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Deconstructing the effects of concentration meditation practice on interference control: The roles of controlled attention and inflammatory activity

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ABSTRACT

Prior work has linked meditation practice to improvements in interference control. However, the mechanisms underlying these improvements are relatively unknown. In the context of meditation training, improvements in interference control could result either from increases in controlled attention to goal-relevant stimuli, or from reductions in automatic capture by goal-irrelevant stimuli. Moreover, few studies have linked training-related changes in attention to physiological processes, such as inflammatory activity, that are thought to influence cognitive function. This study addresses these gaps by examining associations between cognitive performance and cytokines in the context of an intensive meditation retreat. Participants were randomly assigned to complete 3 months of meditation training first, or to serve as waitlist controls. The waitlist-control participants then later completed a separate 3-month training intervention. We assessed participants' interference control with a flanker task and used computational modeling to derive component processes of controlled and automatic attention. We also collected blood samples at the beginning, middle, and end of training to quantify changes in cytokine activity. Participants who completed training evidenced better controlled attention than waitlist controls during the first retreat intervention, and controls showed significant improvements in controlled attention when they completed their own, second retreat. Importantly, inflammatory activity was inversely associated with controlled attention during both interventions. Our results suggest that practice of concentration meditation influences interference control by enhancing controlled attention to goal-relevant task elements, and that inflammatory activity relates to individual differences in controlled attention.

1. Introduction

Emerging research indicates that training in meditation, mindfulness, and other contemplative practices can improve performance on inhibitory control tasks (Gallant, 2016; Gothe et al., 2014; MacLean et al., 2010; Mitchell et al., 2017; Sahdra et al., 2011; Zanesco et al., 2013; Zanesco et al., 2018). An outstanding question that stems from this work concerns the psychological or physiological mechanisms that may account for meditation-based changes in *interference control* (i.e., the cognitive ability to suppress attention to distracting thoughts or stimuli and focus on goal-relevant information). That is, in what ways, and through what routes, might training in meditation influence the typical functioning of cognitive systems? To date, most researchers have attempted to tackle this question by examining the neural correlates of meditation-related improvements in interference control (e.g., Moore et al., 2012; Moynihan et al., 2013; Slagter et al., 2007; Taren et al., 2017). In the current study, we take a different approach: We leverage multiple methods to examine how intensive meditation training influences—and inflammatory cytokine activity relates to—the component cognitive processes that underpin performance on an interference control task.

There is good reason to think that meditation training might affect biological and immunological processes in ways conducive to improvements in attentional control. Traditional accounts of Buddhist meditation emphasize the importance of a calm, serene, and equanimous bodily state for facilitating concentration and sustained attention (Gunaratana, 2002; Wallace, 2006). In addition, many contemporary forms of meditation training—including mindfulness-based stress reduction—aim to increase physical wellness and well-being, while strengthening faculties of attention, awareness, and executive function

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(Creswell, 2017). Although direct empirical support for these connections is lacking, indirect support can be derived from two separate research threads: the effects of meditation training on cognitive performance (e.g., Jha et al., 2007; MacLean et al., 2010), and the effects of meditation training on stress reduction, reactivity, and regulation (Conklin et al., 2019; Creswell and Lindsay, 2014).

In the present study, we examined the role of cytokine activity in relation to cognitive processes that are thought to be influenced by meditation practice. We focused on cytokine activity because previous work has shown that meditation practice can appreciably influence cytokines (Black et al., 2013; Black and Slavich, 2016; Buric et al., 2017; Creswell et al., 2016; Pace et al., 2009) and because the neuroimmune environment of the brain has been found to influence similar cognitive processes (Donzis and Tronson, 2014; McAfoose and Baune, 2009; Shields et al., 2017; Yirmiya and Goshen, 2011). In addition, we focused our investigation on concentrative styles of meditation practice—namely, *shamatha* practices that aim to cultivate calm, sustained attention and experiential states of meditative quiescence. Prior work in our lab has shown that intensive, full-time practice of shamatha meditation can (a) increase the ability to sustain one's attention over time (MacLean et al., 2010; Zanesco et al., 2019), (b) improve the capacity for cognitive control (Sahdra et al., 2011; Zanesco et al., 2018), and (c) modulate biological markers associated with physical well-being (Jacobs et al., 2011).

1.1. Cognitive components of interference control

Improvements in interference control can be explained by way of dissociable cognitive mechanisms. For example, dual-process models of interference control hold that automatic attentional activation to goal-irrelevant task elements occurs in parallel with controlled attention to goal-relevant elements (Ridderinkhof, 2002). In these models, observed behavioral responses represent the summation of these parallel processes, each of which can drive improvements in task performance. For instance, although top-down processes (e.g., controlled attention) are well-known to modulate the Stroop effect (e.g., MacLeod, 1991), bottom-up processes (e.g., automatic attentional activation) appear to contribute to its effects as well (Notebaert et al., 2006). Findings such as these suggest that the cognitive processes underlying interference control may be more varied than is often assumed, and highlight the importance of considering multiple attentional mechanisms when examining how performance on interference control tasks might be modified with training.

In studies of meditation practice, enhancements in interference control have often been attributed to improvements in controlled attention (for a review, see Gallant, 2016). But the generality of this conclusion is not clear. For instance, there is evidence to suggest that training in different styles of meditation, across a range of experience and intensity levels, may influence attentional subsystems in different ways. In one study, improvements in subcomponents of attention were distinguished according to whether people engaged in intensive or non-intensive concentrative meditation training (Jha et al., 2007). In this study, meditation-naïve participants who underwent an 8-week mindfulness-based stress reduction course demonstrated improvements in endogenous attentional orienting, while experienced meditators who engaged in a 1-month concentrative meditation retreat showed improvements in exogenous attentional orienting. In another study, three months of full-time intensive meditation produced changes in event related brain responses thought to reflect both top-down attentional and bottom-up perceptual processes (Zanesco et al., 2019). This latter study used the same participant sample and training program (shamatha practice) as our present report.

The cognitive substrates of meditation-related improvements in interference control remain opaque because few studies dissociate changes in controlled attention (i.e., attention to goal-relevant task elements) from automatic attentional activation (i.e., attention to distracting or goal-irrelevant task elements). This is largely because controlled and automatic attentional processes are hard to differentiate at the behavioral level. Computational cognitive modeling, however, offers a solution by permitting the decomposition of task performance into component processes that underlie global behavioral effects (Farrell and Lewandowsky, 2018). Nonetheless, despite the promise that computational modeling holds for clarifying the cognitive processes altered through meditation practice, it has been largely underutilized as a methodological approach in this area of research (van Vugt et al., 2019).

Drawing on theory, Ulrich et al. (2015) developed a model that fits interference control tasks by combining motor and decisional processes with superimposed controlled and automatic attentional processes. In this model, controlled attention is modeled as attention to goal-relevant information, and automatic attentional activation is modeled as attention to goal-irrelevant information. More concretely, in the flanker task—a task commonly used to assess interference control—this model considers the central stimulus (i.e., the target stimulus) to be the goal-relevant information, whereas it considers the flanking stimuli (i.e., the distracting stimuli) to be the goal-irrelevant information. The model of Ulrich et al. provides excellent fit to empirical data, and is the only model that can comprehensively account for empirical data from all types of interference control tasks (Servant et al., 2016; Ulrich et al., 2015).[1] The conceptual framework of this model, which we use in this study, is illustrated in Fig. 1.

1.2. Immune effects on cognitive performance

There has been progress in understanding the neural mechanisms associated with meditation-related improvements in executive function (Moore et al., 2012; Moynihan et al., 2013; Slagter et al., 2007; Taren et al., 2017). However, less is known about concomitant physiological processes, such as inflammatory activity, that may mediate these effects. Indeed, recent work suggests that inflammatory activity may exert important influences on executive functions, leading to impairments in interference control (Shields et al., 2017). Higher circulating levels of proinflammatory cytokines, such as interleukin (IL)-6, predict worse interference control (Marsland et al., 2006; Mooijaart et al., 2013; Trollor et al., 2012; Trompet et al., 2008), and reduced gray and white matter in the brain (Hinwood et al., 2013; Satizabal et al., 2012; Tu et al., 2013; Wersching et al., 2010). In contrast, anti-inflammatory cytokines, such as IL-10, predict better interference control (Van Exel et al., 2003). Due to the antagonistic—and sometimes co-activating—effects of pro- and anti-inflammatory cytokines, the ratio of IL-6 to IL-10 is often used as an indicator of overall inflammatory activity, and as a predictor of psychological outcomes (e.g., Dhabhar et al., 2009; Fredericks et al., 2010). Importantly, a higher IL-6/IL-10 ratio has been shown to predict worse interference control (Fabregue et al., 2016).

In addition to its effects on interference control, emerging work suggests that the practice of meditation techniques, including mindfulness meditation, can reduce inflammatory activity (Black and Slavich, 2016; Conklin et al., 2019; Creswell et al., 2016; Pace et al., 2009). These effects have largely been interpreted as resulting from the stress-reducing features of meditative techniques, as well as the socio-environmental contexts (e.g., residential retreats) in which meditation is often practiced (Conklin et al., 2019; see Pascoe et al., 2017, for a meta-analysis). In light of these findings, and of the broader work linking stress processes to inflammatory activity (Slavich and Irwin, 2014), we expect that reductions in inflammatory activity are one pathway through which meditation practice might improve

[1] In particular, it is the only model that can account for "negative-going delta plots"—a term given to the empirical phenomenon that interference effects eventually decrease in slower quantiles of reaction times.

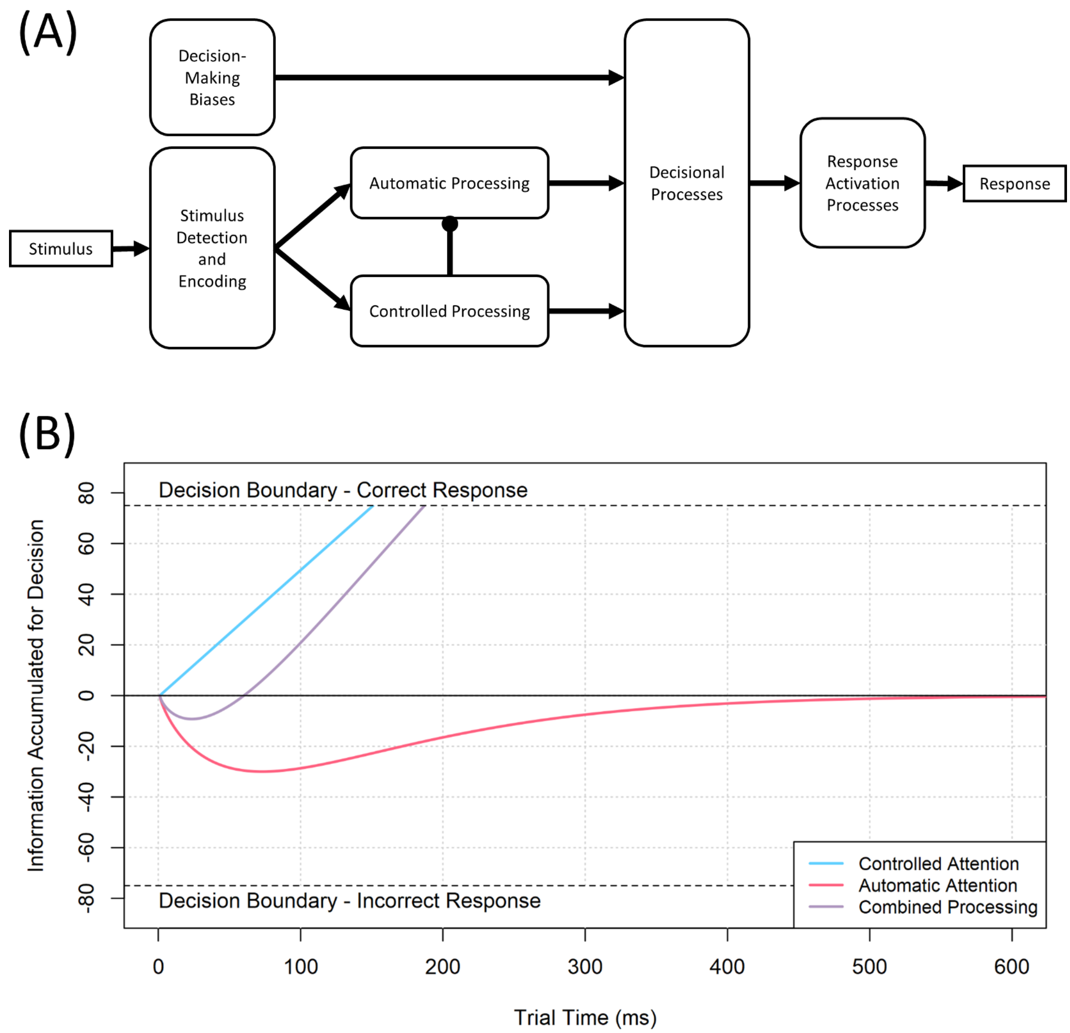

Fig. 1. Theoretical schematic (A) and expected attentional and decisional component values on incongruent trials (B) of the computational model (i.e., the diffusion model for conflict tasks), shown at plausible but arbitrarily specified parameter values. Responses to tasks requiring interference control are modeled as an additive result of the influences of controlled and automatic attentional processes. Note that although this computational model is consistent with the depicted theoretical schematic, this computational model is also consistent with other theoretical perspectives. This figure is based on figures in Ulrich et al. (2015).

interference control. To date, however, no study has tested this hypothesis.

1.3. Current research

We examined the cognitive and immunological mechanisms through which meditation practice might alter interference control. Specifically, we examined the interplay of these processes in the context of an intensive, residential meditation retreat. Residential retreats are a form of meditation training designed to support extended periods of dedicated practice. While on retreat, meditators follow a rigorous schedule of formal practice. This practice is conducted alongside a community of fellow practitioners and under the guidance of experienced teachers. Importantly, retreats can afford methodological advantages for research questions bearing on psychological process or mechanism (King et al., 2019; see also Zanesco et al., 2019). In the present study, we used meditation retreats to study a high dosage of practice, extended across months of training, for the purpose of determining the sensitivity of cognitive and psychobiological outcomes to meditation training.

We conducted a longitudinal, waitlist-controlled experiment examining the effects of intensive concentration meditation. Thirty participants were randomly assigned to a 3-month meditation retreat intervention and 30 participants were assigned to serve as waitlist controls. Later, the waitlist controls completed their own formally identical 3-month retreat intervention. In both groups, interference control was assessed via flanker task performance at mid-intervention (i.e., retreat or control period), after roughly 5 weeks of intensive training or after a 5-week waiting period. Flanker performance was compared between experimental groups (i.e., retreat vs. control) in the first intervention, and within participants (i.e., from waitlist status to active training) at the second intervention. We then used computational modeling to decompose flanker performance into component cognitive processes, thereby providing estimates of controlled and automatic attention. In addition, we longitudinally assessed the ratio of serum levels of the pro-inflammatory cytokine interleukin-6 (IL-6) to the anti-inflammatory cytokine interleukin-10 (IL-10) at the beginning, middle, and end of each retreat.

We had two main predictions. First, we expected that participants in the meditation retreat group would show improved flanker performance relative to waitlist controls. We remained agnostic, however, to whether these improvements would result from relatively stronger controlled attention, relatively weaker automatic attentional activation, or some combination of the two. Our second prediction draws on models of cognitive function that implicate increased low-grade peripheral inflammatory activity in poorer cognitive function (Donzis and

Tronson, 2014; Shields et al., 2017). We hypothesized that poorer controlled attention would be associated with increased low-grade peripheral inflammatory activity prior to and contemporaneous with the interference control assessment across all participants.

2. Methods

2.1. Participants

Volunteers with prior meditation experience were recruited through advertisements in Buddhist print and online publications. We selected participants between 21 and 70 years old who were (a) willing to be randomly assigned to one of two retreat interventions, (b) familiar with intensive meditation practice (having attended at least two 5 to 10 day retreats), and (c) willing to abstain from recreational drugs and tobacco 3 months prior to and during the study, and to abstain from alcohol use during the study. All participants had normal or corrected-to-normal vision and hearing, and no known neurological or Axis I psychiatric impairments (based on the Mini International Neuropsychiatric Interview screen and interview by a licensed clinical psychologist).

Following recruitment (~50% inclusion rate), 30 participants were randomly assigned to an initial retreat group and 30 participants were assigned as waitlist controls. At assignment, the groups were matched on age, sex, handedness, and estimated lifetime meditation practice experience using a stratified matching procedure. Following assignment, we verified that the groups did not significantly differ on a number of trait psychological characteristics including the Big Five Inventory (BFI; John et al., 1991) and the Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006). Of importance for the current analysis, we also confirmed that the groups did not differ in their performance on an inhibitory control task collected prior to group assignment (see Supplemental Material). Descriptive statistics and between-group comparisons on these measures can be found in Table 1. One control participant dropped out between the interventions for reasons unrelated to the study, leaving a sample of 29 participants for the second intervention. All study procedures were approved by the institutional review board of the University of California, Davis. All participants gave full informed consent and were compensated $20 per hour of data collection.

2.2. Training and procedure

The two training interventions took place at a meditation retreat center (Shambhala Mountain Center) in Northern Colorado. Each retreat lasted for 3 months, during which time the training participants lived and practiced meditation onsite at the center. During the first retreat (Retreat 1), participants in the waitlist group continued their daily lives at home but were flown to the retreat center three times (pre-, mid-, and post-retreat) for onsite assessments. Waitlist participants arrived 3 days prior to each assessment to allow for acclimation and adjustment to the retreat environment. Three months after Retreat 1 ended, participants in the waitlist-control group returned to the retreat center to complete their own 3-month meditation retreat.

While on retreat, participants practiced meditation for about 6 to 7 h per day, and met individually once each week with the meditation instructor (B. Alan Wallace). The majority of training consisted of shamatha techniques, which aim to cultivate concentration, attentional stability, and vividness of perception (Wallace, 2006). During shamatha practice, attention is placed on a sensory or mental object, such as the sensations of the breath or the field of arising mental events. While mindfully attending to the object of concentration, the practitioner monitors the quality of their attention, and refreshes focus as necessary. Participants also received ancillary training in the four immeasurables, which aim to promote aspirations of benevolence for oneself and others.

Participants completed an assortment of laboratory tasks as part of their enrollment in the larger intervention (the results from which have been reported elsewhere, e.g., Jacobs et al., 2013; MacLean et al., 2010; Rosenberg et al., 2015; Sahdra et al., 2011). The testing assessments occurred at the beginning (pre), middle (mid), and end (post) of each retreat, and were conducted in two darkened, sound-attenuated field laboratories. Due to logistical constraints, not all measures were assessed at every timepoint. Although blood was taken for cytokine assays at each assessment, the interference control task (i.e., the flanker task) was only completed at the mid-retreat assessment—after about 5 weeks of full-time meditation training and practice.

Table 1
Group Demographics and Participant Characteristics at Pre-assignment.

Variable	Control group (n = 30)	Retreat group (n = 30)	Between-group difference t	p	d
Age	46.4 (15.3)	49.3 (12.7)	0.79	.431	0.20
Females / males	16 / 14	16 / 14	—	—	—
Handedness	28 R, 2 L	29 R, 1 L	—	—	—
Lifetime meditation practice (hours)	2696.5 (3119.0)	2551.4 (2640.7)	0.19	.848	0.05
Big Five Inventory					
Agreeableness	5.47 (0.87)	5.30 (0.87)	0.76	.449	0.20
Conscientiousness	5.19 (0.96)	5.09 (0.84)	0.44	.660	0.11
Extraversion	4.52 (1.06)	4.13 (1.00)	1.47	.147	0.38
Neuroticism	3.21 (0.98)	3.14 (0.85)	0.28	.779	0.07
Openness	5.64 (0.82)	5.73 (0.69)	0.49	.623	0.13
Five Facet Mindfulness					
Awareness	4.75 (1.24)	5.03 (1.00)	0.95	.348	0.24
Describing	5.20 (1.02)	5.36 (1.18)	0.56	.580	0.14
Nonjudging	4.85 (1.28)	5.25 (1.26)	1.22	.227	0.32
Nonreactivity	5.25 (1.06)	5.24 (0.90)	0.04	.970	0.01
Observing	5.52 (0.65)	5.58 (0.86)	0.30	.769	0.08
Baseline cognitive control					
Accuracy (A')	0.90 (0.062)	0.90 (0.072)	$<$ 0.01	$>$ .999	0.00
Reaction time variability (RTCV)	0.30 (0.086)	0.31 (0.084)	0.46	.650	0.12

Note. Means and standard deviations (in parentheses) are displayed for participant characteristics collected at pre-assignment—3 months before the start of the intervention. The control and retreat groups were matched though stratified assignment on age, sex, handedness, and estimated lifetime meditation experience (see also MacLean et al., 2010, Table 1). Item means for subscales of the Big Five Inventory and Five Facet Mindfulness Questionnaire take a range from 1 to 7. Measures of accuracy (A') and reaction time variability (RTCV) are provided from a cognitive control task administered at the pre-assignment baseline (see Supplemental Material). Estimates of lifetime hours were missing for one retreat participant.

2.3. Interference control task

Interference control was assessed using a modified flanker paradigm. Presentation software (Neurobehavioral Systems; https://www.neurobs.com/) was used to deliver stimuli on an LCD monitor (Viewsonic VX-922). Participants were shown an array of five letters, with the center letter being either an X or a Z. The center letters occurred with equal probability across trial types. The four flanking letters were either congruent (e.g., XXXXX) or incongruent (e.g., ZZXZZ) with the center letter.

The task consisted of four blocks of 50 congruent and 50 incongruent trials each (randomized within blocks), for a total of 400 trials. Each trial began with a fixation dot (0 to 1500 ms, sampled from a uniform distribution), followed by the flanker display (100 ms). On each trial, participants pressed the left or right mouse button, respectively, to indicate whether the center letter was an X or a Z.

2.4. Computational modeling

Data from the flanker task were fit to the diffusion model for conflict tasks (DMC; Ulrich et al., 2015), which is a task-general model designed to fit any task with incongruent and congruent trials. The model posits that response selection is driven by superimposed automatic (i.e., bottom-up) and controlled (i.e., top-down) attentional processes. These processes are conceptualized as attentional activation to goal-irrelevant task elements, and intentional attention to goal-relevant task elements, respectively. The automatic attentional process is modeled by the DMC as a scaled gamma function, which begins the trial at zero, reaches a maximum after a short delay, and approaches zero thereafter—following empirical literature showing that task-irrelevant information (e.g., flankers in the flanker task, the meaning of words in the Stroop task) has its strongest effect near trial onset and a lesser effect as a trial continues (Dyer, 1971; Ulrich et al., 2015). The peak amplitude (i.e., the size, A), shape (a), and scale (τ) of this gamma function are fit as model parameters. The controlled attentional process is modeled as a standard Wiener diffusion process with a constant drift rate (μ_c), which indicates the strength of the controlled process (where a higher μ_c indicates stronger controlled attention).

The automatic attentional process decays over time (i.e., approaches zero), whereas the controlled attentional process remains constant (despite random variability). Thus, the predominance of automatic attention early in the decision process gradually shifts to a predominance of controlled attention as time since stimulus onset increases (Ulrich et al., 2015). Once evidence accumulation for a response exceeds a given threshold (i.e., the decision boundary, b), the selected response is encoded into a motor action and is executed during some non-decision time (μ_R), which exhibits trial-to-trial variability (σ_R). The model fits variability in the starting point of this decision process with a parameter describing the shape of the beta distribution of response starting points (α). This parameter is constrained by the decision boundary (b) and reflects the fact that on some trials participants could be primed with a certain response (e.g., by the response given on a prior trial). The standard deviation of the starting point distribution ($\sigma_{\mathbf{X}(0)}$) is calculable given α and b. Fig. 1 depicts a theoretical schematic of the attentional activations and decision boundaries implicated in these processes. The computational model fitting procedure is described in detail in the Supplemental Material. Briefly, the model was fit to trial-level data using cumulative density functions and conditional accuracy functions. Parameter estimates were obtained for each participant through an iterative fitting procedure, and values from the best fitting model were selected as the final parameters for each participant and used in statistical analyses.

2.5. Cytokine assays

Peripheral blood (5 ml) was collected from each participant at an on-site laboratory at the pre-, mid-, and post-retreat assessments. Whole blood was coagulated at room temperature for 30 min in Vacutainer Tubes (Becton Dickinson, Franklin Lakes, NJ). Serum was obtained by centrifugation of whole blood for 15 min at 1100g in a 4 °C refrigerated centrifuge, frozen, and stored at −80 °C for subsequent cytokine quantification.

Serum aliquots were delivered on dry ice to Stanford University for cytokine analysis in the laboratory of Dr. Firdaus Dhabhar. A high sensitivity multiplexed sandwich immunoassay was used to quantify IL-6 and IL-10 concentrations (Mesoscale Discovery, Gaithersburg, MD). The inter- and intra-assay coefficients of variation for each cytokine range from 5 to 10%. The sensitivity for each cytokine was approximately 0.2 pg/ml. IL-6 and IL-10 are commonly assessed pro-inflammatory and immunoregulatory/anti-inflammatory cytokines, respectively. Therefore, we used the ratio of IL-6 to IL-10 as an overall index of inflammatory activity, as has been done in prior studies (Dhabhar et al., 2009; Fabregue et al., 2016). The IL-6/IL-10 ratio was log transformed to correct for skew prior to analyses.

2.6. Data analysis

Following Ulrich et al. (2015), trials with response times shorter than 200 ms or longer than 1200 ms were discarded (0.4% of all trials). All analyses were conducted in **R**, version 3.4.3. The function for simulating DMC trials was coded in **C**++ and called using the Rcpp package, version 0.12.17. The subplex optimization algorithm was called from the subplex package, version 1.5–4. All variables were examined for outliers and values greater than ± 3 SDs from the mean were removed. Reported statistical tests are standard t tests and Pearson correlations.

3. Results

3.1. Preliminary analyses

3.1.1. Inflammatory activity.

We first examined whether levels of inflammatory activity changed as a function of meditation training. For Retreat 1, the ratio of IL-6 to IL-10 was entered into a mixed-model ANOVA with Group (meditation retreat vs. waitlist control) as a between-subjects effect and Time (pre, mid, post) as a within-subjects linear predictor. Surprisingly, the Group × Time interaction was not significant, $F(1, 96.2) = 0.94$, $p = .334$, indicating that participants in the meditation retreat group did not differ from waitlist controls in their trajectories of cytokine changes over the course of the retreat. Nevertheless, the meditation retreat group numerically and linearly decreased in inflammatory activity from the pre-retreat assessment ($M = 0.49$, $SE = 0.19$) to the mid-retreat assessment ($M = 0.24$, $SE = 0.19$), and then to the post-retreat assessment ($M = 0.19$, $SE = 0.19$), $B = -0.147$, $p = .055$ (one-tailed); in contrast, control participants did not (pre-retreat: $M = 0.67$, $SE = 0.18$; mid-retreat: $M = 0.53$, $SE = 0.18$; post-retreat: $M = 0.64$, $SE = 0.19$), $B = -0.021$, $p = .822$. However, the difference in the rate of change between the two groups was not significant, $p = .167$ (one-tailed).

There were no decreases in inflammatory activity among the waitlist participants when they later received their own intervention in Retreat 2, $B = 0.11$, $p = .434$.[2] The means for the waitlist participants during their intervention in Retreat 2 were as follows: pre-retreat $M = 0.59$, $SE = 0.26$; mid-retreat $M = 0.65$, $SE = 0.25$, post-retreat $M = 0.81$, $SE = 0.26$.

[2] These null effects of retreat on inflammatory activity were also present when IL-6 and IL-10 were analyzed separately, instead of their ratio used in our main analyses.

3.1.2. Flanker performance.

We first examined whether the meditation retreat and waitlist-control groups differed in their overall flanker performance (i.e., incongruent RT – congruent RT) at the mid-assessment of Retreat 1. The effect of group on flanker interference was not significant, $t(58) = 0.60$, $p = .549$, $d = 0.16$. The mean interference effects for the retreat and control groups were 29.67 ms and 27.07 ms, respectively (*SE*s = 2.55 and 3.46). We then tested whether the waitlist controls changed in flanker performance from the mid-retreat assessment of Retreat 1 to the mid-retreat assessment of Retreat 2 (as active training participants). Although the waitlist-control participants' mean interference effect decreased numerically when they entered their own retreat (Retreat 2 interference effect: $M = 23.00$, $SE = 3.30$), this change was not statistically significant, $t(28) = 1.32$, $p = .196$, $d_z = -0.25$.

A different pattern emerged for response errors. For Retreat 1, the meditation retreat group made marginally fewer errors on congruent trials ($M = 2.27$, $SE = 0.51$) than did the control group ($M = 3.70$, $SE = 0.66$) at the mid-retreat assessment, $t(58) = 1.73$, $p = .089$, $d = 0.45$. Moreover, the waitlist-control group decreased in errors made on congruent trials from the first to the second retreat ($M = 2.34$, $SE = 0.48$), $t(28) = 2.44$, $p = .021$, $d_z = 0.45$. For incongruent trials, the meditation retreat group ($M = 3.53$, $SE = 0.80$) committed numerically fewer errors than the control group ($M = 5.33$, $SE = 0.91$) in Retreat 1; however the two groups did not differ significantly, $t(58) = -1.49$, $p = .143$, $d = 0.38$. In Retreat 2, the waitlist-control group did significantly decrease in errors made on incongruent trials from the first to the second retreat ($M = 3.55$, $SE = 0.93$), $t(28) = 2.40$, $p = .023$, $d_z = 0.45$.

3.2. Primary analyses

Flanker interference effects and errors can result from weak top-down attentional control, strong bottom-up attentional activation, or a preference for speed in the speed/accuracy tradeoff. This entails that differential effects of meditation on these processes could mask effects on interference control at the behavioral level. Thus, we analyzed the effects of the meditation intervention on underlying processes contributing to performance on the flanker task, estimated via computational modeling.

3.2.1. Computational modeling.

The diffusion model for conflict was an excellent fit to the data, explaining over 99% of variance in the response time and accuracy distributions (see Fig. 2). We found that three modeled parameters, indexing two cognitive processes, differed between the meditation and control groups in Retreat 1. Table 2 lists the parameter estimates and significance values for different attentional subcomponents derived from the computational model. First, the meditation retreat group showed stronger controlled attention than did the waitlist-control group, $t(58) = 2.48$, $p = .016$, $d = 0.64$ (see Fig. 3a). Second, the groups differed on two components of the automatic attention gamma function, $ps \leq 0.001$, such that the retreat group participants had greater total automatic attentional activation, $t(58) = 2.16$, $p = .035$, $d = 0.56$ (Fig. 3b). No other estimated parameters differed significantly between the groups, $ps \geq 0.087$.

For waitlist controls, we found that controlled attention increased from the first retreat (when they served as control participants) to the second retreat (when they engaged in intensive training), $t(28) = 3.56$, $p = .001$, $d_z = 0.66$ (see Fig. 3c). However, total automatic attentional activation did not change from the first to the second retreat, $t(28) = 0.13$, $p = .896$, $d_z = 0.02$, although it increased numerically. Thus, the training-induced effect of greater controlled attention *between groups* in Retreat 1 replicated *within group* in the second intervention, whereas the automatic attentional activation effect did not. No other parameter significantly changed in waitlist participants from the first to the second retreat (Table 2).

3.2.2. Associations between inflammatory activity and estimated parameters.

Drawing on theoretical perspectives which contend that inflammatory activity may itself exert effects on cognitive processes, we next examined whether inflammatory activity, as indexed by the ratio of IL-6 to IL-10, was associated with the estimated model parameters (see Table 3). We correlated the IL-6/IL-10 ratio at the mid-retreat assessment in each retreat with the attentional model parameters derived from flanker task performance measured at this same assessment. As hypothesized, inflammatory activity measured contemporaneously with flanker assessment was significantly associated with poorer controlled attention across all participants in the first retreat, $r(50) = -0.31$, $p = .023$ (Fig. 4a), as well as in the second retreat, $r(24) = -0.46$, $p = .019$, (Fig. 4b).[3] Moreover, these associations held while controlling for age, sex, and BMI, $ps < 0.045$. No other model parameter was significantly associated with inflammatory activity in either retreat (see Table 3).

Finally, we investigated the temporal priority of these associations, by examining (1) whether inflammatory activity at the beginning of retreat (at the pre-retreat assessment) predicted controlled attention (at the mid-retreat assessment, about 5 weeks after the pre-retreat assessment), and (2) whether mid-retreat controlled attention predicted inflammatory activity at the end of retreat (at the post-retreat assessment). Consistent with the idea that inflammatory activity impairs executive cognitive processes, we found that pre-retreat inflammatory activity predicted worse controlled attention at mid-retreat across all participants during Retreat 1, $r(47) = -0.31$, $p = .030$. And, importantly, this pattern was replicated in the second retreat, in which pre-retreat inflammatory activity also predicted worse mid-retreat controlled attention, $r(22) = -0.44$, $p = .031$. Controlled attention at the mid-retreat assessment, however, did not predict inflammatory activity at the end of retreat in Retreat 1, $r(45) = -0.23$, $p = .126$, or in Retreat 2, $r(23) = -0.29$, $p = .148$. Although temporal inferences should be drawn with caution given our sample size, our results suggest a significant association between inflammatory activity and controlled attention when inflammatory activity is assessed prior to or contemporaneously with performance, but not when inflammatory activity is assessed after cognitive performance. This pattern of results could therefore be taken to suggest that inflammatory activity may affect controlled attention to a relatively greater degree than controlled attention may affect inflammatory activity—at least in the timescale of this study.

4. Discussion

Meditation training has generally been associated with better performance on tasks designed to assess executive attention (e.g., Gallant, 2016; MacLean et al., 2010; Moore et al., 2012). Nevertheless, the cognitive effects of practicing meditation are still relatively unclear, as numerous cognitive processes contribute to behavioral outcomes of task performance, and different styles of meditation may impact separable neurocognitive systems in different ways (Lutz et al, 2015). Further, the biological mechanisms underpinning these effects are largely unknown. In this study, we aimed to elucidate these processes by examining the effects of meditation practice on flanker task performance, its component cognitive processes, and its associations with inflammatory

[3] We chose to conduct analyses across all participants because of our prediction, drawn from prior theory, that inflammatory activity would influence cognitive performance regardless of group. When the groups were examined separately, correlation coefficients with controlled attention within each group (training $r = -0.23$; waitlist-control $r = -0.33$) were similar to the coefficient across all participants ($r = -0.31$), and the association between inflammatory activity and controlled attention did not differ between groups, $t(48) = 0.32$, $p = .75$.

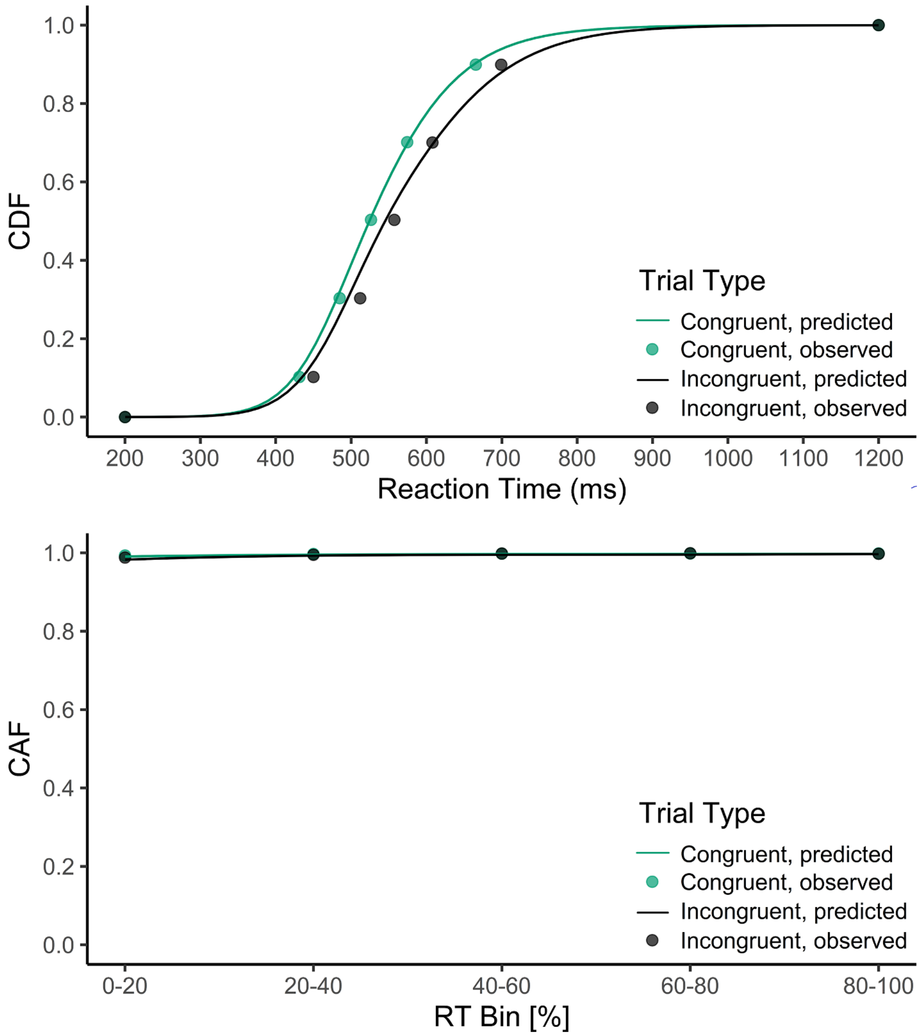

Fig. 2. Model fit across participants' Vincentized distributions. The model was an excellent fit to the data, explaining 99.9% of the variance in the cumulative distribution function (CDF) and 99.6% of the variance in the conditional accuracy function (CAF).

activity. We found that participants randomly assigned to a meditation retreat showed significantly greater controlled attention and total automatic attentional activation than an experience-matched waitlist-control group after 5 weeks of full-time practice and training. Further, the waitlist-control group subsequently improved in controlled attention when they completed their own intensive training in a second retreat. We also found that inflammatory activity—indexed as the ratio of IL-6 to IL-10—was significantly associated with controlled attention across all participants in both interventions.

The most consistent and robust result was the improved strength of controlled attention as a function of meditation retreat (i.e., the drift rate of the superimposed controlled process; Ulrich et al., 2015). This result was observed cross-sectionally in the experimental manipulation of the first intervention, as well as longitudinally across the first and second interventions. Thus, the strengthening of controlled attention appears to be a reliable effect of intensive meditation training that

Table 2
Parameter Estimates from the Diffusion Model for Conflict Tasks.

	Meditation Retreat	Waitlist: Control	Between Groups	Between Groups	Waitlist: Retreat	Within Group	Within Group
Parameter	Mean (*SD*)	Mean (*SD*)	*p*	*d*	Mean (*SD*)	*p*	d_z
Strength of controlled attention (μ_C)	0.522 (0.07)	0.468 (0.09)	**.016**	0.64	0.563 (0.15)	**.001**	0.66
Size of automatic attention function (A)	11.28 (5.33)	11.20 (5.40)	.958	0.01	12.41 (6.94)	.195	0.25
Scale of automatic attention function (*a*)	2.24 (0.74)	3.66 (1.23)	< **.001**	1.40	3.19 (0.97)	.075	-0.34
Peak latency of automatic attention function (t)	162.43 (105.08)	83.62 (68.21)	**.001**	0.89	67.32 (50.38)	.290	-0.20
Total automatic attentional activation (AUC)	4498.7 (3102.6)	3007.2 (2178.1)	**.035**	0.56	3113.5 (2940.7)	.896	0.02
Decision boundary (*b*)	68.36 (18.75)	71.02 (20.09)	.599	-0.14	65.88 (21.32)	.475	-0.13
Mean nondecision time (μ_R)	425.06 (58.43)	399.35 (55.83)	.087	0.45	414.66 (55.96)	.108	0.31
Nondecision time variability (s_R)	53.17 (19.53)	49.82 (17.62)	.488	0.18	48.08 (15.76)	.667	-0.08
Variability in starting point ($s_{X(0)}$)	26.98 (24.90)	31.39 (22.26)	.472	-0.19	29.44 (25.84)	.953	-0.01

Note: Waitlist – Control denotes the Waitlist group during Retreat 1 (prior to their own meditation intervention), whereas Waitlist – Retreat denotes the same Waitlist group during Retreat 2. Between Groups *p* denotes the test of Meditation Retreat – Waitlist Control, whereas Within Group *p* denotes the test of Waitlist Retreat – Waitlist Control. Total automatic attentional activation represents the area under the curve for the automatic attention function.

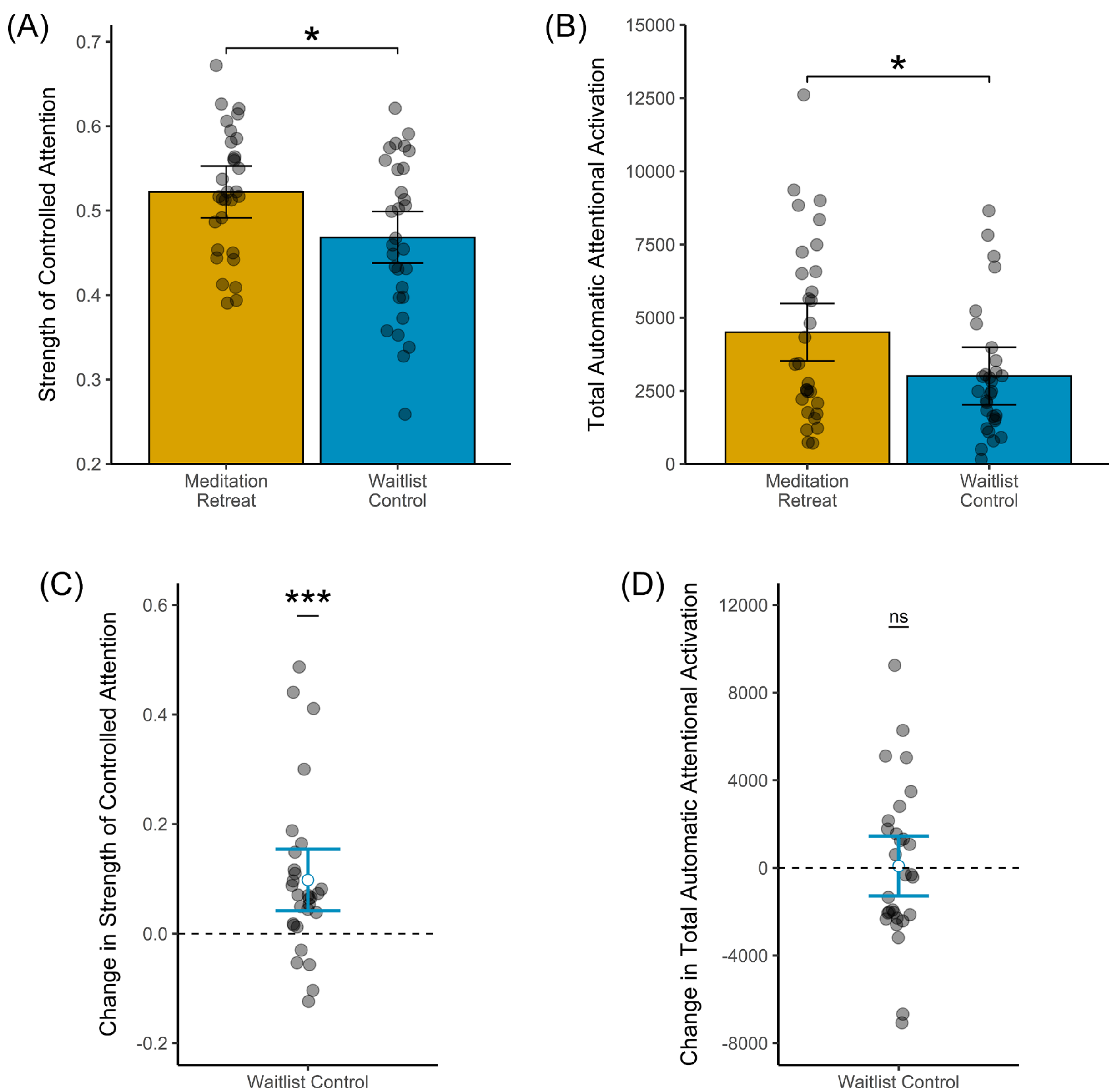

Fig. 3. Effects of retreat on attention. Participants randomly assigned to the retreat group evidenced greater controlled attention (A) and automatic attentional activation (B) than participants assigned to the waitlist-control group during Retreat 1. Similarly, participants assigned to the waitlist-control group significantly improved in controlled attention from their waitlist assessment to their Retreat 2 assessment (C); however, waitlist-control participants did not differ in automatic attentional activation between assessments (D). Error bars illustrate 95% confidence intervals. $^{*}p \leq 0.05$, $^{***}p \leq 0.001$.

Table 3
Correlations between Inflammation and Model Estimates.

	Time 1 (N = 60)	Time 2 (N = 29)
Parameter	r	r
Strength of controlled attention (μ_C)	−.314*	−.458*
Size of automatic attention function (A)	−.327*	−.248
Scale of automatic attention function (a)	.205	.161
Peak latency of automatic attention function (τ)	−.030	−.054
Total automatic attentional activation (AUC)	−.213	−.080
Decision boundary (b)	.102	.082
Mean nondecision time (μ_R)	.050	.090
Nondecision time variability (σ_R)	.049	.005
Variability in starting point ($\sigma_{X(0)}$)	.069	.056

Note: $^{*}p < .05$. Correlations are between the IL-6/IL-10 ratio and each respective parameter estimate.

emphasizes the cultivation of concentration and vivid and stable qualities of attention (i.e., shamatha). These results raise the possibility that some of the observed improvements in cognitive function in past meditation studies (e.g., Gallant, 2016; MacLean et al., 2010), may be attributable, in part, to improvements in controlled attention—though attentional sub-processes were not explicitly modeled in these studies.[4]

We also found that worse controlled attention was associated with a greater inflammatory burden at a contemporaneous assessment across all participants in both retreats. These findings support existing theories that implicate inflammatory activity in weaker cognitive abilities (McAfoose and Baune, 2009; Shields et al., 2017). We further found that higher inflammatory activity measured at the first assessment was associated with worse controlled attention several weeks later at the second (mid-retreat) assessment. This was true across all participants,

[4] For neural data supporting this idea, see Moore et al. (2012), Taren et al. (2017), and Zanesco et al. (2019).

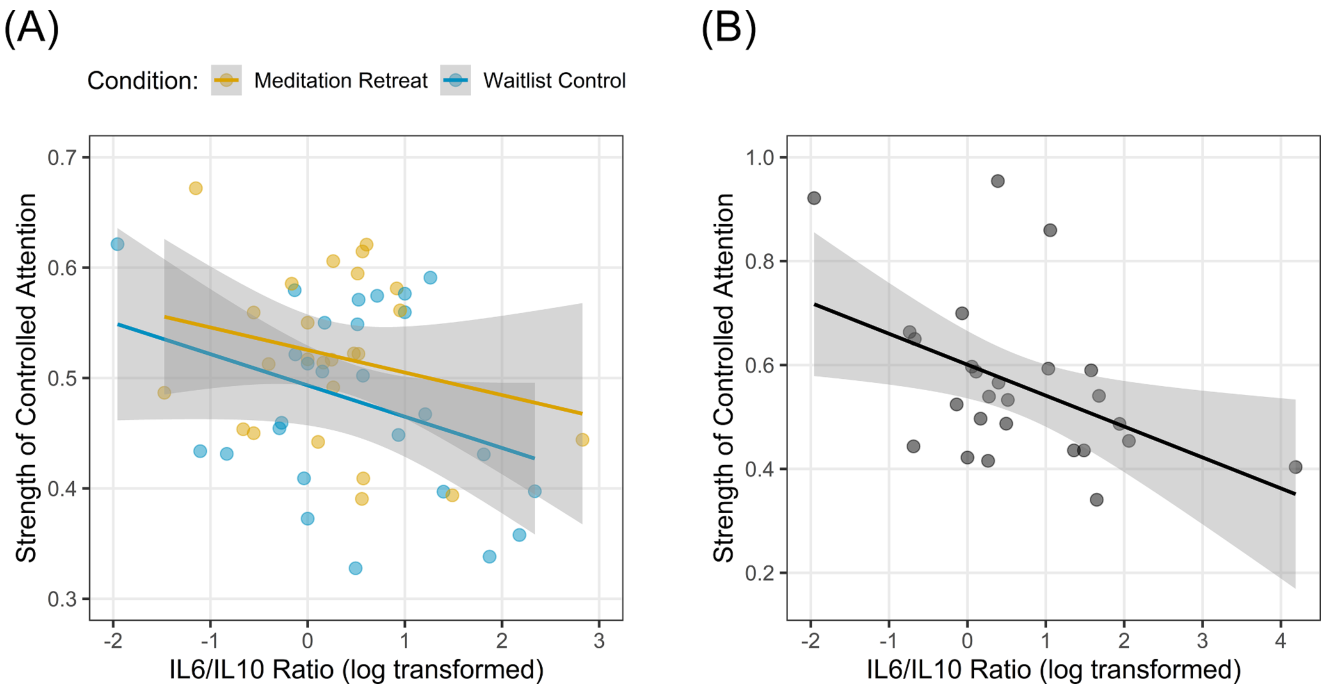

Fig. 4. Associations between inflammatory activity and controlled attention during Retreat 1 (A) and Retreat 2 (B). Inflammatory activity was significantly and inversely associated with controlled attention at each retreat.

and in both interventions. Conversely, levels of controlled attention were not significantly associated with subsequent inflammatory activity. These results support the idea that high levels of inflammatory activity may impair executive function (Trompet et al., 2008; Yang et al., 2018). They provide less support for the idea that higher levels of executive function may lead to reduced inflammatory activity (Hostinar et al., 2015).

Although inflammatory activity was associated with poorer controlled attention across all participants, shamatha meditation retreat did not appear to significantly influence inflammatory activity. While active retreat participants in the first intervention showed a numeric reduction in inflammatory activity, this change did not reach statistical significance and did not replicate in the second retreat. Given prior work suggesting that meditation interventions can reduce inflammatory activity (e.g., Pace et al., 2009), and that inflammatory activity can impair cognitive processes (e.g., Shields et al., 2017), we expected that reductions in inflammatory activity would be one pathway through which our training would influence attentional processes. This prediction was not supported by the results of the current study. Rather, the observed constellation of findings suggest that shamatha meditation and inflammatory activity may relate to controlled attention through independent pathways. It also possible that a larger sample size is necessary to capture meditation-related changes in inflammatory activity.

Interestingly, we also observed a group difference in model estimates of automatic attentional activation, with higher values of overall activation among retreat participants, as compared to waitlist controls, in the first intervention. This finding is consistent with reports of enhanced sensory processing in experienced meditators (e.g., Antonova et al., 2015; Zanesco et al., 2019, from this same study sample), and suggests that engaging in meditation in a retreat environment may lead to enhanced processing of both goal-relevant (modeled as controlled attention) and goal-irrelevant (modeled as automatic attention) task elements. Thus, when practiced intensively, meditation may promote a general increase in the sensory processing of, and attentional response to, *all* task stimuli, regardless of goal-relevance. This pattern, however, did not replicate in our second intervention, when waitlist participants returned to complete a 3-month training intervention. For a discussion of the relationship between automatic and controlled attention in the fitted data, see Supplemental Material.

There are at least two possible explanations for the discrepancy we found in between- and within-subjects effects on automatic attentional activation. First, it could be that meditation actually does increase automatic attentional activation, but that practice effects led to a decrease in task-specific automatic attentional activation among waitlist participants over time. On the one hand, it is thought that meditation training can increase the perceptual awareness (i.e., automatic attentional activation) of visual task stimuli (MacLean et al., 2010, from this same study sample; Naranjo and Schmidt, 2012); on the other hand, it has been shown that completing a conflict task (such as the flanker) on separate testing occasions can reduce automatic attentional activation from irrelevant stimuli (Dulaney and Rogers, 1994). As such, it is possible that meditation training increased automatic attentional activation in both retreats, but that task practice decreased it among waitlist participants completing the task for a second time, leading to an overall null effect for the change in automatic attentional activation in the second intervention. An alternative explanation is that the group difference in automatic attentional activation in Retreat 1 was a spurious finding. The current data cannot directly address these possibilities. Further research should attempt to clarify discrepancies in outcomes of automatic attentional activation in meditation interventions of varying intensities, styles, and practice traditions.

By focusing our investigation on intensive meditation interventions, we were able to determine the plausible locus of effects of concentrative meditation practice on interference control and its relation to inflammatory activity. Nevertheless, we can only speculate as to *why* the meditation retreat, considered as a holistic training intervention (King et al., 2019), led to the observed effects. One possibility is that the meditation retreat may have reduced stress. There is strong evidence demonstrating that stress impairs controlled attention (Arnsten, 2015; Mather and Sutherland, 2011; Sänger et al., 2014; Shields et al., 2016; though see Shields et al., 2019), and that reducing stress may contribute to improvements in executive function (Diamond and Lee, 2011; Gothe et al., 2016; Moynihan et al., 2013; Walter et al., 2010). Meditation training—considered across a range of practice styles and intervention types—is thought to serve a stress-reducing function (Conklin et al., 2019; Creswell and Lindsay, 2014; Kabat-Zinn, 1982; Moynihan et al., 2013). In a residential retreat context, these effects are compounded by removing participants from many of the primary stressors of daily life. Our finding that inflammatory activity—which is upregulated by stress—was inversely related to controlled attention could be taken to support the idea that meditation may enact improvements in controlled attention in part by reducing stress levels. However, it is important to note that the meditation intervention did not reduce inflammatory activity in this study, which is inconsistent with the idea that meditation improves controlled attention via a stress-reduction pathway.

Our study was designed to clarify the global effects of intensive concentrative meditation training on cognitive and biological processes underpinning interference control. An interesting and related issue, which we cannot presently address, pertains to the developmental trajectories of meditation training on attentional processes. The outcomes of any given meditation intervention are likely modulated by a number of design features, including the intensity and duration of the training program, and individual differences in practitioner experience (King et al., 2019). Because the effects of a concentrative meditation retreat on attentional processes could vary based on any one of these factors, there is need to assess the effects of meditation interventions at various levels of these variables. Similarly, we cannot know if our results will generalize to other classes of meditation training. Indeed, prior work has shown that although open monitoring meditation and focused attention meditation both enhance executive control, open monitoring practice—which takes the ongoing flow of experience, rather than a specific object, as its focus—additionally enhances attentional orienting (Tsai and Chou, 2016). Presumably, shamatha meditation, with its strong object orientation (Lutz et al., 2015), would be expected to enhance controlled attention in a manner similar to how regularly practicing self-regulation is thought to improve self-regulatory abilities (Hofmann et al., 2012; Muraven and Baumeister, 2000). An open question is whether other forms of meditation, particularly those incorporating a weaker object orientation, similarly enhance controlled attention, and whether they exert effects through complementary cognitive pathways.

4.1. Strengths and limitations

This study has numerous strengths, including an experimental manipulation of intensive meditation practice, a mixed design including both between-groups and longitudinal comparisons, and statistical methods that allowed us to decompose target outcomes into component cognitive processes of interest. There are also a number limitations that should be noted. First, the sample size was relatively modest, making our null results susceptible to type II errors. Indeed, effect sizes from our non-significant comparisons ranged from small to moderate. Second, we lacked an assessment of interference control at the beginning of training, so were unable to assess changes in controlled attention over the course of the retreat. Third, our sample included individuals with extensive prior meditation experience. As mentioned above, the effects of meditation likely differ between individuals who have acquired some expertise in meditation and those who have not (see also Lutz et al., 2015), potentially limiting the generalizability of our results to experienced meditators. Finally, we recently demonstrated the partial maintenance of improvements in sustained attention and response inhibition over a 7 year period in these same participants (Zanesco et al., 2018). However, the current data did not include a follow-up assessment after the intervention, and thus we cannot directly address the persistence of changes in controlled attention or the role of inflammatory activity in these effects.

5. Conclusion

We found that participants randomized to an intensive concentration meditation retreat demonstrated better controlled attention than did a waitlist-control group. We also found that the waitlist-control group improved in controlled attention after later completing their own intensive training intervention. Although inflammatory activity was not modulated as a function of the retreat intervention, inflammatory activity was inversely associated with controlled attention across participants and conditions, providing further evidence that inflammatory activity may impair top-down cognitive processes. Our findings suggest that concentration meditation works to improve interference control task performance, and perhaps cognitive performance more broadly, by increasing top-down control—rather than by decreasing bottom-up interference—and that these cognitive effects are related to levels of inflammatory activity.

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Appendix A. Supplemental material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2020.06.034.

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