Published in final edited form as:

Pain. 2015 March ; 156(3): 357–358. doi:10.1097/01.j.pain.0000460338.16353.8e.

Heritability of Catastrophizing: the Biopsychosocial Model in Action

Roger B. Fillingim, PhD

University of Florida, Pain Research & Intervention Center of Excellence

The biopsychosocial model of pain posits that the experience of pain is sculpted by complex and bidirectional interactions among biological, psychological and social factors. In recent years, considerable research has attempted to address the “biological” domain by examining genetic contributions to pain. Indeed, both clinical and experimental pain represent substantially heritable phenotypes, such that, on average, genetic variability accounts for 25-50% of the variance in clinical and experimental pain responses [12]. In addition, numerous studies have identified candidate genes that are associated with clinical and experimental pain responses [3; 5], providing more specific information regarding biological pathways that contribute to pain.

Within the context of the biopsychosocial model, “psychological” contributions to pain have also garnered tremendous empirical attention. Psychological variables confer increased risk for development of chronic pain, and psychological functioning predicts pain severity and disability among individuals with existing chronic pain [6; 10]. Among the most widely research psychological factors in recent years, pain catastrophizing has shown consistent and robust associations with acute and chronic clinical pain as well as experimental pain responses [4; 15]. Traditionally, genetic and psychological influences on pain have been conceptualized as independent, though potentially interactive, domains that can influence pain. However, in this issue of PAIN, Trost and colleagues [16] report that pain catastrophizing shows significant heritability, suggesting a substantial genetic (and thereby biological) contribution to this important pain-related psychological construct. Specifically, these investigators examined pain catastrophizing and cold pressor pain responses in 400 twin pairs, roughly half of whom were monozygotic and the other half dizygotic. As expected based on previous findings, cold pressor pain tolerance measures showed heritability estimates slightly above 50%, indicating that slightly more than half of the variance in these pain measures can be attributed to genetic variability. But, for the first time, these investigators demonstrated that pain catastrophizing also showed significant heritability (37%).

That catastrophizing is in part genetically determined should not be surprising, as many psychological phenotypes, including personality, depression, and cognitive function, have shown significant heritability [2; 14]. A particularly interesting finding from the Trost study was that the genetic contribution to catastrophizing was largely independent of the genetic

contribution to pain responses. That is, the association between pain catastrophizing and cold pressor pain tolerance appeared to be a direct relationship rather than a reflection of shared genetic variance. Of course, as the authors note, although catastrophizing shows significant heritability, a majority of the variability in pain catastrophizing remains attributable to environmental factors. In this regard, it was interesting that the authors found pain responses and catastrophizing showed no common environmental variance. The authors suggest that this may reflect an important role for a unique learning environment in catastrophizing's influence on pain. That is, there may be an innate predisposition toward catastrophizing, which may lead to enhanced attention to pain-related information, subsequently facilitating learning that is biased toward negative pain-related outcomes.

While this is the first study to report on a genetic contribution to catastrophizing, previous findings have addressed whether catastrophizing and genetic factors work together to influence pain. Specifically, George and colleagues have reported a series of studies demonstrating that one of the most widely researched pain-related genes (the catechol-O-methyl-transferase or *COMT* gene) interacts with catastrophizing to influence pain. Specifically, these authors demonstrated that individuals with a *COMT* genotype that confers increased pain sensitivity who also reported a high level of pain catastrophizing reported the greatest levels of clinical shoulder pain [9]. Importantly, *COMT* genotype and catastrophizing were not related. They have subsequently replicated these findings in a separate clinical cohort and in two additional cohorts experiencing experimentally-induced shoulder pain [7; 8]. The findings of Trost and colleagues of a genetic contribution to catastrophizing opens the possibility that the *COMT* X catastrophizing interaction may represent a gene-gene interaction in addition to a gene-environment interaction.

The findings reported by Trost and colleagues point to several interesting lines of future research. The results certainly need to be replicated in larger samples, including those experiencing chronic pain. This would further establish the potential clinical utility of the findings, and sufficient sample sizes would permit analysis to determine whether the heritability of catastrophizing varies as a function of sex. This could be an important consideration, since both pain and catastrophizing are typically greater among females, and some investigators have reported sex X gene interactions in predicting pain phenotypes [1; 11; 13]. Also, future studies designed to identify the specific genes associated with catastrophizing would be quite valuable. This could shed light on the neurobiology of catastrophizing, potentially leading to a better understanding of its influence on pain and possibly to novel treatments designed to reduce catastrophizing. Finally, research designed to determine the environmental factors contributing to catastrophizing, and how these factors interact with the potential genetic susceptibility to catastrophizing would be quite informative. This could lead to tailored interventions to prevent or reverse pain catastrophizing in individuals who are at risk.

Trost and colleagues are to be commended for this interesting study and its novel findings. The pattern of results serves as a reminder that our tendency to separate risk factors into different domains (e.g. biological vs. psychological) reflects an artificial distinction based primarily on our own biases and limitations rather than an accurate characterization of how human health is influenced. Continued research efforts such as this one will promote a more

integrated biopsychosocial model of pain, which will ultimately lead to more effective diagnosis and management of pain.

Acknowledgments

This work was supported by NIH/NIDCR Grants U01DE024169 and U01DE017018.

References

- [1]. Belfer I, Segall SK, Lariviere WR, Smith SB, Dai F, Slade GD, Rashid NU, Mogil JS, Campbell CM, Edwards RR, Liu Q, Bair E, Maixner W, Diatchenko L. Pain modality- and sex-specific effects of COMT genetic functional variants. *Pain*. 2013; 154(8):1368–1376. [PubMed: 23701723]
- [2]. Bouchard TJ Jr. McGue M. Genetic and environmental influences on human psychological differences. *JNeurobiol*. 2003; 54(1):4–45. [PubMed: 12486697]
- [3]. Diatchenko L, Fillingim RB, Smith SB, Maixner W. The phenotypic and genetic signatures of common musculoskeletal pain conditions. *NatRevRheumatol*. 2013;10.
- [4]. Edwards RR, Cahalan C, Mensing G, Smith M, Haythornthwaite JA. Pain, catastrophizing, and depression in the rheumatic diseases. *Nature reviews Rheumatology*. 2011; 7(4):216–224.
- [5]. Fillingim RB, Wallace MR, Herbstman DM, Ribeiro-Dasilva M, Staud R. Genetic contributions to pain: a review of findings in humans. *Oral Dis*. 2008; 14:673–682. [PubMed: 19193196]
- [6]. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007; 133(4):581–624. [PubMed: 17592957]
- [7]. George SZ, Dover GC, Wallace MR, Sack BK, Herbstman DM, Aydog E, Fillingim RB. Biopsychosocial influence on exercise-induced delayed onset muscle soreness at the shoulder: pain catastrophizing and catechol-o-methyltransferase (COMT) diplotype predict pain ratings. *ClinJPain*. 2008; 24(9):793–801.
- [8]. George SZ, Parr JJ, Wallace MR, Wu SS, Borsa PA, Dai Y, Fillingim RB. Biopsychosocial influence on exercise-induced injury: genetic and psychological combinations are predictive of shoulder pain phenotypes. *The journal of pain: official journal of the American Pain Society*. 2014; 15(1):68–80. [PubMed: 24373571]
- [9]. George SZ, Wallace MR, Wright TW, Moser MW, Greenfield WH III, Sack BK, Herbstman DM, Fillingim RB. Evidence for a biopsychosocial influence on shoulder pain: pain catastrophizing and catechol-O-methyltransferase (COMT) diplotype predict clinical pain ratings. *Pain*. 2008; 136(1-2):53–61. [PubMed: 17686583]
- [10]. Linton SJ. A review of psychological risk factors in back and neck pain. *Spine*. 2000; 25(9): 1148–1156. [PubMed: 10788861]
- [11]. Mogil JS, Sorge RE, LaCroix-Fralish ML, Smith SB, Fortin A, Sotocinal SG, Ritchie J, Austin JS, Schorscher-Petcu A, Melmed K, Czerminski J, Bittong RA, Mokris JB, Neubert JK, Campbell CM, Edwards RR, Campbell JN, Crawley JN, Lariviere WR, Wallace MR, Sternberg WF, Balaban CD, Belfer I, Fillingim RB. Pain sensitivity and vasopressin analgesia are mediated by a gene-sex-environment interaction. *Nature neuroscience*. 2011; 14(12):1569–1573.
- [12]. Nielsen CS, Knudsen GP, Steingrimsdottir OA. Twin studies of pain. *Clinical genetics*. 2012; 82(4):331–340. [PubMed: 22823509]
- [13]. Olsen MB, Jacobsen LM, Schistad EI, Pedersen LM, Rygh LJ, Roe C, Gjerstad J. Pain Intensity the First Year after Lumbar Disc Herniation Is Associated with the A118G Polymorphism in the Opioid Receptor Mu 1 Gene: Evidence of a Sex and Genotype Interaction. *JNeurosci*. 2012; 32(29):9831–9834. [PubMed: 22815498]
- [14]. Sprangers MA, Bartels M, Veenhoven R, Baas F, Martin NG, Mosing M, Movsas B, Ropka ME, Shinozaki G, Swaab D, Consortium G. Which patient will feel down, which will be happy? The need to study the genetic disposition of emotional states. *Quality of life research: an international journal of quality of life aspects of treatment, care and rehabilitation*. 2010; 19(10):1429–1437.

- [15]. Sullivan MJ, Thorn B, Haythornthwaite JA, Keefe F, Martin M, Bradley LA, Lefebvre JC. Theoretical perspectives on the relation between catastrophizing and pain. *ClinJPain*. 2001; 17(1):52–64.
- [16]. Trost ZS,E, Sullivan M, Vervoort T, Avery AR, Afari N. Heritability of pain catastrophizing and associations with experimental pain outcomes: a twin study. *Pain*. 2015