WITHIN-SUBJECTS' VARIABILITY OF EXPERIMENTAL PAIN AND ITS RELATIONS WITH PAIN SENSITIVITY AND PAIN MODULATION IN FIBROMYALGIA

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Introduction

- Recent findings highlighted the clinical relevance of within subjects' variability of pain scores in response to both experimental and clinical pain **[1,2,3]**.
- Fibromyalgia (FM), a chronic pain condition which is characterized with impaired pain descending modulatory system and larger within-subject pain variability **[4,5,6]**, offers an opportunity to further investigate this topic.
- The aim of this study was to investigate relationships between experimental pain variability and pain sensitivity and pain modulation in FM.

Materials and Methods

- FM patients were recruited from the Rheumatology Department of the Centro Hospitalar de Lisboa Ocidental, Portugal, underwent a battery of experimental pain tests, comprised of various noxious modalities (electrical, thermal, pressure) and assessing pain sensitivity (threshold, tolerance), modulation (Electrical Temporal Summation and Conditioned Pain Modulation of tonic heat and phasic pressure pain) and experimental pain variability (FAST).
- Experimental pain variability was assessed using the Focused Analgesia Selection Test (FAST), a a psychophysically-based laboratory method based on the induction of thermal noxious stimulus of different intensities (44-50ºC). The patients rate the pain intensity of each stimulus applied to the ventral surface of the forearm on a 0-100 numerical rating scale (NRS), in which 0 denotes "no pain" and 100 "the worst pain imaginable. FAST outcome measures are R2, ICC and CoV.
- Information related to symptoms and psychological characteristics was also collected using Brief pain inventory (BPI), Fibromyalgia impact questionnaire (FIQ), 36-Item short form health survey (SF-36), The international physical activity questionnaire (IPAQ), Functional assessment of chronic illness therapy-fatigue (FACIT fatigue) and Hospital depression and anxiety scale (HADS).

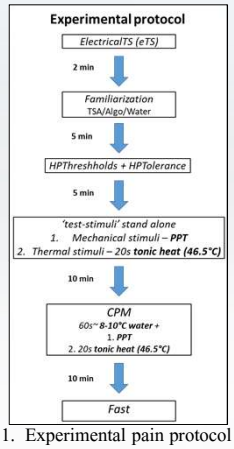


Figure 1. Experimental pain protocol description

Results

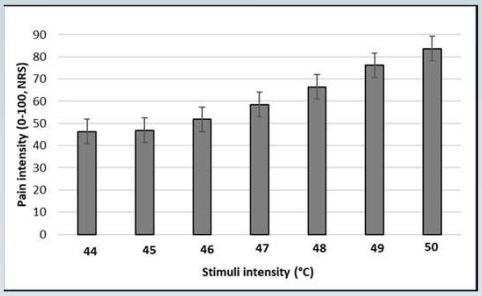
Participants' Characteristics

- Twenty-nine FM patients completed the study with mean ± standard deviation (SD) of 50.41 ± 10.34 years. Beginning of the symptoms among participants was mean ± SD 13.96 ± 11.21.

FAST mean pain and outcomes

- Figure 2 illustrates the FAST mean pain scores. Mean pain scores were significantly different in each temperature (Friedman's test, chi-square 125.79; P <.000) and Post hoc Wilcoxon test revealed that there was a significant difference between each two consecutive stimuli intensities (P<0.05) except between 44°C and 45°C (P=0.510)

Figure 2. FAST Mean pain scores



- FAST outcome measures can be found in table 1

	R^2	ICC	CoV
Mean (SD)	0.469(0.15)	0.546 (0.19)	0.360 (0.36)
Median	0.493	0.575	0.281
Minimum	0.006	-0.139	0.000
Maximum	0.701	0.774	1.560

Table 1. FAST outcome measures

Pain sensitivity measures

- Table 2 illustrates the results for pain thresholds of each stimuli modality and Table 3 the pain modulation results

Test	Mean ± SD	Range
Electrical pain threshold (mA)	16.7±1.30	2.0-5.90
Heat pain threshold (°C)	41.84±4.20	34.80-48.63
Pressure threshold (kg-f)	2.88±1.34	1.07-6.60

Table 2. Pain sensitivity results

	NPS1 (Mean ± SD)	NPS2 (Mean ± SD)	Δ ETS
ETS (mA)	22.59 ± 23.47	46.07 ± 32.14	23.48 ± 22.18
	Test stimulus stand alone (Mean ± SD)	**Test Stimulus under conditioning (Mean ± SD)**	**Δ CPM**
CPM PPT (KgF)	28.81 ± 13.39	34.25 ± 17.01	5.43 ± 11.50
CPM Tonic heat (NPS)	64.37 ± 29.19	67.01 ± 30.16	2.64 ± 13.94

Table 3. Pain modulation results

Correlations between FAST and Pain Sensitivity

- Positive correlations were found between FAST, specifically the CoV outcome measure, and pressure pain threshold (Spearman's r=0.414, P=0.26). CoV also correlated with heat pain tolerance (Spearman's r=0.473, P=0.10). No correlations were found between FAST and electrical or thermal pain thresholds.

Correlations between FAST and Pain Modulation

- No correlations were found between FAST and pain modulation, specifically between FAST outcome measures and the magnitude of electrical temporal summation or conditioned pain modulation.

Associations between FAST Outcomes and Questionnaires

- Correlations between FAST outcome measures and the questionnaires can be found in Table 4.

Spearman Correlation Coefficients of FAST Outcome Measures and Questionnaires

Questionnaires	R^2	ICC	CoV
BPI			
Severity Score	-0.268	-0.233	-0.280
Interference Score	-0.083	-0.123	-0.323
FACIT	-0.101	-0.185	-0.409*
FIQ	-0.172	-0.318	-0.256
HADS			
HADS Anxiety	-0.228	-0.406*	-0.101
HADS Depression	-0.136	-0.200	-0.117
HADS Total	-0.268	-0.356	-0.126
IPAQ	-0.282	-0.361	0.288
SF-36			
SF-36 PCS	0.265	0.434*	0.516**
SF-36 MCS	0.191	0.305	0.326
SF-36 Total	0.280	0.409*	0.394*

Note. *p<0.05; **p<0.01

Table 4. Spearman Correlation Coefficients of FAST Outcome Measures and Questionnaire

Conclusions

- The results showed high pain sensitivity - low pain thresholds and tolerance levels, and a high electrical temporal summation response, indicating the existence of abnormal functioning in the pro-nociceptive pathways. Besides, FM subjects were unable to exhibit pain reduction in CPM i.e. could not recruit the descending inhibitory system, the anti-nociceptive pathways.
- Since FAST R2 and ICC did not correlate with any sensitivity task, we consider that they are measuring a specific pain concept, pain reporting variability, not sensitivity to pain
- No relations were found between the FAST outcome measures and the eTS or CPM, suggesting that FAST procedure is assessing pain variability. It does not seem to assess pain modulation, the fluctuations of pain that the subject might experience related to the functioning of the descending pain modulation system.
- ICC FAST outcome correlated with a few characteristics, similarly to CoV, to lower perception of physical wellbeing and general health perception.

By examining the relationships between FAST outcomes and the static (sensitivity: threshold and tolerance) and dynamic pain measures (CPM and eTS), used in the current study, we found further support that FAST is assessing a specific pain dimension, termed as pain reporting variability, which is distinct from pain sensitivity and modulation.

In summary, as seen in a recent healthy subjects' study* [7], *in FM population there are no relations between the within-subjects' variability in response to experimental stimuli and the sensitivity to pain or pain modulation.

References

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