How The Mind Changes Genes Through Meditation

The mind-body divide has been breached in conventional western medicine, thanks to new research findings in molecular genetics which not only bridge mind and body but also East and West.

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Psychosomatic is Real

Conventional western science and medicine has long held that one's mind or psychological state cannot have physical effects on the body—so much so that subjective feelings of being ill are generally dismissed as "psychosomatic" and hence not a real indicator of how physically unwell the body is. This mind–body divide has truly broken down, as researchers are identifying hundreds and thousands of genes that are affected by our subjective mental states. Feeling constantly sad and depressed can genuinely turn on genes that make us physically unwell and prone to viral infections and chronic diseases, just as feeling particularly relaxed and peaceful can turn off those genes and activate others that help us heal and fight infections.

The emerging field of human social genomics is demonstrating that social conditions, especially our subjective perceptions thereof, can radically change our gene expression states. This has opened up new ways of intervention.

Integrative Medicine's Focus on Disease Prevention

In the United States and other industrialised countries, "integrative medicine" is becoming increasingly important in healthcare delivery in its focus on disease prevention and amelioration through healthy diet, lifestyle, stress management and cultivation of emotional wellbeing. Among the most popular approaches in integrative medicine are traditional deep-relaxation techniques referred to as "yogic/meditative practices", which include yoga and diverse meditation and breathing exercises such as qigong, tai chi, etc.

Over the years, many studies have suggested that such practices have positive effects on the mind–body system and can increase wellbeing and support recovery from disease. Yogic/meditative practices were shown to have positive effects on heart rate, blood pressure and low-density lipoprotein cholesterol and to decrease levels of salivary cortisol, the stress hormone. These findings are consistent with a down-regulation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system, both of which are known to be overactivated by the stressful western lifestyle.

Now, a series of new studies on gene expression profiles in immune cells circulating in the blood are showing that yogic/meditative practices have profound effects at the molecular level.

Mind Over Body as Revealed by Gene Expression Profiles

The first study that used gene expression profiles to probe the effects of meditative practices was small but in depth. The neutrophils (one kind of white blood cells) of five Asian qigong practitioners were compared with six healthy Asian controls.

The qigong group had practised for at least a year, their regimen consisting of a cognitive component in addition to exercise that lasted for one to two hours daily. Gene expression profiles were examined with microarrays for about 12,000 genes. Among them, 250 genes were consistently different between the qigong and the control groups, with 132 down-regulated and 118 up-regulated. Among the differentially expressed genes, the down-regulated included genes related to the ubiquitin degradation pathway (for breaking down proteins) as well as genes encoding ribosomal proteins. Cellular stress-response genes were generally down-regulated in qigong practitioners compared with controls, but the expression of two heat-shock proteins was increased. Expression of genes related to immunity was also increased in the qigong group—genes such as interferon *gamma* (IFNγ) and IFN-related and IFN-regulated genes (involved in fighting viral infections). In an *in vitro* assay, the neutrophils from qigong practitioners had increased bactericidal activity.

Furthermore, the lifespan of normal neutrophils was increased while that of inflammatory neutrophils was decreased through apoptosis.

A second study is particularly interesting. It evaluated gene expression changes triggered by the "relaxation response" (RR), characterised by decreased oxygen consumption, increased exhaled nitric oxide and reduced psychological distress. The practices were quite diverse, ranging from Vipassana or insight meditation, mantra meditation and Transcendental Meditation, to breath focus, Kripalu or Kundalini yoga and repetitive prayer. The study included 19 long-term (average 9.4 years of practice) RR practitioners (group M) and 20 healthy controls tested at baseline (group N1) who underwent eight weeks of training in guided relaxation techniques and were tested again (group N2). Peripheral blood mononuclear cells (PBMC, all blood cells having a round nucleus) were isolated and global transcriptome (totality of transcripts) profiles were determined using microarrays that could probe 47,000 genes and gene variants.

A total of 2,209 genes were differentially expressed between groups M and N1: 1,275 up- and 934 down-regulated. Between groups M and N2, 1,504 genes were differentially expressed: 774 up- and 730 down-regulated. Between N1 and N2, 1,561 genes were differentially expressed: 874 up- and 687 down-regulated. Interestingly, 595 genes were differentially expressed, specifically in group M, suggesting that long-term practitioners of RR give a distinct expression profile.

Similarly, 428 genes were shared between the short- and long-term RR groups (N2 and M) but not with the control N1 group. The type of genes differentially expressed suggested to the authors that gene expression changes in the M and N2 groups might indicate a greater capacity to respond to oxidative stress and associated detrimental effects. And it matters little which RR technique is practised.

The third study investigated changes in gene expression by Sudarshan Kriya (a kind of yoga) and associated practice. It included 42 practitioners and 42 healthy normal controls. RNA was isolated from PBMC and subjected to reverse transcription polymerase chain reaction (RT-PCR) analysis with a focus on genes involved in oxidative stress, DNA damage, cell-cycle control, ageing and apoptosis. In parallel, the blood drawn was assayed for glutathione peroxidase, superoxide dismutase (SOD) and glutathione levels.

Consistent with a previous study, glutathione peroxidase and superoxide dismutase activities and glutathione levels were higher in practitioners compared with controls. Consistent with those findings, glutathione S-transferase mRNA was also significantly higher in practitioners compared with controls. Although not statistically significant, similar increases were found in the antioxidant genes Cu-Zn-SOD and Mn-SOD, glutathione peroxidase and catalase.

All three studies suggest that yogic/meditative practice gives rise to gene expression changes consistent with improved response to environmental stress...

In addition, expression of the anti-apoptotic gene COX2 and stress response gene HSP70 were significantly increased in the practitioners. Thus the authors suggested that the meditative practice might result in a better antioxidant status, at least in part, by changes in the expression of the relevant genes, which may translate to better response to environmental stress.

All three studies suggest that yogic/meditative practice gives rise to gene expression changes consistent with improved response to environmental stress, improved survival of immune cells and improved antioxidant status.

Meditation Overcomes Effects of Loneliness

Lonely older people have increased expression of pro-inflammatory genes and increased risk of illness and death. Behavioural treatments to reduce loneliness and health risks have had limited success. A study was carried out to test how eight weeks of a mindfulness-based stress reduction (MBSR) program compared to a wait-list control group (a group of participants assigned to a waiting list for intervention and acting as the control group for the intervention).

Feeling lonely is a significant risk factor for cardiovascular disease, Alzheimer's disease and death from all causes.

Several previous studies suggested that MBSR may reduce protein biomarkers of inflammation, and inflammation is known to play a major role in the development and progression of many diseases in older people. Research findings also showed that immune cells from lonely older people have increased expression of genes involved in inflammation.

Randomised participants of 40 healthy older adults (aged 55–85 years) not taking any medication and not trained in MBSR were recruited via newspaper advertisements from the Los Angeles area.

The sample was 64% Caucasian, 12% African American, 10% Latino, 7% Asian American and 5% other, and predominantly female (33). They were randomly assigned to intervention and control groups, which did not differ significantly on measured demographic characteristics at baseline.

Six participants (15%) dropped out before completion, five from the intervention group and one from the control group. Fifteen completed the MBSR program and showed significant decreases in loneliness from baseline compared to a small increase in loneliness from baseline in the control group. There was no significant difference between the groups at baseline.

Previous research found that loneliness was related to increases in expression of NF-κB (nuclear factor *kappa*-light-chain-enhancer of B cells) genes. In the study, 256 genes showed ≥ 25% difference in expression: 87 up-regulated in high-lonely individuals, and 169 genes up-regulated in low-lonely individuals at baseline.

Bioinformatics analysis identified greater prevalence of NF-κB genes in the set of genes up-regulated in the high-lonely individuals compared to genes up-regulated in low-lonely individuals.

After MSBR treatment, 143 genes showed ≥ 25% difference in expression between conditions: 69 genes down-regulated in MBSR subjects relative to controls, and 74 genes relatively down-regulated in controls compared to MBSR subjects. Bioinformatics analysis indicated reduced activity of NF-κB genes in MBSR-treated subjects relative to controls.

These changes were not accompanied by changes in behaviour, such as quality of sleep and exercise. One limitation could be that the MBSR classes are providing social support, which is reducing loneliness, although previous findings indicate that social support and social skills training per se were ineffective.

The results showed that yoga intervention not only ameliorated fatigue but also reduced the inflammatory response. There was a clear down-regulation of pro-inflammatory genes in the yoga group.

Yoga Overcomes Fatigue in Breast Cancer Survivors

A new study led by Dr Julienne Bower at the University of California, Los Angeles, in the United States involved breast cancer survivors with persistent cancer-related fatigue. The subjects were randomised to a 12-week Iyengar yoga intervention (n=16) or a 12-week health education control condition (n=15). Blood samples were collected at baseline, at post-intervention and at a three-month follow-up for genome-wide transcriptional profiling and bioinformatics analyses. Plasma inflammatory markers and salivary cortisol were also assessed.

The results showed that yoga intervention not only ameliorated fatigue but also reduced the inflammatory response. There was a clear down-regulation of pro-inflammatory genes in the yoga group. The two groups did not differ significantly at baseline and while the yoga group changed over time, the control group showed no significant changes.

A total of 435 gene transcripts showed ≥15% difference over time: 282 transcripts were up-regulated from baseline after intervention and at three-month follow-up in the yoga group relative to the controls, and 153 transcripts were relatively down-regulated. Particularly prominent among the yoga group's down-regulated genes were type I interferon responses.

Bioinformatic analysis showed reduced activity of NF-κB, increased activity of glucocorticoid receptor and reduced activity of CREB (cyclic AMP response element-binding) protein, a transcription factor, all tending to reduce inflammatory response. In addition, there was a down-regulation of interferon-related transcription factor activity in the yoga group versus controls.

The levels of inflammatory markers at baseline were not different between the groups. One of the markers, sTNF-RII (soluble form of tumour necrosis factor–receptor II), showed a significant increase in the health education group, whereas the levels remained relatively stable in the yoga group. A similar pattern was found for IL-1RA (interleukin-1 receptor agonist). Yoga significantly increased glucocorticoid receptor (GR) activity. Previous research has documented a decrease in GR-mediated gene expression among breast cancer survivors with persistent fatigue, which may contribute to chronic inflammation. This suggests that yoga may cause glucocorticoid receptors to become more sensitive

to the anti-inflammatory effects of cortisol, thereby decreasing inflammatory signalling. Yoga also reduced CREB activity, indicating a reduced sympathetic nervous system signalling through β-adrenergic receptors, which can activate NF-κB genes and up-regulate transcription of pro-inflammatory cytokine genes. Thus, reduction in CREB also reduced inflammatory processes.

In addition, the down-regulation of genes involved in type I interferon (IFN) responses and reduction in IFN-related transcription factors may contribute to reduction in fatigue, as treatment with IFN-α is known to cause symptoms of fatigue in patients with melanoma and hepatitis C.

Meditation Overcomes Stress Among Family Dementia Caregivers

Family caregivers are highly stressed and are at risk of stress-related disease and general health decline. One genome-wide transcriptional profiling study showed that monocytes from family caregivers exhibited heightened expression of genes with response elements for NK-κB and reduced expression of genes with response elements for IRF (interferon regulatory factor) relative to healthy controls.

Forty-five family dementia caregivers were randomised to either Kirtan Kriya Meditation or relaxing music listening for 12 minutes daily for eight weeks, and 39 caregivers completed the study.

Genome-wide transcriptional profiles were collected from peripheral blood leukocytes sampled at baseline and at an eight-week follow-up. The results showed 68 genes differentially expressed: 19 up- and 49 down-regulated. Up-regulated genes included immunoglobulin-related transcripts. Down-regulated genes included pro-inflammatory cytokines and activation-related immediate early genes.

After intervention, both groups improved, showing significantly lower levels of depressive symptoms and better mental health, but the yogic group improvement was higher (43.3% improvement in meditation group compared with 3.7% improvement in the relaxation group), suggesting amelioration of stress-induced cellular ageing. There were 23 subjects in the meditation group and 16 in the relaxation music group. The groups did not differ on any of the baseline characteristics except for BMI [body mass index], which was lower in the meditation group, but BMI was not associated with any of the outcome measures.

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In a separate report on the same family caregivers, not only did the meditation group have significantly lower levels of depressive symptoms and greater improvements in mental health and cognitive functioning compared with the relaxation group, but the improvements were accompanied by an increase in telomerase activity. There were significant correlations between increased telomerase activity and decrease in depression and improvement in mental health score, the latter only in the meditation group.

The telomere is a region of repetitive DNA sequences at the end of a chromosome, which protect the chromosome from deterioration. Shortened telomere length and reduced telomerase, the enzyme responsible for telomere length and maintenance, are associated with premature death and predict a host of health risks and diseases that may be in part regulated by psychological stress.

A study published in 2011 showed that meditation and positive psychological change were associated with higher levels of telomerase activity.

This finding is now confirmed. On average, the incidence and prevalence of clinical depression in family dementia caregivers approached 50%, and they become less resilient to stress with advancing age and at risk of cardiovascular disease and death.

Rapid Epigenetic Changes from Meditation

A hint as to how quickly the activity of genes can be changed by meditation comes from a study on a day of intensive practice of mindfulness meditation in 19 experienced subjects.

The expression of circadian, chromatin modulatory and inflammatory genes was compared to that of a control group of 21 subjects with no meditation experience who engaged in leisure activities in the same environment.

Peripheral blood mononuclear cells were collected before and after the intervention, eight hours apart. Gene expression was analysed using customised quantitative real-time PCR assays. Both groups were also presented with the Trier Social Stress Test (TSST, a lab procedure for inducing stress).

Core clock gene expression at baseline was similar between groups, and their rhythmicity was not affected in meditators by the intensive day of practice.

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All the epigenetic regulatory enzymes and inflammatory genes analysed were similar in basal expression levels in the two groups.

In contrast, after the brief practice there was reduced expression of histone deacetylase genes (HDAC 2, 3 and 9 which modify histone proteins, altering gene expression), changes in global modification of histones (H4ac; H3K4me3) and decreased expression of pro-inflammatory genes (RIPK2 and COX2) in meditators compared with controls.

The expression of RIPK2 and HDAC2 genes was associated with a faster cortisol recovery to the TSST in both groups.

The findings suggest that the regulation of HDAX and inflammatory pathways may represent some of the mechanisms underlying the therapeutic potential of mindfulness-based interventions.

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About the Author:

Dr Mae-Wan Ho is the co-founder and director of the London-based Institute of Science in Society (ISIS), which promotes the public understanding of science as well as social responsibility and sustainability in science and also campaigns against the unethical uses of biotechnology.

She received her BSc in biology and chemistry (Ist Class) in 1964 and her PhD in biochemistry in 1968, both from the University of Hong Kong. Her career spans more than 40 years in research and teaching in biochemistry, evolution, molecular genetics and biophysics.

Dr Ho is the holder of several patents and has received a variety of science-based awards, fellowships and grants. She is the author or co-author of over 200 scientific papers and has written, co-written or edited over a dozen books.

Her own titles include *The Rainbow and the Worm: The Physics of Organisms* (1993, 1998, 2008), *Genetic Engineering: Dream or Nightmare?: The Brave New World of Bad Science and Big Business* (1998, 1999; reviewed in NEXUS 5/03) and *Living with the Fluid Genome* (2003). Her article "Psychic Cells Communicate Across A Physical Barrier" was published in the Science News section of NEXUS 21/05.

For more information, visit the ISIS website at http://www.i-sis.org.uk.

Editor's Note:

This is an edited version of Dr Mae-Wan Ho's ISIS Report of 21 May 2014, available at the ISIS web page http://tinyurl.com/jvglwqp. The complete article with references can be downloaded by ISIS members or on a one-off fee basis.