Mechanisms Linking Daily Pain and Depressive Symptoms: The Application of Diary

Assessment and Bio-Psycho-Social Profiling

by

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ABSTRACT

Despite the strong link between pain and depressive symptoms, the mechanisms by which they are connected in the everyday lives of individuals with chronic pain are not well understood. In addition, previous investigations have tended to ignore biopsychosocial individual difference factors, assuming that all individuals respond to pain-related experiences and affect in the same manner. The present study tried to address these gaps in the existing literature. Two hundred twenty individuals with Fibromyalgia completed daily diaries during the morning, afternoon, and evening for 21 days. Findings were generally consistent with the hypotheses. Multilevel structural equation modeling revealed that morning pain and positive and negative affect are uniquely associated with morning negative pain appraisal, which in turn, is positively related to pain's activity interference in the afternoon. Pain's activity interference was the strongest predictor of evening depressive symptoms. Latent profile analysis using biopsychosocial measures identified three theoretically and clinically important subgroups (i.e., Low Functioning, Normative, and High Functioning groups). Although the daily pain-depressive symptoms link was not significantly moderated by these subgroups, individuals in the High Functioning group reported the lowest levels of average morning pain, negative affect, negative pain appraisal, afternoon pain's activity interference, and evening depressive symptoms, and the highest levels of average morning positive affect across 21 days relative to the other two groups. The Normative group fared better on all measures than did the Low Functioning group. The findings of the present study suggest the importance of promoting morning positive affect and decreasing negative affect in disconnecting the

within-day pain-depressive symptoms link, as well as the potential value of tailoring chronic pain interventions to those individuals who are in the greatest need.

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멀리 미국에서 공부하고 있는 아들을 위해서 항상 응원해 주신 우리 어머니 그리고 아버지 정말 감사드립니다. 가족과 떨어져 있었던 이 긴 시간이 헛되지 않도록 훌륭한 학자가 되겠습니다. 마지막으로, 사랑하는 우리 동생 지선아. 항상 통증과 씨름하면서도 너의 목표를 향해 열심히 살아가는 네가 정말 자랑스럽다. 곧 병마로부터 벗어나 지금까지 힘들었던 너의 시간들을 모두 보상받을 수 있었으면 좋겠다.

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Introduction

Almost 100 million Americans, about one third of the U.S. population, report experiencing chronic pain (National Institutes of Health, 2014). The estimated annual cost of treating problems caused by chronic pain is over \$635 billion, an amount that surpasses the annual cost of treating any other chronic illness (Gaskin & Richard, 2012). Chronic pain is also regarded as a significant risk for developing a number of psychopathological conditions including major depressive disorder, anxiety disorders, borderline personality disorder, and post-traumatic stress disorder (see Dersh, Polatin, Robert, & Gatchel, 2002 for a review). Indeed, chronic pain is a major socioeconomic health problem; and a more nuanced understanding of how chronic pain leads to numerous physical and mental health problems is needed.

Among various deleterious psychological consequences of chronic pain, the link between pain and depressive symptoms is particularly important. First, the prevalence of experiencing depressive symptoms among chronic pain patients is very high. Even with stringent clinical diagnostic criteria of major depressive disorder, epidemiological studies suggest that up to 45 percent of individuals with chronic pain meet the criteria for major depressive disorder (e.g., Demyttenaere et al., 2007; Rush, Polatin, & Gatchel, 2000). A population-based retrospective cohort study also reported that individuals with chronic pain due to fibromyalgia are 2.9 times more likely to be diagnosed with major depressive disorder than healthy individuals in the United States (Weir et al., 2006). Second, depressive symptoms pose a significant threat to effective chronic pain management. Individuals in a depressed state experience higher impairments in social, physical, and occupational functioning (see McKnight & Kashdan, 2009 for a review), making it

difficult to seek and adhere to a chronic pain treatment. This can further induce feelings of helplessness and hopelessness in managing pain and may increase the risk of developing major depressive disorder.

Despite the strong correlational link between pain and depressive symptoms, the underlying mechanisms have not been fully understood, especially in the context of the daily lives of chronic pain patients. Much of the previous research addressing the pain-depression link has been correlational, yielding findings that primarily draw upon nomothetic (i.e., variable-centered) methods that ignore the role of within-person variance (as would be examined within an idiographic, person-centered approach). The prior studies thus provide a limited understanding of how pain and depressive symptoms are connected to each other in a real-world context. Hence, further research is required to better understand *how and through what* mechanisms pain and depressive symptoms are connected to each other. In addition, there is a dearth of research examining how momentary experiences of positive and negative affect play role in pain processing among individuals with chronic pain.

The present study seeks to examine the underlying mechanisms linking pain and depressive symptoms in a nuanced fashion, by utilizing ecological momentary assessment data (i.e., daily diaries) gauging individuals' behavior and experience in real-time and in real-world settings (Shiffman, Stone, & Hufford, 2008). Moreover, statistical techniques will be employed that reflect both a variable- and person-centered approach. In addition, the role of positive and negative affect in processing pain will be explored. Finally, a set of theoretically-based biopsychosocial individual difference variables will be included that may serve either to attenuate or to intensify the pathways from pain to

depressive symptoms. The inclusion of a battery of biopsychosocial variables will inform efforts to develop more effective and efficient chronic pain treatments in the future.

Potential Mechanisms Linking Pain and Depressive Symptoms

Below, a review of the relevant literature provides support for the hypothesized model tested in the present study.

Pain, Pain Appraisal, Activity Interference

Acute pain serves as an automatic, evolved alerting system that signals individuals who are experiencing nociceptive stimulation to withdraw (if possible) or to seek melioration. Acute pain is functional. By contrast, the persistent or chronic experience of pain can lead to impairments in physical functioning and in the pursuit of important personal goals (Affleck et al., 1998, 2001; Karoly & Ruehlman, 2007; Ruehlman, Karoly, & Taylor, 2008; Weiner, Rudy, Morrow, Slaboda, & Lieber, 2006; Wilson & Palermo, 2012). Chronic pain can be pathogenic. For instance, pain's compelling attention grabbing capacity is known to have various deleterious consequences (e.g., Crombez, Van Damme, & Eccleston, 2005; Van Damme, Legrain, Vogt, & Crombez, 2010). Specifically, it has been argued that experience of pain can shift one's attention and behavior to the pursuit of pain-reduction goals, thus interfering with the pursuit of other valued personal goals (see Eccleston & Crombez, 1999; Van Damme et al., 2010 for review).

Pain's interruptive effects on daily activity are not proportional to the level of actual pain experience. One key variable that can exert significant influence on pain's interruptive effects is how individuals appraise pain experience. Pain that is negatively appraised increases pain intensity and also interferes with instrumental performance

(Unruh & Ritchie, 1998). For instance, the Fear Avoidance Model (FAM; Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012; Leeuw et al., 2006; Vlaeyen, Crombez, & Linton, 2016) suggests that the way an individual interprets pain is critical in managing pain. Specifically, when a nociceptive stimulus is interpreted as nonthreatening, then individuals can maintain their engagement in valued daily activities and goals. However, when pain is interpreted as a threat, the priority to control pain becomes dominant and elicits behavioral avoidance which can induce significant functional interference and negative affect (Vlaeyen, Crombez, & Linton, 2016; Zale, Lange, Fields, & Ditre, 2013). Previous literature on pain catastrophizing, a type of negative pain appraisal that is characterized by rumination, magnification, and helplessness, also suggests that such thinking can enhance reports of pain intensity and functional impairment among chronic pain patients (Edwards et al., 2008; Keefe, Brown, Wallston, & Caldwell, 1989; Richardson et al., 2009; Severeijns, Vlaeyen, van den Hout, & Weber, 2001; Sullivan, Stanish, Waite, Sullivan, & Tripp, 1998). On the other hand, individuals who are more capable of accepting and tolerating unpleasant feelings without automatically reacting to and judging them tend to demonstrate less interference in daily living (Lengacher et al., 2012; Ussher et al., 2014). This positive appraisal system is also related to decreased emotional interferences (Ortner, Kilner, & Zelazo, 2007), less psychological distress (Kögler et al., 2015), and less pain symptom severity (Jones, Mist, Casselberry, Ali, & Christopher, 2015). Clearly, cognitive appraisal of pain seems to serve an important mediating role on determining the magnitude of pain's adverse effect on daily functioning.

The Role of Negative and Positive Affect

Negative emotion, which is frequently experienced by individuals with chronic pain, can be one of the major sources of dysfunction in daily living. For instance, previous studies report that negative affect is associated with higher pain and activity interference levels (Dekker, Tola, Aufdemkampe, & Winckers, 1993; Hu & Gruber, 2008). The experience of negative affect can also distort the ways in which individuals appraise their pain. Negative affect reflects a harm-avoidance motivational system (Gray, 1994; Lang, Bradley, & Cuthbert, 1998), which can serve to bias information processing and make individuals *hypervigilant* toward potential threats such as pain (Geisser, Roth, Theisen, Robinson, & Riley, 2000; Watson & Pennebaker, 1989). Furthermore, it is suggested that negative affect can narrow the scope of individuals' attention, thus assisting with immediate action tendencies such as flight or fight mode (Fredrickson, 1998, 2013). Hence, when individuals are in a negative affective state, it is possible that they are more likely to appraise nociceptive stimuli in a negative way and disengage from pursuing their valued goals or activities.

On the other hand, positive affect, part of the approach-oriented appetitive motivational system (Gray, 1994; Lang, Bradley, & Cuthbert, 1998), is known to facilitate the pursuit of valued aspirations (Custers & Aarts, 2005; Finan & Garland, 2015; Fishbach & Labroo, 2007; Ong, Zautra, & Reid, 2015). For example, a recent daily diary study of a community sample of persons with chronic pain showed that higher levels of morning positive affect were associated with lower levels of interference with afternoon work goal pursuit above and beyond morning pain intensity and negative affect (Mun, Karoly, & Okun, 2015). According to the broaden-and-build hypothesis

(Fredrickson, 1998, 2013), positive affect can expand individuals' attention and elevate their mental flexibility, which allows them to build important biological, psychological, and social resources over time (Cohn, Fredrickson, Brown, Mikels, & Conway, 2009; Fredrickson, 2013; Fredrickson, Cohn, Coffey, Pek, & Finkel, 2008; Garland et al., 2010). Hence, positive affect may help individuals lessen the likelihood that they will appraise pain in a constrained and catastrophic manner. For instance, Geschwind, Meulders, Peters, Vlaeyen, and Meulders (2015) examined whether experimentally induced positive affect prevents generalization of pain-related fear of movement. They found that momentarily increasing positive affect reduced the generalization of pain-related fear when participants were in a state of acute pain (Geschwind et al., 2015). In sum, both positive and negative affect appear to serve an important role in influencing negative pain appraisal and interference of daily activities over and above experience of pain.

The Association between Activity Interference and Depressive Symptoms

For individuals with chronic pain, one of the most salient factors related to feeling depressed may be pain's interference with valued daily activities. For instance, Börsbo, Peolsson, and Gerdle (2009) found that the level of depressive symptoms had the highest correlation with disability caused by pain compared to correlations with pain intensity, anxiety sensitivity, pain anxiety, and pain catastrophizing. From a cognitive perspective, repeated interruption of work on important activities or failure to achieve meaningful personal goals due to pain can induce individuals to construct self-defeating negative schemas (Karoly & Jensen, 1987; Jensen, Turner, & Romano, 1991; Jensen & Karoly, 1991), which can likewise contribute to depressive symptoms. Similarly, learned

helplessness theory (Seligman, 1972) hypothesizes that individuals become depressed when they perceive that they have no control over the outcome of a negative situation or event such as the activity interference brought about by random pain flares. The behavioral framework further supports the claim that significant activity interference can induce depressive symptoms. For example, according to Fordyce's (1976) behavioral model of chronic pain, daily interference caused by chronic pain can substantially reduce access to positive/negative reinforcement and reward that used to come about as a result of engagement in those activities. Let us say that an individual used to relieve stress mostly through the rewarding effects of regular exercise. However, if the individual can no longer garner the same reward or benefit due to pain's interference with exercising, he or she is more likely to experience depressive symptoms. Theoretically, self-defeating schemas, helplessness, and reduced access to rewards, all of which fundamentally originate from pain-related interference, can be linked to the experience of depressive symptoms among chronic pain patients.

Consideration of Individual Differences and the Bio-Psycho-Social Perspective

The aforementioned theoretical and empirical associations are based on the assumption that all individuals respond to experiences such as pain, negative and positive affect, or pain's interference with daily activity in the same manner. However, in reality, there is great variation in the way that individuals with chronic pain react to these experiences. For instance, some individuals are better than others at regulating their pain. Also, not all individuals with chronic pain experience depressive symptoms due to pain's interference in daily activities. Hence, it is crucial to ask *how* and *why* similar levels of pain, affect, or pain-related interference are processed and regulated differently across

individuals. Finding an answer to this question would make it possible to tailor or target chronic pain intervention programs to those individuals who are at the highest risk.

Recent studies have, in fact, begun to address this important question. For instance, Mun, Karoly, and Okun (2015) found that individuals reporting a high pain acceptance level showed no significant association between morning pain intensity and afternoon pain's interference with work goal pursuit, whereas individuals with a low or mean level of pain acceptance showed a significant association between the two. In a sample of individuals with fibromyalgia who engaged in a 30-day diary assessment, Finan et al. (2011) found that the within-person association between daily ratings of pain and maladaptive coping (i.e., pain catastrophizing and pain attention) was moderated by variation in the catechol-O-methyltransferase (COMT) gene. Rios and Zautra's study (2011) also revealed that between-person differences in economic hardship significantly moderated the daily association between financial worries and pain intensity.

An important limitation of these studies, however, is that only a limited array of individual differences (either biological, psychological, or social) are examined for practical reasons. This constrained approach does not lend itself well to obtaining a complete understanding of individual differences in the real world. A potential solution to this issue is to incorporate individual differences in the biological makeup, psychological predispositions, and socio-cultural backgrounds of study participants. This is often referred to as the *biopsychosocial framework*. There is a growing consensus in the field of psychology that both mental and chronic health disorders should be understood through this more holistic perspective (Borrell-Carrio, 2004; Engel, 1977). So far, however, no attempt has been made to explore the influence of individual differences on

the link between pain and depressive symptoms using a biopsychosocial framework.

Below I provide a literature review of a number of biopsychosocial individual difference factors that may moderate the experience of pain, affect, pain appraisal, and/or activity interference among individuals with chronic pain.

Biological Individual Differences

Respiratory Sinus Arrhythmia

The autonomic nervous system (ANS) consists of two main divisions: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). The SNS is responsible for fight-or-flight responses during stressful or emergency situations, whereas the PNS is responsible for rest and restoration which inhibit the activation of SNS during sudden changes in environment or after exposure to stress. Among these two systems, the PNS plays a central role in regulation of individuals' stress reactivity and sensitivity (Porges, 1992, 1995, 2007).

Previous studies suggest that the activity of the vagus nerve plays an essential part in the PNS (Allen, Chambers, & Towers, 2007; Berntson et al., 1997). Thus, vagal tone, which reflects the activity of the vagus nerve, is recognized as a general index of PNS function. However, vagal nerve activity cannot be measured without using invasive methods. Hence, respiratory sinus arrhythmia (RSA), capturing the PNS' influence on systematic fluctuation in heart rate during respiration through the vagus nerve is commonly utilized as a proxy measure of vagal tone (Allen et al., 2007; Berntson, Cacioppo, & Quigley, 1993; Berntson et al., 1997; Grossman & Taylor, 2007; Grossman, Stemmler, & Meinhardt, 1990; Porges, 1992, 1995, 2007).

Individual differences in resting RSA have been consistently demonstrated to play an important role in regulating arousal and promoting restoration from psychological stress (Appelhans & Luecken, 2006; Beauchaine, 2001; Porges, 2007). It is suggested that high resting RSA is related to greater flexibility in response to environmental demand and better executive function task performance (Hansen, Johnsen, & Thayer, 2003; Porges, 2007; Suess, Porges, & Plude, 1994; Yaroslavsky, Bylsma, Rottenberg, & Kovacs, 2013). On the other hand, low resting RSA is associated with low executive control, high impulsivity, and deficits in the ability to regulate emotion (Huffman et al., 1998; Krypotos, Jahfari, van Ast, Kindt, & Forstmann, 2011). Furthermore, individuals with low resting RSA are likely to present more mental and physical health issues, such as anxiety (Thayer, Friedman, & Borkovec, 1996) and major depressive disorder (Rottenberg, 2007; Yaptangco, Crowell, Baucom, Bride, & Hansen, 2015). Thus, RSA is a trait level physiological index of restoration from psychological stress that appears to be an important protective factor in managing the experience of pain, negative affect, and pain-related activity interference in the present model.

The Behavioral Approach and Behavioral Inhibition System

The behavioral approach system (BAS) and the behavioral inhibition system (BIS) are the two distinct neurophysiological systems relevant to human adaptation. BAS is an appetitive motivational system that is responsible for approach-related behaviors, emotions (e.g., hope, joy, excitement, and anger), and cognition (e.g., self-efficacy). BAS is activated when individuals perceive environmental cues that are rewarding. On the other hand, BIS is an aversive motivational system that activates avoidant-related behaviors, emotions (e.g., depression and anxiety), and cognition (e.g., hopelessness and

catastrophizing). It is activated in response to threat and punishment-related cues (see Jensen, Ehde, & Day, 2016 for a review).

Extreme levels of either BIS or BAS appear to be maladaptive for individuals with chronic pain (see Jensen et al., 2016). A dominant BIS tendency promotes avoidance and withdrawal behaviors that avert individuals from engaging in meaningful activities.

A skewed BAS tendency can also lead to higher pain and its interference. For example, maintaining a consistently high activity level during an injury or a necessary resting period can contribute to increases in pain and interference in daily living (Fordyce, 1976).

There is little agreement on how to accurately measure BIS and BAS (De Pascalis, 2008). Usually, BIS and BAS are measured using a self-report questionnaire (i.e., Carver & White, 1994) that directly asks participants about their BIS/BAS trait-like tendencies. However, this self-report measure of BIS/BAS can be complemented by a physiological measure called a *startle response* that is associated with subconscious BIS/BAS activation.

The startle response is an automatic, defensive physiological reaction that involves activation of several brain areas, such as the amygdala and thalamus, known to be associated with processing threatening stimuli. The startle response is reliably captured by the magnitude and latency of eye blinking elicited by abrupt white noise (Grillon & Baas, 2003). The startle reflex is usually augmented if it occurs in the context of ongoing aversive (negative) emotion, but is attenuated when one is in an appetitive (positive) emotional state relative to a neutral emotional state (Bradley, Codispoti, & Lang, 2006). To be specific, during the aversive emotional state, individuals are primed to react to potential threats more quickly, whereas a calm and enjoyable emotional state

primes individuals to react more slowly to potential threats, as it is less necessary for individuals to be in a flight-or-fight response mode.

Previous studies show that findings from both BIS/BAS questionnaires and the startle reflex paradigm are significantly related to each other (Hawk & Kowmas, 2003; Peterson, Gable, & Harmon-Jones, 2008). Using both a self-report measure of BIS/BAS and the startle reflex provides more nuanced understanding of how individuals with chronic pain respond to varying degrees of pain and its activity interference.

Sleep Interference

A number of studies have found a robust association between sleep disturbance and pain severity (Haythornthwaite, Hegel, & Kerns, 1991; Smith, Perlis, Smith, Giles, & Carmody, 2000; Stone, Broderick, Porter, & Kaell, 1997). Although it is assumed that the association between pain and sleep is bi-directional, it has been reported that the effect of sleep disruption on pain severity is stronger than the effect of pain on sleep quality (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Raymond, Nielsen, Lavigne, Manzini, & Choinière, 2001).

In some chronic pain disorders, such as fibromyalgia, sleep interference is regarded as one of the major etiological and maintenance factors (e.g., Hamilton, Atchley, Karlson, Taylor, & McCurdy, 2011; Moldofsky, 2008). Sleep interference can lower the pain threshold (Lentz, Landis, Rothermel, & Shaver, 1999; Onen, Alloui, Gross, Eschallier, & Dubray, 2001), impair regulation of somatic focus on pain stimuli (Affleck et al., 1996), and thus can elevate pain sensitivity. Sleep interference is also associated with pain-related activity interference (Kothari, Davis, Yeung, & Tennen, 2015; Menafee et al., 2000; McCracken & Iverson, 2002). McCracken and Iverson's

study (2002) suggests that patterns of sleep and rest significantly predict physical activity interference over and above the influence of depressive symptoms and pain severity.

The influence of sleep interference is also associated with increased depressive symptoms. Naughton, Ashworth, and Skevington (2007) found that sleep disruption and poor sleep quality significantly predicted higher levels of depressive symptoms among chronic pain patients. Sleep intervention studies further support this argument. For example, Edinger, Wohlgemuth, Krystal, and Rice (2005) randomly assigned chronic pain patients to either a cognitive behavioral therapy (CBT) for insomnia group, a sleep hygiene group, or a control group receiving standard care. Their findings suggest that participants in the CBT and sleep hygiene intervention groups reported not only significant reduction in pain but also improvement in overall mood and well-being (Edinger, Wohlgemuth, Krystal, & Rice, 2005). Thus, sleep interference can be an important individual difference in understanding the current pain-depressive symptoms model.

Pain Threshold

The pain threshold is the point at which an individual first perceives a nociceptive stimulus as being painful. A low pain threshold is suggested to be indicative of a potential neurobiological vulnerability (central sensitization), associated with an increased level of substance P in cerebrospinal fluid, which acts to lower the synaptic excitability threshold and irritate second-order spinal neurons (Choy, 2015). There is growing evidence that the sensitized central nervous system can alter the process of nociception and can contribute to persistent pain experience (Sheather-Reid & Cohen, 1998; Sterling, Treleaven, Edwards, & Jull, 2002).

Most studies have utilized pain thresholds to compare individuals with chronic pain and healthy individuals or to make comparisons between different chronic pain groups. For instance, Nørregaard, Bendtsen, Lykkegaard, and Jensen (1997) examined how individuals with fibromyalgia and healthy control groups differed in their thermal, mechanical, and electrical pain thresholds. Mechanical and electrical pain thresholds were significantly lower in FM patients than in controls, whereas there was no significant difference in heat pain threshold between the two groups (Nørregaard et al., 1997).

Pressure pain thresholds of tender point sites were also found to be significantly different between FM patients and healthy controls (Maquet, Croisier, Demoulin, & Crielaard, 2004). Recently, Gormsen, Bach, Rosenberg, and Jensen (2012) found that individuals with neuropathic pain demonstrated higher pain thresholds to both mechanical (i.e., using a pressure algometer) and thermal stimuli (i.e., thermos tester).

Examining differences in pain thresholds between various groups of individuals with chronic pain and healthy individuals is important. However, a wide range of individual differences in pain threshold exists within each group. Individuals who have a very low pain threshold can potentially distort the ways they appraise a pain stimulus and have an exaggerated pain response. This tendency may increase the likelihood of experiencing pain-related activity interference. Therefore, assessing between-person differences in pain threshold can be a useful pain-specific individual difference measure.

Psychological Individual Differences

The Continuum of Depression

Although the present model focuses on depressive symptoms that arise as a consequence of pain and its interference, depression is also known to exert an adverse

influence on pain sensations and upon the activities of daily living for individuals with chronic pain. For instance, Haythornthwaite, Sieber, and Kerns (1991) found that individuals with chronic pain who are depressed reported significantly higher pain intensity levels and greater pain interference relative to those who were not depressed. Raselli and Broderick (2007) confirmed this finding using an ecological momentary assessment design wherein individuals with higher level of depression provided higher ratings of pain across a 2-week period. Longitudinal studies that have been recently conducted provide further evidence that depression can negatively impact pain and disability. Scott, Kroenke, Wu, and Yu (2016), for example, found that depression significantly predicted pain intensity and interference above and beyond pain catastrophizing and anxiety.

Depression also appears to play a key role in distorting individuals' perception of pain's interference. For instance, Huijnen et al. (2011) examined the role of depression in activity interference among individuals with chronic pain. They found that people with higher depression had a higher gap between subjective and objective activity interference as measured by an accelerometry when compared to people with lower depression. In other words, among people with chronic pain, those with higher depression tend to negatively portray their daily activity interference levels. Thus, the present model will take into account the role of individual differences in the continuum of depression.

The Continuum of Anxiety

Anxiety is one of the most common aversive emotions experienced by persons with chronic pain. In fact, individuals with chronic pain are quite commonly diagnosed with various anxiety disorders. For instance, McWilliams, Cox, and Enns (2003) found

that 35 percent of individuals with chronic pain had anxiety disorders including generalized anxiety disorder, panic disorder, social phobia, and agoraphobia using a nationally representative sample.

Physiologically, the experience of anxiety can activate the SNS, which may lower the pain threshold and increase pain receptor activation, inducing greater pain intensity (Naliboff & Rhudy, 2009; Schmidt & Cook, 1999). From a cognitive perspective, anxiety is associated with elevated attention to various internal and external stimuli that may amplify nociceptive experience (Arntz, Dreessen, & De Jong, 1994). Turk (2002) argued that individuals who are hypervigilant and fearful of nociceptive stimuli tend to appraise the stimuli in an exaggerated way. They are also likely to engage in escape and avoidant behaviors that can lead to interference with daily activities.

Previous empirical studies support these claims. Smith and Zautra (2008) investigated the role of anxiety and depression play in pain experience among women with pain due to rheumatoid arthritis or osteoarthritis. They found that individual difference in anxiety and depression were associated with increases in current and next week's pain experience. Individuals with a relatively high level of anxiety experienced twice as much weekly pain compared to those with a high level of depression (Smith & Zautra, 2008). A recent longitudinal study also showed that anxiety at baseline significantly predicted pain severity 12 months later among individuals with chronic musculoskeletal pain (Bair et al., 2013). Furthermore, in a large sample of children and adolescents with chronic pain, anxiety moderated the association between current pain and pain-related functional interference (Simons, Sieberg, & Claar, 2012). For individuals who reported a high level of anxiety, even a low level of pain was related to

high pain-related interference. Individual differences in anxiety may modulate one's experience of pain and its interference over and above depression.

Neuroticism

Whereas depression and anxiety level can vary over time, neuroticism is generally considered to be a stable personality trait or predisposition that is characterized by various negative emotions, such as anxiety, fear, depressive affect, distress, frustration, and jealousy (Thompson, 2008). Previous studies have demonstrated that neuroticism is positively associated with greater bodily sensation experience (Geisser, Roth, Theisen, Robinson, & Riley, 2000) and that individuals with higher neuroticism tend to pay more attention to minor sensations such as aches (Watson & Pennebaker, 1989). Researchers have started to examine the role of neuroticism in chronic pain. For instance, Goubert, Crombez, and Van Damme (2004) found that pain catastrophizing and pain-related fear significantly mediated the association between neuroticism and vigilance to pain. In addition, they also revealed that the association between pain catastrophizing and pain severity is significantly moderated by neuroticism (Goubert et al., 2004). In a study employing ecological momentary assessment of pain intensity and pain unpleasantness for two weeks, individuals with higher neuroticism reported higher ratings of pain across the two week period (Raselli & Broderick, 2007). Although neuroticism may have some overlap with state level of depression and anxiety, it is expected that this stable personality trait may play a unique role in individuals' pain sensation and pain appraisal.

Pain Acceptance

Pain acceptance is characterized by a willingness to engage in activities without defense, control, or avoidance even if pain is present (McCracken, Vowles, & Eccleston, 2004; McCracken & Zhao-O'Brien, 2010). Previous studies found that individuals who exhibit high levels of pain acceptance are more likely to show greater psychosocial functioning and less pain medication use (McCracken & Eccleston, 2005). Furthermore, pain acceptance has been negatively associated with pain intensity, depression, pain-related anxiety, and disability (McCracken & Eccleston, 2003; McCracken, Spertus, Janeck, Sinclair, & Wetzel, 1999; McCracken, 1998). More recently, Mun et al. (2015) found that high pain acceptance levels significantly mitigated the positive association between morning pain and pain's interference with work goal pursuit in the afternoon. These findings suggest that individuals' willingness to engage in daily activities and pursue meaningful values in the presence of pain may serve as an important protective factor for individuals with chronic pain.

Social Individual Differences

Socio Economic Status (SES) and Financial Stress

SES is often operationalized by income, occupation, and/or education level (Dorner et al., 2011; Morgan, Conway, & Currie, 2011; Saastamoinen, Leino-Arjas, Laaksonen, & Lahelma, 2005). Studies suggest that individuals with low income and low education show higher prevalence rates of chronic pain and report higher pain intensity (Morgan, Conway, & Currie, 2011; Saastamoinen, Leino-Arjas, Laaksonen, & Lahelma, 2005). A recent study found that when individuals experienced the same level of pain, those who were in a lower SES group indicated higher pain-related disability (Dorner et

al., 2011). Rios and Zautra (2011) also discovered that individuals with greater overall economic hardship rated higher levels of pain intensity when they experienced financial worries compared to those with less economic hardship.

Financial stress can be experienced by individuals from any SES group, and is known to exert a pervasive negative influence on an individual's life (see Fox & Chancey, 1998 for a review). Financial stress can significantly affect physical and mental health over and above SES (see Skinner, Zautra, & Reich, 2004 for a review). For example, Krause, Jay, and Liang (1991) revealed that elevations of subjective financial stress, dissatisfaction, and insecurity are associated with higher somatic symptoms after controlling for SES. Financial stress is also related to higher depressive symptoms and decreased self-esteem (Keith, 1993; Krause, Jay, & Liang, 1991). Skinner, Zautra, and Reich (2004) employed the daily diary method to examine the role of daily financial stress on health complaints among arthritis patients. They found that more than usual daily financial stress was associated with increased health complaints and negative affect. Individual difference in both SES and financial stress appear to serve important social functions in modulating one's pain experience.

Interpersonal Stress

Chronic pain does not merely impact intra-individual processes in a negative manner, but it also disrupts interpersonal dynamics. For example, studies have found that chronic pain can significantly decrease a partner's relationship satisfaction (Reich, Olmsted, & van Puymbroeck, 2006), can significant impact sexual function (Coates & Ferroni, 1991), increase caregiver burden (Reich, Olmsted, & van Puymbroeck, 2006), and elevate depression (Schwartz, Slater, Birchler, & Atkinson, 1991). Chronic pain

contributes to profound changes in role and communication patterns among couples (Roy, 1985), and can alter a partner's goals, expectations, and perceived purpose in life. Chronic pain adversely influences other interpersonal relationships because patients often seek solicitous support and empathy from others, and demand more resources from their social support system (Keefe et al., 1996; Sullivan, Tripp, & Santor, 2000; Sullivan et al., 2001). For instance, Lackner and Gurtman (2004) found that pain catastrophizing leads to greater interpersonal difficulties as patients demand more support and caretaking. Hence, chronic pain can significantly disrupt and worsen individuals' interpersonal networks and attenuate interpersonal relationship quality.

Likewise, elevated levels of interpersonal stress may lead to or worsen patients' dysfunctional patterns of pain regulation and feelings of depression. Previous findings suggest that a partner's expression of anger, irritation, or disregard significantly predict a patient's higher functional interference, negative affectivity and depressive symptoms (Kerns et al., 1991; Stroud, Turner, Jensen, & Cardenas, 2006). On the other hand, patients' positive daily interaction with their partners is associated with attenuated pain behaviors, pain intensity, and pain-related disability (Leonard, Cano, & Johansen, 2006). There is also evidence that interpersonal conflict (e.g., with family, friends, larger social network) and lack of support from work peers contributes to increase in pain (Faucett & Levine, 1991; Feuerstein, Sult, & Houle, 1985). More recently, Hyphantis, Guthrie, Tomenson, and Creed (2009) found that individuals with severe Irritable Bowel Syndrome (IBS) who have interpersonal issues exhibited longer disease durations while controlling for psychological distress. The study further points out that a decrease in interpersonal problems through psychodynamic interpersonal therapy was associated with

improved health status (Hyphantis et al., 2009). Taken together, assessing individual difference in interpersonal stress emanating from relationships with partners, family members, friends, and/or colleagues may be meaningful in understanding the link between pain and depressive symptoms.

Satisfaction with Social Support in Coping with Pain

Social support has been defined as "resources perceived as being available from others in social networks" (López-Martínez, Esteve-Zarazaga, & Ramírez-Maestre, 2008, pp. 373). Studies report that chronic pain patients who have a higher level of perceived social support are less likely to report pain intensity, distress, and better pain adjustment (Jensen et al., 2002; Waltz, Kriegel, & van't Pad Bosch, 1998).

Some argue that solicitous support, which involves catering to or expressing sympathy in response to the patient's pain behaviors, can positively reinforce the patient's expression of pain (Flor, Kerns, & Turk, 1987) and the display of pain behaviors (Romano et al., 1992). Thus, paradoxically, providing support to pain patients may act to reinforce maladaptive behaviors and result in greater functional interference (Flor, Kerns, & Turk, 1987; Gil, Keefe, Crisson, & Van Dalfsen, 1987; Romano et al., 1992). However, negative responses towards patients' pain behaviors do not significantly attenuate their pain behaviors (Turk, Kerns, & Rosenberg, 1992) or pain intensity (Kerns, Haythornthwaite, Southwick, & Giller, 1990). Rather, it has been reported that negative or disapproving responses towards patients is related to elevation in their depressive symptoms (Kerns et al., 1991; Stroud et al., 2006). These findings do make sense, as chronic pain patients might feel guilty, upset, or helpless about their current state.

According to a comprehensive review, solicitous, distracting, and negative forms of

social responding are positively associated with pain intensity and functional disability (see Leonard, Cano, & Johansen, 2006 for a review). The influence of social support on pain and its adjustment is complex as Gil, Keefe, Crisson, and Van Dalfsen (1987) pointed out. Perhaps, what is important is individuals' *satisfaction* in receiving social support in coping with their pain rather than types of support that they receive.

Biopsychosocial Profiling

Many studies on chronic pain have used moderation analyses (see Aiken & West, 1991 for a review) involving a small number of moderating variables to examine individual differences in the everyday lives of chronic pain patients (e.g., Davis, Okun, Kruszewski, Zautra, & Tennen, 2010; Finan et al., 2011; Mun et al., 2015; Okun, Karoly, Mun, & Kim, 2016). The traditional moderation analysis approach is ideal for testing one or two moderating variables. However, it is not advisable to include a large number of moderators in a regression model simultaneously, because of the excessive complexity of the model and significant reduction of the power to detect higher-order interactions (Cooper & Lanza, 2014). Hence, including all the aforementioned biopsychosocial individual differences in a regression model is statistically challenging.

A more suitable statistical approach that may enable a comprehensive investigation of multiple biopsychosocial individual differences is *latent class (profile) moderation* (see Lanza & Rhoades, 2013; Wang & Ware, 2013). Lanza and colleagues (Lanza, Rhoades, Greenberg, Cox, & Family Life Project Key Investigators, 2011; Lanza, Rhoades, Nix, Greenberg, & Conduct Problems Prevention Research Group, 2010) suggest that latent class (profile) moderation provides an in-depth and personoriented approach to the individual difference profiling of risk and protective factors.

This methodological approach makes it possible to empirically identify subgroups of chronic pain patients who share common biopsychosocial risk and/or protective factors, such as neuroticism, heart rate variability, pain threshold, pain acceptance, and socioeconomic status. By identifying different subgroups with distinct biopsychosocial profiles, we can examine which subgroups possess dysfunctional versus functional patterns of pain, affect, pain appraisal, and pain-related interference regulation, and how these patterns relate to the experience of depressive symptoms.

The Present Study

Despite the strong connection between pain and depressive symptoms, how and through what mechanisms they are connected to each other in the everyday lives of chronic pain patients is not well understood. In addition, only a limited array of individual differences showing some moderating effects on pain, affect, pain appraisal, and pain interference have been investigated in isolation. The present study seeks to address these gaps in the literature and proposes a more comprehensive mechanistic model for linking pain and depressive symptoms.

A recent study by Mun, Karoly and Okun (2015) provides a useful framework for the model of the present study. They examined the influence of morning pain and morning ratings of affect on evening work goal progress as mediated by afternoon pain's interference in work goal pursuit. They also examined the moderating influence of pain acceptance on morning pain intensity and afternoon pain's interference on work goal pursuit. Based on this previous within-day sequential model (Mun et al., 2015), the present study will investigate how the experience of pain and positive and negative affect in the morning influence end-of-day depressive symptoms. Both morning pain appraisal

(i.e., a composite of pain catastrophizing, pain intolerance, and pain reactivity), and afternoon pain's activity interference are assumed to sequentially mediate the relationship between morning pain and evening depressive symptoms. The role of positive and negative affect in this process will be also examined. Furthermore, if subgroups of individuals with distinct biopsychosocial profiles can be identified, then analyses will be conducted to test how the link between daily pain and depressive symptoms is moderated within different subgroups. A hypothesized mechanistic model of pain and depressive symptoms is presented in Figure 1. Specific hypotheses are described below.

Research Hypotheses

Hypothesis 1: On mornings with higher than usual pain levels, appraisals of pain will be more negative.

Hypothesis 2: Over and above the effect of morning pain elevation, morning positive and negative affect may uniquely predict how individuals negatively appraise their pain experience. Specifically, it is expected that the greater than usual experience of morning negative affect will predict increases in negative pain appraisal, whereas the greater than usual experience of positive affect will predict decreases in negative pain appraisal.

Hypothesis 3: Higher than usual negative pain appraisal in the morning will lead to greater pain-related activity interference in the afternoon.

Hypothesis 4: Greater pain-related activity interference in the afternoon will predict higher depressive symptoms in the evening.

Exploratory hypothesis: As no previous study has tried to identify subgroups of individuals with chronic pain representing different biopsychosocial profiles, it is

difficult to anticipate how many subgroups will emerge from a latent profile analysis or which specific pathways will be moderated by distinct biopsychosocial profiles in the present research. However, a general assumption is that if a subgroup with a biopsychosocial profile of high protective factors and low risk factors is identified, then individuals in this group will be less influenced by the deleterious effects of pain, negative affect, negative pain appraisal, or pain's activity interference, and thus will experience less depressive symptoms in the evening. On the other hand, for subgroups with fewer biopsychosocial protective factors and more risk factors, the association will be intensified between morning pain and depressive symptoms as mediated through negative pain appraisal and pain's interference with activity.

Methods

Participants

Individuals with chronic pain from the Phoenix metropolitan area were recruited by newspaper advertisements, online postings, and local doctors' offices as part of a larger psychological intervention study on fibromyalgia (FM). Inclusion criteria for the present study were: individuals who (1) are between the ages of 18 and 72; (2) have pain for three months or more in at least three of four quadrants of the body, or in two quadrants of the body and they had substantial sleep disturbance and fatigue; (3) report pain in at least 11 of 18 tender points during a home visit (described below) consistent with diagnostic criteria for FM established by the American College of Rheumatology (Wolfe et al., 1990); (4) do not have any autoimmune or neuropathic pain disorders; (5) are not currently in other research trials or receiving psychotherapy for pain or

depression; and (6) are not pursuing litigation related to their pain condition. More detailed information on the total sample size for the present study is described below.

Participant Screening

Among the 716 individuals who showed interest in the present study, 444 did not meet the inclusion criteria after the initial phone screening and the tender point exam. Failure was primarily due to lack of interest and/or time to complete the requirements of the study. Those 272 who passed the phone screening had a tender point exam administered by a research nurse. 4 kg of pressure was delivered with a dolorimeter to each of 18 tender points and 3 control points for the tender point exam. Participants were required to report some pain in response to pressure on at least 11 of 18 tender points to be qualified for the present study. This tender point exam cutoff criterion is based on the guidelines of American College of Rheumatology (Wolfe et al., 1990). Two hundred seventy two participants were enrolled into the study. However, 52 individuals dropped out of the study after the enrollment mainly due to their time constraints. Thus, a total of 220 individuals participated in the present study. All participants read and signed a consent form, and completed an initial questionnaire packet that included measures of physical health, emotional health, and pain. A clinical visit by a registered nurse was conducted to assess pain and comorbid health issues of participants. In addition, an assessment of depression, post-stress traumatic disorder, and life events was conducted by a phone interview. After finishing these procedures, participants completed preintervention assessments including: (1) a laboratory session to assess cortisol, emotionmodulated startle responses, pain threshold and tolerance, and resting heart rate variability; (2) 21-day daily diary regarding their interpersonal events, pain, fatigue, sleep quality, mood, and coping; and (3) questionnaires regarding current FM symptoms, and physical and emotional functioning. After completion of all these procedures, participants were then randomly assigned to one of three 7-week FM psychological treatment conditions. After completing the treatment, a post-intervention assessment that is identical to that of the pre-assessment was conducted. Participants also underwent six-and twelve-month follow-up assessments that are based on self-report questionnaires. All procedures for data collection in the current study were approved by the Institutional Review Board at Arizona State University prior to initiating the study. Data for the current study are drawn from pre-intervention questionnaires, laboratory, and daily diary assessments.

Demographics

Among the 220 participants, 195 (88.6%) were female. The mean age of the sample was 51.30 (SD = 11.03) and participants came from diverse ethnic backgrounds (78% Caucasian, 2.7% African American, 14.3% Hispanic, 4% Native American, 1.3% Asian, and 4.5% other). Their education level was also varied across participants (15.2% had a high school diploma or less education, 17% had post graduate education, 46.6% attended some college or had earned an Associate's degree, and the remaining 17.5% had a Bachelor's degree). In terms of their relationship status, 55.3% of participants indicated that they were either married or living with a romantic partner, 8.1% reported never married, 27.4% were divorced, and 5.8% were widowed. Despite having chronic pain, 23.3% of participants were working full-time, and 27.4% were working part-time.

Procedure

Laboratory Assessments

Participants attended a three-hour laboratory session to complete a number of laboratory tests. Based on each participant's availability, these laboratory sessions were scheduled in the morning (start time between 9 and 10 AM) or the afternoon (start time between 1 and 2 PM). Approximately half of the sessions were conducted in the morning (48%). In each lab session, participants were first fitted with facial electromyography (EMG) and electrocardiography (EKG) electrodes and asked to rest for 10 minutes while their heart rate responses were recorded. Afterward they participated in a startle probe protocol while their facial EMG responses were recorded. After completing the startle probe task, participants were provided with a 10-minute rest period before participating in a pain threshold and tolerance assessment.

Physiological data acquisition procedure. Laboratory staff placed Ag/Ag Cl conducting electrodes with gel on a participant's (1) forehead (i.e., ground), (2) left corrugator muscle (i.e., frowning muscle), (3) left zygomatic muscle (i.e. smiling muscle), and (4) left orbicularis muscle (i.e., startle eye blink) to record participants' EMG activity. An extra Ag–AgCl electrode was also attached to a participant's left and right wrist to collect EKG data. In the present study, electrode impedance for all electrodes fell below $10 \text{ k}\Omega$. A BioPac MP 100 system (Biopac Systems, Inc.) was used to record both EMG and EKG activity. The raw EMG and EKG signals were sampled digitally at 2000 Hz and were amplified through BioPac EMG bio-amplifiers.

After placing all electrodes, participants were asked to sit quietly for approximately ten minutes to become accustomed to the laboratory environment. During

this period, 10 minutes of resting ECG data were collected through use of AcqKnowledge data acquisition software. Participants were not allowed to talk or move during the ECG recording. No instructions were provided to them on how to breathe. Then, they received digitalized and standardized voice instructions transmitted through headphones. The same instructions also appeared in writing on a monitor in front of participants while they are listening to the instructions. Participants were prompted to view some slides that varied in emotional content (i.e., positive, negative, and neutral) and then rated the level of valence and arousal of each slide after it was presented. The instruction also included that participants would periodically hear a brief noise over the headphones, and a sample of that noise was delivered. This acoustic stimulus consisted of a 95 dB, 50 milliseconds (ms) burst of white noise. Headphones were calibrated prior to each session to establish proper voltage and decibels of the probe. Then, participants were presented with three sample slides, two of which included an acoustic startle burst, to familiarize them with study procedures. Participants were allowed to ask any questions prior to proceeding to the actual data collection phase.

Individuals were exposed to a total of 36 slides (i.e., 12 negative, 12 neutral, and 12 positive) depicting affective content while their eye blink startle reflex and facial EMG were recorded. These slides were drawn from the International Affective Picture System (IAPS; Lang, Bradley, Cuthbert, 1998). Positively and negatively valenced slides were selected to be of comparable, high levels of arousal, based on normative ratings. Examples of photos from the negative emotion category included a snake, a burn victim, and a toilet. Examples of photos from the neutral emotion category included an umbrella, shoes, and a lamp. Examples of photos from the positive emotion category included

images of romantic couples, sailing, and nature scenes. The slide presentation order was randomized within blocks of six slides. Each block had two slides of each valence category (i.e., negative, neutral, or positive). Prior to displaying each slide, an orienting symbol (i.e., "+") was first presented for three seconds to alert the participant of an upcoming slide. Each slide was then displayed for six seconds followed by their self-report ratings of emotional valence and arousal for that slide. For two-thirds of the slides within each emotional valence category (i.e., 8 positive, 8 neutral, and 8 negative), an acoustic startle burst was presented while participants are viewing slides. The startle probe was randomly presented 3, 4, or 5 ms after a slide was displayed to prevent participants from habituating to the startle stimulus. EMG data were recorded with a computer through use of *AcqKnowledge* data acquisition software. Waveforms were displayed in real time were constantly monitored by lab staff members in a separate room while participants viewed slides on a computer in their own room.

Diary assessment procedure. For the diary assessment, a cell phone was provided to each participant for the duration of the assessment. Research staffs met with each participant and provided them with detailed instructions and training on how to complete the daily phone diaries. Participants were asked to complete four diary reports per day for 21 days through an automated system that called the cell phone. The automated system also delivered audio recorded questions, and participants used phone keypad to respond these questions. The first morning assessment time was decided by participants to occur approximately 30 minutes after their normal waking time. The remaining three calls occurred at 11:00 am (morning), 3:30 pm (afternoon), and 7:00 pm (evening). If participants missed one of these calls, they were allowed to call into the

system within three hours of time window to complete the diary questions. Research staff members thoroughly monitored participants' diary completions to reduce missing data. If participants missed calls for several days in a row, staffs contacted participants to help them with any potential barriers to complete the diary assessment. Participants were paid \$2 for each day they completed diaries, with a bonus of \$1/day for rates of diary completion that were more than or equal to 50%. As a result, the overall diary completion rate across 21-days was high. Participants completed 3,796 of 4,620 (82.2%) observations possible across the sample.

Measures

Within-Person Variables

Most of the within-person variables (i.e., pain, affect, pain appraisal, pain's activity interference) were measured multiple times during the day. However, selection of each variable was based upon the hypothesized within-day sequential model of pain and depressive symptoms (see Figure 1).

Morning pain: Pain intensity was measured by a standard pain rating scale (Jensen, Karoly, & Braver, 1986). Participants were asked to report their overall level of pain in the past two to three hours using a numerical scale that ranges from 0 (no pain) to 100 (pain as bad as it can be).

Morning Positive Affect: Positive affect is a composite of four items (i.e., energetic, calm, cheerful, and ease) which were chosen from the PANAS (Watson, Clark, & Tellegen, 1988). Positive affect score was calculated as the average ratings of the four items. Energetic and cheerful represent positively valenced emotion with high arousal. Calm and ease are emotions that represent positive valence with low arousal. Participants

were asked to rate the intensity of each positive affect items that they might have felt over using a scale ranging from 1 (not at all) to 5 (completely). The within-person reliability for the four morning positive affect was .66.

Morning Negative Affect: Negative affect is also a composite of four items (i.e., lonely, afraid, sad, angry) that are selected from PANAS (Watson & Clark, & Tellegen, 1988). Negative affect score was calculated as the average ratings of the four items. Angry and afraid represent negatively valenced emotion with high arousal. Lonely and sad are emotions that represent negative valence with low arousal. Participants were asked to rate the intensity of each negative affect items that they might have felt using a scale ranging from 1 (not at all) to 5 (extremely). The within-person reliability for the four morning negative affect was .86.

Morning Negative Pain Appraisal: Negative pain appraisal is measured by a mean of four diary items. Participants were instructed to report the degree to which they experienced specific cognitions in the past two to three hours on a five-point scale ranging from 1 (not at all) to 5 (completely). The first measure is pain catastrophizing, an item selected from the Pain Catastrophizing Scale (Sullivan, Bishop, & Pivik, 1995): "You felt your pain was so bad you couldn't stand it anymore". The second item is pain irritation which was measured by asking participants "How much were you irritated by your pain?" The third item, pain uncontrollability, was measured by asking participants "You were able to control your pain" (adapted from Affleck, Tennen, & Apter, 2001) and it was reverse coded. Lastly, pain reactivity was measured by asking participants "How much were you able to feel your pain without having to react to it?". The pain reactivity

scale was also reverse coded. The within-person reliability for the four morning negative pain appraisal was .60.

Afternoon Pain's Activity Interference: Participants answered the following item that measures pain's activity interference: "During the past 2-3 hours, how much did your pain interfere with your ability to carry on with your activities?" The scale ranged from 1 (not at all) to 5 (completely).

Evening Depressive Symptoms: The level of daily depressive symptoms was measured in the evening using five items assessing common symptoms of depression drawn from the Patient Health Questionnaire (Kroenke, Spitzer, & Williams, 2002). Items were rated on a 3-point scale (1= no, 2 = yes, slightly, and 3 = yes, very much). Items included: "Did you feel... (1) a lack of interest in your activities; (2) down on yourself; (3) restless or slowed down; (4) an increase or decrease in appetite; and (5) difficulty concentrating or making decisions?" A mean of these items was used to create a composite of depressive symptoms score for each day and the within-person reliability was .64.

Between-Person (Individual Difference) Variables

Note that sources of between-person variables that are used in the present study are the various assessments that occurred during the pre-intervention phase, including responses to standardized self-report questionnaires, the average of 21-day diary assessments, and several physiological measures.

Respiratory Sinus Arrhythmia (RSA): From digitalized raw ECG recordings, inter-beat interval (IBI) series were extracted by using QRSTool Software (Allen et al., 2007). Each IBI series was hand-corrected for artifacts including missed, erroneous, or

ectopic beats. Heart rate variability in the high frequency (HF) band (.12–.4 Hz), which is suggested to represent vagal influences (see Berntson et al., 1997 for a review) was derived by CMetX Cardiac Metric Software (Allen et al., 2007). This was then used to estimate one's respiratory sinus arrhythmia. The CMetX program converts IBI series to a time-series that is sampled at 10 Hz with linear interpolation. A 241-point optimal finite impulse response digital filter designed using FWTGEN V3.8 (Cook & Miller, 1992) with half-amplitude frequencies of a .12–.40 Hz was applied to the 10 Hz time-series representation of the IBI series. The natural log of the variance of the filtered waveform was used as the estimate of RSA. By examining the dominant frequency in the power spectrum of the respiration waveform all participants were verified to be breathing within the respiratory frequency range (.12 – .40 Hz). This indicates that participants were neither breathing too slowly nor quickly and also ensures that the RSA capture participants' respiratory variations in heart rate more accurately.

Electromyography of Startle Reflex: Visual inspection of recorded EMG waveforms was first conducted to detect potential artifact due to participants' physical movement. Startle responses that depart more than three standard deviations from the mean response for each subject were deleted. The raw EMG data were band-pass filtered with the range of 90-1000 Hz, rectified and smoothed with a 200-ms moving window. Magnitude of eye blink responses was identified by determining the peak value between 20 and 200 ms following the startle probe. To calculate magnitude of startle reflex, the mean voltage of the orbicularis muscle during the 60-ms before the startle probe stimulus (i.e., baseline) was subtracted from the peak voltage that occurred between 20-200 ms after the onset of startle probe. In terms of determining the magnitude of startle in

response to each category of valence (i.e., positive, neutral, and negative), the average startle magnitude across all probed slides regardless of valence for each participant was subtracted from the average startle magnitude for each valence type. Then, the startle magnitudes of each category of valence were standardized using z-score for each participant. These z-scored average startle magnitudes for each valence type (positive, neutral, and negative) were used in the current analysis.

Behavior Inhibitory System and Behavior Activation System (BIS/BAS): The BIS/BAS Scale developed by Carver and White (1994), and consists of 20 items was used to measure individual differences in BIS and BAS levels. Previous studies demonstrated its good validity (e.g., Gomez & Gomez, 2005). Items are based on a 4-point Likert scale that ranges from 1 (Strongly Disagree) to 4 (Strongly Agree). The BIS (7 items) captures one's sensitivity to punishment and avoidant motivation. On the other hand, the BAS (13 items) assesses sensitivity to reward and appetitive motivation. The Cronbach's alphas of BIS and BAS were .83 and .84, respectively.

Sleep Quality (from daily diary): The measure of sleep quality is based on the average of 21-day daily diary data. Previous night sleep quality was measured by 3 items that were selected from the Pittsburgh Sleep Quality Index (Buysse et al., 1991), which has been demonstrated to have good validity and reliability. Each morning right after participants woke up, they were asked to report whether they had trouble staying asleep on a 4-point Likert scale (1 = "not at all" to 4 = "quite a bit"), the quality of their sleep on a 101-point scale (0 = "extremely poor sleep" to 100 = "extremely good sleep"), and how refreshed they felt upon awakening on a 101-point scale (0 = "not at all refreshed" to 100 = "extremely refreshed"). The last two items were rescaled (i.e., linear transformation)

from a 0 to 100 scale to a 0 to 5 scale by dividing each score by 20 to be comparable to the scaling of other variables in the model to ease interpretation of findings. This transformation does not affect correlations, the proportion of variance explained, or the significance of results (see Cohen, Cohen, West, & Aiken, 2003). The trouble staying asleep item was reverse coded. A composite of sleep quality was made by computing the mean of the three items and the Cronbach's alpha was .78.

Pain threshold: Participants' heat pain threshold was assessed using Medoc TSA II Neurosensory Analyzer (Medoc Ltd, Israel). The thermal stimuli were delivered via a thermode to participants above the inner right forearm. Before inducing the thermal pain, participants were informed that they could cease the laboratory procedure at any time by removing their arm from the thermode. First, to assess pain threshold, the thermode temperature was increased from 38 °C to a maximum of 50 °C. An instruction was given to participants to press a button on the response unit as soon as they sensed that the thermal stimuli was painful. A total of 5 trials were conducted with a 90 second inter trial interval. The average temperature of these 5 trials was used as the pain threshold measure. Although participants' pain tolerance and suprathreshold perceptions of pain unpleasantness were also assessed, the present study only focuses on utilizing the pain threshold measure. More detailed information regarding pain tolerance and pain perception are available in a previously published manuscript (see Yeung, Davis, & Ciaramitaro, 2016 for a review).

Continuum of Depression: The Hamilton Depression Inventory (Reynolds & Kobak, 1995) was used to evaluate individuals' depressive symptoms. It is a 23 item self-report version of the Hamilton Depression Rating Scale (Hamilton, 1960, 1967) that is

interview-based. The HDI has strong reliability and validity, and has been suggested to be highly correlated with clinical interview results (Kasch, Rottenberg, Arnow, & Gotlib, 2002; Kobak & Reynolds, 2000; Reynolds & Kobak, 1995). The Cronbach's alpha of HDI was .88.

Continuum of Anxiety: Individual differences in anxiety level were measured by the Mental Health Inventory (MHI) anxiety subscale. MHI is a 38 item self-reported measure of psychological distress and well-being which has good reliability and validity (Veit & Ware, 1983). The MHI has 5 subscales (anxiety, depression, loss of behavioral/emotional control, positive affect, and emotional ties) and the MHI anxiety subscale is based on 10 items such as "feeling rattled, upset, or flustered" or "difficulty trying to calm down". The Cronbach's alpha of MHI was .92

Pain Acceptance: The Chronic Pain Acceptance Questionnaire (CPAQ; McCracken, Vowles, & Eccleston, 2004) is a 20-item self-report of pain acceptance. CPAQ has a 7-point Likert rating scale that ranges from 0 (Never) to 6 (Always) and has two subscales that are activity engagement and pain willingness. The activity engagement subscale consists of 11 items that measure the extent to which one pursues life activities while experiencing pain (e.g., "I lead a full life even though I have chronic pain"). Pain willingness subscale has 9 items measure the extent to which one is willing to experience pain without trying to control it (e.g., "I need to concentrate on getting rid of my pain"). A higher total score represents higher pain acceptance. The Cronbach's alpha of CPAQ total score was .78

Neuroticism: Neuroticism was measured by 12 items that comprise the neuroticism subscale of the Big Five personality inventory (Costa & McCrae, 1987).

Ratings for each item ranges from 1 = disagree strongly to 5 = agree strongly. Examples of the items are "I can be moody," "I can be tense," and "I get nervous easily." Higher score indicates greater neuroticism and four items were reverse coded. A composite was made by taking mean of all 12 items. The Cronbach's alpha of neuroticism was .87

Socio Economic Status (SES): Both education level and income were assessed as measures of SES. Seven ordinal categories were employed to represent the level of education attained (1 = 8th grade or less, 2 = some high school, 3 = completed high school, 4 = vocational or trade school, 5 = completed some college, 6 = college graduate, and 7 = completed some graduate school). In terms of income, participants were asked to indicate their annual family income (i.e., income from work, interest, and social security) by choosing 1 of 19 categories representing incremental income ranges. Income categories ranged from under \$3,000 to \$150,000 and over. Each category represented an approximate \$2,000 increment from under \$3,000 to \$150,000 and over. For example, the second category ranged from \$3,000 to \$4,999 and the third category was the next \$2,000 increment, \$5,000 to \$6,999.

Financial Worry (from daily diary): To assess overall perceived stress due to finances, participants were asked to rate how much they worried about finances every day using 21-day daily diary on a 4-point scale (1 = "Not at all" to 4 = "Extremely"). Daily financial worry was averaged across 21-days.

Interpersonal Stress (from daily diary): Interpersonal stress was measured in regard to family members and friends. Two questions were asked: (1) "Overall, how stressful were your relations with your family members today?", (3) "Overall, how stressful were your relations with friends today?". The responses were scored on a 5-

point scale ranging from 1 (not stressful at all) to 5 (extremely stressful). The total interpersonal stress score was computed by taking the mean score of these two items and averaged across 21-days.

Satisfaction with Social Support in Coping Pain (from daily diary): Participants were asked to rate their satisfaction with how their (1) spouses or partner and (2) people other than spouse or partner (i.e., family members, friends, and co-workers) responded to their pain coping on a 5-point Likert scale ranging from 1 (not at all satisfied) to 5 (completely satisfied) every day for 21-days. This measure was modified from Holtzman & DeLongis' (2007) diary item that assessed satisfaction with spouse responses among chronic pain patients. A mean of these two items were averaged across 21-days.

Data Analysis Plan

As a preliminary analysis, descriptive statistics including mean, standard deviation, skewness, kurtosis, observed range, and intraclass correlation (ICC; only for within-person variables) were computed for the study variables. ICC provides useful information on how the variation in a daily diary variable is partitioned into within- and between-person variability. For individual difference variables, multivariate outlier analyses were conducted by using Cook's distance as criteria (cutoff value = 1; Cook, 1977), as clustering is sensitive to outliers. Intercorrelations for within- and between-person variables were also computed.

A series of statistical analyses were conducted to test the study hypotheses. First, because the data of the present study has a two-level hierarchy [days (level-1) are nested within persons (level-2)], multilevel structural equation modeling (MSEM) was used to account for the nestedness and to correctly estimate regression coefficients and standard

errors. TYPE = TWOLEVEL command in Mplus software version 7 (Muthén & Muthén, 2012) was used to run MSEM. MSEM has some advantages over using traditional multilevel models. First, MSEM makes it possible to fit more complex multilevel models (Preacher, Zyphur, & Zhang, 2010). Second, MSEM provides model fit indices. Third, MSEM allows for construction of latent variables and can account for measurement error (Preacher, Zhang, & Zyphur, 2011). Fourth, MSEM automatically partitions within- and between-person level variances by estimating both within- and between-person models simultaneously, and thus centering each study variable is unnecessary. In other words, the regression coefficients at each level can be directly interpreted at the corresponding levels of analysis (Preacher et al., 2010). Note that the between-person model within MSEM is fundamentally cross-sectional as variables are the means of repeated measures (e.g., 21-days). In addition, as the main study hypotheses are based on within-person level, only the within-person MSEM model are examined and reported here.

Once the MSEM model demonstrated adequate fit [CFI greater than .90 (Kline, 1998), SRMR less than .10 (Kline, 1998), and RMSEA less than .08 (Byrne, 2001)], the exploratory hypothesis of the present study was tested by conducting latent profile analysis (LPA). LPA is a special case of finite mixture modeling that is used to identify unobserved subgroups within a population (Nylund, Asparouhov, & Muthén, 2007). The indicators that were included in the LPA were all individual difference variables that are described above (total 17 indicators; see Table 1). However, as there was a large number of indicators with a relatively small sample size for running LPA, it increased the likelihood of encountering some model convergence problems. When this occurred repeatedly due to having a large number of LPA indicators, then the number of indicators

was reduced by conducting exploratory factor analyses. Once reasonable factors that represent the large number of variables were identified, then these factors were used as indicators of LPA.

In terms of determining the optimal number of classes for conducting LPA, several model fit criteria were used: (1) the Bayesian information criteria (BIC; Schwarz, 1978) and a sample-size adjusted BIC (Adj BIC; Sclove, 1987), with smaller values indicating a better-fitting model; (2) likelihood ratio tests including the Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (VLMR; Lo, Mendell, & Rubin, 2001) and the Bootstrap Likelihood Ratio Test (BLRT; McLachlan & Peel, 2000) that compares whether k number of class is significantly better than that of k-1 class. A p-value less than 0.05 represents that the model fit of k class is significantly better than a model of one fewer class; (3) entropy (Ramaswamy, Desarbo, Reibstein, & Robinson, 1993), a measure of classification certainty with a value that is close to 1.0, indicating less uncertain classification of individuals; and (4) theoretical justification and interpretability of the latent classes (e.g., Grimm & Ram, 2009; Jung & Wickrama, 2008; Muthén & Muthén, 2000; Muthén, 2004). In conducting mixture models, it is quite common to encounter a local maximum, not the global maximum, that has the largest log likelihood among all possible parameter values. Thus, to prevent the model from converging into a local maximum solution, different sets of starting values were used and the model was run multiple times to ensure the best fitting model solution (Muthén, 2004).

Once the best fitting model was identified, the classification information was used to test the exploratory hypothesis (see Figure 1). When entropy was high enough (i.e., close to 0.8), the most likely class membership was exported from LPA analyses.

Previous studies suggest that when the entropy is high (i.e., around 0.8), exporting the most likely classification membership is less likely to introduce significant bias (Asparouhov & Muthén, 2013; Clark & Muthén, 2009; Muthén & Muthén, 2012).

Using the exported grouping variable from LPA, a series of one-way ANOVAs were first conducted to compare the differences between means of all within-person study variables (i.e., morning pain, affect, negative pain appraisal, afternoon pain's activity interference, and evening depressive symptoms) among different subgroups. Post-hoc analyses were conducted if significant omnibus *F*-test results emerged from the ANOVAs. Specifically, if the homogeneity of variance assumption was met, the Tukey HSD post-hoc test was used. However, if the assumption is not met, the Games-Howell post-hoc test was used.

After testing mean differences of within-person study variables, multiple group analysis (Jöerskog & Sörbom, 1979) was conducted to examine whether regression paths in the within-person model differ by subgroups of individuals with fibromyalgia who were identified through LPA. First, two models were compared using a chi-square difference test: (1) a configurable model that allows all the within-person level paths to be freely estimated across groups, and (2) a constrained model that restricts all paths at the within-person level to be equal across groups. Fundamentally, this analytic approach is similar to the omnibus *F*-test in ANOVA. Second, if there was a significant chi-square difference between the configurable vs. constrained model, then each regression path was examined to see if there are any significant differences across groups.

The joint significance test of three path mediation was used to test the mediated effect. According to Taylor, MacKinnon, and Tein's (2008) simulation study, the joint

significant test of three-path mediation is the most convenient method to test a three-path mediated effect with excellent control of Type I error rates and good statistical power. Use of this test for examining the three-path mediated effect requires three paths to be statistically significant at an alpha level of 0.05. These paths are: (1) the effect of the independent variable on the first mediator, (2) the effect of the first mediator on the second mediator, and (3) the effect of the second mediator on the dependent variable. If all three paths are significant at a *p*-value less than 0.05, then a significant indirect (mediated) effect can be inferred.

Results

Preliminary Findings

Tables 2, 3, and 4 summarize the descriptive statistics (including bi-variate correlations) of within- and between-person study variables. Skewness and kurtosis of all study variables were within the acceptable range (Skewness cutoff = 2; Kurtosis cutoff = 7; West, Finch, & Curran, 1995). Through multivariate outlier analyses, using Cook's distance of 1 as a criterion, no influential cases were identified. ICCs of within-person variables ranged from 0.41 to 0.59. For instance, 59% of variance in morning negative affect was explained by between-person differences. Results of ICCs indicate that there is a sufficient amount of within- and between-person variability within the data to estimate multi-level models.

The decision was made to remove all startle reflex variables from subsequent analyses for two main reasons: (1) although startle reflex results may somewhat complement BIS/BAS measures, including three extra startle reflex variables in addition to two BIS/BAS variables may significantly burden LPA model convergence; and (2) as

shown in Table 4, there were strong negative correlations among all three EMG variables. This is contrary to what was assumed and it is difficult to explain how this result emerged.

Findings of Multilevel Structural Equation Modeling

Overall, the model fit the data well, χ^2 (df = 2) = 9.335, p < .01, CFI = .999, SRMR-within = .007, SRMR-between = .002 and RMSEA = 0.029. Figure 2 presents the standardized path estimates of the within-person model. On mornings when pain (B =.42, SE = .02, p < .001) and both positive affect (B = -.30, SE = .02, p < .001) and negative affect (B = .13, SE = .02, p < .001) were higher than a person's usual level, ratings of morning negative pain appraisal were higher. When a participant reported higher morning negative pain appraisal than his or her usual level, he or she also reported higher than usual afternoon activity interference due to pain (B = .15, SE = .02, p < .001), while controlling for morning pain, positive and negative affect, and morning pain's activity interference. Higher pain's activity interference in the afternoon, in turn, was associated with higher depressive symptoms in the evening (B = .22, SE = .02, p < .001), over and above morning pain, affect, and negative pain appraisal. Based upon the test of joint significance, the following significant three-path mediated effects from morning pain, negative and positive affect, and evening depressive symptoms were found: (1) morning pain \rightarrow morning negative pain appraisal \rightarrow afternoon pain's activity interference \rightarrow evening depressive symptoms; (2) morning positive affect \rightarrow morning negative pain appraisal \rightarrow afternoon pain's activity interference \rightarrow evening depressive symptoms; and (3) morning negative affect \rightarrow morning negative pain appraisal \rightarrow afternoon pain's activity interference \rightarrow evening depressive symptoms. Some significant direct effects

were also revealed. Morning pain (B = .07, SE = .02, p < .01) and morning positive affect (B = -.07, SE = .02, p < .01) significantly predicted afternoon pain's activity interference. Evening depressive symptoms were also significantly predicted by both morning positive affect (B = -.16, SE = .02, p < .001) and negative affect (B = .14, SE = .02, p < .001).

Findings of Exploratory Factor Analyses

When LPA was run with all level-2 indicators, the model failed to converge starting from a 2-class model. Hence, as discussed in the analytic plan, exploratory factor analyses (EFA) with oblimin rotation were used to reduce the number of LPA indicators. Results of initial EFA suggested a 4-factor model to be the best fitting model. The model fit was good, χ^2 (df = 41) = 57.721, p = .04, RMSEA = 0.04, CFI = .98, and SRMR = .04. However, five variables (i.e., scores of RSA, BAS, pain threshold, sleep quality, and education) did not belong to any of four factors that were identified. Hence, the decision was made to include these five variables separately as indicators of the LPA model. EFA was rerun excluding these five variables and a 3-factor model was found to be the best fitting model, which showed adequate model fit, χ^2 (df = 12) = 34.670, p < .001, RMSEA = 0.09, CFI = .97, and SRMR = .04. Table 5 presents rotated factor loadings for each factor. The first factor is called 'High BIS and Neuroticism', the second factor is called 'High Depression/Anxiety and Low Pain Acceptance', and the third factor is called 'Low Income and Social Support with High Financial and Interpersonal Stress'. Factor scores were exported from Mplus and included as indicators of LPA in addition to five variables (i.e., scores of RSA, BAS, pain threshold, sleep quality, and education) that did not belong to any of these factors. Note that in order to ease the interpretation of LPA findings, all of the LPA indicators were standardized to z-scores.

LPA Classification Findings

The results of the systematic LPA model fitting process are presented in Table 6. Based on various fit indices and theoretical justification, the 3-class model was chosen as the best fitting model. Neither the 4-class or 5-class model was chosen because they showed a greater BIC and entropy value compared to the 3-class model, as well as non-significant VLMR and BLRT results.

Figure 3 shows the estimated pattern of these three classes. The first class (n = 42; 19.1%), labeled as 'Low Functioning Group', was characterized by high level of biopsychosocial risk factors such as BIS, neuroticisms, anxiety, depression, stress, and relatively low level of protective factors including pain threshold, pain acceptance, and sleep quality. The second class, labeled as 'Normative Group', was by far the largest (n = 118; 53.6%), with average levels on all biopsychosocial risk and protective factors. The third class, labeled as 'High Functioning Group', included 60 (27.3%) individuals. Those in this group displayed low levels of biopsychosocial risk factors and relatively high levels of protective factors.

Group Mean Differences in Within-Person Study Variables Across 21-days

A series of one-way ANOVAs were conducted to examine the effect of different subgroups (which were identified by LPA) on the means of all within-person study variables (i.e., mean of morning pain, positive affect, negative affect, negative pain appraisal, afternoon pain's activity interference, and evening depressive symptoms). Table 7 provides a summary of findings of the one-way ANOVAs in regard to each variable.

As the omnibus *F*-test results were all statistically significant, post-hoc analyses were conducted. The Tukey HSD was used for dependent variables that met the homogeneity of variance assumption (i.e., mean of morning pain, negative pain appraisal, afternoon pain's activity interference, evening depressive symptoms) and the Games-Howell test was used for those that did not (i.e., mean of morning positive and negative affect). As shown in Figures 4 to 9, findings of post-hoc analyses revealed significant group differences (i.e., Low Functioning vs. Normative; Normative vs. High Functioning; and Low Functioning vs. High Functioning) on all outcome variables. To be specific, the Low Functioning group showed highest mean scores of morning pain, negative affect, negative pain appraisal, afternoon pain's activity interference, and evening depressive symptoms and the lowest mean score of morning positive affect. On the other hand, the High Functioning group showed the lowest mean scores of pain, negative affect, negative pain appraisal, activity interference, and depressive symptoms and the highest mean score of positive affect.

Results of Multiple Group Analysis

Multiple group analysis was conducted to test potential moderation effects of different biopsychosocial profiles on structural paths in MSEM. However, the result of the chi-square difference test between two models (i.e., configurable model vs. constrained model) showed that the difference of model fit between the freely estimated and the constrained model was not statistically significant, χ^2 (df = 40) = 53.47, p = .08. Thus, exploring differences in each regression path across different groups was not done as it was thought to be too exploratory.

Effect size

Thus far there has been no study that suggests which effect size estimate is the most accurate to use in a multilevel framework (Peugh, 2010). However, generally, calculating the variance explained (i.e., R-squared) by predictors in a model is regarded as a useful effect size index in MLM (Singer & Willett, 2003). Using this method, it was found that 42.5% of morning negative pain appraisal variance at the within-person level was explained by morning pain, positive affect and negative affect. In the case of afternoon pain's activity interference, 13.2% of variance was explained by morning pain, positive and negative affect, and an additional 3.4% of unique variance was explained by morning negative pain appraisal. Lastly, for evening depressive symptoms, 11.9% of variance was explained by morning pain, positive and negative affect, and negative pain appraisal, and an additional 3.7% of unique variance was explained by afternoon pain's activity interference.

Discussion

Numerous studies report the robust link between pain and depressive symptoms (Demyttenaere et al., 2007; Rush, Polatin, & Gatchel, 2000; Weir et al., 2006). However, the majority of studies that have examined the underlying mechanisms between the two have been cross-sectional (e.g., neuroimaging studies) and/or predominantly focused on investigating nomothetic (i.e., between-person) mechanisms. To date, no previous studies have investigated within-person mechanisms *through which* pain experience is associated with depressive symptoms among individuals with chronic pain, nor how various individual differences play a role in such processes. The present study sought to address this gap in our knowledge by proposing a within-person model of the pain-depressive

symptoms link while taking the influence of numerous biopsychosocial individual difference factors into consideration.

In the present study, both morning negative pain appraisal (a composite of momentary pain catastrophizing, pain irritability, pain intolerance, and pain reactivity) and afternoon pain's activity interference were proposed as sequential mediators in the association between morning pain and evening depressive symptoms. It was also expected that both positive and negative affect would serve a unique role in predicting negative pain appraisal over and above pain experience, because affect has been shown to exert a pervasive influence on individuals' overall cognition (Adolphs, & Damasio, 2001; Forgas, 2008; Hoffman, 1986). Finally, the present study tested the exploratory hypothesis that subgroups of individuals in the sample who share a homogenous level of biopsychosocial risk and protective factors could be identified empirically through use of latent profile analysis (LPA). As LPA is fundamentally a data-driven and exploratory analysis, no specific hypotheses were made about how many and what kinds of subgroups would be identified from the analysis. However, it was expected that if distinct subgroups were identified from LPA, there would be significant group differences in individuals' reports of pain, affect, pain cognition, activity interference, and depressive symptoms across 21 days, as well as moderation effects by group regarding the paindepressive symptoms link.

The results of the study were largely consistent with the main hypotheses, and further revealed three empirically-derived subgroups of individuals within the sample in the exploratory analyses. Potential explanations and clinical implications of the present

findings, theoretical and methodological speculations about the unexpected findings, and future research direction are discussed below.

Morning Pain to Evening Depressive Symptoms through Negative Pain Appraisal and Pain's Activity Interference

Consistent with expectations, on days when an individual experienced more than the usual level of morning pain, he or she was more likely to report higher negative pain appraisal in the morning. Prior studies have found that pain is a salient internal threat signal that captures individuals' attention (Crombez, Van Damme, & Eccleston, 2005; Van Damme, Legrain, Vogt, & Crombez, 2010). This attention capture can set the motivational stage for individuals to engage in certain coping behaviors (e.g., efforts to escape from pain or diminish pain). From an evolutionary perspective, the positive relationship between pain and negative pain appraisal can be viewed as functional because *false-positive behavior* (i.e., trying to escape from pain or control pain when there is no actual threat of pain) is better than *false-negative behavior* (i.e., trying not to escape from pain nor control pain when there is actual threat of pain) for an individual's survival.

Elevation of negative pain appraisal, however, comes with costs. In the present study, higher negative pain appraisal in the morning was associated with higher pain activity interference in the afternoon, even after controlling for the effect of morning pain, affect, and morning pain's activity interference. When the sensation of pain is negatively interpreted, individuals are more likely to try to control or escape from the aversive feeling. Doing so can significantly interfere with their on-going goal pursuit. To provide a more illustrative example, let us say that an individual with chronic pain was

planning to engage in a rewarding social activity (e.g., going to a weekly language exchange meeting), but noticed that his or her level pain intensity that day was higher than is typical. This recognition may activate the negative pain appraisal process, resulting in a shift of their attention and motivation to either eliminating the pain or reducing it. As a result of this attentional and motivational change, the individual may persist in attempting to control pain while disengaging from enjoyable social activities. Findings from recent studies that have used daily diary methods indirectly support the notion: morning pain has been associated with weaker activation of goal schemas (i.e., anticipatory goal-related mindset that is measured by goal planning, goal attainability, and perceived goal importance), which in turn, predicts lower levels of goal pursuit and striving later in the day (Karoly, Okun, Enders, & Tennen, 2014; Mun, Karoly, Okun, Kim, & Tennen, 2015).

In line with a previous study (Börsbo, Peolsson, & Gerdle, 2009), pain's activity interference was found to be the strongest within-day predictor of depressive symptoms. Several theoretical explanations as to how repeated experience of activity and goal interference can lead to development of clinical depression can be found in the extant literature. For instance, the cognitive-motivational framework suggests that repeated interruption of important personal goals due to pain can induce individuals to develop self-defeating negative schemas (Karoly & Jensen, 1987; Jensen, Turner, & Romano, 1991; Jensen & Karoly, 1991), which in turn can contribute to the elevation of depressive mood and symptoms. In contrast, a behavioral framework (Fordyce, 1976) posits that the loss of reward as a consequence of pain's interference with individuals' meaningful activity engagement can lead to development of depression.

Nonetheless, these explanations do not directly apply to the current finding with regard to the within-day relationship between pain's activity interference and non-clinical depressive symptoms. A useful model that may help us understand this within-day association between activity interference and depressive affect is the *control systems* framework (Carver, 2015; Carver & Scheier, 1990, 1998, 2013; Powers, 1973).

According to this view, individuals' experience of sadness, depression, or grief fundamentally comes from apparent failure to make progress toward a desired end-state (i.e., goal). However, a depressive state does not necessarily cause individuals to develop a clinical level of depression. In fact, it is argued that aversive emotional experiences can facilitate goal directed behaviors (Carver, 2015). For instance, a recent daily diary study of individuals with chronic pain found that on days when individuals reported non-pursuit of work goals in the afternoon, they experienced higher negative affective reactions which, in turn, facilitated same-day work goal resumption (Okun, Karoly, Mun, & Kim, 2016).

The question then arises, how do individuals become clinically depressed through repeated experience of pain? Unfortunately, the current study cannot unequivocally address this question. However, several factors are plausible contributors to the development of clinical depression among individuals with chronic pain. First, the development of clinical depression may be associated with *chronicity* of goal failures. In the short-term, negative emotions arising from goal failure may facilitate resumption of goal pursuit (e.g., Klinger, 1975; Okun, Karoly, Mun, & Kim 2016; Schrooten, Karsdorp, & Vlaeyen, 2013). However, if this pattern continues frequently over time, individuals may become hopeless and helpless in pursuing their goals and develop a self-defeating

schema that can induce clinical depression (Karoly & Jensen, 1987). Second, in addition to chronicity of goal failure, development of clinical depression may be related to the *types of goals* (or activities) that are being interfered with. Interruption of goals that have higher personal value can lead to higher levels of a depressive state. Therefore, individuals whose important personal goals are repeatedly interrupted by pain may be more likely to develop clinical depression. Third, individuals with *higher emotional inertia* (i.e., the tendency for emotional states to be resistant to change) might be more prone to developing clinical depression. If individuals have difficulty in flexibly moving out from a highly depressive state, then it becomes a challenge for them to re-initiate important personal goals. In fact, previous studies indicate a robust positive association between emotional inertia and psychological maladjustment in general and depression severity in particular (Koval, Kuppens, Allen, & Sheeber, 2012; Kuppens, Allen, & Sheeber, 2010).

The Role of Negative and Positive Affect

The current findings also demonstrated that on days when an individual experienced more than the usual level of negative affect, he or she was more likely to report higher negative pain appraisal over and above the effect of morning pain and positive affect. This finding is consistent with the argument that negative affect—a component of the harm-avoidance motivational system (Gray, 1994; Lang, Bradley, & Cuthbert, 1998)— can narrow the scope of individuals' attention to potential threat, such as pain, and can induce bias in information processing (Geisser, Roth, Theisen, Robinson, & Riley, 2000; Fredrickson, 1998, 2013; Watson & Pennebaker, 1989).

It is also noteworthy that while controlling for all other morning and afternoon predictors, morning negative affect was a significant predictor of evening depressive symptoms. Although this association was not previously tested at the within-person level, one longitudinal study found that negative affect reactivity to daily interpersonal and non-interpersonal stress predicted changes in depressive symptoms two months later, controlling for baseline depressive symptoms (Parrish, Cohen, & Laurenceau, 2011). Perhaps, starting one's day with elevated negative affect makes individuals become more sensitive to internal and external stressors as a result of their narrowed attention, a process that may increase their chances of being in a depressive state later in the day. This possibility remains speculative, however. Additional research testing this possibility needs to be conducted before firm conclusions can be drawn.

One of the most intriguing variables in the pain-depressive symptoms link was morning positive affect, which was not only a significant predictor of morning negative pain appraisal but also a significant predictor of afternoon pain's activity interference and evening depressive symptoms. In regard to the negative association between positive affect and negative pain appraisal, this finding is in line with several previous studies that suggest that positive affect can expand one's overall attention and mental flexibility (Cohn, Fredrickson, Brown, Mikels, & Conway, 2009; Fredrickson, 2013; Fredrickson, Cohn, Coffey, Pek, & Finkel, 2008; Garland et al., 2010), both of which can potentially lessen the negative evaluation/interpretation of pain sensation (e.g., Geschwind et al., 2015). For example, a recent daily diary study of individuals with fibromyalgia revealed that more than the typical experience of positive affect in the afternoon was associated

with less pain expectancy in the evening (Mun, Thummala, Davis, Karoly, & Tennen, 2017).

The finding that higher morning positive affect is related to a lower level of pain's activity interference in the afternoon is consistent with recent empirical findings as well.

Using a daily diary of 123 individuals with chronic pain, Mun, Karoly, and Okun (2015) found that those with higher than usual morning positive affect reported less interference from pain in the pursuit of work goals in the afternoon, while controlling for morning pain and negative affect. Although based upon a non-chronic pain sample, relatedly, Schöndube, Kanning, and Fuchs' (2016) study using daily diary data also indicated that when individuals experience higher than usual levels of positive affect in the morning, they were likely to engage in longer duration exercise during that day. Positive affect seems to serve an important role in providing enhanced control over individuals' engagement in important life activities and goals even in the face of everyday challenges, such as experience of pain (e.g., Haase, Poulin, & Heckhausen, 2012).

The significant association between morning positive affect and evening depressive symptoms was also an interesting finding of the present study. Contrary to the obtained pattern with negative affect, starting one's day with a more than usual level of positive affect may lessen sensitivity to both interpersonal and non-interpersonal stressors through increased psychological flexibility, a process that can prevent individuals from experiencing depressive symptoms later in the day.

Implications from Three-Path Mediated Effects

Findings of the three-path mediations suggest that the relationships between morning pain, positive, and negative affect, and evening depressive symptoms are

sequentially mediated through morning negative pain appraisal and afternoon pain's interference. Although the ideal way to short-circuit the pain-depressive symptoms link is to substantially decrease pain, numerous meta-analyses and systematic reviews suggest that psychosocial interventions for chronic pain, such as cognitive-behavioral therapy (CBT), mindfulness, and acceptance commitment therapy (ACT), do not dramatically reduce the level of pain intensity (Astin, Beckner, Soeken, Hochberg, & Berman, 2002; Dixon, Keefe, Scipio, Perri, & Abernethy, 2007; Glombiewski, Sawyer, Gutermann, Koenig, Rief, & Hofmann, 2010; Hoffman, Papas, Chatkoff, & Kerns, 2007; Morley, Eccleston, & Williams, 1999; Reiner, Tibi, & Lipsitz, 2013; Veehof, Oskam, Schreurs, & Bohlmeijer, 2011).

Perhaps, a more realistic psychological intervention that can sever the day-to-day pain-depressive symptoms link is to help individuals decrease negative affect by boosting positive affect. In fact, the present study shows that both morning positive and negative affect are significant predictors of morning negative pain appraisal while controlling for the effect of morning pain. Elevation of positive affect and decrease of negative affect may likely reduce negative pain appraisal when individuals experience more than the usual level of pain. The good news is that numerous empirical studies have garnered robust evidence that positive emotion can be increased to a certain level by engaging in simple, brief (as short as 8 minutes), and regular positive activities (see Lyubomirsky & Layous, 2013 for a review) such as writing letters to express gratitude (Lyubomirsky, Dickerhoof, Boehm, & Sheldon, 2011; Seligman, Steen, Park, & Peterson, 2005), counting one's blessings (Emmons & McCullough, 2003; Lyubomirsky, Sheldon, & Schkade, 2005), performing kind acts toward others (Lyubomirsky, Sheldon, & Schkade,

2005), visualizing optimistic future selves (King, 2001; Layous, Nelson, & Lyubomirsky, 2012), and practicing a loving-kindness meditation (Fredrickson, Cohn, Coffey, Pek, & Finkel, 2008; Zeng, Chiu, Wang, Oei, & Leung, 2015). Encouraging individuals to engage in these simple, brief, and flexible positive affect enhancing activities would be a realistic intervention target for individuals with chronic pain in addition to traditional chronic pain treatments (e.g., CBT, ACT, and mindfulness).

The current findings of mediated effects also imply the importance of considering the *timing* of intervention delivery, which has not received much attention from researchers or clinicians so far. Understanding *when* would be the best time to maximize an intervention's benefit is a critical research question that has direct clinical utility. For instance, according to findings of the present study, as well as previous findings reporting the unique effect of *morning* positive affect on cognition and behavior (e.g., Kothari, Davis, Yeung, & Tennen, 2015; Mun, Karoly, & Okun, 2015; Mun, Karoly, Okun, Kim, & Tennen, 2015; Mun, Thummala, Davis, Karoly, Tennen, & Zautra, in press; Schöndube, Kanning, & Fuchs, 2016), boosting positive affect *early in the day* might be more effective in disconnecting the within-person pain-depressive symptoms link than doing so in the afternoon or at night. This is, however, a preliminary argument. An important future research avenue would be testing whether there is a significant difference in individuals' reports of daily depressive symptoms depending on when the participants engaged in positive activities.

Biopsychosocial Profiling

The study also explored the possibility that biopsychosocial variables might be used to identify subgroups of individuals, and that those subgroups might distinguish

more adaptive copers from more vulnerable individuals. Prior to conducting the LPA analysis, a no specific hypothesis was put forward regarding how many and what kinds of subgroups would be identified from LPA. However, three subgroups that are both theoretically and clinically interesting were identified from 220 individuals with fibromyalgia. The first group, which was labeled as a "low functioning group", consisted of about 20% of the sample and was characterized with high levels of biopsychosocial risk factors and low levels of protective factors. Specifically, individuals in this group reported having high emotional distress (i.e., anxiety, depression), high neuroticism, low pain tolerance capacity (i.e., pain acceptance, pain threshold), an avoidant motivational system, low levels of social resources, and a relatively low level of sleep quality compared to other groups. The second group, labeled the "normative group" consisted of about half of the sample, and showed an overall average level of all biopsychosocial protective and risk factors. Lastly, the third group, labeled the "high functioning group," consisted of about one third of the sample and displayed almost the opposite patterns of biopsychosocial profiles compared to the "low functioning" group. Some intriguing findings and issues were raised from the biopsychosocial profiling analyses, which are discussed below.

A sizeable number of participants (about 30%) in the sample presented with good biopsychosocial resources and characteristics that have been known to play an important role in coping with and adjustment to pain-related issues. Averaging the diary reports regarding daily experiences to derive between-person values provides the opportunity to discuss how these subgroups differ on more stable aspects of their daily lives, thereby contributing to our understanding of the implications of subgroup membership. ANOVAs

and post-hoc tests showed that there are clear group differences in the level of individuals' reports of morning pain, positive and negative affect, negative pain appraisal, afternoon activity interference, and depressive symptoms across 21-days. The findings generally aligned as one would expect. Specifically, individuals in the High Functioning group reported the lowest level of average morning pain, negative affect, negative pain appraisal, afternoon pain's activity interference, and evening depressive symptoms.

Moreover, they displayed the highest level of average morning positive affect. The Normative group fared better on all measures than did the Low Functioning group.

These findings are consistent with previous arguments that there can be subgroups of chronic pain patients and that providing a uniform intervention (either medical or psychosocial) for them would result in less than ideal outcomes because each group's characteristics and specific needs are different (Turk & Flor, 1989; Turk, Okifuji, Sinclair, & Starz, 1996). For instance, in the present study, perhaps individuals in the High Functioning group already possesses enough biopsychosocial resources to adaptively cope with or adjust to pain-related problems. By contrast, individuals in the Low Functioning and Normative groups may need some tailored psychosocial interventions to effectively cope with pain and prevent depressive symptoms. Based upon the biopsychosocial profile difference between the Low Functioning group and Normative group, it appears that individuals in the Normative group may need a holistic approach to increase biopsychosocial protective factors and decrease risk factors. On the other hand, individuals in the Low Functioning group might benefit more from interventions that are tailored to focus on mitigating avoidant behavior, emotional

distress, interpersonal stress, as well as increasing pain acceptance and social support for pain coping.

Most psychological interventions of chronic pain, in fact, have only shown smallto-moderate effect sizes in decreasing pain and improving physical and emotional functions (Astin, Beckner, Soeken, Hochberg, & Berman, 2002; Dixon, Keefe, Scipio, Perri, & Abernethy, 2007; Glombiewski, Sawyer, Gutermann, Koenig, Rief, & Hofmann, 2010; Hoffman, Papas, Chatkoff, & Kerns, 2007; Morley, Eccleston, & Williams, 1999; Veehof, Oskam, Schreurs, & Bohlmeijer, 2011). This may be the case because (1) participants who do not need any additional resources to assist them with managing their pain contribute to the low effect sizes in many intervention studies, and (2) the one-sizefit-all interventive approach may not adequately benefit the different subgroups of individuals with chronic pain. Note that effect size is usually calculated by taking the mean outcome difference between two groups (control vs. intervention group). Thus, we should not only interpret the results of chronic pain intervention studies more *cautiously*, but also implement psychological interventions for chronic pain more efficiently. To provide more cost-effective psychosocial interventions for those individuals who suffer from chronic pain, attention should be focused on tailoring existing psychosocial interventions to those who are in need and can benefit from them. Delivering tailored interventions based on patients' biopsychosocial characteristics would be more costeffective than prescribing uniform interventions to all patients (Turk, Okifuji, Sinclair, & Starz, 1996). Hence, as a preliminary step, testing the utility of a pre-intervention screening process based upon individuals' biopsychosocial profiles might offer an important direction for research.

The present study is one of few to test the utility of comprehensive biopsychosocial profiling using advanced statistical techniques. Somewhat surprisingly, the majority of biological variables were not decisive factors for sorting individuals into different subgroups. For instance, levels of RSA, sleep quality, pain threshold, and BAS were not dramatically different across subgroups. One possible explanation for this finding involves issues with measurement of biological data. Acquisition of reliable and valid biophysiological data is challenging. For instance, a recent review on the utilization of heart rate variability (HRV) in research argued that there are several methodological issues with measuring and interpreting HRV data that have not been well-recognized in the field (Laborde, Mosley, & Thayer, 2017). It is also well-known that physiological data, such as EMG and EEG, require very careful data acquisition and involve a complex and time consuming data cleaning process (e.g., Luck, 2014; Türker, 2007). Moreover, many individuals with chronic pain regularly consume prescribed psychotropic medications (e.g., anti-depressant, anxiolytics, opioids, medical marijuana, etc.), which makes it difficult to control their use prior to acquiring their biological data. Overall, there are numerous factors that can contribute to less precise measurement of biological data in individuals with chronic health problems, which, in turn, can also reduce statistical power. More effort is needed in the future to develop more reliable and precise measures of physiological processes. Such efforts could be enhanced through fundamental discussions about the current biopsychosocial framework.

Biopsychosical profiles as a moderator

Contrary to expectation, the within-person model of pain-depressive symptoms was not significantly moderated by subgroup group profiles. For instance, there was no

significant difference across subgroups in the association between morning pain and morning negative pain appraisal. A number of factors may have contributed for this null finding. First, given that the sample size was not very large and sample sizes were unequal across groups, there may have been low power to detect cross-level interactions. Second, we cannot discount the possibility that the present study may have failed to include some important biopsychosocial risk or protective factors as indicators in the biopsychosocial profile analysis. Third, perhaps this null finding might represent how the real world functions. As experiences of pain, negative and positive affect, activity interference, or pain appraisal are all salient and our cognitive and behavioral reactions to these experiences are often automatic, there may be very limited space for individual differences to exert significant influence on modulating momentary experiences.

Future Directions

The findings of the current study prompt several interesting and important potential directions for future research. First, an immediate avenue for using biopsychosocial profiles (i.e., latent profiles) that was identified in the current study is to test moderation effects on the outcomes of psychosocial interventions (i.e., intervention groups status x biopsychosocial profile subgroups). The present study is based on secondary data analysis of a larger study that tries to evaluate the efficacy of three different chronic pain interventions (i.e., cognitive-behavioral therapy vs. mindfulness-based intervention vs. psychoeducation group). Hence, subgroups that were identified in the pre-intervention period can be easily applied to these intervention data. Testing the latent class (profile) moderation of intervention effects (cf. Cooper & Lanza, 2014) can foster the examination of two important research questions: (1) who benefits most from

evidence-based psychosocial interventions of chronic pain?; (2) do individuals respond differently across different interventions based upon their biopsychosocial profiles? Addressing these questions will be important to tailoring chronic pain interventions and to maximize the benefits of implementing psychological pain interventions especially tailored to individuals who need them.

Second, although biopsychosocial profiles did not significantly moderate the pain-depressive symptoms link, individuals in the High Functioning group consistently showed significantly lower levels of pain, negative pain appraisal, negative affect, pain's activity interference, and depressive symptoms, and higher level of positive affect across 21-days. However, these group differences are based on a relatively short period time. Perhaps, the group differences would have become more pronounced with the passage of time (e.g., several months or a few years later). Longitudinally observing how different groups of individuals with distinct biopsychosocial profiles differentially adjust to pain and pain-related issues could be another possible future research avenue.

Third, previous literature suggests that one of the best ways to understand the impact of pain sensation on pain cognition, affect, task interruption, and psychological adjustment is examining how these connections are modulated by self-regulatory processes (e.g., Karoly, 1985, 2010; Karoly & Jensen, 1987). Self-regulation is a complex process that guides individuals' goal-directed activities over time and across various challenges (Karoly, 1993) and thus, the core of self-regulation pivots on individuals' goals. Examining goal-related measures such as goal cognition, goal hierarchy, goal progress, goal striving behavior, and goal conflict might be useful in illuminating *how* pain disrupts individuals' engagement in meaningful activities and leads

to clinical depression. The good news is that these goal-related variables can be quite easily measured through self-report (or via an informant) using ecological momentary assessment (e.g., Bender, Woike, Burke, & Dow, 2012; Hardy, Crofford, & Segerstrom, 2011; Harris, Daniels, & Briner, 2003; Mun, Karoly, & Okun, 2015; Mun, Karoly, Okun, Kim, & Tennen, 2015).

Limitations

There are several limitations of the present study that require some attention. First, this study only focused on the underlying mechanisms of pain and depressive symptoms. Investigating the underlying mechanisms of pain and anxiety symptoms at both the within- and between-person level is also important because co-morbidity of chronic pain and anxiety disorder is quite common (Asmundson, & Katz, 2009; McWilliams, Cox, & Enns, 2003). Second, previous studies indicate that being in a depressive state may cause changes in individuals' sensation of pain (e.g., Bair, Robinson, Katon, & Kroenke, 2003). However, this finding was not explored within this study as depressive symptoms were measured only a single time (in the evening) each day. In future studies, assessing both depressive symptoms and pain intensity multiple times during the day will be useful to understanding the momentary association between the two. Third, the paths from morning pain, negative and positive affect to morning negative pain appraisal are cross-sectional. Therefore, no causal inferences should be made with regard to these associations. However, within this study, it was thought that the experience of pain and affect can momentarily influence one's cognition in the present rather than a few hours later. Therefore, 'morning' negative pain appraisal was used instead of the variable that was measured in the afternoon. Fourth, the one-item

measure of pain's activity interference ("During the past 2-3 hours, how much did your pain interfere with your ability to carry on with your activities?") used in the present study lacked specificity. Some participants may have had some difficulty in understanding which activity this measure was referring to because individuals were often multi-tasking. More specific measures of activity or functional interference of pain should be used in future studies. Fifth, items that comprise the negative pain appraisal measure were somewhat arbitrary. This is primarily because there was no previously validated negative pain appraisal measure that could be utilized in a daily diary study. More rigorous investigation of the validity and reliability of the day-to-day measure of negative pain appraisal is needed. Last, the present findings have some limits in terms of generalizability, as the sample is strictly based upon fibromyalgia (a specific type of chronic pain disorder) and the participants of the study were primarily mid- to upperclass individuals in the community. Replications of the present findings in other noncancer chronic pain populations (e.g., arthritis, chronic low back pain, headache pain, irritable bowel syndrome, etc.) is required.

Conclusion

This is the first study that has examined the within-day mechanisms of the pain-depressive symptoms link and the unique role of positive and negative affect. In addition, the feasibility of biopsychosocial profiling in testing the moderation effect of the pain-depressive symptoms link was explored. Findings of the present study suggests that morning pain, positive affect, and negative affect are all uniquely associated with morning negative pain appraisal, which in turn positively predicted afternoon pain's activity interference. Afternoon pain's activity interference was the strongest predictor of

evening depressive symptoms. These findings suggest the importance of promoting morning positive affect and decreasing negative affect and negative pain appraisal, both of which can be realistic targets of psychosocial chronic pain interventions. Although there were no moderation effects in the association between pain-depressive symptoms link across different subgroups, a group of individuals that represented an overall higher level of biopsychosocial protective factors and lower level of risk factors tended to display the lowest level of average pain, negative affect, negative pain appraisal, activity interference and depressive symptoms across 21-days. The findings of the present study therefore can contribute meaningfully to understanding the mechanisms of adaptive pain adjustment, as well as to efforts to tailor existing chronic pain interventions to those individuals who are in the greatest need and who would most benefit from them. Future replications and extensions of the present study using both ecological momentary assessment data and comprehensive biopsychosocial measures would be helpful for developing cost-effective chronic pain management programs that can not only treat, but also prevent the development of major depressive disorder.

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APPENDIX A

TABLES

Table 1

List of individual difference variables that will be used as indicators of LPA

Name of Variable	Characteristics	Assessment Method	
1. Respiratory Sinus Arrhythmia	Biological	EKG	
2. Behavioral Inhibition System	Biological	Self-report measure	
3. Behavioral Activation System	Biological	Self-report measure	
4. Startle reflex during positive affect	Biological	EMG	
5. Startle reflex during neutral affect	Biological	EMG	
6. Startle reflex during negative affect	Biological	EMG	
7. Sleep quality	Biological	21-day daily diary	
8. Pain threshold	Biological	Sensory Nerve	
9. Continuum of depressive symptoms	Psychological	Evaluation Self-report measure	
10. Continuum of anxiety	Psychological	Self-report measure	
11. Neuroticism	Psychological	Self-report measure	
12. Pain acceptance	Psychological	Self-report measure	
13. Education	Social	Self-report measure	
14. Income	Social	Self-report measure	
15. Financial stress	Social	21-day daily diary	
16. Interpersonal stress	Social	21-day daily diary	
17. Social support satisfaction in coping pain	Social	21-day daily diary	

Table 2

Descriptive statistics and bi-variate correlations of level-I (within-person) variables ($n = 3716 \sim 3939$ observations)

9						I	1.80	0.54	1-3c	0.31	-0.73	0.47
5					I	0.29**	2.67	1.15	1-56	0.15	-0.81	0.41
4				I	0.37**	0.25**	2.65	0.87	1-5 ^b	0.10	-0.36	0.47
en			I	0.35**	0.20**	0.23**	1.63	0.85	1-56	1.52	1.71	0.59
2		1	-0.39**	-0.49**	-0.28**	-0.29**	2.59	0.90	1-5 ^b	0.29	-0.40	0.50
1	ı	-0.33**	0.24**	0.55**	0.29**	0.19**	48.74	24.30	0-100a	-0.09	-0.80	0.49
Variables	1. Morning Pain	Morning Positive Affect	3. Morning Negative Affect	4. Morning Negative Pain Appraisal	5. Afternoon Pain's Activity Interference	6. Evening Depressive Symptoms	Mean	Standard Deviation	Possible Range	Skewness	Kurtosis	ICC

Note. All level-1 variables were person-mean centered and thus the correlations represent pure level-1 correlations.

²0 = No pain, 100 = Pain as bad as it can be; ^b1 = Not at all, 5 = Completely; ^c1 = No, 2 = Yes, slightly, 3 = Yes, very much;

Table 3 $Descriptive \ statistics \ of \ level-2 \ (individual \ difference) \ variables \ (N=136 \sim 220)$

Name of Variable	Mean	SD	Skewness	Kurtosis	Observed Range
1. Log Respiratory Sinus Arrhythmia	4.76	1.21	-0.30	-0.03	1.06-7.43
2. Behavioral Inhibition System	3.60	0.73	-0.46	0.31	1-5
3. Behavioral Activation System	3.59	0.52	0.11	0.08	1-5
4. Startle reflex during positive affect	-0.18	0.73	0.51	-1.13	-1.15-1.15
5. Startle reflex during neutral affect	0.22	0.75	-0.30	-1.26	-1.15-1.15
6. Startle reflex during negative affect	-0.04	0.74	0.26	-1.34	-1.15-1.15
7. Pain Threshold	42.39	3.72	-0.45	-0.72	33.7-49.6
8. Sleep Quality	2.50	0.57	-0.04	0.39	0.95-4.18
9. Continuum of depressive symptoms	2.11	1.51	0.27	-0.72	0-5
10. Continuum of anxiety	3.23	1.09	0.20	-0.86	1.11-5.89
11. Neuroticism	3.15	0.78	-0.14	-0.37	1.33-5
12. Pain acceptance	3.42	1.01	0.18	-0.58	1-6
13. Education	6.39	1.55	-0.21	-0.46	2-9
14. Income	12.22	4.82	-0.87	-0.15	1-19
15. Financial stress	2.29	0.95	0.85	0.16	1-5
16. Interpersonal stress	1.78	0.59	0.84	0.44	1-3.81
17. Social support satisfaction in coping pain	2.86	1.04	0.19	-0.75	1-5

Bi-variate correlations of level-2 (between-person) variables (N = $136 \sim 220$)

1. RSA 2. BIS 3. BAS 3. Code and a consistive and a consi		Variables	1	2	3	4	5	9	7	∞	6	10	11	12	13	14	15	16	17
- 0.04 - 0.06 0.12 - 0.06 0.12 - 0.03 0.29" 0.54" 0.54" 0.07 0.03 0.06 0.09 0.26" 0.24" - 0.07 0.13 - 0.06 0.08 0.15' 0.13 0.05 0.01 0.00 0.00 0.00 0.00 - 0.50" - 0.48" 0.09 0.10 0.04 0.10 0.02 0.05 0.10 0.09 0.08 0.11 - 0.52" - 0.48" 0.09 0.11 0.02 0.05 0.11 0.07 0.01 0.04 0.00 0.00 - 0.00 0.00 0.00 0.00 0.00 0	-	. RSA	-	80:0	-0.11	-0.05	0.02	0.02	-0.09	-0.01	-0.03	-0.05	-0.00	90:0	0.03	-0.04	60:0	0.10	-0.06
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	7	. BIS		ı	-0.04	-0.06	0.12	90:0-	-0.12	-0.03	0.29**	0.39**	0.64**	-0.27**	0.03	-0.03	0.26**	0.24**	-0.14
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	co.				ı	-0.07	0.13	90:0-	80.0	0.15	-0.13	-0.05	-0.05	0.13	-0.01	0.09	0.08	-0.01	0.13
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4	. Startle reflex when positive				ı		-0.48**	60:0	-0.10	0.04	0.10	-0.02	-0.05	0.00	-0.00	0.09	-0.13	-0.05
- 0.00 -0.07 -0.05 -0.09 0.12 0.00 -0.03 -0.07 -0.03 - 0.09 -0.18' -0.17' -1.6' .22" -0.06 -0.01 -0.04 -0.16' - 0.26" -0.27" -0.17' 0.22" -0.05 0.21" -0.15' -0.09 - 0.65" 0.58" -0.70" -0.01 -0.33" 0.28" 0.34" - 0.62" -0.47" -0.02 -0.13 0.32" 0.38" - 0.62" -0.47" -0.02 -0.13 0.32" 0.40" - 0.50" -0.11 0.20" 0.31" 0.40" - 0.02 -0.03 0.31" 0.14 -0.16' - 0.02 -0.03 0.31" 0.14 -0.16' - 0.03 -0.03 0.07 - 0.03 -0.03 0.07	2	 Startle reflex when neutral 					ı	-0.52**	-0.09	0.11	0.02	-0.05	0.11	-0.07	-0.01	90.0	-0.02	0.15	-0.03
- 0.09 -0.18" -0.17" -1.6" 22" -0.06 -0.01 -0.04 -0.16" - 0.26" -0.27" -0.17" 0.22" -0.05 0.21" -0.15" -0.09 - 0.65" 0.58" -0.70" -0.01 -0.33" 0.28" 0.34" - 0.62" -0.47" -0.02 -0.13 0.32" 0.38" - 0.62" -0.47" -0.02 -0.13 0.32" 0.38" - 0.50" -0.11 -0.20" 0.31" 0.40" - 0.50" -0.01 0.31" -0.14 -0.16" - 0.02 -0.03 0.07 - 0.03 -0.03 0.07	9	 Startle reflex when negative 						ı	-0.00	-0.00	-0.07	-0.05	-0.09	0.12	0.00	-0.03	-0.07	-0.03	0.09
0.26" -0.27" -0.17" 0.22" -0.05 0.21" -0.15" -0.09 - 0.65" 0.58" -0.70" -0.01 -0.33" 0.28" 0.34" - 0.62" -0.47" -0.02 -0.13 0.32" 0.38" - 0.50" -0.11 -0.20" 0.31" 0.40" - 0.05 0.01 0.31" -0.14 -0.16" - 0.02 -0.05 0.07 - 0.03 0.31" -0.14 -0.16"	7								ı	60:0	-0.18	-0.17*	16		90:0-	-0.01	-0.04	-0.16	0.07
- 0.65* 0.58* -0.70* -0.01 -0.33* 0.28* 0.34** - 0.62* -0.47* -0.02 -0.13 0.32* 0.38** - 0.50* -0.11 -0.20* 0.31** 0.40** - 0.05 -0.11 0.20* 0.31** 0.40** - 0.01 0.31** -0.14 -0.16** - 0.02 -0.05 0.07** - 0.034** -0.29** - 0.40**	00	 Sleep Quality 								ı	-0.26	-0.27**	-0.17*	0.22**	-0.05	0.21**	-0.15	-0.09	0.26"
- 0.62" -0.47" -0.02 -0.13 0.32" 0.38" 0.50" -0.11 -0.20" 0.31" 0.40" 0.01 0.31" -0.14 -0.16" - 0.02 -0.05 0.07 - 0.34" -0.29" - 0.40"	6). Depression									ı	0.65	0.58	-0.70	-0.01	-0.33**	0.28	0.34"	-0.27**
0.50** -0.11 -0.20** 0.31** 0.40** 0.01 0.31** -0.14 -0.16* - 0.02 -0.05 0.07 0.34** -0.29** - 0.40**	_	0. Anxiety										ı	0.62	-0.47**	-0.02	-0.13	0.32**	0.38**	-0.33
0.01 0.31" -0.14 -0.16" - 0.02 -0.05 0.07 - 0.34" -0.29" - 0.40"	-	1. Neuroticism											ı	-0.50**	-0.11	-0.20	0.31"	0.40	-0.35
- 0.02 -0.05 0.07 0.34** -0.29** - 0.40**	_	2. Pain Acceptance												ı	-0.01	0.31**	-0.14	-0.16	
-0.34** -0.29** - 0.40**	_	3. Education													ı	0.02	-0.05	0.07	0.05
040,,,	_	4. Income														ı	-0.34"	-0.29**	0.31"
	_	Financial Stress															ı	0.40	-0.22
	Т	Interpersonal Stress																ı	-0.39
	-	7. Social Support Satisfaction																	'

* p < .05, ** p < .01, *** p < .001

Table 5

Oblimin rotated EFA factor loadings

Variables	Factor 1	Factor 2	Factor 3
	(High BIS and	(High Depression	(High Financial &
(Factor Labels)	Neuroticism)	& Anxiety and	Interpersonal Stress
		Low Pain	and Low Income
		Acceptance	with Social Support
			in Pain Coping)
BIS	0.76*	-0.09*	-0.02
Neuroticism	0.83*	0.12	0.06
Depression	-0.03	0.98*	0.04
Anxiety	0.29*	0.44*	0.15
Pain acceptance	-0.13	-0.68*	0.11
Financial stress	0.06	-0.00	0.52*
Interpersonal stress	0.03	-0.02	0.72*
Income	0.19	-0.19	-0.43*
Social Support	-0.11	0.04	-0.48*

^{*}*p* < .05

Table 6 ${\it Model Fit Information for Class Determination of Latent Profile Analysis Models (N=220)}$

Number of Classes	BIC	Adjusted BIC	VLMR	BLRT	Entropy
1 Class	4865.994	4815.288	N/A	N/A	N/A
2 Class	4712.918	4633.690	p <.001	p <.001	0.756
3 Class	4689.315	4581.564	p = .07	p <.001	0.777
4 Class	4704.319	4568.046	<i>p</i> =.52	p <.001	0.762
5 Class	4728.614	4563.820	p = 0.44	<i>p</i> =.12	0.772

Table 7

Results of one-way ANOVA and means and standard deviations for each group

 $\mathbb{E}(2,217) = 41.75 \quad p < .001$ $\mathbb{E}(2,217) = 51.07 \quad p < .001$ $\mathbb{E}(2,217) = 44.37 \quad p < .001$ $\mathbb{E}(2,217) = 20.15 \quad p < .001$ $E(2,217) = 29.32 \quad p < .001$ $F(2,216) = 53.48 \quad p < .001$ Sig 2.17 (0.73) Functioning Group (N = 60)M (SD)38.87 (17.32) 3.09 (0.65) 2.18 (0.46) 1.19 (0.22) 1.51(0.31)Group (N = 118) M (SD)50.48 (16.09) 2.48 (0.51) 1.66 (0.56) 2.74 (0.56) 1.86(0.33)Normative 2.75 (0.72) Low Functioning Group (N = 42)M (SD)59.02 (15.07) 2.11 (0.53) 2.32 (0.84) 3.16 (0.55) 2.16 (0.31) 3.24 (0.62) Mean of Morning Negative Pain Appraisal Mean of Evening Depressive Symptoms Mean of Afternoon Pain's Activity Mean of Morning Negative Affect Mean of Morning Positive Affect Mean of Morning Pain Dependent Variable Interference

APPENDIX B

FIGURES

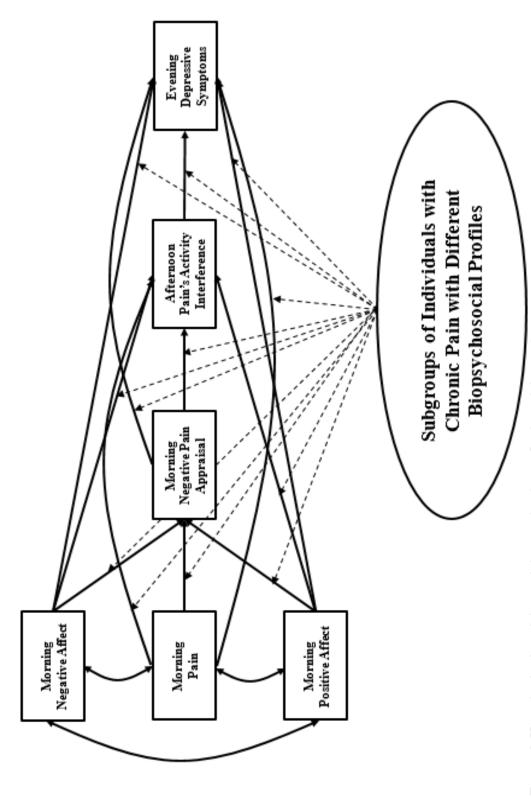


Figure 1. Hypothesized model examining mechanisms of pain and depressive symptoms.

Note. Morning pain's activity interference was controlled in the actual model but it is not shown in this figure due to visual parsimony.

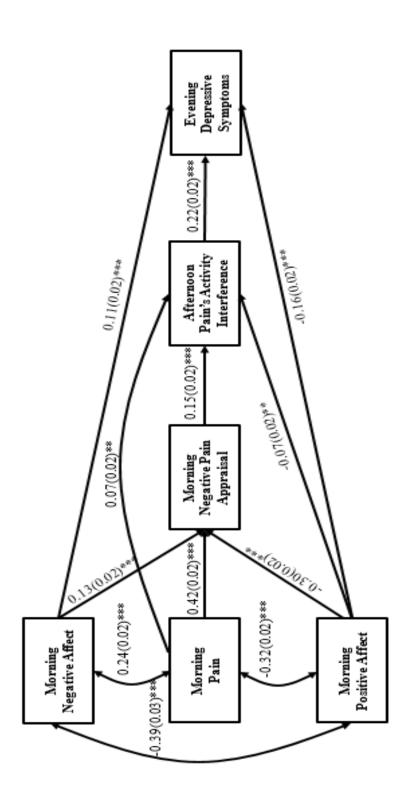


Figure 2. Findings of within-person mechanisms of pain and depressive symptoms.

Note. Only significant paths are shown here and morning pain's activity interference was controlled in the actual model is not shown in this figure due to visual parsimony. All paths estimates are standardized regression coefficients. Values in brackets are standard errors.

$$p < .05, **p < .01, ***p < .001$$

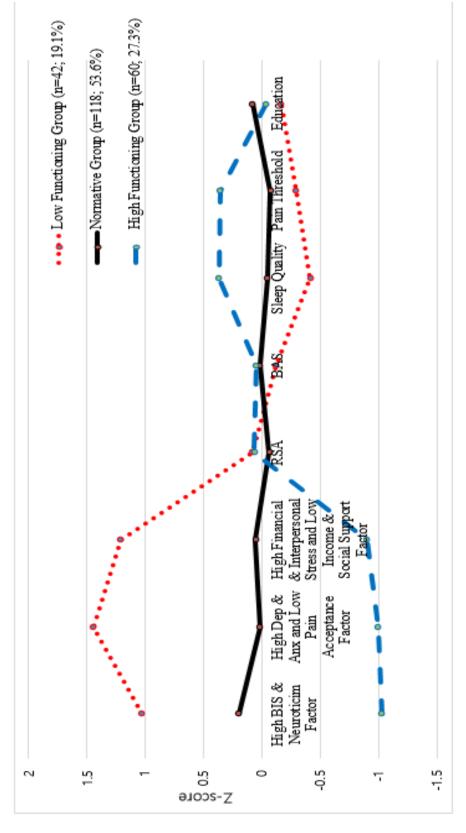


Figure 3. Results of the Latent Profile Analysis of Biopsychosocial Risk and Protective Factors

Note. BIS = Behavioral Inhibition System, BAS = Behavioral Activation System, Dep = Continuum of depression, Anx = Continuum of

anxiety, RSA = Respiratory Sinus Arrhythmia.

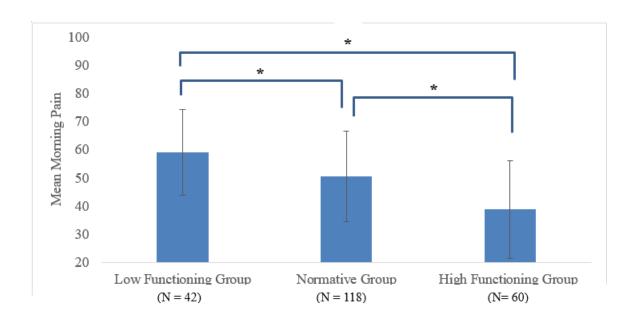


Figure 4. Mean of morning pain across different LPA subgroups.

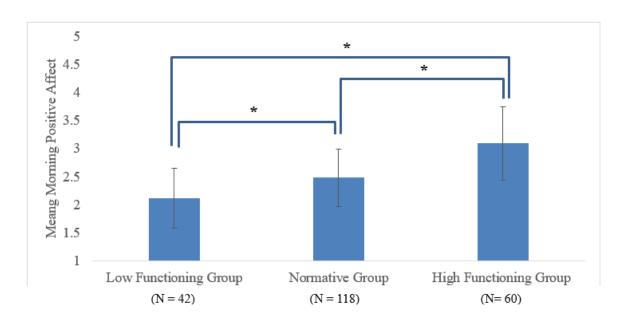


Figure 5. Mean of morning positive affect across different LPA subgroups.

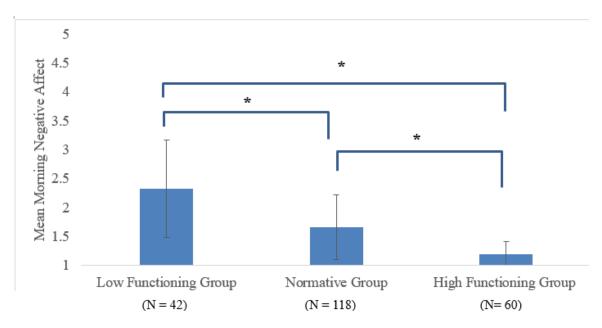


Figure 6. Mean of morning negative affect across different LPA subgroups.

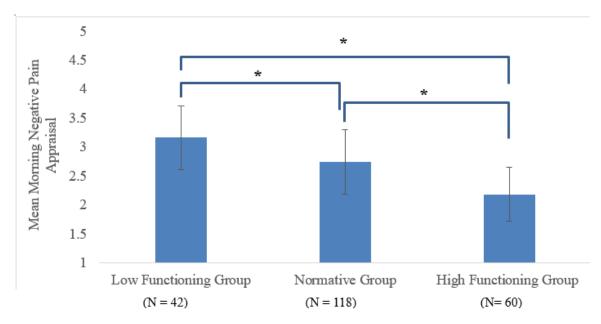


Figure 7. Mean of morning negative pain appraisal across different LPA subgroups.

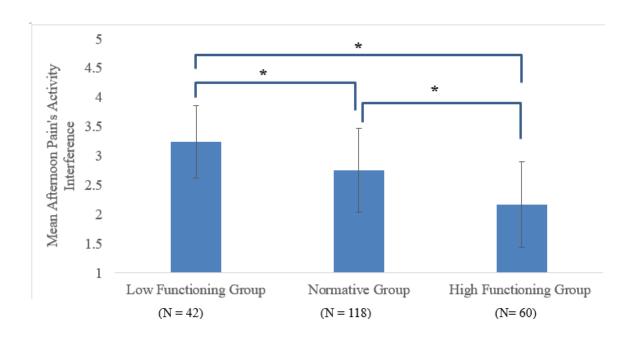


Figure 8. Mean of afternoon pain's activity interference across different LPA subgroups.

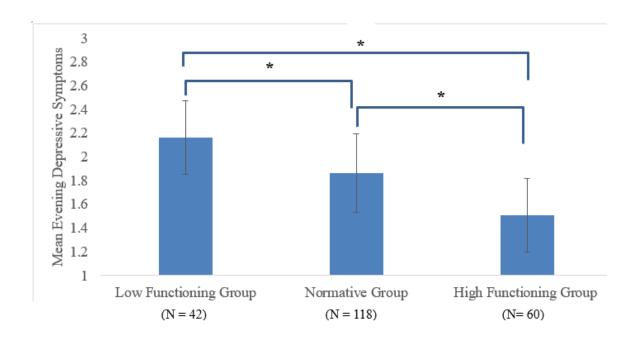


Figure 9. Mean of evening depressive symptoms across different LPA subgroups.