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Naltrexone renders one-session exposure therapy less effective: A controlled pilot study

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Abstract

In vivo exposure has become the gold standard treatment for specific phobia. The endogenous opioid system is one mechanism proposed to explain why exposure provides such quick and effective treatment for specific phobia. The effect of naltrexone on fear and avoidance behavior was investigated among 15 specific phobia participants who received exposure treatment. Participants were randomly assigned to receive naltrexone, placebo, or no drug prior to attending one-session exposure treatment. Mixed effects regression results revealed that across time, the naltrexone group tolerated significantly less time in the room with the feared animal (Behavioral Avoidance Index) as compared to the placebo and no drug groups. Phobic individuals assigned to the naltrexone group had significantly higher fear ratings across time in comparison to the placebo group. Results provide support for the endogenous opioid system as a potential underlying biological mechanism associated with behavioral changes during in vivo exposure.

Keywords: Phobias; Naltrexone; Endogenous opiates; Behavioral assessment

Randomized controlled trials indicate that exposure is the most efficacious treatment for specific phobia (Booth & Rachman, 1992; Menzies & Clarke, 1993; Ost, Johansson, & Jerremalm, 1982). It has been suggested that the specific variant of in vivo exposure is the treatment of choice for this disorder (Marks, 1987). Phobic individuals have been successfully

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treated with one-session in vivo exposure in 3 h or less and have maintained a significant reduction in the key symptoms of fear and avoidance at subsequent 1-year follow-up sessions (Koch, Spates, & Himle, 2004). Behavioral interpretations have been put forth to explain the mechanism of action that produces such effective and reliable outcomes. The most common interpretation is that severe distress levels are significantly reduced in the presence of phobia-specific stimuli because of response extinction. In essence, extinction involves a reduction in the strength of learned responses through repeated responding that is not reinforced by escape or avoidance (Barlow, 1988). When phobic individuals are repeatedly confronted with fearful stimuli without the experience of negative consequences occurring, their fear and avoidance is significantly reduced. Less is known about the underlying biological mechanisms that may help to facilitate such processes.

A prime biological candidate that may be associated with behavioral responses during exposure therapy is the endogenous opioid system. Powerful and effective analgesic effects are produced by endogenous opioids (e.g., endorphins, enkephalins, and dynorphins) during inescapably aversive situations (Besson, Privat, Eschalier, & Fialip, 1996; Hunziker, 1992; Hyson, Ashcraft, Drugan, Grau, & Maier, 1982). In addition to their pain reducing effects, it has been suggested that opioids also have an anxiolytic (anxiety reducing) effect (Rang & Dale, 1991). Individuals with specific phobia may be able to adapt via reduced fear and avoidance to an exposure intervention because of the release of these naturally produced analgesics. The influence of the endogenous opioid system on specific phobia treatment has been examined by comparing the effects of an opioid antagonist (naloxone or naltrexone) to placebo (Arntz, Merckelbach, & de Jong, 1993; Egan, Carr, Hunt, & Adamson, 1988; Merluzzi, Taylor, Boltwood, & Gotestam, 1991). The common hypothesis is that an opioid antagonist would disrupt the effects of naturally produced endogenous opioids that are presumed to help a person with specific phobia adapt to exposure therapy, leading to behavioral disruptions in treatment such as early withdrawal from the treatment session (Merluzzi et al., 1991). The few studies that examined the effect of an opioid antagonist on specific phobia treatment show some evidence consistent with behavioral disruptions in treatment. Behavioral avoidance outcomes have shown that participants given an opioid antagonist had greater drop out rates (Merluzzi et al., 1991), took longer to complete one of the treatment steps (Merluzzi et al., 1991), and maintained a greater distance from the phobic stimuli during a behavioral assessment (Arntz et al., 1993).

To our knowledge, research has yet to address behavioral avoidance in terms of the duration a person is able to stay in the room with a feared stimulus during a behavioral assessment. Duration was of particular interest to the present study because opioid-mediated effects may be correlated with the length of time a person endures exposure to an aversive stimulus in an inescapable scenario such as exposure treatment. Results from non-human studies (i.e., rats exposed to inescapable shock) have found that 20 min of intermittent shock rather than 3 min of continuous shock is necessary for the opioid system to become activated (Maier, Sherman, Lewis, Terman, & Liebeskind, 1983). At this point in time, one can only speculate as to the length of time required to activate the endogenous opioid system in humans. Phobics can be successfully treated in 99 min (Koch et al., 2004), suggesting that endogenous opioids may be released in 99 min or less.

The present study was designed to replicate and expand on data linking the opioid system with fear and avoidance behavior. Similar to previous studies, the present study employed a comparison between an opioid antagonist (naltrexone) and placebo. An additional no drug control group also was included to control for potential placebo effects (i.e., the activation of the endogenous opioid system due to the administration of a placebo; Amanzio & Benedetti, 1999). There were two adaptive behavioral responses of interest: subjective reports of fear and duration