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# Generalization of Pain-Related Fear Based on Conceptual Knowledge

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**Increasing evidence suggests that pain-related fear is key to the transition from acute to chronic pain. Previous research has shown that perceptual similarity with a pain-associated movement fosters the generalization of fear to novel movements. *Perceptual generalization of pain-related fear* is adaptive as it enables individuals to extrapolate the threat value of one movement to another without the necessity to learn anew. However, excessive spreading of fear to safe movements may become maladaptive and may lead to sustained anxiety, dysfunctional avoidance behaviors, and severe disability. A hallmark of human cognition is the ability to extract conceptual knowledge from a learning episode as well. Although this conceptual pathway may be important to understand fear generalization in chronic pain, research on this topic is lacking. We investigated acquisition and generalization of *concept-based pain-related fear*. During acquisition, unique exemplars of one action category (CS+; e.g., opening boxes) were followed by pain, whereas exemplars of another action category (CS-; e.g., closing boxes) were not. Subsequently, spreading of pain-related fear to novel exemplars of both action categories was tested. Participants learned to expect the pain to occur and reported more pain-related fear to the exemplars of the CS+ category compared with those of the CS- category. During generalization, fear and expectancy generalized to novel exemplars of the CS+ category, but not to the CS- category. This pattern was not corroborated in the eyeblink startle measures. This is the first study that demonstrates that pain-related fear can be acquired and generalized based on conceptual knowledge.**

*Keywords:* pain-related fear; acquisition; generalization; category-based learning; associative learning

The ability to learn which stimuli in the environment signal threat has an important adaptive advantage, because it enables us to initiate appropriate defensive responses that protect us from future harm (Vlaeyen, 2015). Nevertheless, adaptive learners face the challenge of how to deal with variations in the appearances of signaling stimuli. *Stimulus generalization* (Honig & Urcuioli, 1981; Kalish, 1969) allows individuals to extrapolate the predictive value of one stimulus to perceptually similar stimuli and minimizes the necessity to learn everything anew. As a consequence, the advanced capacity to detect similarities between unique but related stimuli fosters swift adaptation to a dynamic environment.

Pain is a vital motivator in learning because it typically alerts the individual of impending or actual bodily threat. It has been shown that associative learning is crucially involved in the acquisition of fear of movement-related pain (Meulders, Vansteenwegen, & Vlaeyen, 2011). In particular, using a voluntary joystick movement (VJM)

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paradigm, Meulders and colleagues (2011) showed that after (repeated) pairing of a painful electrocutaneous stimulus (unconditioned stimulus [pain-US]) with an initially neutral joystick movement (conditioned stimulus [CS]), this movement (CS+) elicited protective responses such as fear and avoidance (conditioned response [CR]), whereas another neutral joystick movement (CS-) that was not paired with pain did not evoke such CRs. Differential pain-related fear learning was apparent in self-reports and psychophysiological measures (startle eyeblink measure), as well as behavior (movement-onset latency)—that is, participants reported more fear in response to the CS+ than to the CS-, showed elevated startle responses to the CS+ compared with the CS-, and were slower in initiating a movement that was painful (CS+) than one that was not (CS-). For example, if a person performs a bending exercise (CS+) during yoga class and gets a shooting pain in the back (pain-US), this person might start to associate bending movements with pain, learn that yoga is dangerous, and begin to avoid going to yoga class altogether (CRs). From an associative learning perspective, this fear of movement-related pain might extend to a range of novel movements resembling this original pain-associated bending movement (i.e., more similar movements may induce more fear/avoidance). For example, this person might also become afraid to bend over to pick up an object and start to avoid a wide range of bending-related movements.

This type of fear generalization is typically referred to as *perceptual pain-related fear generalization*. Previous research in healthy participants has shown that fear spreads selectively to novel movements that have a perceptual feature in common with the original CS+ but not to movements having a feature in common with the CS- (Meulders & Vlaeyen, 2013). More specifically, after being trained with a joystick movement straight to the left (CS+) that was followed by pain and a joystick movement straight to the right (CS-) that was not followed by pain (or vice versa), spreading of fear to four novel diagonal movements (generalization stimuli [GSs]) was tested. More specifically, participants were requested to perform novel movements directed to the left-top, the left-bottom, the right-top, and the right-bottom corners of the computer screen. Results confirmed that when the straight movement to the left served as the CS+, the diagonal movements to the left (GS+) elicited more fear measured with both self-report and startle amplitude than did the diagonal movements to the right (GS-). However, when the CS+ was the straight movement to the right, the response pattern was reversed (Meulders & Vlaeyen, 2013). In another study (Meulders, Vandebroek, Vervliet, & Vlaeyen, 2013), we again trained participants with joystick movement to the left followed by pain, and joystick movements to the right not followed by pain (or vice versa), and tested novel intermediate movements lying between the CS+ and the CS-. The results corroborate previous findings at least in the startle eyeblink measures. More specifically, we showed a *pain-related fear generalization gradient*—that is, there was a linear decrease in startle amplitudes for GSs approaching the original CS-. Another study using a left-right hand judgment conditioning paradigm with pictures of hand postures as CSs and a painful electrocutaneous stimulus as the pain-US showed a similar gradient at least in the verbal measures (fear and expectancy; Meulders, Harvie, Moseley, & Vlaeyen, 2015). In this study, one hand posture (CS+; e.g., extreme hand flexion) was consistently paired with pain and another hand posture (CS-; e.g., extreme hand extension) was not. During generalization, we tested the spreading of fear and US-expectancy to a set of novel hand postures (GSs) with six grades of perceptual similarity to the CS+. Results confirmed that novel GSs that were more similar to the CS+ triggered more pain-related fear and US-expectancy than did those more similar to the CS-. Taken together, accumulating evidence suggests that pain-related fear can spread based on perceptual similarity.

A certain degree of fear generalization is adaptive, but excessive generalization to technically safe stimuli may become maladaptive and pathological. In a replication of Meulders and Vlaeyen (2013), we demonstrated that patients with fibromyalgia syndrome do not show selective fear generalization like healthy pain-free controls, but overgeneralize their fear to all novel (diagonal) movements (GSs). In a hand pain scenario contingency learning task with hand postures as cues and the words “pain” and “no pain” as outcomes, participants were asked to rate the likelihood that a fictive hand pain patient would feel pain when moving the hand into certain postures (Meulders et al., 2014). One hand posture (e.g., extreme hand flexion) was consistently paired with the word “pain” and another hand posture (e.g., extreme hand extension) was paired with “no pain.” During generalization, we tested the spreading of pain expectancy to a set of novel hand postures (GSs) with six grades of perceptual similarity to the pain-associated hand posture. Unilateral chronic hand pain patients showed flatter, asymmetric generalization gradients compared with healthy pain-free controls, with higher pain expectancy ratings for novel postures that were more similar to the CS-. At the CS+ side of the gradient, pain expectancy ratings did not differ between patients and controls, indicating a lack of safety learning rather than excessive fear in response to actual threat.