

LOVING-KINDNESS MEDITATION'S EFFECTS ON NITRIC OXIDE AND PERCEIVED WELL-BEING: A PILOT STUDY IN EXPERIENCED AND INEXPERIENCED MEDITATORS

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Background: Meditation is associated with lower blood pressure, but little is known about how loving-kindness meditation affects nitric oxide (NO) metabolism, a key mediator of cardiovascular physiology associated with vasodilation.

Methods: We studied seven inexperienced and five experienced healthy meditators at one study visit, after they refrained from eating nitrate-rich foods for at least 12 h. Participants completed questionnaires on demographics and meditation practices. We measured nitrite and nitrate and self-reported stress at baseline, after a neutral reading period (prior to meditation), immediately after, and 10 min following a standardized 20-min loving-kindness meditation.

Results: The 12 subjects had a mean age of 51 years, and two were male. Stress was significantly lower at baseline in the experienced group (15 vs. 49 on 100 point scale, $P < .05$) as was heart rate (HR) [68.1 ± 0.5 beats per minute (bpm) vs. 73.4 ± 0.7 bpm, $P < .05$]. Stress levels fell significantly with meditation (52 vs. 11, $P < .05$), while relaxation increased (55

vs. 89, $P < .05$) in the inexperienced group. Plasma nitrite levels were not significantly higher, but nitrate levels were more than twice as high ($P < .05$) for experienced vs. inexperienced meditators before and after loving-kindness meditation.

Conclusion: Loving-kindness meditation is associated with stress reduction in inexperienced meditators. Experienced meditators had higher nitrate levels, trended toward having higher nitrite levels, and had significantly lower stress levels than inexperienced meditators. Nitric oxide metabolism may be involved in the cardiovascular effects of persistent meditation practice. Larger longitudinal studies would be fruitful to better understand the mechanisms involved.

Key words: Compassion, meditation, nitric oxide, relaxation, cardiovascular

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INTRODUCTION

Meditation is commonly practiced for both spiritual and health purposes.^{1,2} Meditation encompasses a heterogeneous group of practices, e.g., sitting practices such as mindfulness

practices and the relaxation response and moving practices such as yoga.³ Despite this diversity, most meditation practices include training attention and developing a neutral cognitive/emotional perspective of acceptance and nonattachment to outcomes. These practices are associated with physiologic effects on the central and autonomic nervous systems, cognition, perceptions of pain, mood, and lower blood pressure.^{4–18} However, few studies have explored the effect of meditation on nitric oxide (NO) bioavailability, which is a key mediator of cardiovascular physiology.^{19–21} One study showed that experienced Zen meditators had higher levels of serum nitrate + nitrite than age-/gender-matched subjects who did not meditate, but this study has not been replicated for other types of meditation.²⁰

Direct detection of NO is difficult due to its reactivity and fast conversion into nitrite, nitrate, and nitrosothiols in the blood.^{22–24} Therefore, measurements of NO metabolites such as nitrite and nitrate are often done.²⁵ NO reacts rapidly with hemoglobin inside red blood cells to form nitrate.²⁶ Plasma nitrate concentrations are influenced by a number of factors including dietary intake, saliva production, bacterial synthesis

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in the bowel, inhalation of nitrogen oxides, and renal function, diminishing the ability to use nitrate measurements to differentiate between these factors and changes in NO bioavailability.^{27,28} Because plasma nitrate concentrations are nearly 100 times higher than plasma nitrite concentrations, the common measure of the sum of the two effectively only measures nitrate. Thus, measures of the sum of nitrite and nitrate as a function of meditation (as used in earlier research) cannot conclusively be interpreted in terms of NO bioavailability.²⁰ Instead, changes in plasma nitrite concentration directly relate to NO bioavailability, indicating that plasma nitrite is a better marker for NO bioavailability.²⁷

One type of meditation, which is the subject of growing research, is loving-kindness meditation.²⁹ This practice deliberately cultivates a sense of good will, loving-kindness, or compassion toward oneself and others. Preliminary studies suggest that loving-kindness meditation, like other sitting and moving practices, has physiologic and clinical effects.^{30–41} However, we were unable to find studies exploring compassion meditation's effects on NO bioavailability. Such studies would be useful to inform clinical research on compassion meditation in patients with cardiovascular disease.

The purposes of this study were to determine the feasibility of measuring self-reported well-being and NO in experienced and inexperienced meditators, replicate earlier observation of higher nitrate among experienced meditators compared with inexperienced or non-meditators, and assess differences in measures between control states before and after compassion meditation to begin to understand the causal relationship for differences in physiologic parameters in experienced and inexperienced meditators.

METHODS

This pilot study was conducted in the Clinical Research Unit (CRU) at the Wake Forest University School of Medicine during July and August 2012. Each subject served as his/her own control for a single study visit. Subjects were recruited by email from a convenience list of colleagues at the University known to have an interest in meditation or physiology research. The recruitment email contained a link to a Research Electronic Data Capture (REDCap) screening survey to determine eligibility. Eligibility was confirmed in a telephone interview with the study coordinator. Subjects were eligible if they were 18 years or older, willing to come to the CRU for the study, have blood drawn, complete study questionnaires, practice a specific type of loving-kindness meditation for 20 min during the study, and abstain from vigorous exercise and nitrate containing foods in the 12 h prior to the study visit. Subjects were eligible if they reported either less than 10 h of meditation practice in the previous three months and less than 100 h of lifetime meditation practice (inexperienced meditators) or more than 300 h of lifetime meditation experience (experienced meditators). Subjects were ineligible if they reported having cardiovascular disease, hypertension, autoimmune disorders, cancer, or regularly used beta-blocking medications or nitrate medications. Subjects received free parking and a \$20 gift card in recognition of their volunteering for the 90-min study visit. The study was

approved by the Wake Forest University Health Sciences Institutional Review Board (IRB).

Study Procedure

When a subject arrived at the CRU, she/he was greeted by the study coordinator who escorted him/her to a private room, confirmed eligibility, and administered informed consent. Subjects sat in a comfortable chair while completing study questions online for approximately 30 min. Study questions included demographic (age, gender, and race/ethnicity); types and amount of sitting and moving meditation experience; a widely used empathy measure, the 28-item Interpersonal Reactivity Index (IRI) (which has four subscales for fantasy, perspective-taking, empathic concern, and personal distress)^{42–50}; the 24-item Compassion Scale (for which we analyzed the three positive subscales for kindness, common humanity, and mindfulness)⁵¹; the 15-item internationally used Mindful Attention Awareness Scale (MAAS)^{52–58}; and three 100-mm visual analog scales for stress, relaxation, and peacefulness which we used in earlier studies.^{37,59}

A CRU nurse then entered the study room to insert an intravenous catheter to collect blood specimens to measure plasma nitrate and nitrite as biomarkers of nitric oxide bioavailability. Less than 2 cc of blood was collected for each blood draw: after the 10-min control period (reading), immediately after the 20-min intervention (compassion meditation), and 10 min after the intervention. Specimens were labeled, transported within 20 s to a centrifuge, and spun down at 4000 rotations per minute (rpm) for 3 min. The plasma was removed, frozen on dry ice, and stored at -80°C for later analysis.

After the study nurse placed the intravenous catheter, the study coordinator instructed the subject to read from a standard text (*Mindsight* by Daniel Siegel) for a 10-min resting control period. Subjects were then asked to complete the three visual analogue scale (VAS) measures and had blood drawn before the study intervention.

The study intervention consisted of a standard loving-kindness meditation practice. Subjects were given a card with four statements (Figure 1). Subjects were asked to silently repeat one sentence per breath for a cycle of four breaths and to repeat the cycle continuously for 20 min. When subject's minds wandered, they were instructed to return to the sequence of four statements coupled with breathing.

Following the study intervention, subjects were again asked to complete the three VAS measures and had their blood drawn. They were then invited to rest silently in the study room for 10 min, abstaining from using cell phones, text, email, etc. Following the 10 min of rest, subjects again completed the three VAS measures and had a final blood draw.

Compassion Meditation for the Study Visit

1. May all beings be safe and secure.
2. May all beings be healthy and comfortable.
3. May all beings be happy and peaceful.
4. May all beings be free from suffering and its causes.

Figure 1. Compassion meditation for the study visit.

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