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Invited Review

Mind–body therapies and control of inflammatory biology: A descriptive review

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ABSTRACT

The use of mind–body therapies, including Tai Chi, Qigong, yoga, and meditation, has grown steadily in recent years. These approaches have been shown to be effective in reducing symptoms and improving quality of life, and research has begun to examine the impact of these therapies on biological processes, including inflammation. A review of 26 randomized controlled trials was conducted to describe the effects of mind–body therapies (MBTs) on circulating, cellular, and genomic markers of inflammation. This qualitative evaluation showed mixed effects of MBTs on circulating inflammatory markers, including CRP and IL-6, and on measures of stimulated cytokine production. More consistent findings were seen for genomic markers, with trials showing decreased expression of inflammation-related genes and reduced signaling through the proinflammatory transcription factor NF-κB. Potential mechanisms for these effects are discussed, including alterations in neuroendocrine, neural, and psychological and behavioral processes.

1. Introduction

Mind–body therapies, or MBTs, have been broadly defined as a group of therapies that emphasize use of the brain in conjunction with the body to assist the healing process (Spencer and Jacobs, 2003). These therapies, the majority of which are based on ancient practices and traditions, are believed to have beneficial effects on mental and physical health and are widely used to manage symptoms and improve well-being. Indeed, in a nationwide survey of community-dwelling adults in the US conducted in 2007, 19% reported that they had used at least one mind–body therapy in the past year, and rates are even higher among clinical populations (Barnes et al., 2008). Over the past two decades, the efficacy of these approaches has been subjected to empirical scrutiny through randomized controlled trials conducted in clinical and non-clinical populations. Meta-analyses of these trials suggest that MBTs are effective in reducing symptoms and improving quality of life and certain functional outcomes (Bussing et al., 2012; Goyal et al., 2014; Wang et al., 2004).

Alterations in inflammatory processes are thought to play a role in many of the symptoms and conditions that are responsive to MBTs, including fatigue, depression, and pain (Irwin and Cole, 2011). Given the importance of inflammation on these patient-reported outcomes, a growing number of trials have evaluated effects of MBTs on markers of inflammation. The goal of this review is to qualitatively evaluate the evidence that MBTs lead to changes in these markers, and to discuss potential mechanisms and issues in this emerging area of research. We include results of randomized controlled trials that assessed inflammatory cytokine activity at multiple levels, including circulating, cellular, and genomic markers of inflammation.

We focus here on four types of MBTs that have received considerable research attention and are widely available to clinical and community populations: Tai Chi, Qigong, yoga, and meditation. *Tai Chi* and *Qigong* are practices from traditional Chinese medicine that combine specific movements or postures, coordinated breathing, and mental focus. *Yoga* has its origins in ancient Indian philosophy; as practiced in the West, it typically includes physical postures, breathing, and meditation or relaxation, though there is considerable variability across different schools of yoga and specific interventions. *Meditation* refers to a broad range of practices that involve training the mind, typically to focus attention. In particular, mindfulness meditation teaches individuals to bring attention to present moment experiences with openness, curiosity, and non-judgment.

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To identify studies for inclusion in this qualitative review, we searched MEDLINE (from 1946), through November 1, 2014. Searches were limited to human studies and the English language. We searched using the following terms: mind–body therapies, tai chi, qigong, meditation, mindfulness, or yoga; and inflammation, cytokines, or proinflammatory. In addition, we screened the reference lists of selected reviews and primary articles for additional publications.

2. Effects of MBTs on circulating markers of inflammation

2.1. CRP

The most common inflammatory marker assessed in the MBT trials reviewed here is C reactive protein (CRP), a well-established marker of inflammatory activity. We identified 14 RCTs that reported effects of a MBT on CRP, described in Table 1. The majority of these trials evaluated Tai Chi or Qigong ($n = 7$), with additional studies of yoga ($n = 3$) and meditation ($n = 4$). Various control conditions were used including health education, usual care or wait-list, aerobic exercise, and cognitive behavioral therapy (CBT). All studies assessed CRP at pre- and post-treatment, and several also included follow-ups from 6 weeks to 3 months post-treatment, although one had a one-year post-treatment follow-up (Irwin et al., 2014b, 2015).

A previous meta-analysis had reported that these various types of MBTs, typically lasting eight to twelve weeks, yielded decreases in circulating levels of CRP (Morgan et al., 2014). However, results inclusive of research published since that review show that findings for CRP were evenly split; seven of the trials yielded decreases in circulating levels of CRP, and seven yielded no significant changes in this marker. Hence, at best, it appears that MBTs have mixed effects on CRP, although this conclusion is tempered by the absence of a meta-analytic approach as compared to the prior review. There is some evidence that Tai Chi or Qigong, and possibly yoga, which incorporate physical activity components, are more likely to reduce levels of CRP, relative to meditation; the majority of studies using Tai Chi/Qigong or yoga showed decreases in CRP, whereas none of the meditation studies showed this effect (though two reported marginally significant reductions of CRP; Creswell et al., 2012; Malarkey et al., 2013). Nevertheless, the number of studies categorized by treatment type is too small to make any conclusions about the relative benefit of one treatment or another.

Interestingly, patient type may be more relevant, as those studies that enrolled participants who were likely to have elevated levels of CRP at baseline due to depression, cancer diagnosis, diabetes, or cardiovascular disease appear to show decreases in CRP; such decreases in response to intervention were not found in studies that focused on healthy adults or healthy older adults for whom substantial medical co-morbidities were an exclusion criteria. The latter conclusion is supported by meta-analytic results from Morgan et al. (2014) who found that CRP was likely to be reduced following mind–body therapies in populations with disease conditions, but not in healthy persons.

However, even this conclusion is mixed. Bower et al. found no change in CRP in two trials conducted with breast cancer survivors; one used a 12-week yoga intervention for survivors with persistent fatigue (Bower et al., 2014) and the other used a 6-week mindfulness intervention for younger breast cancer survivors (Bower et al., 2015). Likewise, Irwin et al. in two different populations, breast cancer survivors (Irwin et al., 2014a) and older adults with insomnia (Irwin et al., 2014b, 2015), found inconsistent results. Tai Chi yielded a decrease in CRP in older adults with insomnia when administered for 16 weeks (Irwin et al., 2014b, 2015), but not in breast cancer survivors with insomnia in which Tai Chi was administered for only 12 weeks (Irwin et al., 2014a). Average levels of CRP were similar in these two independent samples suggesting that higher baseline levels in one vs. the other did not account for differential responses. Alternatively the duration of Tai Chi administration in the breast cancer survivors may have been too short to detect changes. CRP is regulated in part by IL-6, and Tai Chi-related reduction of IL-6 at 16 weeks (Irwin and Olmstead, 2012) is reportedly followed by reductions of CRP at 24 weeks (Lavretsky et al., 2011). Interestingly, we had previously reported that cognitive behavioral therapy for insomnia (CBT-I) induced a remission of insomnia in the older adults, and this remission was associated with sustained decreases in CRP during the one-year follow-up period (Irwin et al., 2014b, 2015). Nevertheless, other studies have found decreases in CRP to occur as early as 8–10 weeks after administration of a mind–body treatment (e.g., Oh et al., 2008, 2010, 2012; Pullen et al., 2008, 2010).

There is another issue related to the interpretation of these results. As noted in Table 1, some of the reported "decreases" in the intervention group are accounted for by increases in the control condition, either due to a confounding influence in the controls that produced the reported increase in CRP or that the intervention resulted in an attenuated age-related increase in inflammation; the latter seems a more tenuous explanation given that many of the interventions only lasted weeks to months.

2.2. IL-6

A total of 12 trials were identified which examined effects of a MBT on circulating concentrations of the proinflammatory cytokine IL-6, including studies using Tai Chi or Qigong ($n = 4$), yoga ($n = 3$) and meditation ($n = 5$). Again, a variety of controls were used such as wait list, education, or social support. Overall, it appears that IL-6 does not show any consistent changes following the administration of these various MBTs, with three studies showing modest decreases, and the remaining nine studies showing no change. Two of the three trials that found decreases in IL-6 were trials of yoga for patients with heart failure, a group with pronounced elevations in inflammation (Pullen et al., 2008, 2010). None of the Tai Chi/qigong or meditation trials yielded decreases in IL-6. However, it is notable that decreases in IL-6 were found among individuals with higher baseline levels of this marker in a trial of Tai Chi in healthy older adults (Irwin and Olmstead, 2012) and among individuals with more hours of meditation practice in trials of mindfulness (Bower et al., 2015) and compassion meditation (Pace et al., 2009).

2.3. TNF-α and other circulating inflammatory cytokines

Seven of the listed studies also evaluated the effects of mind–body therapies on other inflammatory markers such as TNF-α, IL-1 receptor antagonist (IL-1RA), and IL-18. The limited data for any of these other circulating outcomes do not allow for any conclusions, although two of the studies that administered yoga and measured TNF or its soluble receptor found stable levels in the yoga group vs. controls (Bower et al., 2014; Rao et al., 2008). Both of these trials focused on breast cancer patients and one specifically targeted women with cancer-related fatigue, who have previously been shown to have elevated concentrations of soluble TNF receptor type II (sTNF-RII; Bower et al., 2011).

3. Effects of MBTs on cellular markers of inflammation

Systemic changes in circulating markers of inflammation might be due to effects of MBTs on the release of cytokines such as IL-6 from non-immune sources such as adipose tissue. To evaluate