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Physical and Psychological Correlates of Fatigue and Physical Function: A Collaborative Health Outcomes Information Registry (CHOIR) Study

John A. Sturgeon, Beth D. Darnall, Ming-Chih J. Kao, and Sean C. Mackey

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford Systems Neuroscience and Pain Laboratory, Stanford University School of Medicine, Palo Alto, California.

Abstract: **Fatigue is a multidimensional construct that has significant implications for physical function in chronic noncancer pain populations but remains relatively understudied. The current study characterized the independent contributions of self-reported ratings of pain intensity, sleep disturbance, depression, and fatigue to ratings of physical function and pain-related interference in a diverse sample of treatment-seeking individuals with chronic pain. These relationships were examined as a path modeling analysis of self-report scores obtained from 2,487 individuals with chronic pain from a tertiary care outpatient pain clinic. Our analyses revealed unique relationships of pain intensity, sleep disturbance, and depression with self-reported fatigue. Further, fatigue scores accounted for significant proportions of the relationships of both pain intensity and depression with physical function and pain-related interference and accounted for the entirety of the unique statistical relationship between sleep disturbance and both physical function and pain-related interference. Fatigue is a complex construct with relationships to both physical and psychological factors that has significant implications for physical functioning in chronic noncancer pain. The current results identify potential targets for future treatment of fatigue in chronic pain and may provide directions for future clinical and theoretical research in the area of chronic noncancer pain.**

Perspective: ***Fatigue is an important physical and psychological variable that factors prominently in the deleterious consequences of pain intensity, sleep disturbance, and depression for physical function in chronic noncancer pain.***

Key words: *Fatigue, depression, chronic pain, sleep, physical functioning, Collaborative Health Outcomes Information Registry (CHOIR).*

Chronic pain contributes significantly to physical dysfunction, which increases health care costs in the United States through decreased work productivity and higher health care utilization.[20] On an individual level, pain demonstrates deleterious effects on physical functioning through several mechanisms, including pain intensity,[21] sleep problems,[31] and depression.[27] Another key mechanism is fatigue, which commonly accompanies pain but has a multifactorial etiology, including pain intensity, inflammatory processes, and psychological factors. Fatigue has been defined as an overwhelming and persistent feeling of exhaustion that interferes with one's ability to function.[10] Fatigue contributes to physical dysfunction in chronic illness[39] and chronic pain populations[7,33] but remains a relatively poorly understood construct.

Fatigue in Chronic Noncancer Pain

To date, scientific inquiry has primarily examined fatigue in specific chronic medical and neurologic populations, such as patients with cancer,[24] human immunodeficiency virus,[16] and multiple sclerosis.[42] However, a significant comorbidity between chronic noncancer pain conditions and fatigue has been noted.[12,17,37] Fatigue is a significant complaint in individuals with rheumatoid arthritis,[41] osteoarthritis,[33] fibromyalgia,[29]

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Address reprint requests to John A. Sturgeon, PhD, Stanford University School of Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford Systems Neuroscience and Pain Laboratory, 1070 Arastradero, Suite 200, MC 5596, Palo Alto, CA 94304. E-mail: jasturge@stanford.edu

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chronic low back pain,[17] and chronic abdominal pain,[8] and complaints of fatigue predict poorer physical functioning in these conditions.[29,33] Despite its implications for functioning, however, fatigue has remained relatively understudied and may not be thoroughly considered in the context of chronic pain treatment outside of certain pain disorders. Some of the difficulty in the use of fatigue as a clinical target may stem from its multifactorial nature.

Contributors to Fatigue in Chronic Noncancer Pain

Fatigue has been defined as a multidimensional construct, composed of both physical and psychological factors.[45] In chronic pain, a positive relationship between pain intensity and fatigue has been reported,[50] though this finding has not been replicated in all studies.[37] Psychological factors also contribute to fatigue in chronic pain. An indirect effect of pain on fatigue has been noted through sleep disruption.[18] Similarly, there is a notable relationship between depression and fatigue in chronic pain. Reports of low energy or significant fatigue are a diagnostic criterion for depression,[2] and elevated rates of depression have been consistently reported across a variety of pain populations.[32] Further, longitudinal studies have identified a reciprocal relationship between depression and fatigue, such that individuals with increased fatigue appear to be at increased risk of developing a future major depressive episode.[1] Similarly, individuals with depression are more likely to report significant fatigue in the future.[44] Further, there may be significant sex-based differences in experience of pain,[23,47] depression,[43,47] and fatigue[4] because of biological or psychosocial differences, further highlighting the complexity of fatigue in chronic pain.

Study Hypotheses

Given that fatigue, pain, sleep disturbance, and depression have disruptive, but potentially overlapping, influences on physical functioning,[21] it is important to examine whether these variables have unique implications for physical functioning. The current study utilized data from the Collaborative Health Outcomes Information Registry (CHOIR), using a set of open-source tools for assessing patient-reported health status (Patient Reported Outcome Measurement Information System [PROMIS]).[10] The CHOIR, derived from a larger, comprehensive study known as the Stanford-NIH Open Source Health Registry, collects longitudinal data using set measures (including PROMIS) that are collected at initial clinic visits and at fixed intervals thereafter, as well as follow-up appointments. Data from the CHOIR were used to assess fatigue, depression, sleep disturbance, physical function, and pain-related interference in a diverse sample of individuals with chronic pain conditions. We expected that pain intensity, sleep disturbance, and depression would independently contribute to severity of fatigue. Further, consistent with previous studies, we expected that fatigue would account for a significant degree of the relationships of pain intensity, sleep interference, and depression with ratings of pain-related interference and physical function.

Methods

All procedures were approved by the institutional review board at the Stanford University School of Medicine, and all patients provided informed consent prior to completing any measures from the data registry.

Participants

Data were collected from 2,487 patients who presented for initial medical evaluations between September 2012 and May 2014 at the Stanford Pain Management Center, a large, tertiary care pain clinic. The sample was 62.6% female (n = 1,556). The predominant ethnicity in the current sample was white (63.2% of the overall sample), followed by Asian (7.2%), African American (3.4%), Native Hawaiian or Pacific Islander (.7%), and American Indian or Alaska Native (.4%). Nearly one-fifth of the sample (19.7%) reported an ethnicity of "Other," and 5.4% of the sample did not endorse an ethnicity. Median education in the patient sample was a completed associate's degree or equivalent occupational or technical program certification. Mean age in the current sample was 49.7 years (range = 18–93 years). Regarding pain diagnoses, the largest proportion of patients were referred to the pain clinic for thoracolumbar pain (20.7% of the sample), followed by other musculoskeletal pain (11.5%), fibromyalgia and/or myofascial pain (8.8%), orofacial pain (7.8%), nerve pain (7.2%), neck pain (7.0%), abdominal pain (4.1%), and pelvic pain (4.1%). A full list of pain diagnoses for the current sample can be found in Supplementary Appendix 1. At the time of the initial visit, 1,791 patients (92.1% of the sample) carried a single pain diagnosis, 183 patients (7.4% of the sample) had 2 pain diagnoses, 11 patients (.4% of the sample) had 3 pain diagnoses, and 2 patients (.1% of the sample) carried 4 pain diagnoses. Pain diagnosis information was unavailable for 500 patients in the current sample.

Procedures

At clinic check-in for their initial medical appointments, patients were provided a tablet computer that allowed them to complete a series of questionnaires. PROMIS measures were administered using a computerized adaptive testing (CAT) approach[9,22]; rather than assessing a set number of items per subscale, the CAT approach identifies the optimal items within each domain based on prior responses from the respondent. CAT assessments are considered superior to traditional standard scale assessments because of the smaller number of items needed for effective assessment of each construct, as well as increased reliability of measurement.[28] The CHOIR includes CAT versions of the PROMIS measures adapted with an in-house algorithm (SNAPL-CAT). SNAPL-CAT was implemented using the same CAT algorithm as the one used by the Northwestern University Assessment Center, which has provided open access to PROMIS instruments.[22]