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Title: Pain pressure threshold, a new way to assess dyspnea-pain counter-irritation?

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**Body:** Introduction. Counter-irritation is the attenuation of a painful sensation by a newly occurring heterotopic stimulus that must be noxious in nature. Dyspnea-pain counter-irritation has been described with experimental dyspnea of the work/effort type, with dyspnea inhibiting laser evoked cortical potentials and RIII flexion reflex. Pain pressure threshold (PPT) using algometry is an easy to use and reliable model to induce acute experimental pain. Objectives. Assess the effects of experimental work/effort dyspnea on PPT. Methods. Inspiratory threshold loading was used to induce experimental dyspnea (work/effort) in 14 young and healthy volunteers. PPT were obtained using a pressure algometer at baseline and at two different intensities of dyspnea; visual analogic scale (VAS) ratings  $\geq 6$  and  $\geq 8$  cm. Force was applied incrementally on non-dominant trapeze, biceps and deltoid muscles of the subjects during 3 conditions: baseline, VAS dyspnea ≥ 6 and VAS dyspnea ≥ 8. Results. PPT increased significantly with increasing dyspnea ratings; trapeze (35.3 N to 44.2 N to 46.3 N; F = 8.3, p = 0.01), biceps (29.2 N to 33.7 N to 42.0 N ; F = 13, p = 0.001) and deltoid (41 N to 50.1 N to 52.9 N; F = 8.7, p = 0.01) for baseline, VAS dyspnea  $\geq 6$ and VAS dyspnea ≥ 8 respectively. Dunn's multiple comparison test showed that VAS dyspnea ≥ 6 significantly increased PPT for the deltoid only, while VAS dyspnea ≥ 8 increased PPT for all 3 muscle sites. Conclusion. Work/effort dyspnea significantly increases PPT, with an apparent dose-response relationship. PPT is an easy to use method for assessing dyspnea-pain counter-irritation, that could be used to indirectly but more objectively measure dyspnea in clinical populations.