Published in final edited form as:
Psychosom Med. 2013 May ; 75(4): 413–421. doi:10.1097/PSY.0b013e31828c4cb4.

PSYCHOLOGICAL AND PHYSIOLOGICAL PREDICTORS OF ANGINA DURING EXERCISE-INDUCED ISCHEMIA IN PATIENTS WITH CORONARY ARTERY DISEASE

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Abstract

Objective—This study compares sensory-biological, cognitive-emotional, and cognitive-interpretational factors in predicting angina on an exercise treadmill test (ETT).

Methods—163 patients with ETT-induced ischemia and coronary artery disease (CAD) in the NHLBI Psychophysiological Investigations of Myocardial Ischemia (PIMI) study were given an ETT, and 79 patients reported angina during the ETT. We assessed the following as predictors of self-reported anginal pain: sensory-biological factors (β-endorphin reactivity, hot pain threshold, and maximum ST-segment depression), cognitive-emotional factors (negative affect and symptom perception), and cognitive-interpretation (self-reported history of exercise-induced angina). Models were covariate-adjusted with predictors examined individually and as part of component blocks.

Results—Logistic regression revealed that history of angina (OR=17.41, 95% CI=7.16–42.34) and negative affect (OR=1.65, 95% CI=1.17–2.34), but not maximum ST-segment depression, hot pain threshold, β-endorphin reactivity, nor symptom perception were significant predictors of angina on the ETT. The component block of sensory-biological variables was not significantly predictive of anginal pain ($chi^2_{block} = 5.15$, $p = 0.741$). However, the cognitive-emotional block ($chi^2_{block} = 11.19$, $p = 0.004$) and history of angina (cognitive-interpretation) ($chi^2_{block} = 54.87$, $p < 0.001$) were predictive of ETT angina. A model including all variables revealed that only history of angina was predictive of ETT pain (OR = 16.39, $p < 0.001$), although negative affect approached significance (OR = 1.45, $p = 0.07$).

Conclusion—These data suggest that in patients with ischemia, cognitive-emotional and cognitive-interpretational factors are important predictors of exercise angina.

Keywords

angina; depression; anxiety; treadmill test

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Coronary artery disease (CAD) is the leading cause of death in the United States (1). Angina is a common clinical manifestation of CAD and important in diagnostic algorithms for myocardial infarction (MI; 2). Though prevalent, angina is absent in about half of first MIs and in most episodes of myocardial ischemia (3,4). The absence of angina in many coronary events can be a dangerous clinical problem; without anginal pain, there is no warning signal for the occurrence of potentially dangerous myocardial ischemia. In addition, anginal complaints and exercise treadmill angina are often used to guide diagnosis and treatment of CAD (2). Thus, determining when ischemia will or will not result in anginal pain is a clinically important problem.

One hypothesis is that anginal pain occurs when ischemia is more severe (5). Although severity of ischemia is an important trigger, even severe ischemia does not always predict anginal pain (6,7), and patients with CAD may report anginal pain in the absence of evidence of any ischemic event (8). Therefore, investigators have examined multiple determinants of anginal pain other than the presence of myocardial ischemia or ischemic severity.

Pain threshold might also account for individual variability in anginal symptoms. Individuals with higher pain thresholds are less likely to experience anginal pain, and patients with silent ischemia have higher pain thresholds compared to those with symptomatic ischemia (9–12). Changes in stress-induced analgesia or changes in pain perception mechanisms via release of endogenous endorphins also account for some of the differences in anginal perception (13,14). However, some (15) but not all studies (12,16,17) have demonstrated that β-endorphin levels are associated with asymptomatic ischemia and less anginal pain.

Anxiety and depression symptoms are prospectively associated with cardiac disorders (18–20) and also pain perception (21). Stress and anxiety affect angina thresholds (22). This relationship may be due, in part, to patients' anticipation of pain or tendency to report negative emotions (affect) in certain situations (12). Furthermore, psychosocial traits relating to symptom perception may be an important predictor of silent versus symptomatic ischemia (23,24). Depressive symptoms are related to cardiac symptoms (25). Using data from the NHLBI PIMI study, the present investigators have demonstrated a relationship between anxiety and depressive symptoms and both history of angina and anginal pain latency (26). Depressed patients are more likely to develop post-MI angina (22), and depression not only plays a role in the development of CAD in general, but of anginal pain in particular (22,27). Depressive symptoms also influence features of angina such as pain latency (26), intensity and duration (28,29), even when controlling for ischemic severity. Thus, individuals high in symptom perception might be more likely to report pain during ischemia.

Anginal history is an important predictive factor for exercise-induced angina, and also of CAD disease morbidity and mortality (30). Anginal pain history may not only lead to exercise-angina because of its association with the disease process but also because it is related to psychological factors, such as anticipation of pain during stress testing and daily life activities (8), or by influencing the perception of other nociceptive stimuli (12).

Thus, multiple mechanisms explaining angina during stress testing have been offered. The predictors of anginal pain reviewed above represent sensory and biological variables, cognitive and emotional variables, and memory of prior pain. These findings are consistent with the recognition that contributors to pain include sensory-biological, cognitive-emotional, and cognitive-interpretational processes (33). The different components of pain are likely to be differentially affected by the factors reviewed above. For example, the

sensory-biological component of anginal pain may be primarily affected by factors including ischemic severity (5), pain threshold (9–12), and opioid response (13–15). Factors affecting the cognitive-emotional component may include neuroticism (31), traits of anxiety and depressive symptoms (21), and symptom perception (23,24).

Cognitive-interpretation factors affecting pain relate to the contextual body of knowledge that influences the perception and understanding of painful stimuli. These factors can be difficult to measure, but memory bias in chronic pain is well-established (32) and therefore history of angina might be considered, in part, to represent a factor influencing the cognitive-interpretational factor of pain (32,33).

Therefore, one purpose of the present study is to understand the interrelations of the psychological, physiological, and clinical processes that may affect the presence or absence of exercise-induced angina. In addition to representing individual predictor variables we also categorized these variables into 3 pain components (sensory-biological, cognitive-emotional, and cognitive-interpretational; 33) and more broadly assessed whether pain components identified in the pain literature differentially affect exercise angina.

Data from the NHLBI Psychophysiological Investigations of Myocardial Ischemia (PIMI) study provide an opportunity to examine the individual and combined effects of these multiple predictors of exercise angina in the same study. Therefore this study will assess the value of ischemic severity, β-endorphin reactivity, and hot pain threshold (sensory-biological), depressive and anxiety symptoms, and symptom perception (cognitive-emotional) and history of exercise-induced anginal pain (cognitive-interpretational) in predicting angina during exercise stress testing. This categorization into pain components will be used to assess the similarity of findings in the present study to those in the broader pain literature.

We hypothesized that each of these variables would be important in determining anginal chest pain, and that the combined effects of these variables would be more predictive of exercise-angina than any of these variables alone. Secondarily, we also explored whether certain variable groupings were more important predictors of anginal pain on the ETT, and whether the effect of these factors changed in the presence of the others.

Methods

The present study used the publicly accessible database from the NHLBI Psychophysiological Investigations of Myocardial Ischemia (PIMI) study. The methods of this study have been described in detail previously (34,35), and the relevant methods will be briefly reviewed here. The relevant portions of the PIMI study data were collected between June 1993 and September 1994.

Participants

The PIMI study enrolled 196 patients, of which 163 (22 women) with complete data on the variables of interest were included in this study. Eligibility criteria included either a positive angiogram (≥50% narrowing of at least one major coronary artery) or previous MI; and a positive ischemic response to an exercise treadmill test (ETT) while off anti-ischemic medications (e.g., beta-blockers). Exclusion criteria were: pregnancy; MI within three months of the ETT; major cardiac surgeries; unstable angina in the past month; other serious illness or neurologic disease; inability to discontinue medication for testing; and abnormalities in the ECG that would interfere with the interpretation of the ambulatory ECG.

Patients were recruited through participation in a previous study (18), catheterization and exercise laboratories, and chart review. The consent of the attending physician was required for participation and to monitor the stopping of medication. All participants provided informed consent and the project was approved by relevant Institutional Review boards.

Patient demographics showed that patients were mostly white (141 patients, 86.5%). About half of the patients were retired (75 patients, 46.0%), 68 patients (41.7%) were working either full- or part-time, and 20 (12.3%) were disabled or unemployed. Seventy-five patients (46.0%) had a history of myocardial infarction, and 6 patients (3.7%) had congestive heart failure. Eighty-one patients (49.7%) had hypertension, and 23 (14.1%) had diabetes. Most patients reported a history of cigarette smoking (121 patients, 74.2%), and 28 patients (17.2%) were current smokers.

Procedures

Participation consisted of an initial medical qualifying visit, followed by a clinic visit. During the initial visit, patients performed a multistage ACIP protocol treadmill test (ETT) while off anti-ischemic medication (36). The clinic visit then consisted of two half days of testing where patients were given a battery of psychological questionnaires and performed mental and physical stress tests on different days. Data were collected with respect to psychological, physiological, and medical correlates of anginal pain. Patients underwent a bicycle stress test, pain threshold testing using the Marstock task (37), and blood draws for β-endorphin levels. Patients were asked to be off anti-ischemic medications during the ETT in order that the test would not be affected by medication. The following analyses use data from the physical stress day, and the qualifying ETT. Data from radionuclide bicycle and mental stress testing have been presented in prior publications (11, 38–40).

Measures

Anginal pain—For the purposes of the analyses described below, anginal pain was determined as present or absent (yes=1/ no=0) during the ETT (41). This measure provides an analogue to diagnostic pain reports used in the clinic. All patients had a positive ETT indexed through ECG while off anti-ischemic medications. Ischemia during the ETT was defined as a greater than 0.1 mV ST-segment depression, as previously described (11). Reasons for stopping the test included excessive angina, shortness of breath, fatigue, evidence of severe ischemia, and physician judgment.

Sensory-biological measures—

1. *Maximum ST-segment depression.* Data from the ECG for the ETT was used to identify maximal ST-segment depression. This measure reflects severity of ischemia during the ETT.
2. *Pain threshold.* Hot pain thresholds (HPT) were obtained using the Marstock test of sensory perception (37). In this task, patients are asked to indicate when a thermal probe feels warm and cool, and then painfully hot or cold. The hot pain thresholds identified this way provide a proxy for visceral pain thresholds. Lower temperatures at which patients report pain indicate that individuals are more pain-sensitive.
3. *Opioid response.* Blood was obtained through intravenous lines before and during bicycle stress testing. β-endorphin levels were measured after a 30-minute rest period and at peak exercise (35). Reactivity in β-endorphin levels was calculated by subtracting rest levels from peak levels.

Cognitive-emotional measures—

1. *Depressive and anxiety symptoms (Negative Affect).* Depressive symptoms were measured using the Beck Depression Inventory (BDI; 42), a widely used and highly validated measure of depressive symptoms. The BDI is a 21-item questionnaire scored on a 4-point scale with scores ranging from 0 to 63. Anxiety symptoms were measured using the state version of the State Trait Anxiety Inventory (STAI; 43). The STAI is a series of 20 questions that asks individuals to rate their current (state) anxiety symptoms on a 4-point Likert-type scale. The STAI was designed to assess anxiety as distinct from depression in adults. STAI scores can range from 20 to 80, with higher scores being indicative of greater state anxiety. To avoid problems caused by multicolinearity in regression analyses, a Negative Affect score was calculated by summing the standardized scores for depressive and anxiety symptom measures and used in all analyses.

3. *Symptom perception.* The modified Autonomic Perception Questionnaire (MAPQ; 44) was used to measure levels of symptom perception (23,24). The MAPQ is 21-item questionnaire that provides an indication of the individual's tendency to perceive and report bodily symptoms.

History of angina measure—The Rose Questionnaire (30) portion of the Anginal Syndrome Questionnaire (45) was used as a measure of history of exertional angina. This measure, which is coded as a binary measure (yes=1/ no=0), for history of angina has been validated to detect chest pain due to coronary causes (46) and is predictive of subsequent CAD (47). Specifically, the Rose Questionnaire asks whether individuals recall experiencing pain during exercise. The present study uses patient reports of presence of angina in the past 3 months. Anginal history was considered a measure of anginal pain-related memory bias in the present study. The rationale for this is that given that all individuals in this study had documented CAD and ischemia on the ETT their reports of anginal history are arguably less important diagnostically than cognitively as a measure of prior anginal pain experience. In prior research, increased memory for endorsed pain-related words have been considered to represent cognitive bias for pain (48). Accordingly, presence of a memory of pain during exertion is here taken to indicate a cognitive-interpretational process that will influence subsequent interpretations of chest sensations during exertion.

Statistical analyses

First, we created a correlation matrix to examine whether predictors represented distinct independent constructs or clustered together into categories. Then, a series of hierarchical logistic regression models evaluated whether each predictor was independently associated with angina at exercise, controlling for covariates. Next, 3 hierarchical logistic regression models were created to examine the contribution of each category of variables (sensory-biological, cognitive-emotional, cognitive interpretational) to the prediction of anginal pain during exercise. Finally, a full model was created to examine the total combined effect of all variables in their categories. All regression analyses controlled for age, sex, history of hypertension, history of diabetes, and history of MI as *a priori* covariates because of their known relationship to anginal pain perception (49–51). Analyses were performed using IBM SPSS version 19.

Results

Table 1 presents patient demographic characteristics by presence or absence of angina on the ETT. The total sample means for all predictors are as follows: maximum ST-segment

depression (mean = 1.99 mm, SD = 0.61, range = 1.00–4.00), hot pain threshold (mean = 45.91°C, SD = 4.08, range = 34.3–53.0), β-endorphin reactivity (mean = 1.29, SD = 3.25, range = −10.20–14.20), BDI (mean score = 6.04, SD = 6.14, range = 0–36), STAI (mean score = 31.62, SD = 9.90, range = 20–66), MAPQ (mean score = 91.43, SD = 46.37, range = 8–232), history of angina (% yes = 48.5).

Intercorrelations of predictor variables

The correlation matrix (Table 2) shows that, as expected, there were significant correlations among depression, anxiety, and symptom perception variables, indicating that cognitive-emotional variables were correlated. These variables were also related to history of angina. Maximum ST-segment depression, β-endorphin reactivity, and hot pain threshold were largely uncorrelated with each other and with other variables. The exception to this was maximum ST-segment depression, which was associated with anxiety, negative affect, and history of angina.

Women were more likely to report a history of angina and depressive symptoms, and had lower hot pain thresholds. Age was positively associated with severity of ischemia and negatively correlated with depressive symptoms and symptom perception.

Models predicting exercise-induced angina

Multivariate logistic regressions considering each variable separately and controlling for covariates indicated that negative affect and history of angina were significant predictors of the presence of ETT anginal pain. Though their individuals overall models were not significant, both depression and anxiety seemed to contribute an independent effect. Covariates included age, sex, history of hypertension, history of MI, and history of diabetes. The models for hot pain threshold, β-endorphin reactivity, and maximum ST-segment depression, and for symptom perception (MAPQ) did not significantly predict exercise-angina (see Table 3).

Targeted category models predicting exercise-induced angina

Three models were created to compare the predictive value of each cluster of variables assumed to affect different pain components. Each model included first a covariate block and then a variable cluster block (sensory-biological, cognitive-emotional, cognitive-interpretational). Covariates included age, sex, history of hypertension, history of MI, and history of diabetes. The covariate block was not significant in any of the three models ($\chi^2_{block} = 4.04$, $p_{block} = 0.54$). The model evaluating factors affecting the sensory-biological component (Table 4) was not significantly predictive ($\chi^2 = 5.15$, $p = 0.74$). The sensory-biological block, which consisted of maximum ST-segment depression, hot pain threshold, and β-endorphin reactivity, was also not significantly predictive and added little to the total model ($\chi^2_{block} = 1.11$, $p_{block} = 0.77$).

In contrast, the model cognitive-emotional factors was significantly predictive of anginal pain ($\chi^2 = 15.23$, $p = 0.033$), and the block consisting of negative affect and symptom perception was also significant ($\chi^2_{block} = 11.19$, $p_{block} = 0.004$). The model representing cognitive interpretation component was also significant ($\chi^2 = 58.91$, $p < 0.001$). Anginal history was significantly predictive of anginal pain on the ETT($\chi^2_{block} = 54.87$, $p_{block} < 0.001$). This model was re-run including anxiety and depression separately. The total model was marginally significant ($\chi^2 = 15.23$, $p = 0.055$), and anxiety (OR = 1.05, $p = 0.24$) and depression (OR = 1.02, $p = 0.28$) were not independently significant. When each was entered into the model separately the variables were significant with comparable effect sizes. The cognitive-emotional model with BDI and MAPQ ($\chi^2 = 14.04$, $p = 0.051$) showed that BDI was a significant predictor of exercise-angina (OR = 1.07 $p = 0.04$), and the cognitive-

emotional model with STAI and MAPQ (χ^2 = 13.79, p = 0.055) showed that anxiety was a significant though slightly weaker predictor of exercise-angina (OR = 1.04, p = 0.04).

Full model predicting exercise-induced angina

Next we assessed the association of these factors with angina when all 3 variable blocks (sensory-biological, cognitive-emotional, cognitive-interpretational) were entered into the same model (Table 5). The covariate (χ^2_{block} = 4.04, p_{block} = 0.54) and the variables grouped to represent the sensory-biologic factors (χ^2_{block} = 1.11, p_{block} = 0.77) remained non-significant. The block representing cognitive-emotional variables provided a significant increased in the model's predictive value (χ^2_{block} = 10.86, p_{block} = 0.004), and anginal history was robustly significant (χ^2_{block} = 47.37, p_{block} < 0.001). The full model was predictive of anginal pain (χ^2 = 63.38, p model < 0.001). Among the individual predictors, anginal history alone remained significant in the full model, and negative affect was marginally significant.

Discussion

The present study evaluated six factors implicated as predictors of exercise anginal pain. Considered individually and controlling for medical risk factors, negative affect (depressive and anxiety symptoms) and history of exertional angina were significant predictors of ETT angina. The negative affect variable was an important predictor of angina pain above and beyond the effects of the other variables, however, the effect of negative affect was considerably smaller than that of history of angina.

Relevance of Depression and Anxiety Symptoms

The association between negative affect and ETT angina is consistent with effects found in other studies. Depressive and anxiety symptoms correlated highly with each other, and also correlated with history of pain. A prior publication with the PIMI data set reported that anxiety and depression predicted both history of angina and time to angina (26). The relationship between psychological symptoms and history of pain is consistent among studies (22,52) and supports the notion that there is an affective component to reporting a pain history. This covariation could be due to individuals with a pain history being more likely to develop psychological symptoms as sequellae to recurrent pain. A physiological mechanism connecting psychological symptoms to the development of anginal pain has also been suggested (22,27). Though this mechanism has not yet been clearly demonstrated, the overlap of the emotional and physical pain pathways that probably underlies this mechanism has been described (53).

History of Exertional Angina

The strongest individual predictor was by far history of exercise-induced angina. Patients with a history of exercise-induced angina may learn to associate angina with exercise, and this may alter the experience of physical symptoms during exertion (8). A connection between exercise and anginal pain in these patients may result from a cognitive process or from a "re-wiring" of the nociceptive pathways in the myocardium or the CNS (54,55). Anginal pain history may not only lead to exercise-angina because of its association with the disease process, but also because it is related to psychological factors, such as depression and anxiety (26), or anticipation of pain during stress testing and daily life activities (8).

On initial examination, the strong association between history of pain and angina on ETT might be seen as simply reflecting that both measures assess the underlying CAD pathophysiology resulting in chest pain, or that patients are accurate in describing whether they have pain during exercise. However, several facts argue against the sufficiency of this

interpretation. First, only 51 of the 79 participants who reported pain on the ETT also reported a history of angina in the past 3 months on the Rose questionnaire. Second, the correlation between history of angina and ETT angina ($r=0.56$, $p = <0.001$) though significant, indicates that they are still moderately independent measures. Every patient in these analyses had ischemia on the treadmill test. Therefore, if anginal pain reports simply reflect presence of ischemia, we would expect all patients to report pain. In addition, we would not expect discordance between reports of pain during treadmill testing and during exertion in daily life, where patients presumably also had ischemia. It is also possible that the individuals not reporting pain in the past 3 months simply did not have enough physical exertion to trigger ischemia with angina. However, what is more likely is that these individuals were somehow distracted enough from their internal symptoms as to simply not perceive or remember angina during ischemia when it occurred. Third, only 31% of patients, all of whom had documented CAD, reported both history of angina in the past 3 months and angina on the ETT. These results indicate that a minority of patients display consistency between anginal history and ETT angina.

Conceptual grouping of variables

Grouping them according to the pain components they represent (sensory-biological, cognitive-emotional, and cognitive-interpretational), only the cognitive-interpretational block and a variable representing depression and anxiety symptoms were significant predictors. These results provide some support for specific theories of pain reporting. Patients with higher levels of anxiety and depression seem to be more likely to report pain on the ETT. As such, the broader construct of neuroticism may explain some of the pain reports here. There is an extensive literature relating negative affect and personality traits to disease and symptom reporting (31,56,57). The present study replicates findings that there is a direct relationship between negative affect and symptom reporting. It is also possible that there is a common etiology between physical pain and psychological distress (53), and that each of these variables reflect different aspects of pain. Because depression and anxiety may be involved in the development of CAD, this study provides evidence to suggest that negative affect might be involved in both disease etiology as well as in reporting of pain symptoms.

The present results are consistent with Melzack's Neuromatrix theory of pain (54, 58), developed to explain phenomena specific to chronic pain that could not be explained by the Gate Control theory (59). The Neuromatrix theory states that chronic pain develops through a combination of nociceptive pathways (sensory), situational interpretation (cognitive), cognitive-emotional factors (affective), and central modulatory and inhibitory factors. These forces produce a "pain signature" in the central nervous system that corresponds to a given type of chronic, recurrent pain, in this case angina. With repeated occurrences of this pain, the "pain signature" becomes more well-practiced and its underlying neurocircuitry becomes potentiated to the point where any given component of the pain (e.g., the sensory component) is no longer necessary to triggering the pain. Contextual factors alone might suffice. This theory might best explain why biological factors seem to be less strongly related to ETT angina than pain history, anxiety, and depression.

In all models, we did not observe significant effects for symptom reporting, β-endorphin reactivity, or hot pain threshold which has been previously related to pain latency in this sample (11). We also did not find significant effects of maximum ST-segment depression. Symptom reporting, though significantly correlated to angina in the correlation matrix, did not seem to play a strong predictive role in ETT anginal pain perception. These non-significant factors might not be statistically or clinically robust predictors of the presence versus absence of experimental anginal pain, although they may predict pain features such as latency, duration and intensity (11,26).

The present analyses do not suggest that these factors play no role at all. It is possible that no effect of sensory-biological factors was seen precisely because all patients had ischemia in this study. Ischemic severity and other factors may not be important in recurring pain like angina because the “pain signature” is already well-established, and therefore cognitive and emotional factors take on a greater importance.

Alternatively, these non-significant factors might not be statistically or clinically robust predictors of the presence versus absence of experimental anginal pain, although they may predict pain features such as latency, duration and intensity (11,26). Furthermore, research examining associations among disease, symptom reporting, and psychological factors suggest a more complex interplay among these variables (57,58), and that some factors, for example β-endorphins, may either mediate or moderate the associations between psychological factors and pain perception. The present study was not designed to test these more complex models, and further research might seek to establish what sort of interplay exists among the components of pain.

Study Limitations

This study did not include a measure of angiographic severity of disease, but the results suggest that disease severity is unlikely to have accounted for the entire predictive value of anginal history and psychological variables since all patients had documented CAD and prior evidence of ischemia. The lack of predictive relationships between ischemic severity, pain threshold, and β-endorphin reactivity for ETT angina indicates that the relationship between history of angina and ETT angina are not entirely mediated by cardiac disease processes. Given the different measurement parameters and measurement variability among predictors in this study, it is not possible to compare the strength of cognitive-emotional, cognitive-interpretational, and sensory-biological factors. However, the pattern of results indicates clearly that the effects of most variables are smaller than the effect of anginal history. The multivariate models may be unstable due to the fact that only 9 patients had a history of angina with no angina during the ETT. As such, models including this variable may obscure the true effect of other variables because of over-fitting. Also, the PIMI recruitment procedures may have selected for patients who represent a somewhat healthier than average CAD population, and there was a relatively small representation of women (35). Withdrawing medications could also have effects, such as sensitization of receptors, which could have affected predictors and outcome variables in the study. Finally, our operationalization of pain component categories is imperfect at best, and therefore the conclusions about the broad cognitive-interpretational pain component can be questioned. History of pain clearly represents more than a cognitive-interpretational factor since it also is a marker of the ischemic disease process. Conceptual conclusions of the study may also be limited by the fact that many of the predictors were measured after the ETT.

In sum, taking into account these limitations, the present study findings are consistent with the notion that clinical anginal pain is the result of a potentially learned response greatly influenced by contextual and emotional factors. Angina on the ETT is used as a clinical component of CAD diagnosis and a guide to treatment selection (2), and future research and clinical assessment and treatment may benefit from a more conceptual approach to the problem of angina.

Acknowledgments

The opinions and assertions expressed herein are those of the authors and are not to be construed as reflecting the views of the USUHS or the U.S. Department of Defense. Preparation of this article was assisted by NIH grant (Principle investigator: Dr. David S. Krantz NHLBI 1RO1 HL085730).

This study reports data from the NIH publicly accessible data set of the NHLBI-sponsored Psychophysiological Investigations of Myocardial Ischemia (PIMI) study, which can be accessed at https://biolincc.nhlbi.nih.gov/studies/pimi/.

Abbreviations

BDI	Beck Depression Inventory
CAD	coronary artery disease
ECG	electrocardiogram
ETT	exercise treadmill test
HPT	hot pain threshold
MAPQ	modified Autonomic Perception Questionnaire
MI	myocardial infarction
RAQ	Rose Angina Questionnaire
STAI	State Trait Anxiety Inventory

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Table 1

Participant characteristics.

	Silent ischemia N (%) N=84	Symptomatic ischemia N (%) N=79	*P*
Age			0.29
40–49 yo	9 (10.7%)	7 (8.8%)	
50–59 yo	17 (20.2%)	23 (29.1%)	
60–69 yo	44 (52.4%)	31 (39.2%)	
70+ yo	14 (16.7%)	18 (22.8%)	
Sex			0.54
Men	74 (88.1%)	67 (84.8%)	
Women	10 (11.9%)	12 (15.2%)	
Years of education[†]			0.52
5 and 11 years	16 (19.0%)	22 (27.8%)	
12 years	24 (28.6%)	17 (21.5%)	
13 and 15 years	16 (19.0%)	15 (17.9%)	
16 and 27 years	28 (33.3%)	24 (30.4%)	
Living alone	10 (11.9%)	21 (26.6%)	0.017
Working			0.035
full-time	28 (33.3%)	24 (30.4%)	
part-time	5 (6.0%)	11 (13.9%)	
Retired	45 (53.6%)	30 (38.0%)	
'other'	6 (7.1%)	14 (17.7%)	
History of MI	35 (41.7%)	40 (50.6%)	0.25
History of CHF	4 (4.8%)	2 (2.5%)	0.45
History of hypertension	38 (45.2%)	43 (54.4%)	0.24
History of diabetes	13 (15.5%)	10 (12.7%)	0.60
BMI - mean (SD)	31.21 (16.05)	28.11 (4.20)	0.26
Maximum ST-segment depression	2.05 (0.64)	1.92 (0.58)	0.20
Hot pain threshold	45.98 (3.78)	45.84 (4.40)	0.84
β-endorphin baseline	4.81 (2.96)	4.74 (3.06)	0.89
β-endorphin reactivity	1.31 (3.39)	1.28 (3.12)	0.95
BDI	4.80 (4.59)	7.35 (7.25)	0.009
STAI	29.74 (9.21)	33.62 (10.26)	0.012
MAPQ	83.77 (42.94)	99.57 (48.71)	0.029
History of angina	9 (10.7%)	51 (64.6%)	<0.001

MI = myocardial ischemia; CHF = coronary heart failure, BMI = body mass index, BDI = Beck Depression Inventory, STAI = State Trait Anxiety Inventory, MAPQ = modified Autonomic Perception Questionnaire.

[†]1 patient had missing data and was not included in these analyses.
Continuous variables analyzed by independent samples t-tests, categorical variables analyzed by Chi-square tests.

Table 2

Intercorrelations among variables.

	HPT	β-end	Max ST	BDI	STAI (state)	Negative affect	MAPQ	RAQ	Sex	Age	ETT angina	Ischemic Latency	Chest pain (3 months)
HPT		0.02	0.12	0.15	0.01	0.09	−0.02	−0.07	−0.16*	0.00	−0.02	0.02	−0.05
β-end			0.10	0.01	0.08	0.05	−0.01	0.06	0.03	0.09	−0.01	−0.01	−0.11
Max ST				−0.09	−0.19*	−0.16*	−0.04	−0.16*	−0.05	0.25**	−0.10	−0.20**	−0.16*
BDI					0.59**	0.90**	0.35**	0.16*	0.19*	−0.18*	0.21**	−0.11	0.19*
STAI (state)						0.89**	0.26**	0.23**	0.14	−0.09	0.20*	−0.05	0.21**
Negative affect							0.34**	0.22**	0.18*	−0.15	0.23**	−0.09	0.22**
MAPQ								0.24**	0.06	−0.20*	0.17*	−0.07	0.22**
RAQ									0.18*	−0.08	0.56**	−0.12	0.70**
Sex										−0.03	0.05	−0.27**	0.25**
Age											0.01	−0.23**	−0.06
ETT angina												−0.16*	0.64**
Latency													−0.20**
Chest pain (3 months)													

* $p < 0.05$,

** $p < 0.01$

BDI = Beck Depression Inventory; HPT = Hot pain threshold; MAPQ = Modified Autonomic Perception Questionnaire; RAQ = Rose Angina Questionnaire; STAI = State Trait Anxiety Inventory.

Table 3

Logistic regression models of individual factors controlling for medical variables.

	B	S.E	OR	95% CI	*P*
Hot pain threshold	−0.01	0.04	0.99	0.91–1.07	0.78
β-endorphin reactivity	−0.00	0.05	1.00	0.91–1.10	0.95
Maximum ST-segment depression	−0.29	0.28	0.75	0.43–1.29	0.30
Negative affect *	0.50	0.18	1.65	1.17–2.34	0.005
Anxiety symptoms	0.43	0.02	1.04	1.01–1.08	0.013
Depression symptoms	0.08	0.03	1.08	1.02–1.15	0.010
Symptom perception	0.01	0.00	1.01	1.00–1.02	0.023
History of angina **	2.86	0.45	17.41	7.16–42.34	<0.001

** p for Model <0.001,

* p for Model < 0.05

Table 4

Logistic regression multivariate models evaluating sensory-biological, cognitive-emotional, and cognitive-interpretational factors in prediction of ETT angina. (A) Sensory-biological model; (B) Cognitive-emotional model; (C) Cognitive-interpretational model.

	N	B	S.E	OR	95% CI	*P*
A. Sensory-biological model	163					0.74
Covariates						
Sex		0.29	0.49	1.34	0.51–3.49	0.55
Age		0.14	0.20	1.15	0.79–1.69	0.47
History of hypertension		0.40	0.33	1.50	0.78–2.85	0.22
History of diabetes		−0.34	0.48	0.71	0.28–1.82	0.48
History of MI		0.39	0.35	1.47	0.75–2.90	0.26
Biological factors						
Hot pain threshold		−0.01	0.04	0.99	0.92–1.08	0.89
B-endorphin reactivity		0.00	0.05	1.00	0.91–1.10	0.99
Max ST-segment depression		−0.29	0.28	0.751	0.43–1.31	0.31
B. Cognitive-emotional model	163					0.03
Covariates						
Sex		0.11	0.51	1.12	0.41–3.03	0.82
Age		0.27	0.21	1.31	0.87–1.95	0.20
History of hypertension		0.35	0.34	1.42	0.73–2.74	0.30
History of diabetes		−0.49	0.50	0.61	0.23–1.62	0.32
History of MI		0.54	0.35	1.72	0.87–3.40	0.12
Cognitive-emotional factors						
Negative affect		0.42	0.18	1.53	1.06–2.19	0.022
Symptom perception		0.01	0.00	1.01	1.00–1.01	0.15
C. Cognitive-interpretational model (anginal history)	163					<0.001
Covariates						
Sex		−0.43	0.62	0.65	0.20–2.18	0.49
Age		0.25	0.23	1.29	0.82–2.02	0.27
History of hypertension		0.37	0.39	1.45	0.63–3.13	0.34
History of diabetes		−0.50	0.58	0.61	0.19–1.89	0.39

	N	B	S.E	OR	95% CI	*P*
	History of MI	0.52	0.40	1.67	0.76–3.68	0.20
Cognitive-interpretational factor						
	History of angina	2.86	0.45	17.41	7.16–42.34	<0.001

Table 5

Logistic regression full model of significant predictors, including covariates.

	N	B	S.E	OR	95% CI	*P*
Full model	163					<0.001
Covariates						
Sex		−0.59	0.65	0.56	0.16–1.96	0.36
Age		0.33	0.25	1.39	0.86–2.25	0.18
History of hypertension		0.41	0.41	1.50	0.67–3.34	0.32
History of diabetes		−0.62	0.59	0.54	0.17–1.71	0.29
History of MI		0.55	0.42	1.73	0.75–3.97	0.20
Biological factors						
Hot pain threshold		−0.00	0.05	1.00	0.90–1.11	0.99
B-endorphin reactivity		−0.05	0.06	0.95	0.85–1.07	0.43
Max ST-segment depression		0.07	0.34	1.07	0.55–2.09	0.85
Cognitive-emotional factors						
Negative affect		0.37	0.21	1.45	0.97–2.16	0.07
Symptom perception		0.00	0.01	1.00	0.99–1.01	0.81
Cognitive-interpretative						
History of angina		2.80	0.47	16.39	6.51–41.26	<0.001

Psychosom Med. Author manuscript; available in PMC 2014 May 01.