Scholarly Undergraduate Research Journal at Clark

Volume 1 Article 10

October 2015

# Biochemical Effects of Meditation: A Literature Review

William C. Daube
*Clark University*

Charles E. Jakobsche
*Clark University*

# Biochemical Effects of Meditation: A Literature Review

William C. Daube, Charles Jakobsche

William Daube '15 lives in Medford, Massachusetts and studies Chemistry. His research interests include understanding the chemical dynamics and composition of the troposphere via various types of spectroscopy. He hopes to eventually pursue graduate studies in either atmospheric chemistry or environmental engineering. In his spare time, he participates in Club Basketball and performs duties as the President of CUBS (Big Brothers Big Sisters).

## Abstract

Meditation is an activity that can help reduce stress and anxiety from daily life as well as help cultivate overall feelings of peacefulness, relaxation, and contentment. This review describes several studies that have been used to assess how meditation can influence the body at the molecular level. The presented results focus on small-molecule metabolites, which are broadly defined as naturally-produced molecules that weigh less than approximately 1000 Da. The results show that meditation can significantly affect hormones and neurotransmitters such as cortisol, dehydroepiandrostrone, serotonin, melatonin, and epinephrine. Some common and modern experimental techniques that are relevant to these studies are also discussed, as well as some challenges of accurately interpreting the results. Overall, understanding the molecular-level effects of meditation can provide a more detailed understanding of its physiological effects because many of the affected molecules are known to be linked to changes in stress responses and mood.

## Meditation Overview

Meditation is known for its ability to help relax and de-stress the mind and body. While there are many different approaches to meditation, including transcendental meditation, Buddhist and Dhammakaya meditation, mindfulness-based stress reduction, progressive muscle relaxation, and multiple types of yoga, some common core ideas include focusing on the present moment, being aware of one's self and one's surroundings, clearing one's mind from distractions, and purposefully controlling one's breath and physical movements. As an example of a common practice, a typical transcendental meditator would spend 15–20 minutes in the morning and again in the evening, seated with eyes closed and mentally focusing on silently repeating a word or phrase to calm the mind and reduce mental distractions.

Practicing meditation can promote physiological responses in the body such as decreased blood pressure and reduced breathing rate. Pioneering work by Herbert Benson described these effects as the "relaxation response," which is produced by activation of the parasympathetic nervous system.[1] The relaxation response is opposite to the more commonly known "fight-or-flight response," which is produced by the activation of the sympathetic nervous system.[2] The content of this review focuses on specific biochemical changes at the molecular level that can result from practicing meditation.

## Analytical Techniques

Experimental techniques for analyzing concentrations of biological chemicals involve two general stages: first, acquiring a biological sample from the subject and then, measuring the concentration of a molecule of interest. Some compounds can be measured from saliva or urine samples, which are relatively simple to acquire. However, other compounds are best measured from blood serum or plasma samples, which must be obtained by trained experts. Additionally, needles are often inserted hours before the experiment in order to produce data that is not affected by any short-term stress effects from the puncture. Some metabolites can be quantified by simple gas chromatography or high-pressure liquid chromatography, but in many cases more complex assays are required. One common assay for measuring the usually very small concentration of metabolites in serum is a radioimmunoassay. In this experiment, the sample is mixed

with a known concentration of a synthetic version of the metabolite that has been made to contain a radioactive atom (for example 125I). The isolated, non-radioactive metabolite and the synthetic, radioactive one compete to bind to immobilized antibodies. After washing away the unbound molecules, the amount of radioactivity produced by the antibody-bound metabolites can be compared to a standardized curve in order to calculate the original concentration of the isolated metabolite. A second useful technique in an enzyme-linked immunosorbent assay (ELISA), which also uses immobilized antibodies to bind the isolated metabolite, but then uses enzyme-catalyzed generation of color or fluorescence as a readout instead of radioactivity.

Regardless of which biochemistry technique is used, the details of the experimental procedures that relate to the human subjects must also be carefully planned. Many metabolites undergo natural changes in concentration throughout the day, and others are affected by eating particular foods, smoking, or other daily activities. Age and gender can also significantly affect some metabolites. While no two people or two situations will provide a perfectly matched negative-control experiment for a test condition, having a stronger understanding of the metabolites of interest enables experiment designers to create better control groups. For experiments assessing the immediate effects of meditation, experiment designers must decide what the control subjects should do while the test group is meditating; sitting, relaxing, keeping eyes open or closed, conversing, or watching TV are all options that can be considered. For experiments assessing the long term effects of regular meditation, it can be difficult to isolate the effects of meditation versus effects that result from other lifestyle choices (diet, for example) that may be more common in meditators versus non-meditators. In all cases it is important to have large enough sample sizes so that appropriate statistical analyses can be used to validate the significance of any observed differences. To show the statistical significance of the experimental results described in this review, respective p-values are included, which indicate the probability of such strong correlations being randomly produced if the underlying hypotheses were not true.

## Metabolites and Biomarkers

Among the metabolites affected by meditation, the hormone cortisol (Figure 1) is perhaps the best studied. Physical and psychological stress cause the body to increase its cortisol levels. Cortisol molecules travel throughout the body to activate various biological responses intended to improve the body's short-term performance in stressful situations, which is often called "the fight or flight response".[3] Biological effects of increased cortisol include increased blood pressure, blood sugar levels, and metabolism, which provides an extra boost of energy and suppression of the immune system, to divert energy towards the more immediate need. Chronic stress and long term elevation of cortisol cause the body to remain in this activated state and are associated with numerous diseases.[4] Thus, cortisol is generally considered a biochemical indicator of stress and a risk factor for associated medical conditions.

In one study, Jevning and coworkers report that the average plasma concentration of cortisol in a group of fifteen experienced transcendental meditators decreased by a statistically significant ($p < 0.01$) 27% after a 30-minute meditation session.[5] In contrast, a group of fifteen control subjects untrained in meditation, who were simply allowed to rest instead of meditating, did not show a statistically significant change. As a follow-up experiment, the control subjects were trained in transcendental meditation and retested after three to four months of practice. After thirty minutes of meditation, this group did show a decrease in average cortisol but it was not as large of a decrease as the experienced meditators had produced ($p < 0.3$). All three groups (experienced meditators, controls, and controls after training) showed similar levels of cortisol in the time period before meditating or resting.

In a second study, Sudsuang and coworkers reported that after a six-week training period in Buddhist meditation, and meditating immediately prior to testing, a group of fifteen Thai boys age twenty to twenty-five showed an average 24% reduction ($p < 0.01$) in serum cortisol levels compared to their levels before the training began.[6] A control group of thirty boys who stayed home on vacation instead of being trained showed no significant change in cortisol. Interestingly, a group of twenty-seven boys who were trained, but described themselves as not being able to find tranquility during the meditation, also did not show any significant change in cortisol levels. Together these results not only suggest that meditation can help reduce stress by lowering cortisol levels, but also that successful meditation is more than simply resting the body and is a mental skill that can be learned and improved through practice.

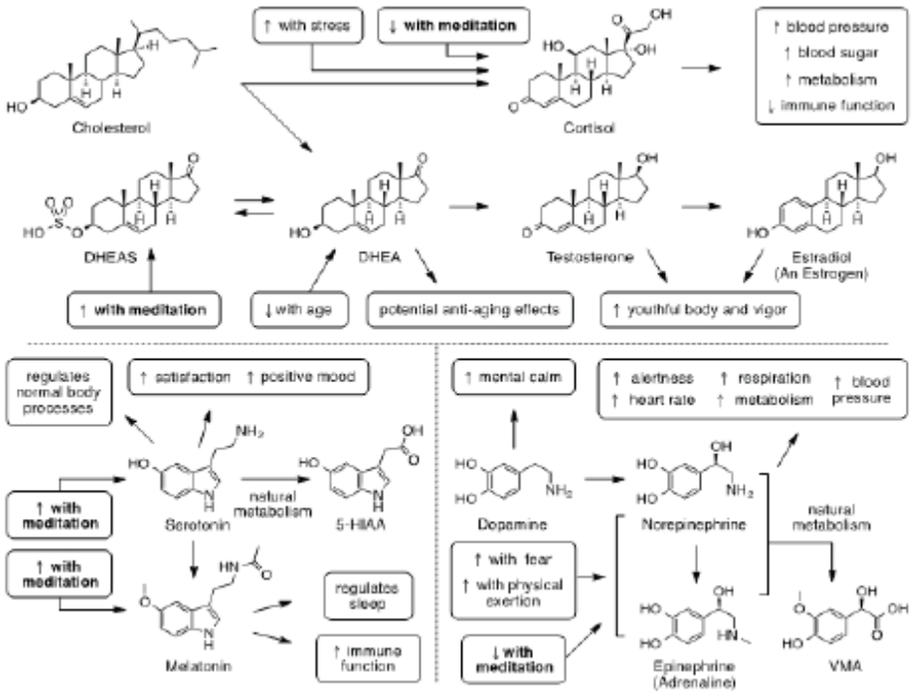


*Figure 1: Summary of some biochemical and physiological pathways relevant to meditation*

Dehydroepiandrostrone (DHEA) and its sulfate ester (DHEAS) are hormones that are abundant in the human body and serve as the biological precursor for other steroid-type hormones including testosterone and estrogen. Although DHEA and cortisol are similar in chemical structure and both made from cholesterol via several steps, their biological effects are completely different. Much interest in DHEA relates to its observed decrease with age and potential applications as "anti-aging" treatments for memory-loss, low-REM sleep, or skin issues.[7]

DHEAS levels have been reported to correlate with meditation activity. In a large scale study, Glazer and coworkers measured DHEAS's serum concentration in 423 people who regularly practiced transcendental meditation and 1252 people who did not.[8] Higher average levels of DHEAS were observed in the meditators groups for both men ($p = 0.001$) and women ($p < 0.001$). Women showed increases, mostly in the 17–54% range, for every age group studied (20–74 years old) and men showed increases in most older age groups (45 to over 70 years old). The authors note that while it is possible that other lifestyle differences between the meditator and non-meditator groups may be responsible for the differences in DHEAS, their results suggest that neither diet, smoking, nor alcohol consumption directly caused the observed differences in DHEAS. Currently, not enough is known to specifically define how or if higher levels of DHEAS may directly, or indirectly through modifying testosterone, estrogen, or cortisol levels, relate to improved health or youthful vigor.

Serotonin acts as a neurotransmitter in the central nervous system and is also involved in the digestive tract. It helps regulate physiological mechanisms such as maintaining body temperature, motor control, circadian rhythms, and also affects mood by producing a general sense of satisfaction and relaxation.[9] Feelings of depression and anxiety are often associated with low serotonin levels, and several antidepressant drugs including Prozac function by increasing serotonin-based biological pathways.[10] Serotonin is naturally metabolized into 5-hydroxyindole-3-acetic acid (5-HIAA) before being excreted, so 5-HIAA concentrations can serve as indicators of serotonin levels. In one experiment, Bujatti & Riederer analyzed urine concentrations of 5-HIAA in eleven subjects who regularly practiced transcendental meditation compared to fifteen healthy control subjects.[11]

At the beginning of the test, the meditators already showed more than twice the average concentration of 5-HIAA compared to the control group ($p = 0.01$) and after thirty minutes of meditation, the meditator's 5HIAA levels rose to more than triple that of the control subjects ($p = 0.005$) who had spent the thirty minutes engaged in light activity and conversation, and whose 5-HIAA levels had not significantly changed. In another experiment, Walton and coworkers compared urine samples from twenty-two college students who regularly practice transcendental meditation to thirty-three control students.[12] Analysis of urine excreted during the night and early morning showed approximately 70% higher average concentrations of 5-HIAA in the meditators compared to the control subjects ($p < 0.015$). Together these results not only suggest that meditation can increase serotonin levels, but that these levels can remain elevated throughout the day and night. Serotonin has been called the "rest and fulfillment hormone,"11 and it seems possible that its effects could contribute to a general sense of happiness in those who meditate regularly. This hypothesis is supported by a study by Yu and coworkers that used a qualitative assessment of mood-states to

identify mood changes in a group of fifteen individuals following a twenty minute session of focused-attention breathing meditation.[13] After meditation, the subjects showed reduced average scores for tension and anxiety ($p < 0.01$), depression ($p < 0.001$), anger and hostility ($p < 0.05$).

The hormone melatonin plays an important role in regulating the sleeping–waking cycle.[14] Melatonin levels increase in the evening and night as it is synthesized from serotonin. Interestingly, the biosynthesis of melatonin is inhibited by strong light, presumably to help match the sleeping–waking cycle with the natural day–night cycle. In addition to promoting sleep, melatonin's biological effects include depression of the central nervous system, reduction of pain sensitivity, upregulation of the immune system, and promotion of general feelings of happiness.[15] Some anti-insomnia drugs function by increasing melatonin pathways. Melatonin has also been shown to suppress the growth of some types of cancer.[16,17]

In one study, Tooley and coworkers have reported that after performing transcendental meditation–Sidhi for sixty minutes in the late evening, a group of ten meditators showed an average plasma concentration of melatonin that was 22% higher ($p < 0.01$) than was observed in the same subjects on a different night after they sat quietly without meditating. The groups did not show any difference in melatonin concentration before meditating and half the group acted as the control group on each night. The authors note that ambient lighting levels were maintained substantially below the intensities that are known to influence melatonin production. The results of this experiment suggest that meditating before going to sleep may help the body transition into sleep and enhance the many known benefits of sleeping well. Indeed, Brand and coworkers have reported that a group of nine experienced meditators scored substantially better on a qualitative sleep-quality index ($p = 0.02$) than did a control group of eleven novices.[19] After eight weeks of training in mindfulness-based stress reduction meditation, the novices' sleep-quality scores improved ($p = 0.008$), but not to the levels scored by the long-term meditators.

Epinephrine (also called adrenaline) and norepinephrine are two related hormones that are associated with biological responses to fear and physical exertion.[20] These molecules temporarily produce high levels of alertness, which could help a person survive a dangerous situation. Epinephrine increases heart rate, respiratory rate, blood pressure, and metabolism. Norepinephrine increases heart rate, serves as a neurotransmitter in areas of the brain associated with alertness, and is the biological precursor for the synthesis of epinephrine.

In one experiment, Infante and coworkers compared the plasma concentrations of epinephrine and norepinephrine of nineteen regular practitioners of transcendental meditation versus sixteen healthy control subjects.[21] Average morning concentrations of epinephrine and norepinephrine in the meditators were approximately 30% lower ($p < 0.01$) and 40% lower ($p < 0.01$) respectively than those in the control subjects. Epinephrine and norepinephrine levels can also be measured by measuring urine concentrations of vanillylmandelic acid (VMA), which is a metabolic product of each. Bujatti & Riederer's experiment showed that both before and after a thirty minute session of meditation, or light activity for the control group, a group of regular meditators had VMA concentrations approximately 50% lower than those measured for control subjects ($p = 0.025$). Conversely, Walton and coworkers' experiment 12 suggests that elevated VMA levels can be more substantially influenced by high sodium intake (62% increase, $p = 0.002$) than by regular meditation (21% decrease, $p = 0.1$). While these studies highlight the importance of comparing meditators to well-matched control groups, the overall results do suggest that people who regularly meditate can maintain lower levels of adrenaline and thereby maintain a more relaxed mindset.

## Connecting the Pieces

Although studying individual metabolites one by one can identify specific biochemical effects of meditation, the data must be integrated together to produce a broader understanding of the overall effects. Elias and coworkers have hypothesized that during meditation the body switches from glucose metabolism to fatty acid metabolism and that the altered concentration of product molecules being produced may lead to increased production of gamma-aminobutyric acid (GABA) in the brain.[22,23] GABA is an inhibitory neurotransmitter and its increase can relax the mind. In one study, Guglietti and coworkers used transcranial magnetic stimulation to analyze brain activity before and after a sixty minute meditation session.[24] A group of thirty-five people who meditated showed a 10% increase ($p = 0.02$) in average cortical-silent period, which is a measurement used to evaluate overall neural inhibition caused by GABA-activated pathways.

A control group of thirty-five people who watched television instead of meditating showed no change in their average cortical silent period. In a study that measured GABA directly, Streeter and coworkers reported that practicing yoga can elevate GABA levels,[25] which is relevant to meditation because the similarities between the mental relaxation achieved through yoga and through meditation are well known. Some physiological responses produced by fasting are also similar to those produced by meditation, and Jevning and coworkers note that fasting also produces a shift away from glucose and towards fatty acids as the primary energy source.[26] Thus, it is possible that during meditation it is the combination of reduced muscle activity and reduced mental activity that causes a reduced energy demand that enables the biological shift away from glucose-based metabolism and towards a more restorative body state.

## New Experimental Directions

A newer field of research that has been gaining interest in recent years is the area of metabolomics.[27] Similar to genetics (which studies genes) or proteomics (which studies proteins), metabolomics aims to simultaneously study all the small-molecule metabolites in a given biological system by identifying which metabolites are affected by a particular experimental condition, for example. To provide sufficient resolution to deconvolute mixtures of many molecules, experimental techniques often involve multidimensional analysis. Some techniques include LC-MS-MS, which is high performance liquid chromatography feeding directly into mass spectrometry separation followed by mass spectrometry analysis, or multidimensional NMR, nuclear magnetic resonance. While various databases containing information on over 40,000 human metabolites have been established, we are unaware of any studies that have utilized a metabolomics approach to further define the specific biochemical effects of meditation.

## Conclusion

The mind has an incredible amount of control over the body. Beyond conscious movements of skeletal muscles, a person's mental state can influence subconscious body functions such as heart rate, blood pressure, and even the production of biochemical molecules. A substantial amount of scientific research has shown that meditation can influence the biological concentrations of a number of human hormones and neurotransmitters, many of which are known to be linked to biological control of stress and mood. These findings correlate well with the well-known positive influences of meditation on relaxation and contentment. One challenge of meditation research is setting up appropriate negative-control groups to enable specific comparisons to be made and to identify the specific effects of meditation on biochemistry. Other challenges include running these experiments on a large enough scale to provide statistically valid results and identifying enough affected metabolites to be able to provide a complete understanding of the biochemical impacts of meditation. Interestingly, many of the biochemical pathways that can be affected by meditation have also served as the biological targets of medical drugs developed to treat a variety of mental and physical symptoms. Thus, we believe that meditation, as well as other healthy-living habits, may have the potential to serve as a drug-free approach to treating or preemptively reducing a variety of stress-related conditions and depressive mood disorders that have become all too common in modern society.

## References

[1] Benson, H.; Klipper, M. Z. The Relaxation Response. Harper Collins, New York, 2009 (1975).

[2] Cannon, W. B. Wisdom of the Body. W. W. Norton & Company, New York, 1963 (1932).

[3] (a) Fukuda, S.; Morimoto, K. Environ. Health and Preventative Med. 2001, 6, 9–14. (b) Fukuda, S.; Morimoto, K. Environ. Health and Preventative Med. 2001, 6, 15–21.

[4] Esch, T.; Fricchione, G. L.; Stefano, G. B. Med. Sci. Monit. 2003, 9, RA23–34.

[5] Esch, T.; Fricchione, G. L.; Stefano, G. B. Med. Sci. Monit. 2003, 9, RA23–34.

[6] Sudsuang, R.; Chentanez, V.; Veluvan, K. Physiology & Behavior 1991, 50, 543–548.

[7] Friess, E.; Trachsel, L.; Guldner, J.; Schier, T.; Steiger, A.; Holsboer F. American Journal of Physiology-Endocrinology and Metabolism 1995, 31, E107.

[7] Friess, E.; Trachsel, L.; Guldner, J.; Schier, T.; Steiger, A.; Holsboer F. American Journal of Physiology-Endocrinology and Metabolism 1995, 31, E107.

[8] Glaser, J. L.; Brind, J. L.; Vogelman, J. H.; Eisner, M. J.; Dillbeck, M. C.; Wallace, R. K.; Chopra, D.; Orentreich, N. Journal of Behavioral Medicine 1992, 15, 327–341.

[9] Gershon, M.; Tack, J. Gastroenterology 2007, 132, 397–414.

[10] Corey, E. J.; Czakó, B.; Kürti, L. Molecules and Medicine; Wiley, Hoboken, NJ, 2007.

[11] Bujatti, M.; Biederer, P. Journal of Neural Transmission 1976, 39, 257–267.

[12] Walton, K. G.; Pugh, N. D.; Gelderloos, P.; Macrae, P. The Journal of Alternative and Complementary Medicine 1995, 1, 263–283.

[13] Yu, X.; Fumoto, M.; Nakatani, Y.; Sekiyama, T.; Kikuchi, H.; Seki, Y.; Sato-Suzuki, I.; Arita, H. International J. Psychophysiology 2011, 80, 103–111.

[14] Vanecek, J. Physiological Rev. 1998, 78, 687–721.

[15] Solberg, E. E.; Holen, A.; Ekeberg, Ø.; Østerud, B.; Halvorsen, R.; Sandvik, L. Medical Science Monitor 2004, 10, CR96–CR101.

[16] Carlson, L. E.; Speca, M.; Patel, K. D.; Goodey, E. Psychoneuroendocrinology 2004, 29, 448–474.

[17] Massion, A.; Teas, J.; Hebert, J. R.; Wertheimer, M.; Kabat-Zinn, J. Medical Hypotheses 1995, 44, 39–46.

[18] Tooley, G. A.; Armstrong, S. M.; Norman, T. R.; Sali, A. Biological Psychology 2000, 53, 69–78.

[19] Brand, S.; Holsboer–Trachsler, E.; Naranjo, J. R.; Schmidt, S. Neuropsychobiology 2012, 65, 109–118.

[20] Carrasco, G. A.; van de Kar, L. D. Eur. J. Pharmacol. 2003, 463, 235–272.

[21] Infante, J. R.; Torres-Avisbal, M.; Pinel, P.; Vallejo, J. A.; Peran, F.; Gonzalez, F.; Contreras, P.; Pacheco, C.; Roldan, A.; Latre, J. M. Physiology & Behavior 2001, 72, 141–146.

[22] Elias, A. N.; Wilson, A. F. Medical Hypotheses 1995, 44, 287–291.

[23] Elias, A. N.; Guich, S.; Wilson, A. F. Medical Hypotheses 2000, 54, 660–662.

[24] Guglietti, C. L.; Daskalakis, Z. J.; Radhu, N.; Fitzgerald, P. B.; Ritvo, P. Brain Stim. 2013, 6, 397–402.

[25] Streeter, C. C.; Jensen, J. E.; Perlmutter, R. M.; Cabral, H. J.; Tian, H.; Terhune, D. B.; Citaulo, D. A.; Frenshaw, P. F. The Journal of Alternative and Complementary Medicine 2007, 13, 419–426.

[26] Jevning, R. Physiology & Behavior 1988, 43, 735–737.

[27] Patti, G. J.; Yanes, O.; Siuzdak, G. Nat. Rev. Molec. Cell Biol. 2012, 13, 263–269.