

Title: Endocannabinoid and BDNF Associated with Positive Month Long Psychological Changes with a 4-day Intense Guided Meditative Retreat

Introduction: It is widely accepted that meditation has positive effects – particularly for reducing stress and anxiety. Additionally, there have been instances where people have described intensely peaceful and blissful experiences associated with meditation. There have been many anecdotal instances in Bhava Spandana Program (BSP), a 4-day advanced meditation retreat offered by Isha Foundation. This program has been conducted for >30 years under the careful guidance of a recognized spiritual master and yogi, Sadhguru. Previous BSP participants have reported feelings of blissfulness, ecstasy, intense happiness, inclusive perception and higher states of consciousness during and after the program. For this study, we wish to objectively measure participant responses on their experiences of the program. We want to correlate this to objective biomarker data. For the purpose of this study, we chose to focus on the endocannabinoid system. Endocannabinoids, such as anandamide, have shown to be linked to enhanced mood and feelings of blissfulness. This study aims to show if the endocannabinoid system is involved in the positive mood responses mentioned in the meditation retreat. Finally, this study assesses the longer term impact on participants’ well-being one month after the retreat.

Methods: After obtaining IRB approval and written informed consent, adults participating in a 4-day meditation program held at Isha Institute of Inner Sciences, McMinnville, TN were studied.

Surveys: Participants were invited to participate in extensive online surveys within 2 weeks before and after the meditation program. The online surveys included validated scales for depression (*20-items Center for Epidemiologic Studies Depression Scale (CES-D)*), anxiety (*8-item Emotional Distress – Anxiety – Short Form*), 15 item Mindful Attention Awareness Scale (MAAS) and 42-item Ryff’s Psychological Well-Being Scale (PWB) and a 0-10 happiness scale. Paired t-tests are used to analyze the data. One to two month post- BSP surveys were closed on January 2, 2018; and the results are being analyzed to study persistent benefits of BSP.

Biomarkers: In addition, before and after meditation blood levels of objective biomarkers including endocannabinoids including anandamide and brain derived neurotropic factor (BDNF) were analyzed in 142 participants to explain neurobiological mechanisms of bliss/happiness, psychological benefits and higher levels of consciousness.

Results:

Surveys: 370 BSP meditation participants completed pre and post meditation online surveys in October 2017. Statistically significant ($p < 0.0001$) reductions in anxiety and depression scores, improvement in happiness score, improvements in psychological well-being and in mindful attention and awareness were observed after meditation compared to baseline pre-meditation levels (Table 1).

Table 1. Before and after BSP psychological survey responses

Psychological Scales	N	Pre-Meditation	Post-Meditation	p-value
Depression Scale - CESD	323	9.9 ± 8.7	7.4 ± 5.8	<.0001
Anxiety Scale	310	1.9 ± 0.8	1.5 ± 0.6	<.0001
Mindful Attention & Awareness Scale	319	4.1 ± 1.0	4.8 ± 0.8	<.0001
Happiness Score	309	6.2 ± 1.8	8.2 ± 1.4	<.0001
Psychological Well-being (PWB) Total Score	310	188.0 ± 27.2	203.2 ± 20.9	<.0001
PWB Autonomy	310	30.2 ± 6.4	33.2 ± 5.9	<.0001
PWB Environmental Mastery	310	28.6 ± 5.0	30.9 ± 4.5	<.0001
PWB Personal Growth	310	35.4 ± 5.2	37.3 ± 4.2	<.0001
PWB Positive Relations	310	32.0 ± 6.2	34.9 ± 5.5	<.0001
PWB Purpose in Life	310	30.4 ± 5.5	32.2 ± 4.9	<.0001
PWB Self-Acceptance	310	31.4 ± 6.9	34.8 ± 5.3	<.0001

Biomarkers: Before and after meditation objective blood biomarker levels, mainly endocannabinoids and BDNF were analyzed in 142 participants. Compared to baseline pre-BSP levels, all post-BSP biomarker levels were significantly higher. Anandamide, the main endocannabinoid, responsible for bliss and joy increased significantly; in certain participants many fold increases were observed after BSP; these findings underpin experienced and survey observed happiness and wellbeing after BSP. We found similar changes with BDNF after BSP explaining better overall focus and attention observed with surveys.

In addition to pre vs. post BSP biomarker comparisons, we looked at proportion of participants with >10% change in levels. The findings suggest there are inter-individual variations in objective biomarkers, similar to their experiences and happiness levels. Some of our future genetic, epigenetic and gene expression studies hopefully will explain mechanistic aspects of these variations (Table 2).

Table 2. Before and after BSP blood chemical (biomarker) changes

Endocannabinoid	N	Pre-BSP	Post-BSP	Change	p-value	Participants (%) with >10% increase after BSP
Anandamide	142	0.58 (0.16)	0.75 (0.21)	0.17 (0.22)	<.0001	71%
2-AG	142	2.2 (1.6)	4.2 (3.1)	2.0 (2.8)	<.0001	75%
1-AG	142	4.4 (3.3)	14.3 (11.3)	9.8 (10.6)	<.0001	92%
Tot AG	142	6.6 (4.8)	18.5 (14.2)	11.9 (13.2)	<.0001	90%
DEA	142	0.21 (0.07)	0.27 (0.09)	0.06 (0.07)	<.0001	69%
OLA	142	22.4 (36.5)	30.9 (45.4)	8.5 (50.7)	0.0481	57%
BDNF	142	17,152 (8,048)	23,097 (5,526)	5,945 (8,414)	<.0001	63%

Discussion: This is the first large study to show a short, intense guided meditation can decrease anxiety and depression, while improving mindful attention, awareness, psychological well-being and happiness, and increase positive neurotransmitters including anandamide and BDNF. Importantly, we have objective blood biomarker changes validating subjective changes in happiness, well-being, focus and attention.

Survey responses showed very significant improvements ($p < 0.001$) for all scales assessed. Furthermore, 6 of 7 endocannabinoid markers measured showed very significant improvement ($p < 0.001$) post program compared to pre program. This data demonstrates that many of the positive psychological effects from the meditation program could be attributed to an activation of the endocannabinoid system. More impressively, many of the positive psychological effects remained after one month (data not shown). Even though the presence of anandamide is short-lived, there is a lasting impact of the intense, blissful experience on the participant psyche.

Whether it's a feeling of "runner's high" or getting high, many of these euphoric feelings can be attributed to elevated anandamide levels. The expression of anandamide and other endocannabinoids have been linked to positive feelings of marijuana usage, chocolate consumption, and exercise. Many of the benefits associated with meditation, such as lowered anxiety and depression, can be explained by a significant increase in endocannabinoids.

Meditation practices are tools not only for anxiety, depression and stress management but also to promote holistic wellbeing and happiness. Moreover, guided meditation practices are easily learnable and they have the advantage of being safe, effective and low cost compared to alternative strategies to reduce stress, anxiety and depression; and while improving focus, wellbeing and happiness. This study demonstrated that meditation provides many positive benefits by activating the endocannabinoid system. Additional studies need to be conducted to further understand how meditation provides positive benefits.