Observational Study

The Result of Acute Induced Psychosocial Stress on Pain Sensitivity and Modulation in Healthy People

Michel Mertens,MSc[1,2], Linda Hermans, MD, PhD[2,3], Jessica Van Oosterwijck, PhD[1–4], Lotte Meert, MSc[1,2], Geert Crombez, PhD[5], Filip Struyf,PhD[1], and Mira Meeus, PhD[1–3]

From: [1]Research Group MOVANT, Department of Rehabilitation Sciences and Physiotherapy (REVAKI), University of Antwerp, Wilrijk, Belgium; [2]Pain in Motion International Research Group, www.paininmotion.be, Belgium; [3]Department of Rehabilitation Sciences and Physiotherapy, Ghent University, Ghent, Belgium; [4]Research Foundation–Flanders (FWO), Brussels, Belgium; [5]Ghent Health Psychology Lab, Department of Experimental-Clinical and Health Psychology, Faculty of Psychology and Educational Sciences, Ghent University, Ghent, Belgium

Address Correspondence:
Mira Meeus
Universiteitsplein 1
2610 Wilrijk, Belgium
E-mail:
mira.meeus@uantwerpen.be

Background: Pain can be influenced by several factors, including stress. Stress can have various reactions on pain. These reactions are influenced by several internal factors such as gender, age, and experience with stress or pain.

Objectives: To determine the effect of acute stress on mechanical hyperalgesia (with pressure pain thresholds [PPT]), endogenous pain facilitation (measured by temporal summation [TS]), and inhibition (measured by conditioned pain modulation [CPM]) in healthy people and to determine which factors are responsible for this stress result.

Study Design: Pre-posttest design.

Setting: Healthy volunteers from Belgium.

Methods: One hundred and one healthy pain-free patients underwent a modified Trier Social Stress Test. Prior and following the stress manipulation, PPT, TS, and CPM efficacy were determined in the mm. trapezius and quadriceps and overall. Furthermore, possible explanatory factors, such as fear of pain, pain catastrophizing, pain hypervigilance, and daily activity levels, were assessed using questionnaires.

Results: We found a significant stress result on widespread pain sensitivity, with an increase of PPT ($P < 0.001$), unchanged TS ($P > 0.05$), and a decrease in CPM efficacy ($P < 0.001$). Factors associated with the stress result were age, previous surgery, attentional focus on the conditioning stimulus during CPM, fear of pain, and daily activity levels.

Limitations: The efficacy of the stress manipulation was not examined, and the lack of a control group prevented to examine a real stress-effect. Furthermore, no physiologic parameters were measured as possibly influencing internal factors for the stress-result.

Conclusions: The increase in PPT was not a clinically significant change, whereas the decrease in CPM was meaningful. None of the factors predicted the stress result in all experimental pain measurements, and the predictions that were observed only explained a small proportion of the observed effects.

Key words: Psychosocial stress, pain sensitivity, pain modulation, pain inhibition, pain facilitation, moderator, predictor, healthy people

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Pain can be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (1) and might be considered as a defense response to an aversive or noxious stimulus (2). Pain can be influenced by several factors, such as

current disease activity (3), emotional or psychological factors (e.g., coping and illness beliefs) (3-5), tissue damage (4,6) and stress (7-10).

The effect of acute stress on pain has been investigated in healthy people, as well as in various disorders. In healthy people, acute stress can result in pain inhibition (11-13), pain facilitation (14), or have no effect on pain (12,15-17). These contradictory reactions to acute stress might be explained by 2 different mechanisms. First, stress may activate pain inhibitory mechanisms by inducing a physiologic arousal reaction (by an increase in cortisol and norepinephrine levels) (18) or distraction (19). Opposite, hyperalgesic effects can be seen as a consequence of increasing vigilance to the stress-inducing (aversive) stimuli (20). Furthermore, several external and internal factors might explain the variability in responses.

In laboratory settings, where the effects of experimentally induced acute stress on experimentally induced pain are assessed, internal factors might influence this response. These factors include gender (2,21), age (2), experience with stress or pain (2,4), personality or individual difference variables (e.g., catastrophizing) (2,4), and attention or anticipation to pain (2,22). These factors can influence both the direction of pain perception and the degree of hypo- or hyper-algesia with various aversive stimuli (22).

Besides of the uncertainties regarding the analgesic effects of acute stress in pain, which is evaluated by self-reported pain intensity or assessment of pressure pain thresholds (PPTs), there is little evidence on how acute stress may interfere with the efficacy of endogenous pain inhibition or facilitation in healthy people. Some studies examined effects of acute stress on pain facilitation (by evaluating temporal summation [TS]) or pain inhibition (by evaluating conditioned pain modulation [CPM]) with PPTs in healthy people, but the results remain conflicting (23-26). Furthermore, no study has investigated if and how internal factors influence the stress effect on PPT, TS, and CPM.

Gaining insight in the effects of stress on pain modulatory mechanisms can help us understand how stress and pain interrelate, and how stress and its management can play a role in pain-related disorders and be a target for therapeutic interventions. Also, the contribution of internal factors to the response to stress is an important aspect to assess to predict stress sensitivity and identify possible treatment targets to modulate stress sensitivity or resilience of an individual.

Therefore the first aim of the study was to determine the effect of acute stress on mechanical pain sensitivity measured by PPTs, endogenous pain facilitation measured by TS, and endogenous pain inhibition measured by CPM in healthy people. The second aim was to determine which internal factors could influence the stress-induced hypo- or hyperalgesic effect in healthy volunteers. Based on the earlier described information and the review of Butler and Finn (2), it is expected that the following internal factors, such as gender, age, chronicity or recurrence of stress, prior experienced stress, physical activity, personality and behavior characteristics, expectations of fear and pain, and whether the patient was focused on or distracted from the conditioning stimulus, had an influence on the stress-result.

## METHODS

Study Design and Setting

This pre–post study took place at the research unit of the Department of Rehabilitation Sciences and Physiotherapy of the Ghent University. The study was approved by the ethical committee of the university hospital.

Patients

One hundred and one healthy pain-free patients between the ages of 18 and 65 years were recruited via personal acquaintances of researchers or employees of the Department of Rehabilitation Sciences and Physiotherapy. Patients were eligible if they had no current pain or history of chronic pain complaints. Pregnant women, or women who gave birth less than 1 year ago, were not eligible for study participation. Before the start of the experiments all patients provided written informed consent.

Procedure

First, the patients were asked to complete a set of 7 questionnaires. These questionnaires included a general questionnaire, the Long-Term Difficulties Inventory (27), the List of Threatening Events (28), the International Physical Activity Questionnaire-short form (29), the Pain Catastrophizing Scale (30), the Pain Vigilance Awareness Questionnaire (31), and the 9-item Fear of Pain Questionnaire (32). Second, the patients underwent the experimental measures. The complete protocol is described elsewhere (33) and schematically shown in Fig. 1.

Fig. 1. *Complete study protocol with different test measurements. Sec.: seconds.*
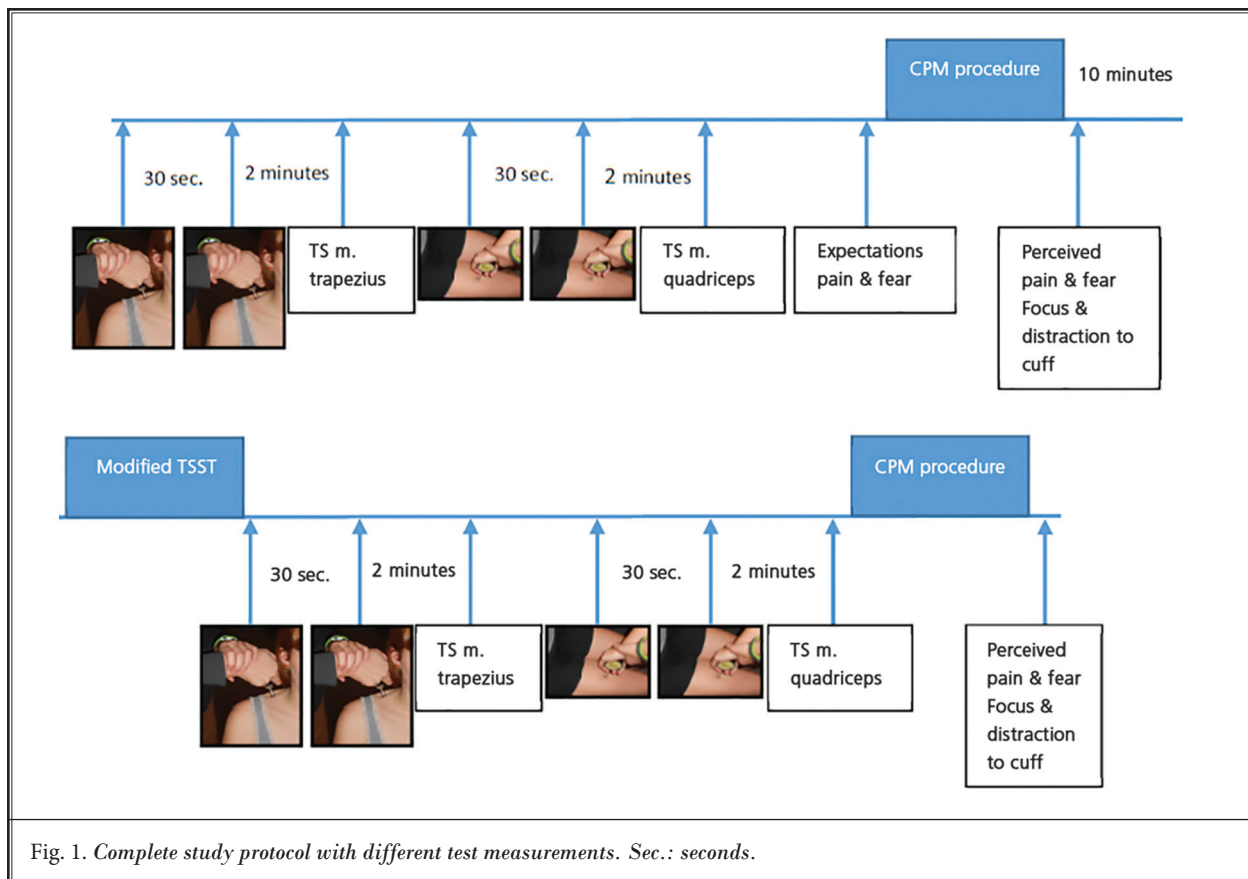
Ten minutes after the prestressor evaluations, the patients were subjected to an acute bout of psychosocial stress with a modified Trier Social Stress Test (TSST). Immediately after this stressor the poststressor evaluations were performed by executing the pain inducing measures (PPT, TS, CPM) again (as presented in Fig. 1).

Prior to the application of the CPM, the patients were asked to rate their expected pain and fear for the conditioning stimulus on a 5-item Likert scale, ranging from "No" to "A lot". Afterwards, the patients were asked to rate their perceived pain and fear and focus and distraction toward and from the conditioning stimulus on a 5-item Likert scale ranging from "No" to "A lot".

Experimental Pain Measures

Mechanical PPT

The PPTs were determined at the center of the muscle belly of the mm. trapezius transversus (as described elsewhere previously [34,35]) and rectus femoris of the quadriceps (as described elsewhere previously [36,37]) on the dominant side while seated in a chair with arm rests. Mechanical pressure pain was applied on these muscles using an analogue algometer with a rubber tip of 1 cm^2 (Wagner Force Dial FDK 10 or 40 [Wagner Instruments, Greenwich, USA]). To determine the PPT, the assessor applied a gradually increasing pressure at a speed of 1 kg/second until the patient indicated that the stimulus was experienced as annoying and uncomfortable. This was repeated after 30 seconds. The PPTs for the respective test sites were calculated as the average of the 2 consecutive measurements. PPTs have shown good to excellent reliability (38-40).

TS

Provoked TS was performed following the procedure of Cathcart et al (35). TS was induced by 10 consecutive repetitions of mechanical pressure applied with the algometer at PPT intensity on the surface of the concerning muscle belly of the trapezius and
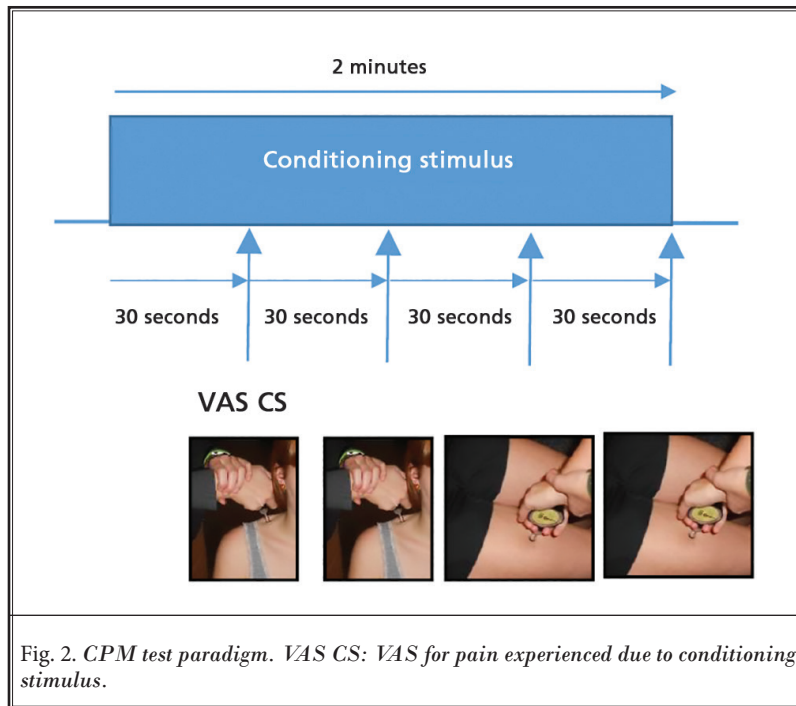
Fig. 2. *CPM test paradigm. VAS CS: VAS for pain experienced due to conditioning stimulus.*

quadriceps muscle. The patient rated the pain intensity of the first, fifth, and 10th repetition on a plastic Visual Analog Scale (VAS), ranging from 0 (no pain) to 10 (worst imaginable pain). The result of TS is the difference between the 10th pulse and the first pulse; this was found a reliable method (35).

CPM

CPM efficacy was evaluated by examining the effect of a conditioning stimulus on a test stimulus. The test stimulus existed out of mechanical pressure pain elicited as described earlier in the mechanical PPTs section. The conditioning stimulus existing out of single ischemic occlusion was applied to the nondominant arm. This protocol was described elsewhere (38,41) and slightly adapted. In contrast to the previous protocol, the patients performed only 30 seconds of contractions before the cuff was applied. The CPM protocol, schematically shown in Fig. 2, was than performed. Immediately after the application of the last test stimulus the cuff was deflated. The CPM-effect was calculated as

$$\frac{\text{PPT during CPM - PPT at baseline}}{\text{PPT at baseline}}$$

Herein is a positive value, a positive effect of CPM.

Stress Manipulation

The original TSST, described elsewhere previously (42), was slightly adapted because of practical reasons. In contrast to the original TSST and similar to the study of Kertz et al (43), the patients did not really have to present in front of a jury and camera but only the preparation phase was conducted. The announcement of the experiment is used as an psychosocial stress test. In consultation with a psychologist (GC) this announcement seemed to be sufficient to induce stress in the patients.

Statistical Analyses

Data were analyzed using the IBM Statistical Package for Social Sciences Version 25 (SPSS, IBM Corporation, Armonk, NY).

Prior to analyses normal distribution of data were checked with the Shapiro-Wilk test. For analysis of the stress result on PPT, TS, and CPM for the mm. trapezius and quadriceps and overall values (mm. trapezius and quadriceps combined) a paired sample t-test or a Wilcoxon signed-ranks test was used for normally and nonnormally distributed data, respectively.

The stress-result was determined by subtracting the prestress overall values of PPT, TS, and CPM from the poststress overall values. Furthermore, the number of positive and negative responders and nonresponders to the CPM paradigm were determined both before and after the stress task for both muscles and overall. Patients were considered a responder if they scored 5.3% (44) higher or lower compared with the baseline PPT measurement. Finally, the difference in positive responders prior and after the stress task was determined with a χ^2 test.

To determine which factors influenced the stress-result, a forward stepwise multiple linear regression was performed for stress-result on PPT, TS, and CPM with the overall values (dependent variables). The following personal factors were used as regressors: age, gender, surgery (yes/no), medication (yes/no), sports last week (yes/no), and total score on each of the 7 questionnaires for

all dependent variables. For the CPM as dependent variable expectation of pain and fear related to the CPM procedure, focus to the cuff and distraction were added as possible regressors. The criteria for inclusion in the model were set at 0.05 and for exclusion at 0.10. The significance level was set at $P = 0.05$.

RESULTS

Population Characteristics

The study population consisted of 101 healthy volunteers (50 men and 51 women) with a mean (± standard deviation [SD]) age of 23.78 ± 6.68 years. Other characteristics are shown in Table 1.

Stress-Result

The mean (± SD) and range values for the PPT, TS, and CPM pre- and poststress are shown in Table 2. The Shapiro-Wilk test showed only normal distribution for CPM effect of the m. trapezius prestress and overall prestress, therefore the Wilcoxon signed-rank test was used for analyzing the stress-results.

The Wilcoxon signed-rank test showed a significant increase in PPT m. trapezius (Z = –5.34; $P < 0.001$), m. quadriceps (Z = –3.74; $P < 0.001$), and overall (Z = –4.44; $P < 0.001$), whereas no significant difference was found for TS of mm. trapezius and quadriceps and overall after stress induction ($P > 0.05$). For CPM on m. trapezius (Z = –4.49; $P < 0.001$), m. quadriceps (Z = –4.49; $P < 0.001$), and overall (Z = –5.25; $P < 0.001$) a significant decrease was found after stress induction, although the CPM effect was still positive on group level. Table 3 shows the number of responders and nonresponders to the CPM paradigm at both the mm. trapezius and quadriceps and overall. No significant difference in number of positive responders were found for mm.

Table 1. *Population characteristics*.

	Total group (n = 101)
Age (years)	23.78 ± 6.68 (18-55)
LDI	4.02 ± 2.57 (0-14)
LTE	0.85 ± 0.90 (0-4)
PCS	11.68 ± 7.24 (0-32)
OVAQ	31.38 ± 10.16 (10-57)
FPQ-9	23.83 ± 4.30 (14-32)
Surgery (yes (%))	58 (57.4%)
Medication (yes (%))	26 (25.7%)
Sports last week (yes (%))	65 (64.4%)
IPAQ-sf	
Inactive	14 (13.9%)
Minimally active (%)	36 (35.6%)
Health enhancing physical activity (%)	51 (50.5%)

Data presented as mean ± SD (range) or in percentage; n: number; LDI: Long-Term Difficulties Inventory; LTE: List of Threatening Events; PCS: Pain Catastrophizing Scale; PVAQ: Pain Vigilance Awareness Questionnaire; FPQ-9: Fear of Pain Questionnaire-9; IPAQ-sf: International Physical Activity Questionnaire short form.

trapezius ($\chi^2 = 1.686$; df = 1; $P = 0.194$), quadriceps ($\chi^2 = 0.401$; df = 1; $P = 0.527$), and overall ($\chi^2 = 1.162$; df = 1; $P = 0.281$) between pre- and poststress.

Expectations about the conditioning stimulus are shown in Table 4. Table 5 shows the results regarding pain from the conditioning stimulus pre- and poststress, perceived pain and fear, and focus and distraction to the cuff pre- and poststress.

Factors Influencing Stress-Result

Mean stress-result and regression models are shown in Table 6.

This indicated a significant effect of age on stress-

Table 2. *PPT, TS, and CPM at the mm. trapezius and quadriceps pre- and postmodified TSST.*

	PPT		TS		CPM					
					Prestress test			Poststress test		
	Prestress test	Poststress test	Prestress test	Poststress test	PPT during CPM	Difference PPT prestress test and PPT during CPM	CPM effect	PPT during CPM	Difference PPT poststress test and PPT during CPM	CPM effect
m. trapezius	2.71 ± 1.48 (0.88–9.90)	3.24 ± 1.80 (1.15–10.40)	0.73 ± 1.49 (–3.10–7.80)	0.71 ± 1.41 (–1.80–7.80)	3.43 ± 1.87 (1.05–10.50)	0.71 ± 1.10 (–2.55–5.43)	0.30 ± 0.29 (–0.37–1.07)	3.62 ± 2.01 (0.78–10.55)	0.37 ± 0.68 (–0.85–2.60)	0.14 ± 0.24 (–0.47–1.20)
m. quadriceps	5.52 ± 2.70 (1.85–15.25)	6.19 ± 2.73 (2.25–14.30)	0.63 ± 1.56 (–3.90–6.60)	0.80 ± 1.27 (–2.10–6.20)	6.48 ± 2.78 (2.78–15.35)	0.96 ± 1.58 (–2.50–6.03)	0.24 ± 0.33 (–0.25–1.46)	6.51 ± 2.85 (2.40–15.60)	0.32 ± 1.06 (–3.00–6.00)	0.07 ± 0.17 (–0.29–0.66)
Overall	4.12 ± 0.19 (1.39–11.75)	4.72 ± 0.21 (1.74–10.60)	0.68 ± 0.14 (–2.85–6.30)	0.75 ± 0.12 (–1.80–6.25)	4.95 ± 2.18 (1.94–11.68)	0.84 ± 1.17 (–2.53–4.55)	0.27 ± 0.03 (–0.22–1.00)	5.06 ± 2.28 (1.85–12.13)	0.35 ± 0.72 (–1.45–4.15)	0.10 ± 0.02 (–0.30–0.79)

Table 3. *Numbers and percentages of responders and nonresponders to the CPM paradigm at the mm. trapezius and quadriceps.*

| | Responders | | | | | | Nonresponders | |
| | Prestress test | | | Poststress test | | | Prestress test | Poststress test |
	Positive	Negative	Total pre	Positive	Negative	Total		
m. trapezius	83 (82.2)	9 (8.9)	92 (91.1)	64 (63.4)	18 (17.8)	82 (81.2)	9 (8.9)	19 (18.8)
m. quadriceps	71 (70.3)	19 (18.8)	90 (89.1)	52 (51.5)	24 (23.7)	76 (75.2)	11 (10.9)	25 (24.8)
Overall	82 (81.2)	8 (7.9)	90 (89.1)	64 (63.4)	15 (14.8)	79 (78.2)	11 (10.9)	22 (21.8)

Table 4. *Expectations about the conditioning stimulus.*

Expected Pain	
No	21 (20.8%)
Little	46 (45.5%)
Reasonable	27 (26.7%)
Much	7 (6.9%)
Very much	0 (0%)
Expected Fear	
No	64 (63.4%)
Little	27 (26.7%)
Reasonable	7 (6.9%)
Much	2 (2%)
Very much	1 (1%)

Data shown as number (percentage).

Table 5. *Results about pain during conditioning stimulus, perceived pain and fear, focus and distraction to the cuff pre- and poststress.*

	Prestress test	Poststress test
VAS (conditioning stimulus)	2.83 ± 1.88 (0.10–8.80)	2.33 ± 1.81 (0.10–7.50)
Perceived pain		
No	4 (4%)	9 (9.4%)
Little	56 (55.4%)	55 (57.3%)
Reasonable	29 (28.7%)	27 (28.1%)
Much	11 (10.9%)	5 (5.2%)
Very much	1 (1%)	0 (0%)
Perceived fear		
No	74 (73.3%)	78 (81.3%)
Little	21 (20.8%)	16 (16.7%)
Reasonable	5 (5%)	1 (1%)
Much	1 (1%)	1 (1%)
Very much	0 (0%)	0 (0%)
Attentional focus on the conditioning stimulus		
No	8 (7.9%)	15 (15.6%)
Little	43 (42.6%)	47 (49%)
Reasonable	27 (26.7%)	26 (27.1%)
Much	19 (18.8%)	7 (7.3%)
Very much	4 (4%)	1 (1%)
Distraction from the conditioning stimulus		
No	15 (14.9%)	22 (22.9%)
Little	58 (57.4%)	48 (50%)
Reasonable	23 (22.8%)	19 (19.8%)
Much	5 (5%)	7 (7.3%)
Very much	0 (0%)	0 (0%)

Data shown as mean ± SD (range) and number (percentage).

result with PPT ($F(100) = 10.949$; $P = 0.01$). For TS the FPQ score, IPAQ score in metabolic equivalent of task (MET), and age showed a significant influence on stress-result ($F(100) = 7.135$; $P < 0.001$). The stress-result in CPM was influenced by prior surgery, reasonable focus on the inflatable cuff poststress, and little focus on the inflatable cuff prestress ($F(95) = 7.421$; $P < 0.001$).

These different factors only explained 10.0% to 16.9% of the pre–post stress difference on the different experimental pain measures.

Discussion

The aim of this study was to determine the result of acute stress on mechanical algesia measured with PPTs, pain facilitation measured by TS, and endogenous pain inhibition measured by CPM and to determine which internal factors could account for the stress-induced pain modulatory effects in healthy volunteers. The results of this study suggest that an acute bout of experimentally induced psychosocial stress results in increased PPTs, unchanged TS, and decreased CPM efficacy. Factors influencing the stress-result in the current study were age, prior surgery, fo-cus on the cuff during the conditioning stimulus, fear of pain, and self-reported physical activity–related energy expenditure. In the next section, these results will be discussed.

Table 6. *Stress-result for PPT, CPM, and TS and their multiple linear regression models.*

	Mean ± SD	Factor	B	β	Sign	R	R2	Adjusted R2
PPT	0.60 ± 0.12	Constant	−0.776		0.076	0.316	0.100	0.090
		Age	0.058	0.316	0.001			
TS	0.08 ± 0.11	Constant	0.508		0.510	0.425	0.181	0.155
		FPQ score	−0.061	−0.233	0.015			
		IPAQ in METs	0.00005	0.208	0.029			
		Age	0.034	0.199	0.037			
CPM	−0.17 ± 0.03	Constant	0.065		0.255	0.441	0.195	0.169
		Surgery	−0.218	−0.387	< 0.001			
		Reasonable focus on cuff poststress	−0.169	−0.269	0.006			
		Little focus on cuff prestress	−0.139	−0.245	0.016			

Data shown as mean ± SD and the coefficients of the model with the model summary.
FPQ: fear of pain questionnaire; IPAQ: International Physical Activity Questionnaire; METs: metabolic equivalent of task; B: unstandardized B; β: standardized beta; Sign.: significance of the factor.

The Influence of Stress on Pain

PPTs

We found a significant increase in widespread PPTs of 0.60 (± 0.12) kg/cm^2 after psychosocial stress manipulation. Because the minimal detectable change for PPT is 1.16 kg/cm^2 (converted) (39) this is not considered a clinically significant change and might have occurred due to chance or measurement error. Several studies found contrasting results, 2 studies (15,23) found no significant effect of mental stress, whereas one study (14) found a decrease in PPT during a period of natural stress. Differences in results between our study and the other literature could be explained by difference in type of induced stress (psychosocial vs. mental vs. natural, and acute vs. longer periods of stress) and pain location (mm. trapezius and quadriceps vs. mm. temporalis and masseter).

The increase in PPTs after a stressful task might be a consequence of the activation of pain inhibitory mechanisms. Our hypothesis about the activation of these mechanisms is that they are activated by distraction (19). During the PPT measurement after the announcement of the psychosocial stress task, patients could have been more focused on their task and less to the PPT measurement, which could result in higher PPTs.

TS

No significant stress-result was found for TS. This result is in line with the result of Cathcart et al (24), who also did not find a difference in TS after inducing cognitive stress. In contrast, one study (26) found a decrease in TS after inducing emotional and physical stress, and one study (25) found an increase in TS after inducing cognitive stress. Both differences might be explained by the type of induced stress (psychosocial vs. emotional and physical vs. cognitive stress).

CPM

We found a significant decrease in CPM efficacy as a result from the psychosocial stress manipulation from 0.27 (± 0.03) to 0.10 (± 0.02). Prestress there were 89.1% responders from whom 81.2% responded positive. This indicates that our test paradigm is sufficient to measure a CPM effect. Poststress there is a decrease in the number of responders, and the number of negative responders and nonresponders increased. This indicates that poststress less people activated their pain inhibitory mechanism, and some more people (14.8-23.7% poststress vs. 7.9-18.8% pre-stress) even activated their pain facilitating mechanism.

This result is in line with the result of Coppieters et al (25). They also found a decrease in CPM effect at the m. trapezius (from 0.75–0.23) after a cognitive stressful task. The decrease (69%) they observed after the stressful task was larger than the decrease we observed (53%). Cathcart et al (24) found no effect of a cognitive stress task in CPM at the m. trapezius and finger. This difference in results might be explained by different conditioning procedures, type of stress induction, and body region measured. Cathcart et al (24) used a procedure during which the conditioning pain stimulus existed out of an occlusion cuff that was kept at a constant pain intensity, whereas in the current study a

constant cuff pressure of 240 mm Hg was used. After inducing psychosocial stress, the endogenous pain inhibition mechanism was affected because there was a lower CPM efficacy score and less positive responders. This could be a consequence of the cognitive change of the perceived conditioning pain (45-47), which is significantly reduced after the stress inducing task (from VAS 2.83–2.33 [$Z = -3.575$; $P < 0.001$]). The decrease in pain perception of the conditioning stimulus might be a result of patients focusing less on the cuff after the induction of stress compared with before the stress induction ($Z = -3.921$; $P < 0.001$) and herewith pain perception changed.

In summary, the differences in results between various studies might be explained by the type of induced stress, the location of the pain measurement, and the used CPM test paradigm. All these different factors result in different reactions and responses (18).

Influencing Factors of the Stress-Result

Various factors were found explaining the stress-result on the different pain measures.

The stress-result in PPT could be predicted by age, with being of older age resulting in achieving a larger stress-result and explaining 10.0% of the variability.

The small nonsignificant change in TS after psychosocial stress might be predicted by fear of pain, daily activity levels, and age, explaining 15.5% of the variability. Higher levels of pain-related fear results in a decrease of the stress-result in TS, whereas higher daily activity levels expressed as METs and higher age results in an increased stress-result of TS.

The negative stress-result on CPM after induced psychosocial stress might be partially predicted by previous surgery, low attentional focus toward the conditioning stimulus during CPM evaluation at baseline, and those with higher attentional focus toward the conditioning stimulus following the stress induction. These factors explained 16.9% of the variability of the stress-result. All these factors resulted in a decrease of the stress-result in CPM.

We are not aware of studies that determined factors explaining the stress-result in healthy patients with PPT. However, it is proposed that gender (2,18,21), age (2,18), experience (exposure to any number of stressful or painful stimuli prior to testing) (2,4,18), genetic and psychological personality characteristics (4,18), and environmental factors (4,18) influence the response to pain after stress events.

However, no single factor was found in all these measurements. This indicates that we have to consider the way we assess pain perception and pain modulating mechanisms. In addition, the stress-result was only explained by these factors for 10.0% to a maximum 16.9%. This indicates that the factors added in the current study can only partly explain the stress-result and there are other factors that also contribute to this difference. Some of these factors might be genetic (48), personality characteristics (2), cardiovascular responses (8), and changes in physiologic arousal (21).

Limitations

In the current study, the task used to manipulate stress was not examined on its efficacy to do so, and therefore it is unclear whether the stressful task was sufficient to reach the stress threshold. In addition, because of the lack of a control group, the stress-result might be a consequence of repeated testing as well (49) instead of a true stress-result. In future studies the perceived stress should be evaluated as well, and a control group should be included.

During the conditioning stimulus, prior to application of the inflatable cuff, patients had to perform contractions of the lower arm muscles for 30 seconds. This was performed for increasing the ischemia in the nondominant arm, which should result in more conditioning pain. Another consequence of these contractions is a possible hypoalgesic effect. In healthy people, effects of exercise-induced hypoalgesia were found with muscle contractions (50,51), this could result in lower pain intensity scores for the conditioning stimulus. As a consequence of this reduced pain perception the possibility exists that no or a smaller effect of the conditioning stimulus on the test stimulus was present and consequently diminishing the resulting CPM effect. Although there is no golden standard to measure CPM, we cannot testify regarding the construct validity of the used CPM paradigm, however, the high responder rates for the used paradigm prior to manipulation indicate that the used paradigm allows to measure the intended concept of CPM.

A relatively young group of patients were examined (23.78 ± 6.68 years), which makes generalization to a general population difficult. In addition, prevalence of chronic pain increases with age (52), and therefore these results cannot be used to compare the effects of acute stress in many chronic pain populations. Future studies should incorporate more and higher age categories for possible generalization.

Finally, physiologic changes can explain pain perception and sensitivity to stress, as it has been found that pain sensitivity is linked primarily to cardiovascular responses, such as heart rate and blood pressure (8), and changes in physiologic arousal (21). In the current study, no physiologic responses to stress were measured or considered, and therefore their confounding influence cannot be excluded. It is highly likely that including such factors would have increased the explanatory role of internal factors as contributors to the stress-result on pain.

CONCLUSIONS

We found an increase in PPTs (although it was not a clinical change), no change in TS, and a decrease in CPM efficacy after psychosocial stress induction, documenting that pain sensitivity and modulation is influenced by psychosocial stress.

Various factors, such as age, physical activity, previous surgery, presence of fear, and focus to the conditioning stimulus, were found to influence the stress-result on pain sensitivity and modulation. However, none of these factors predicted the effect in all the experimental pain measurements, hampering the clinical interpretation of these findings. Furthermore, there are more factors (e.g., cardiovascular responses, physiologic arousal, etc.) known that contribute to stress and these should be assessed in future studies as well.

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