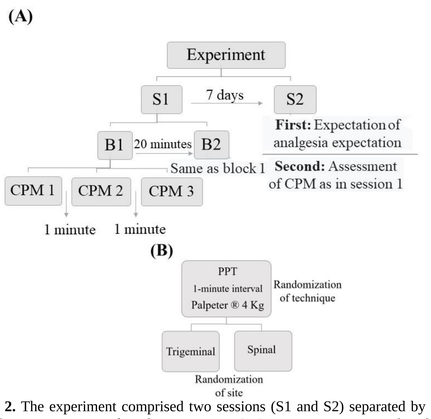


Figure 2. The experiment comprised two sessions (S1 and S2) separated by a 7-day interval. In expectation of analgesia session (S2), participants received audiovisual instructions and suggestions. Each session consisted of two blocks (B1 and B2) separated by a 20-minute interval. Within each block, three repetitions of conditioned pain modulation (CPM) were performed with a 1-minute interval between them (A). During each repetition, the conditioned pain modulation (CPM) was assessed in the trigeminal and spinal region consecutively, using both the unconditioned and conditioned test stimulus (TS) in a parallel. Two types of TS were applied following a 1-minute interval: pressure pain threshold (PPT) and Palpeter® 4Kg (B). This protocol was repeated three times within each block, and the order of the TS and regions was randomized.

Group division made for each technique applied in each region

Observed score = True score + Standard Error of Measurement (SEM)

SEM do TS Basal $= \sqrt{(\sigma 2ex + \sigma 2residual)}$

σ2ex: variance due to systematic differences between the repeated measures of the baseline test stimuli between block 1 and block 2.

σ2residual: indicates the variance of the random error.

CPM = TS conditioned – TS unconditioned

Inhibitor: difference greater than 2xSEM in at least one repetition in B1 for each analysis.

Non-inhibitor: difference less than 2xSEM in all 3 repetitions in B1 for each analysis.

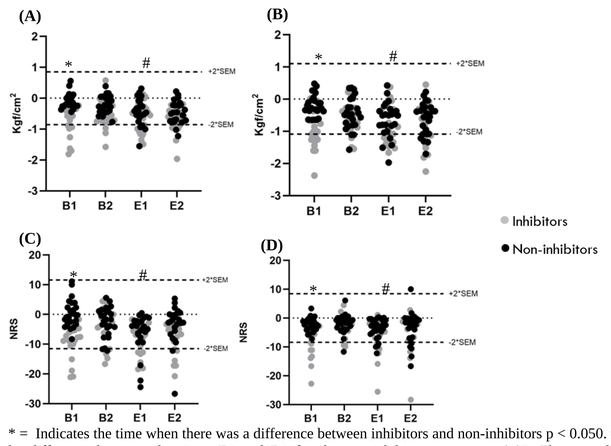
Results

Table 1. Frequency of inhibitors and non-inhibitors individuals at different evaluation times of conditioned pain modulation (CPM) for each region and test stimulus technique. Considering division according to the standard error of measurement (SEM) of each session.

	PPT trigeminal				PPT spinal			
	Inhibitor		Non-inhibitor		Inhibitor		Non-inhibitor	
	N (%)	95% CI	N (%)	95% CI	N (%)	95% CI	N (%)	95% CI
Baseline session								
Block 1	21 (48.8%)	33.3 – 64.5	22 (51.2%) [ac*]	35.5 – 66.7	18 (41.9%)	27 – 57.9	25 (58.1%) [ab]	42.1 – 73
Block 2	17 (39.5%)	25.5 – 55.6	26 (60.5%) [a]	44.4 – 75	20 (46.5%)	31.2 – 62.3	23 (53.5%) [b]	37.7 – 68.8
Expectation of analgesia session								
Block 1	27 (62.8%)	46.7 – 77.0	16 (37.2%) [bc]	23 – 53.3	28 (65.1%)	49.1 – 79	15 (34.9%) [c]	21 – 50.9
Block 2	29 (67.4%)	51.5 – 80.9	14 (32.6%) [b]	19.1 – 48.5	24 (55.8%)	39.9 – 70.9	19 (44.2%) [bc]	29.1 – 60.1
	Palpeter ® 4 Kg trigeminal				**Palpeter ® 4 Kg spinal**			
	Inhibitor		Non-inhibitor		Inhibitor		Non-inhibitor	
	N (%)	95% CI	N (%)	95% CI	N (%)	95% CI	N (%)	95% CI
Baseline session								
Block 1	18 (41.9%)	27 – 57.9	25 (58.1%)	42.1 - 73	14 (32.6%)	19.1 – 48.5	29 (67.4%)	51.5 – 80.9
Block 2	12 (27.9%)	15.3 – 43.7	31 (72.1%) [a]	56.3 – 84.7	11 (25.6%)	13.5 – 41.2	32 (74.4%) [b]	58.8 – 86.5
Expectation of analgesia session								
Block 1	29 (67.4%)	51.5 – 80.9	14 (32.6%) [c]	19.1 – 48.5	18 (41.9%)	27 – 57.9	25 (58.1%) [a]	42.1 – 73
Block 2	24 (55.8%)	39.9 – 70.9	19 (44.2%)	29.1 – 60.1	13 (30.2%)	17.2 – 46.1	30 (69.8%)	53.9 – 82.8

PPT = pressure pain threshold. 95% CI = 95% confidence interval. * = different letters indicate significant differences between evaluation times for each combination of region and test stimulus technique ($p < 0.05$, Cochran's Q test followed by Dunn's test with Bonferroni correction for multiple comparisons).

Figure 2. Mean of conditioned pain modulation (CPM) in blocks 1 and 2 of the baseline session (B1 and B2) and blocks 1 and 2 of the expectation of analgesia session (E1 and E2) for both groups (inhibitors and non-inhibitors), according to the division performed in B1, considering both test stimulus techniques in the two evaluation regions: pressure pain threshold (PPT) in the trigeminal region (A) and spinal region (B), as well as Palpeter® 4Kg in the trigeminal region (C) and spinal region (D).



* = Indicates the time when there was a difference between inhibitors and non-inhibitors $p < 0.050$. # = Indicates the difference between the times E1 and B1 for the non-inhibitor group $p < 0.05$. The error line indicates 2*standard measurement error (SEM) calculated in session 1. It is noteworthy that the inhibitors showed modulation greater than 2*SEM in one of the 3 repetitions in B1, and graph 2 represents the mean CPM of the 3 repetitions at each time point of each analysis.

Conclusion

The expectation of analgesia emerges as a **clinically relevant** pathway for **activating** the descending pain inhibitory system. Moreover, the absence of an additional effect in inhibitors hints at **saturation** or a potential **"ceiling effect"** in this analgesic response. As such, it becomes imperative to consider the **influence** of these **cortical mechanisms** for an accurate and pertinent **profiling** of pain modulation.

Different activation pathways and not necessarily a **"failure"** in the descending inhibitory system

References

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