

## **Meditation aids psychiatric disorder management and enhance adaptive immunity via up-regulating parasympathetic tone**

Wan-Chung Hu

Postdoctorate

Genomics Research Center

Academia Sinica

Taipei, 115, Taiwan

### **Abstract**

Meditation is a common practice in certain religions. Non religion meditation practice is now more and more popular. Meditation can provide a stress relief method via relaxation reaction. It can enhance parasympathetic tone and suppress sympathetic tone. Sympathetic nerve system is a fear-and-fight stress machinery accompanying steroid secretion. Majority of anxiety and depression patients are found hypersecretion of glucocorticoid with enhancing stress response. Meditation can lower cortisol, up-regulate dopamine/serotonin/oxytocin/endorphin to reduce stress reaction. In addition, parasympathetic system enhances adaptive immunity and suppresses innate immunity; sympathetic system enhances innate immunity and suppresses adaptive immunity. Thus, meditation can help us to booster host adaptive immunity to cope with infections. Thus, mediation can be useful for managing psychiatric disorders as well as enhancing host immunity.

### **Review**

Meditation is more and more popular in modern society. Non-religion meditation provides us a relief to cope with stress life events. Besides of the relief, meditation can also have other benefits for health.[1, 2] In this review article, the mechanism of meditation and its usage to treat several illnesses will be discussed, especially psychiatric disorders such as anxiety and depression.

Meditation is practiced by rest and reducing breathing rate. Via this biofeedback method, it can lower basic metabolic rate and enhance parasympathetic tone (reduce heart rate, blood pressure, and respiratory rate). Although it is not sleep status, it is mimicking sleep condition by inducing drowsiness related theta wave. Usually, meditation has three stages. In the first stage, alpha wave will be slowly

prolonged. In the second stage, theta wave appears with drowsiness period. In the third stage, beta wave with spindles appears compared to sleep's first and second stage.[3-5] Parasympathetic nerve system is more activated during sleep. In the most popular meditation practice, transcendental meditation(TM), it can lower oxygen consumption greatly. During awake, body oxygen consumption is 250 ccm per minute. During sleep, the body oxygen consumption can maximally reduce 8% after 5 hr sleep. But, during TM, it can lower body oxygen consumption as high as 20% within 5 minutes. During TM, it can also reduce heart rate and blood pressure significantly. Thus, meditation can provide more parasympathetic activation compared to sleep.[6, 7] During long-term meditation, the grey matter density of amygdala will decrease and that of ventral motor nucleus and solitary nucleus will increase.[8] Amygdala nucleus is related to sympathetic fear-and-fight response, and the ventral motor and solitary nucleus is related to vagal parasympathetic system.[9-13]

Because sympathetic nerve system and parasympathetic nerve system are antagonists to each other, the activation of parasympathetic system means suppression of sympathetic system. Sympathetic system is activated during awake to maintain alertness to cope with daily life stress events. Sympathetic innervation to adrenal gland can also stimulate glucocorticosteroid stress hormone secretion. This is host stress response.[14, 15] Sympathetic nerve system is the fear-and-fight machinery and it can also up-regulate host innate immunity to cope with acute fulminate bacterial infection.[16, 17] By up-regulating parasympathetic and down-regulating sympathetic, the secretion of stress hormone, glucosteroid, can also be reduced during meditation. Parasympathetic system, on the contrary to sympathetic system, can inhibit innate immunity and enhance more long-term adaptive immunity.[18, 19] Since steroid can suppress host immunity, especially adaptive immunity such as lymphocytes, it can also suppress T helper cell driven mediators such as dopamine(TH17 mediator) and serotonin(TH2 mediator).[20, 21] Thus, by suppressing cortisol, it can help to up-regulate dopamine and serotonin in our body during meditation.[22] Oxytocin activation during meditation can further enhance the parasympathetic activity.[23]

In clinical studies, increased HPA activity with increased cortisol level is seen in 20-40% of depressed outpatients, 40-60% of depressed inpatients, 30% obsessive-compulsive disorder. Dexamethasone non-suppression is also found in many depressive patients (69% in depressed patients and 78% in depression with serious suicidality) with a blunted ACTH response to CRH challenge.[24, 25] A large group of depressed patients also shows a blunted TSH response to TRH challenge.

HPA axis and thyroid axis anomalies are also found in bipolar disease patients. High level of cortisol can suppress POMC as well as ACTH for feedback regulation. In an animal model, overexpression of glucocorticoid receptor can cause mood disease(emotional lability) in mice. Cortisol can also suppress TSH level via feedback regulation. Thus, it can explain the blunted TSH or ACTH response due to TRH or CRH challenge respectively. If the level of POMC is low, then the end product of POMC,  $\beta$ -endorphin or Met-enkephalin, is also down-regulated. In several studies, low level of endorphin or enkephalin is also noted in depressive patients. Sympathetic tone overactivation could be the reason for up-regulated cortisol. Stress can enhance sympathetic tone to induce norepinephrine and epinephrine release acting on adrenal gland. It is worth noting that unexpected stress will trigger more epinephrine and familiar stress will trigger more norepinephrine. In clinical studies, overactivation of sympathetic system is observed in major depression. Then, adrenal gland can highly release corticosteroid, and this may explain the Dexamethasone non-suppression. Thus, stress event causes high cortisol and subsequent  $\beta$ -endorphin suppression to cause depressive disorder. By suppressing cortisol, meditation can up-regulate endorphin as well as dopamine/serotonin to enhance euphoria sensation. Dopamine/serotonin/histamine control our body's sex/hunger/thirsty. Dopamine is related to sex orgasm and serotonin is related to food fullness satisfactory sensation. Current anti-psychiatric drugs act on dopamine and serotonin systems. Meditation can further aid medications to relieve depression.

In bipolar disease, HPA axis anomaly is also noted. Here, I also propose the mechanism for bipolar disease. Severe stress can cause CRH release in hypothalamus. Then, CRH can stimulate POMC release and subsequent ACTH and  $\beta$ -endorphin. The high level of  $\beta$ -endorphin can be related to maniac episode of bipolar disorder. Relative lower cortisol is related to higher dopamine and serotonin. Then, ACTH can cause cortisol secretion. High cortisol can suppress POMC production. Then,  $\beta$ -endorphin level becomes low. Dopamine and serotonin level will also be lower. It will be associated with the depressive episode of bipolar disorder. In bipolar disease, maniac episode usually happens before depressive episode. And, additional stress event will cause another cycle of maniac-depressive disorder. In a genetic study, the most important genes associated with bipolar disease is CRH and proenkephalin. Another paper shows that phospholipase C plays an important role in mood disease such as bipolar disorder. That matches my hypothesis. Thus, the pathogenesis of bipolar disorder is also revealed. Meditation can be helpful for depressive episode of bipolar disease.

Compared to mood disorder with cortisol hypersecretion, anxiety disorder is related to merely sympathetic nerve system overactivity. Sympathetic system is a fear-and-fight machinery. Acute threat is mediated by brain regions such as locus coeruleus and the amygdala. The amygdala participate in the encoding of fear memory and aversive conditioning. Acute fear also activates sympathetic nerve system via locus coeruleus. It results in tachycardia, tremor, and diaphoresis which are commonly seen in anxiety disorders. By suppressing sympathetic system, meditation can also help to reduce anxiety disorders such as general anxiety disorder, panic disorder, phobic disorder, post traumatic stress disorder, and other acute stress disorder.

As for substance addiction, meditation can also support the management. Alcohol abuse is one leading problem. Alcohol metabolism can produce acetyl-CoA which is the building block of steroid such as cortisol. In chronic alcoholism, high cortisol level is usually observed in these patients. Cortisol will produce short term alertness (Cortisol euphoria) and longterm depression by suppressing endorphin. Thus, alcoholism is usually accompanying depressive disorder. Meditation can reduce sympathetic stress reaction as well as cortisol level, so it can help to manage alcohol abuse.[26, 27]

Another major group of drug abuse is sympathemimetic agents such as amphetamine, cocaine, nicotine, and low dose marijuana. These drugs can also chronically over-activate sympathetic system to enhance alertness and dopamine/cortisol related euphoria. Meditation can enhance parasympathetic tone and suppress sympathetic tone. Thus, it can also help to manage these kinds of drug abuse.

Finally, meditation has effects via enhancing parasympathetic system itself. It can help to reduce palpitation and hypertension. It can also enhance body adaptive immunity against viruses, parasites, and intracellular bacteria.[28] Antibody titer against influenza was found to elevate after meditation.[29] Thus, meditation has the effect to increase host immunity. For example, AIDS patients have impaired adaptive immunity. Thus, meditation could help these patients to improve their immunity.

## Conclusion

Meditation can enhance parasympathetic nerve system as well as suppress cortisol and increase dopamine/serotonin/endorphin/oxytocin. Via the above effects, it provides many healthy benefits to cope with many psychiatric illnesses such as

drug/substance addiction, depression, anxiety, bipolar disease, and OCD. It can also help to manage hypertension and enhance body immune response. Thus, meditation should be introduced to modern medicine as a complementary treatment method for the above disorders.

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