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CLINICAL RESEARCH

MONITOR Is experimentally induced pain associated with Received: 2014.03.18 Accepted: 2014.03.27 socioeconomic status? Do poor people hurt Published: 2014.07.17 more? ABCDEF 1 Ana Miljković* Authors' Contribution: 1 Medical School, University of Split, Split, Croatia Study Design A ABCDEF 2 Ana Stipčić* 2 University Department of Health Care Studies, University of Split, Split, Croatia 3 Centre for Palliative Medicine, Medical Ethics and Communication Skills, Medical Data Collection B BE 3 Marijana Braš Statistical Analysis C School, University of Zagreb, Zagreb, Croatia BE 3 Veljko Đorđević Data Interpretation D 4 Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, Manuscript Preparation E ПΚ BE 3 Lovorka Brajković Literature Search E 5 Surgery Clinic, Clinical Hospital Centre Split, Split, Croatia **BE 4 Caroline Hayward** Funds Collection G 6 Centre for Global Health, Split, Croatia BE 5 Arsen Pavić BCDE 1,6 Ivana Kolčić ABCDEFG 1.6 Ozren Polašek * Both authors equally contributed to this manuscript

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Background: The association of pain and socioeconomic status is widely reported, yet much less clearly understood. The aim of this study was to investigate the association of experimentally induced pain threshold and tolerance with socioeconomic status.

Material/Methods: The study sample consisted of 319 adult subjects from the population of the island of Vis, Croatia, which was previously shown to have a high level of social homogeneity. A manual dolorimeter was used to measure mechanical pressure pain threshold (least stimulus intensity) and pain tolerance (maximum tolerance stimulus intensity) on both hands. Pain tolerance interval was defined as the difference between pain tolerance and threshold. Years of schooling and material status were used as socioeconomic estimates.

Results: Both of the socioeconomic estimates were significantly correlated with pain threshold, tolerance, and tolerance interval (P<0.001). The mixed modeling analysis, controlled for the effects of age, gender, and 4 psychological variables, indicated that education was not a significant predictor in any of the 3 models. However, lower material status was significantly associated with lower pain tolerance (P=0.038) and narrower pain tolerance interval (P=0.032), but not with pain threshold (P=0.506). The overall percentages of explained variance were lower in the tolerance interval model (20.2%) than in pain tolerance (23.1%) and threshold (33.1%), suggesting the increasing share of other confounding variables in pain tolerance and even more so in tolerance interval model.

Conclusions: These results suggest a significant association between experimentally induced pain tolerance and tolerance interval with material status, suggesting that poor people indeed do hurt more.

MeSH Keywords: Croatia • Pain • Population • Social Class

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MEDICAL

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Background

The complexity of human pain sensation has been a matter of ongoing discussions [1-4]. Despite the vast amount of research, quantification and measurement of pain still remains one of the most problematic issues in contemporary pain medicine [5]. A commonly used approach to measure pain is to use a dolorimeter (also referred to as an algometer) [6], which quantifies the mechanical stimulus intensity associated with subjective pain sensation. This approach provides 2 estimates, known as the pain threshold (the minimal stimulus intensity that provokes pain sensation) and pain tolerance (the upper level of stimulus associated with tolerable pain). Most published studies have focused on either threshold or tolerance, while fewer studies investigated both of these measures simultaneously. Failure to do so may result in limited conclusions, since it is both threshold and tolerance that define the range in which an individual feels and tolerates pain.

In an attempt to understand the determinants of pain sensation, researchers have invoked a number of factors, including socioeconomic inequalities. The social component of pain is well accepted [7-10] and a number of studies have already shown an association of socioeconomic status with pain across different populations and research settings [7,11,12]. Most commonly, such studies used education, occupation, and material status (defined through use of a household possessions index) as the estimates of socioeconomic conditions, or occasionally other proxies, like housing [13-15]. Regardless on the general idea of worsening pain sensation in the less affluent, the results from the studies are occasionally conflicting, showing that, for example, education may be associated with pain in some cases [16], while in others it may not [17]. In contrast, results for material status are far more convincing. Economic hardship was shown to affect and strengthen pain sensation [18], supporting the view that an elevated level of psychosocial stress has an effect on pain threshold [19]. Other studies have shown that improvements in material status have positive effects on pain threshold and tolerance or even that handling money prior to hot water immersion had a positive alleviating effect on pain sensation [20]. It should also be noted that most previous studies focused on specific subgroups of the population, most commonly people with chronic pain, patient samples, or even students, thus possibly leaving out an important piece of information on the effects of socioeconomic status on pain threshold and pain tolerance in a population-based setting. Therefore, the aim of this study was to investigate the association of experimentally induced pain measures, both threshold and tolerance, with socioeconomic estimates in the adult population of the island of Vis, Croatia.

Material and Methods

This study was performed as part of "10,001 Dalmatians", a large-scale genetic epidemiology project implemented in the isolated populations of the Croatian Adriatic islands [21], aiming to map genes for complex traits and a wide range of diseases [22–28]. The sample for this study consisted of subjects aged 25–88 years, who were part of the sub-sample from the island of Vis, a small and remote island in the Adriatic Sea. The subjects were initially recruited into this project in 2003, with re-sampling taking place in 2007. The subjects were invited on the basis of postal invitations (sent to all registered inhabitants, based on the voting register). The sample is therefore not considered to be representative for the entire population, but is very informative as it encompasses a profile of the entire population (as opposed to similar studies that often used highly homogenous samples, such as students).

For purposes of this study, we undertook a field visit to the same setting in 2011, aiming to supplement the data with pain-based measurements, additional surveys, and to re-measure some previously measured phenotypic measurements.

All subjects signed the informed consent prior to entering the study and the entire study was approved by the Ethics Committee of the School of Medicine, University of Split.

Pain-based measurements

Two pain measurements were made for the purpose of this study: mechanical pain threshold (least stimulus intensity) and mechanical pain tolerance (maximum tolerance stimulus intensity). Using these 2 measurements, we also calculated the third one - pain tolerance interval - defined as the difference between the tolerance and threshold, and is considered to be a range of pain sensation at which a subject can feel the pain but is able to tolerate it. One trained female measurer initially explained the procedure to each subject, followed by a demonstrational measurement. A total of 3 consecutive measurements of pain threshold were made on both hands, as suggested by previous studies [6]. The measurement protocol was based on mechanical pressure applied at a nearly perpendicular angle to the middle phalanx of the index finger. The pressure was gradually increased at a similar velocity, until the subjects felt pain and said "stop" to denote the pain threshold. A Wagner ForceOne dolorimeter was used in the measurement.

After at least 30 min and active involvement in other measurements (including blood pressure, electrocardiogram, and anthropometrical measurement), subjects were asked to re-take the measurement, which was considered as the actual measurement. Three consecutive measurements at the same site were also taken, both on left and right hands. Average value was calculated using all 3 measurements for each hand, followed by the calculation of the average value for both hands, which was then used in the analysis. During the second measurement cycle, we also measured mechanical pain tolerance in 2 consecutive attempts on the index finger of each hand. The measurement was performed in a similar way to the threshold, with the exception that subjects were now asked to tolerate as much pain as possible, until the point at which they said "stop", to denote the maximum tolerable signal intensity.

Based on these 2 measures, we also defined a pain tolerance interval as the difference between pain tolerance and pain threshold. This interval denoted the range in which an individual feels and tolerates pain, which is possibly more informative than either of the 2 original measures separately.

In addition to pain measurements, we also asked subjects if they used any form of analgesic drug within the past 48 h. All subjects who had difficulties in site of measurement due to finger injuries or arthritis, as well as those who reported serious discomfort associated with the measurement, were excluded from the analysis (n=14). Additionally, subjects who were diagnosed with neuropathic pain and fibromyalgia were excluded from the analysis (n=7).

Socioeconomic estimates

Two measures of socioeconomic status were used; education (defined as the years of schooling) and material status (defined through use of a household possessions index). The first estimate was based on a simple count of the number of completed years of schooling. The second was a composite index, consisting of 16 separate items, which was adjusted to suit to the properties of this population, and has previously been shown to have sufficient variability to provide a wide spectrum of estimates even in a homogenous population such as that in the island of Vis [29]. The index was defined as the equally weighted sum of the binary answers to question about whether the subjects had any of the following: running water installation, toilet within the house, bathroom, central or gas heating, wooden floors, phone, video recorder or a DVD, freezing chest, 2 TV receivers, dishwasher, computer, book collection (over 100 books), art collection, car, another flat/holiday house, and a boat.

Psychological measures

To broaden the possible set of confounding variables, we also performed psychological testing using 2 instruments. The first was a 48-item Eysenck short form [30], used to score subjects according to 3 distinctive domains: extroversion, neuroticism, and psychoticism. We also asked respondents to fill in a General Health Questionnaire, which is a 30-item, self-reported questionnaire that provides estimates of recent psychological distress [31]. Both surveys were previously analyzed and validated in the study population [32].

Statistical analysis

Both pain measurements were based on averaging of the repeated measurements (3 for pain threshold and 2 for pain tolerance) to suppress the possible effects of random error. Bivariate statistical methods were used in the initial analysis step, including t-test for independent samples and dependent samples (the later was used for the comparison of the leftand the right-hand measurements). Pearson's test was used for the correlation analysis. Chi-square test was used for the analysis of categorical variables (a single exception from this was made in the analysis of handedness, where Fisher's exact test was used due to the small number of cases). To account for the effects of confounding variables, mixed modelling was used. Three models were made: 1 each for pain threshold, upper tolerance limit, and tolerance. The same set of predictor variables was used in all 3 models, including age, gender, and 3 psychological variables (extroversion, neuroticism, and psychoticism) and a proxy for general health (General Health Questionnaire), coupled with the information on whether the subjects took any kind of analgesic drug within the past 48 h. Descriptive analyses were performed using SPSS ver. 19.0 (IBM SPSS). Fisher's exact test was calculated using Simple Interactive Statistics Analysis (http://www.quantitativeskills. com/sisa/statistics/) for the analysis of the gender differences in handedness. Mixed modeling was performed in Solar [33] to adjust for the existence of familial relatedness among subjects. Significance was set at P<0.05.

Results

A total of 319 subjects were included in this study, with 124 men (38.9%) and 195 women (61.1%). Men and women did not differ in age, but they reported significantly different years of schooling and material status (Table 1). Most subjects reported that they were right-handed, and only 1 subject reported being completely left-handed (Table 1).

The initial analysis of the pain measures indicated strong gender differences, with markedly higher scores in men for all 3 measures (Table 1). Women also reported more frequent use of analgesic drugs within the past 48 h than men did (Table 1). Additional analyses yielded a strong negative correlation of age with pain tolerance and pain tolerance interval (r=-0.23 and r=-0.35, respectively, both P<0.001), while association with pain threshold was insignificant (r=-0.12; P=0.825). Comparison of the pain threshold and tolerance between the Table 1. Descriptives of the analyzed sample and pain measurements.

	Men (n=124)	Women (n=195)	Р	
Age (years)	61.52±12.75	61.73±12.77	0.887	
Handedness				
Right	119 (96.0)	184 (94.4)	0.120*	
Left	0 (0)	1 (0.5)		
Ambidextrous	5 (4.0)	10 (5.1)		
Years of schooling	11.82±3.39	9.69±3.24	<0.001	
Material status estimate	10.52±2.34	9.22±2.57	<0.001	
Pain threshold (N/cm²)				
Right hand	57.49±11.45	43.21±10.39	<0.001	
Left hand	54.72 <u>+</u> 11.33	41.60±9.61	<0.001	
Average	56.11±11.09	42.41±9.75	<0.001	
Pain tolerance (N/cm²)				
Right hand	77.93 <u>±</u> 18.56	57.02±16.00	<0.001	
Left hand	72.83 <u>±</u> 18.67	53.09±15.07	<0.001	
Average	75.38±18.14	55.06±14.96	<0.001	
Pain tolerance interval (N/cm²)	19.27±13.37	12.65±10.26	<0.001	
Used analgesic drug within past 48 hours	10 (8.1)	33 (16.9)	0.020	
Psychological characteristics (EPQ-R)				
Neuroticism	4.00±2.97	5.77±3.45	<0.001	
Extrovertism	8.51±2.72	8.20±2.75	0.322	
Psychoticism	3.06±1.39	2.91±1.27	0.329	
General health questionnaire	54.98±9.42	59.78±12.30	<0.001	

The numbers are means ± standard deviations or absolute numbers and percentages (in brackets); * Fisher's exact test.

left- and right-hand measurement revealed a significant difference (both P<0.001), which was strongly expressed even in pain tolerance (Table 1). We did not detect a significant association of education and the use of analgesic drugs within the past 48 h (P=0.436). In contrast, subjects with lower material status reported significantly more frequent use of analgesics (P=0.016).

Correlation between pain measurements and other variables indicated significant results for 3 pain measures and both socioeconomic indices (Table 2). Furthermore, neuroticism was negatively associated with all 3 pain measures, suggesting that subjects who scored higher on the neurotic scale had lower pain threshold and tolerance (Table 2). Additionally, the association between psychoticism and pain threshold was also significant (Table 2).

Mixed modeling was used to create 3 separate models, for each pain measure. The results indicated significance for gender and psychoticism for pain threshold (Table 3). Pain tolerance was significantly associated with age, gender, and material status, a result similar to that of pain tolerance interval (Table 3). The percentages of variance for each of the 3 models were showing a gradual decrease, with 33.1% of explained variance for pain threshold, 23.1% for pain tolerance, and 20.2% for pain tolerance interval (Table 3). In total, material status explained up to 8.6% of total variance of pain tolerance and 7.5% of pain tolerance interval variance (Table 3).

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	Age	Pain threshold	Pain tolerance	Pain tolerance interval	Education	Material status	Neuro- ticism	Extro- vertism	Psycho- ticism	General health
Age	-	-0.01	-0.23	-0.35	-0.38	-0.28	0.15	-0.14	-0.08	0.19
Pain threshold	0.825	-	0.79	0.23	0.19	0.21	-0.12	-0.03	0.15	-0.09
Pain tolerance	<0.001	<0.001	-	0.78	0.30	0.34	-0.15	0.04	0.10	-0.13
Pain tolerance interval	<0.001	<0.001	<0.001	-	0.28	0.32	-0.13	0.09	0.01	-0.11
Education	<0.001	0.001	<0.001	<0.001	-	0.38	-0.28	0.15	-0.05	-0.19
Material status	<0.001	<0.001	<0.001	<0.001	<0.001	-	-0.27	0.18	0.01	-0.30
Neuroticism	0.011	0.044	0.007	0.025	<0.001	<0.001	-	-0.33	-0.09	0.60
Extrovertism	0.018	0.636	0.467	0.100	0.010	0.001	<0.001	-	0.01	-0.34
Psychoticism	0.184	0.011	0.100	0.977	0.392	0.919	0.125	0.813	_	-0.07
General health	0.001	0.107	0.024	0.052	0.001	<0.001	<0.001	<0.001	0.236	-

Table 2. Correlation between socioeconomic and psychological estimates and pain-related measurements*.

* Values above diagonal are correlation coefficients, while those below are significances. The matrix was based on 295 subjects with all measurements.

Table 3. Results of the mixed modeling analysis for pain measurements as outcome variables.

Variable	Pain threshold	Pain tolerance	Pain tolerance interval
Gender	<0.001	<0.001	<0.001
Age	0.507	0.001	<0.001
Years of schooling	0.533	0.359	0.513
Material status	0.506	0.038	0.032
Analgesic used in past 48 hours	0.316	0.314	0.563
Neuroticism	0.555	0.378	0.471
Extrovertism	0.291	0.089	0.848
Psychoticism	0.001	0.670	0.376
General health	0.195	0.141	0.193
Percent variance, material status	3.23	8.58	7.52
Percent variance, total model	33.10	23.07	20.15

Discussion

The results of this study suggest that socioeconomic status was associated with experimentally induced mechanical pain tolerance and pain tolerance interval. This finding becomes even more interesting in conjunction with the lack of a similar result for pain threshold, suggesting that the effect of socioeconomic inequalities is limited to pain tolerance and tolerance interval only. A possible explanation for this finding involves the underlying physiological mechanisms that define pain threshold and tolerance sensation, while tolerance relies more on environmental and psychological factors [34].

The link between education and pain has been variously labeled in previous studies, ranging from strong to no correlation [16,17]. While such finding could be regarded as due to a lack of consistency, it could also be a consequence of the nature of socioeconomic inequalities. Under the assumption that most measures of socioeconomic inequalities will be correlated [35], studies that used only 1 socioeconomic estimate

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in bivariate analysis could be providing a confounded result. Such a result was obtained in this study, in which education was strongly correlated with pain in correlation analysis, but the use of multivariate analytic methods yielded no such significance and suggested that only material status was associated with pain tolerance and tolerance interval.

One of the possible ways to replicate the results of this study could be to investigate the general pattern of pain sensation in a deteriorating socioeconomic situation, especially in an economic recession. Such a situation, in which nearly the entire population is affected by reduced economic possibilities, should therefore increase the use of analgesic drugs. An example of this could be the consumption of painkillers within the UK National Health Service, which was shown to increase during recession [36]. Although this finding cannot be claimed as the direct confirmation of the findings of this study, it nevertheless suggests that material status deterioration affects analgesic drug consumption, possibly reflecting worsening pain sensation across the population in times of economic hardship.

This study also showed that pain threshold does not seem to change with age, a finding that has been previously reported [34]. On the other hand, tolerance was negatively associated with age, suggesting that elderly people have a diminished tolerance interval. Gender-based differences were also reported here, suggesting that women had lower threshold and tolerance, and consequently narrower tolerance interval, as described before [37]. Although such a result may be considered as the direct proof of lower threshold and tolerance in women, such conclusions have to be made very cautiously because research results can be influenced by various socio-cultural variables, rather than providing simple biological measures [38]. This was also true in this study, in which a methodological approach could yield overestimated gender differences. The gender of the person performing measurements is known to affect the pain threshold results such that subjects of opposite gender to the measurer tend to provide better results (ie, higher threshold and tolerance) [39]. Since we only employed a single female measurer, these results could overestimate the gender difference. A more definitive answer to this question should reside in the simultaneous measurement of population-based subjects by measurers of both genders in order to avoid measurer gender bias. We also confirmed a previously reported difference in handedness [40], but failed to provide more definitive answers due to the widespread policy of negating left-handedness and converting left-handed people to right-handed, which is present in the entire region [41]. Lastly, psychological factors such as neuroticism or extroversion were reported to have an effect on some domains or types of pain [42]. We included psychological variables in the mixed model, only to show that the observed bivariate associations were confounded by other variables and that neither extroversion nor neuroticism were significantly associated with either pain measure, despite some previous results to the contrary [43,44].

The main advantages of this study were nearly all outlined in a paper that suggested a way forward towards better understanding of the association between socioeconomic inequalities and pain [10]. The use of multiple socioeconomic estimates, population-based sampling (as opposed to a more homogenous sampling in clinical settings), and further adjustment to other variables that could affect pain [10], such psychological estimates, were all employed in this study. Furthermore, we used a population-specific measure of material status, which was derived especially for this population [29], because generic socioeconomic estimates may often be of limited use across different studies and different populations [35]. Lastly, due to the existence of familial relatedness in the sample, we used mixed modeling to offset the possible over-estimation of results that could occur if such an adjustment was lacking [33].

The limitations of this study include a relatively small sample size. Another limitation is the lack of pain perception surveys or other clinically relevant information on other pain modalities that could provide more information on individual pain experience and attitudes. However, it should be noted that some previous studies did not report a significant association of pain threshold and tolerance with self-reported pain sensitivity [45]. Furthermore, the results obtained in this study may be population-specific [35,46], suggesting that this result requires an independent replication. Another potential limitation of this study is the limited possibility for generalization of results, especially to chronic pain. Regardless on these limitations, the results of this study show that material status may have a modifiable effect on pain tolerance and tolerance interval in a population-based setting in which previous high levels of socioeconomic equalities were observed, suggesting that poor people indeed do hurt more.

Conclusions

The results of this study suggest a significant association between experimentally induced pain tolerance and tolerance interval with material status, suggesting that people with lower socioeconomic status hurt more.

Statement

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