What do we really know about distance-based spatial summation of noxious stimuli in humans? A Systematic Review. Emily Reid, Daniel Harvie, Charles Spence & Lorimer Moseley

When the area of noxious stimulation to the skin is increased, the intensity of the pain that is evoked also increases and the intensity of summation at which pain is first evoked decreases. This is spatial summation (SS), and is a well-accepted characteristic of the nociceptive system. While area-based SS seems well defined, there is more ambiguity with respect to distance-based SS, where an increase in the distance between multiple stimuli increases pain intensity. Although it too is widely accepted, the experimental evidence underpinning distance-based SS has not been formally critiqued.

OBJECTIVE

We aimed to determine the evidence for distance-based spatial summation of nociceptive stimuli, and to define the limits at which it gives rise to conditioned pain modulation.

METHODS

A systematic search of the literature was executed according to the PRISMA and Cochrane guidelines. Studies were included if they measured pain in response to two identical noxious stimuli, delivered at two or more different separations. Records were screened by two investigators and data were extracted by one, double checked by a second. A modified McMaster’s appraisal tool was used by two reviewers to test for risk of bias.

RESULTS

After screening, the full-text of 13 studies was retrieved. Eight studies were included and authors were contacted. Full data were available for seven studies, which tested distance-based SS of noxious contact heat (4), laser heat (1), contact cold (1), or mechanical (1) stimuli.

Records identified through databases: Scopus (n=173), Web of Science (n=147), EMBASE (n=103), MEDLINE (n=76), PubMed (n=75), Academic Search Premier (n=33), CINAHL (n=13), Cochrane Collaboration (n=8), AMED (n=4), Pedro (n=5). Total n = 632.

Eligibility     Screening     Identification

Records after duplicates removed n = 245
Records title & abstract screened n = 245
Full-length articles assessed for eligibility n = 24
Studies assessed eligible for review n = 8
Studies included in qualitative synthesis n = 7
Stage performed by two independent researchers
Stage performed by one researcher

Contact heat

0.5°C/s
4°C/s

Defrin et al. 2006

Contact cold

0.92
0.94
0.96
0.98
1.00

Defrin et al. 2011

PPI relative to single stimulus

0 10 20 30 40
Separation (cm) between paired stimuli

0.08
0.10
0.12

Defrin et al. 2011

PPI relative to single stimulus

0 10 20 30 40
Separation (cm) between paired stimuli

LASER HEAT

MECHANICAL

Control & Fibromyalgia

Staud et al. 2007

Control

Arm

Abdomen

March et al. 2010

Staud et al. 2007

HPT = heat pain threshold; CPT = cold pain threshold; PPI = perceived pain intensity; ABD = abdomen; n = sample size; NC = control group; FM = fibromyalgia.

Results from the modified McMaster Critical Appraisal tool revealed that all studies had moderate to high risk of bias. There was consistency between the studies - all showed higher pain intensity for two stimuli than for one - but also variability - some showed greatest spatial summation at small separation (0cm), others at large separation (10cm) and still others had no difference between separations.

CONCLUSION

There are no data that interrogate distance-based SS to electrical or chemical stimuli and the limits of SS of thermal and mechanical stimuli are not clear. This review highlights deficiencies in the current understanding of SS of noxious information, and raises the possibility that our acceptance of distance-based spatial summation is premature.