Mind Matters: Turn Off Genetic Vulnerabilities by Reducing Stress

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Because of its mechanistic and reductionist bias, mainstream medicine has always been slow to acknowledge that our minds play a vital role in our physical health. This was especially the case in the sixties and seventies, when there was an ongoing debate about whether or not our thoughts and feelings could directly influence our biochemistry. In those days, the materialists had the upper hand, but the rising tide of evidence eventually forced them to give ground. Toward the end of that era, my book Mind as Healer, Mind as Slayer, published in 1977 by Delta/Doubleday, was among the first to herald this once-elusive mind-body connection. In that book I defined stress as a condition that affects both mind and body, and I showed how it contributes to four major types of chronic illness: heart disease, cancer, arthritis, and respiratory illnesses. Along with my other colleagues in the emerging field of integrative medicine, I have been able to demonstrate through my subsequent research and writing that we can reduce our chances of getting those and other degenerative diseases if we commit ourselves to managing our stress effectively.

In fact, I went even further in my research. I discovered that some people had the ability to master the connection of their mind and body. As I followed the thread of research, I met and studied adept meditators who—under strictly controlled conditions—were able to demonstrate that they could exert a remarkable degree of control over pain, bleeding, and infection once they had achieved a meditative state in the laboratory. These people were the pioneers, the exemplars, for those of us who aspire to turn our minds into lifelong allies for health and healing. Jack Schwarz, a Dutch meditation teacher, was perhaps the most impressive of these masters. He had learned to control his own pain and bleeding when he was tortured as a prisoner in a Nazi concentration camp. When my colleagues and I first began to study him under exacting laboratory conditions at the University of California School of Medicine in San Francisco, Jack seemed ordinary at first. He exhibited perfectly normal baseline responses to pain and a normal bleeding time when he was not meditating. Next we asked him to meditate in the controlled conditions of the lab. When I subjected him to pain during his meditation session, we were amazed to observe that his brain waves showed none of the electrical changes normally associated with pain. We then went so far as to ask him to subject himself to pain with a self-inflicted wound by pushing a sharpened, unsterile knitting needle entirely through his left bicep. We discovered to our surprise that he was able to reduce the bleeding by accelerating the time it took for his blood to clot. In a later documentary film for the Canadian Broadcasting Corporation, Schwarz again pushed a sharpened knitting needle completely through his bicep without any display of discomfort. As astounding as that was to witness, he insisted that the real significance of his demonstration was that all of us—not just exceptional individuals—are able to wield such a profound influence over our body. That insight has remained a major theme in my work ever since. Very few of us will become so adept that we can impale ourselves with knitting needles, nor would we want to of course! But I believe that we all have the mental, emotional, and spiritual capacity to fully manage the levels of stress we experience every day.

When I first published my study of Jack Schwarz, it was controversial. Not everyone in the media or in the medical community accepted the idea that we could actually control our own nervous systems. But today the important truth that all of us are born with a natural ability to self-regulate stress is a cornerstone of modern medicine, or at least integrative medicine. More recently, an unexpected and perhaps an even more exciting chapter is unfolding. With the knowledge explosion in human genetics, the same debate is back again, but in a new form: Can our minds directly influence our genes? What's different this time is that genetic testing and retesting gives us an unprecedented ability to precisely monitor the biological effects of our mental and emotional states. In other words, this time we can prove—almost right away—that we can modify gene expression by cultivating relaxed, healthy, and positive states of consciousness and self-awareness. We don't need to wait for long-term studies or engage in a lifetime of meditation or other consciousness practices in a vague hope that we might one day succeed. All we need is a blood test to see exactly how

Excerpted from Change Your Genes, Change Your Life *by Dr. Kenneth R. Pelletier* our genetic biomarkers have changed in response to our current behavior. Let's consider just a few examples of such influence among the many studies that pioneering researchers worldwide have carried out in recent years, beginning with a scientific look at the lifelong epigenetic effect of childhood stress.

Epigenetic Changes from Early-Life Trauma

Early-life stress matters—we have proof that it has a measureable epigenetic effect. Research shows that undue strain or abuse experienced during a child's development affects that young person's epigenome far into adulthood, altering patterns of stress response and often leaving the child with lifelong physical vulnerabilities or emotional disabilities that require treatment. These early epigenetic influences literally burn trauma into the brain and body, or what I prefer to call the body-mind. In brief, here are three remarkable instances of how "mind as slayer" can bring about negative genetic alterations resulting from childhood trauma:

- A study of 448 Dutch soldiers showed that early-life trauma changed more than 45,000 genes in the hippocampus, causing these men to be more vulnerable to emotional stress and PTSD later in life. (The hippocampus is thought to be the brain's center of emotion and memory, and the heart of the autonomic nervous system.)
- A study of 204 undergraduate women whose DNA was collected before and after a campus shooting had startling results. The specific epigenetic modifications created by this early trauma predicted which of these women would later suffer from PTSD-related symptoms as a result of experiencing or being in proximity to the shooting.
- In another study of early trauma, 25 people with a history of abusive childhoods who died by suicide were compared to 16 controls who had died suddenly, but who did not have abusive histories. Genetic analysis focused on 23,551 hippocampal genes. The group that had experienced abuse showed extreme expression (either greater or lower methylation) in 362 neuronal genes. This result means that the functional ability of their genes to assess and respond to danger had been radically changed by child abuse, and may in turn have resulted in their suicide. This unique study suggested that childhood trauma can alter the expression of genes that regulate neuronal function.[1]

The Impact of Early-Life Trauma and Stress on Telomeres

Can early-life trauma affect our telomeres? A 2012 study at Duke University suggests that it can, corroborating earlier studies that have found that children who are physically abused or bullied tend to have shorter telomeres. As discussed earlier, telomeres are the biochemical structures at the tips of chromosomes whose shrinkage has been linked to aging and disease; as cells divide, these structures grow shorter, limiting the number of times a cell can reproduce. Previous research had already identified an association between stress and accelerated telomere loss. Plus, shortened telomeres were sometimes shown to correlate with other health problems including aging, smoking, obesity, mental illness, heart disease, and chronic fatigue. Telomere erosion has also been related to both oxidative stress and inflammation, but such links are not always present in telomere research. "There's a lot of doubt in the field," says Dr. Joao Passos, PhD, a cellular aging specialist at Newcastle University. "For as many studies that show telomere length as a good predictor of health outcomes, there are many that find no relationship."[2]

That Duke University study was more advanced in design than many previous efforts and led to a distinctive outcome. These Duke researchers used data from the Environmental Risk Longitudinal Twin Study, which followed British twins from birth. The team selected 236 of these children, half of whom had experienced at least one form of violence. Using DNA samples collected at ages 5 and 10, the investigators assessed how many times a particular gene had copied itself. Significantly, they found that gene replication was indeed lower among children who had experienced violence. The team not only noted a clear relationship between violence and shortened telomeres, but it also discovered a significant association between the number of violent experiences and the amount of telomere loss. According to one coauthor of the study, Dr. Avshalom Caspi, PhD, "Children who experience physical violence appear to be aging at a faster rate."[3] Parents and caregivers may well wonder whether this process can be reversed once it is set in motion in childhood. Some studies suggest that making healthful lifestyle changes, such as reducing stress, eating well, and exercising, can slow down the rate of telomere loss. But much more research is needed in this important field.

Altering the Expression of Prostate Cancer Genes

There is little question that early-life trauma has a direct and enduring impact on our genes, but it's not a one-way street. Just as mental stress and adversity can affect our genes, so also is it possible to have a positive impact through the mind. That is when "mind as healer" becomes a reality. In fact, some research shows that intervening to reduce stress through the development of better habits can push our genes toward healthy expression and directly enhance our wellness and longevity. For example, in part because of this insight about the biological influence of the mind, we have recently witnessed a sea change in the diagnosis and treatment of prostate cancer. In 2012, the U.S. Preventive Services Task Force advised against the routine prostate cancer screening that provides doctors with PSA readings, since positive results on this test often lead to premature and excessive medical interventions with major negative side effects. Significantly, this advisory was based on the finding that the onset of prostate cancer is reversible through lifestyle changes. Along this line, one new direction in the treatment of prostate cancer involves an intensive lifestyle and nutrition program focused on influencing the genes involved in prostate cancer. In 2008, a group of researchers at the UCSF School of Medicine in San Francisco enrolled 31 men with a low-risk form of prostate cancer who agreed to decline immediate surgery, hormonal therapy, or radiation while undergoing careful surveillance for the progression of their prostate tumors. Instead of the usual medical interventions, these men undertook an intensive, three-month program in which they followed a low-fat, plant-based diet and engaged in stress management practices. When comparing their PSA readings at the start and completion of the program, the researchers found these practices had decreased the expression of the genes associated with prostate cancer.[4]

Dramatic Genetic Changes from Massage

Direct body-mind interventions by caregivers can also positively change gene expression. For example, new research has revealed for the first time that the kneading of sore muscles by a massage practitioner can turn off genes associated with inflammation and turn on genes that help muscles heal. A unique study based on this hypothesis was designed and led by Dr. Mark Tarnopolsky, MD, PhD, a neurometabolic researcher at McMaster University in Canada. Tarnopolsky had suffered a severe hamstring injury in an accident and had received massage therapy as an essential part of his rehabilitation regimen. The massage therapy he received seemed to be so effective that Dr. Tarnopolsky set out to investigate the biochemistry behind it. He was surprised to find that, despite the widespread popularity of massage, researchers in that field knew surprisingly little about its molecular and genetic effects. Two key benefits of massage had previously been well-documented: an increase in blood circulation in the massaged areas, and the general release of endorphins (which decreases pain and increases sensations of pleasure). Researchers knew these positive results were possible, but no one had yet explained how and why these effects occur. Dr. Tarnopolsky wanted to answer these and other questions.

Tarnopolsky and his colleagues designed and conducted their own study, recruiting 11 young men willing to undergo a grueling upright cycling session that left their muscles damaged and sore. Ten minutes later, a massage therapist massaged one of their legs. The researchers took tissue samples from the quadriceps of both legs of each of the volunteers at three points: once before the workout, once ten minutes after the massage, and once three hours after the workout. Then they compared the genetic profiles of each sample. Samples taken before the massages but after the exercise were not a surprise. Researchers detected a greater presence of cell repair activity as well as acute inflammation in the post-workout samples than in the pre-workout samples; this was consistent with the established fact that exercise activates genes associated with these two processes. But what did surprise them were the clear differences between the massaged legs and the unmassaged ones after the exercise. Massaged legs showed 30 percent more expression of a gene that helps muscle cells build mitochondria, the cellular engines that turn a cell's fuel into energy. Even more impressive, these men also had three times less amount of a chemical that turns on genes associated with inflammation. Dr. Tarnopolsky's results prove that massage reduces inflammation caused by exercise and promotes faster healing of affected areas. Incidentally, the study found no evidence to support widely believed claims that massage removes lactic acid, a by-product of exertion long blamed for muscle soreness. Most important, this study underscores the truly amazing finding that the human touch during massage actually induces positive changes in gene expression, leading directly to muscle healing and improved body-mind health.

Stress Hormones Can Cause Epigenetic Changes

For both mice and men, science is revealing the genetic and biochemical pathways through which chronic exposure to stress hormones can change gene expression. During stressful situations, we produce beneficial hormones called glucocorticoids (GC) that affect many bodily systems. GCs are anti-inflammatory, but they also work in the body's immunity pathway. Because this class of hormones is known to be immunosuppressive, drugs containing pharmaceutical versions of this hormonal family are sometimes used to treat diseases caused by an overactive immune system, such as allergies and asthma. Then again, too much of a good thing can cause new problems. Many past studies have found that an excessive amount of glucocorticoids can alter gene expression in the brain. And some researchers have suggested that such influences extend even wider, in part because the distribution of the effects of GCs are mediated by what is known as the hypothalamic-pituitary-adrenal axis (HPA)—a network that links the hypothalamus and the pituitary gland in the brain with the adrenal glands near the kidneys. Thus, a more advanced question concerns how GCs affect the genes that regulate the entire HPA axis. A group led by Drs. James Potash, MD, PhD, and Gary Wand, MD, at Johns Hopkins University set out to answer this question by testing the hypothesis that hormones affect the entire HPA axis through epigenetic modification.

These researchers added corticosterone (a glucocorticoid secreted by the adrenal gland) to the drinking water of mice for four weeks. After exposure, and again after a four-week recovery period without corticosterone, the scientists examined the expression levels of five HPA-axis genes. In particular, they measured the degree of methylation in each gene (a common form of epigenetic modification). In the September 2010 issue of Endocrinology, the researchers reported that mice given corticosterone exhibited an altered expression of three of the five HPA-axis genes, which they attributed to decreased methylation. Now, it turns out that methylation in these same genes has also in the past been associated with PTSD and mood disorders. These newer findings by the Johns Hopkins researchers suggest that epigenetic modification (through methylation) occurs because of the excessive secretion of the GC hormone. "This gets at the mechanism through which we think epigenetics is important," says Potash. "Epigenetic marks added to DNA through life experience may prepare an animal for future events. If you think of the stress system as preparing you for fight or flight, you might imagine that these epigenetic changes might prepare you to fight harder or flee faster the next time you encounter something stressful."[5] Those of us who face stressors such as unreasonable work deadlines are—unlike our cousins in the animal world—unable to fight or flee, and such chronic stress may lead these emotionally trapped humans to experience a variety of hormonal disorders that are then "baked in the cake" epigenetically. This new research suggests that epigenetic changes may play a key role in creating stress-related diseases, and could point to effective treatments.

Meditation Positively Alters Gene Expression

Today's popular mindfulness and meditation practices come in many forms and are now known to have more than a few measurable effects on mental health. For example, the secular meditation-training program known as mindfulness-based stress reduction (MBSR) has long ago been shown to reduce depressive symptoms. More recently, MBSR researchers at Duke University wanted to know how the beneficial effects of this practice on depressives might vary according to demographics. For example, what happens if we factor in a person's religious belief system? Or, how does age or gender modify the effect of MBSR on depression? To answer such questions, a team of researchers led by Dr. Jeffrey M. Greeson, PhD, MS, of the Duke Integrative Medicine Center studied the variations in depressive symptom outcomes among 322 adults who enrolled in an eight-week MBSR program. Remarkably, they discovered that depressive symptom severity decreased significantly, showing statistically significant reductions across all the identified subgroups—including religious affiliation, intention for spiritual growth, gender, and baseline symptom severity.

Discussion of their findings by Greeson and his colleagues is worth paraphrasing in detail: The current results suggest that changes in depressive symptoms following MBSR are explained, in part, by increased mindfulness of thoughts and feelings and by an enhanced perception of spirituality in daily life. Given the connection between spirituality and mental health, mindfulness practice could parallel religious and spiritual practices, such as prayer and meditation.… Other MBSR outcome studies have reported that reduced depressive symptoms may be partially explained by lower levels of rumination, a known risk factor for depression.… Equally likely, the decrease in depressive symptoms may arise from the practice of disengaging from depressive thoughts and recognizing that they are just mental events rather than truth—a core skill called decentering.[6] Because of this significant link to the reduction of depression, I would suggest that the next logical step for Greeson's team should involve research into the epigenetic effects of MBSR. In fact, such an epigenetic link has already been discovered in a related form of meditation. The well-known form of meditation known as the relaxation response technique has recently been shown to not only have measurable psychological benefits, but also discernible effects on gene expression.

Nearly 40 years ago, Dr. Herbert Benson, MD, of Harvard Medical School identified a discrete mind-body process that he named the relaxation response and showed it to be the physiologic opposite of the well-known fight-or-flight response. Benson describes it as a state of deep rest attained through breathing, meditation, yoga, and related practices. His so-called relaxation-response meditation technique is now widely used to help patients manage a variety of medical conditions from anxiety and chronic pain to cancer. In an important additional breakthrough in 2013, researchers led by Benson at Massachusetts General Hospital and Beth Israel Deaconess Medical Center reported that the relaxation response triggers changes in gene expression that can affect the body's immune function, energy metabolism, and insulin secretion. One of Dr. Benson's collaborators at Beth Israel Deaconess is Dr. Towia Libermann, PhD, the co-senior author of the study. According to Libermann, the evidence arising from their study clearly links the relaxation response to rapid changes in gene expression. Libermann reported that genes involved both in immune disturbances and inflammation pathways were repressed after participants practiced the relaxation technique, while another set of pathways involved in mitochondrial function and energy production were epigenetically enhanced.[7] In the study, 26 participants were longtime practitioners of the relaxation response and 26 others who had never experienced it before were trained in the technique. Researchers used gene profiling to identify changes in these subjects' gene expression. "These changes," Libermann said, "occurred in both groups, but were more pronounced among the long-time relaxers." Libermann, who had worked with Benson for the previous decade, says he was drawn to this research "to convince myself that there's really something going on here, and it's not just a placebo effect.…I'm [now] pretty convinced." He and Benson are currently investigating whether the relaxation response triggers molecular-level changes in people with hypertension, inflammatory bowel disease, irritable bowel syndrome, and other diseases.[8]

In a 2008 study that had focused on the long-term practice of the technique, Benson and Libermann also discovered changes in stress-response genes. Blood samples from participants were analyzed to determine effects on 22,000 genes, and revealed significant changes in the expression of several important groups of genes over time. In particular, genes that manage energy metabolism were found to be upregulated because of the relaxation response, and pathways controlled by the activation of a protein called NF-κB—which is known to play a prominent role in inflammation, stress, trauma, and cancer—were suppressed by the practice. Because of these positive results, Benson and Libermann have concluded that "relaxation causes multiple gene-expression changes that create 'mitochondrial resilience' by stabilizing key cellular processes during the adaptation to oxidative stress and by enhancing cell survival and function. The rapidity of these changes is noteworthy, as is the finding that more changes occur with more practice."[8]

Building on these results, researchers have demonstrated with convincing evidence that mindfulness meditation can induce immediate and direct modification of gene expression. Previous studies had shown dynamic epigenetic responses to diet or exercise within just a few hours, but for the first time, two new studies have demonstrated evidence of epigenetic changes following a single period of mindfulness practice. The first is a landmark study published in 2014 in Psychoneuroendocrinology by researchers in Wisconsin, Spain, and France that provides evidence of gene changes following a daylong period of mindfulness practice. After eight hours of disciplined sitting, meditators showed a range of genetic and molecular alterations, including reduced levels of pro-inflammatory gene expression that were not observed in the non-meditating control group. "Most interestingly," writes Dr. Perla Kaliman, PhD, of the Institute of Biomedical Research in Spain, who was the first author of the article, "the changes were observed in genes that are the current targets of anti-inflammatory and analgesic drugs.… Our findings set the foundation for future studies to further assess meditation strategies for the treatment of chronic inflammatory conditions." Another leader of the study, Professor Richard J. Davidson, PhD, founder of the Center for Investigating Healthy Minds at the University of Wisconsin-Madison, noted, "We can think of genes possessing a molecular volume control that ranges from low to high that will govern the extent to which the gene produces the protein for which it is designed. The genes that we found to be down-regulated with mindfulness meditation practice are those implicated in inflammation."[9]

Just as remarkable is a 2013 study from Harvard Medical School that showed immediate effects from a far briefer period of meditation. In this study, gene profiles were analyzed in 26 long-term meditators before and after a mere 20-minute practice session. These profiles were compared to 26 novices who were not meditators. In the long-term meditators, there was an increased expression of genes involving energy metabolism, mitochondrial function, insulin secretion, and repair of telomeres. Additionally, the genes involved in inflammatory response and oxidative stress were suppressed or turned off. Researchers were amazed that such changes could take place after only 20 minutes of practice by skilled meditators. Clearly, the changes in the state of consciousness in the minds of the meditators created a cascade of biological events that led to altered gene expression, which in turn changed specific biochemical pathways that govern their health and illness. With these important studies, we now have compelling evidence of the power of the mind to move our genes and body chemistry toward optimal states of health and longevity. ■

References

1. Labonté B, Suderman M, Maussion G, et al. Genome-wide epigenetic regulation by early-life trauma. Arch Gen Psychiatry 2012;69:722–731.

2. Rowland K. Childhood stress leaves genetic scars. 2012. Online document at: www.sciencemag.org/news/2012/04/childhood-stress-leaves-genetic-scars

3. Shalev I, Moffitt TE, Sugden K, et al. Exposure to violence during childhood is associated with telomere erosion from 5 to 10 years of age: A longitudinal study. Mol Psychiatry 2013;18:576–581.

4. Leigh S. Working up a sweat may protect men from lethal prostate cancer. 2015. Online document at: www.ucsf.edu/news/2015/11/253051/working-sweat-may-protect-men-lethal-prostate-cancer

5. Wein H. Stress hormone causes epigenetic changes. 2010. Online document at: www.nih.gov/news-events/nih-research-matters/stress-hormone-causes-epigenetic-changes

6. Greeson JM, Smoski MJ, Suarez EC, et al. Decreased symptoms of depression after mindfulness-based stress reduction: Potential moderating effects of religiosity, spirituality, trait mindfulness, sex, and age. J Altern Complement Med 2015;21:166–174.

7. Bhasin MK, Dusek JA, Chang BH, et al. Relaxation response induces temporal transcriptome changes in energy metabolism, insulin secretion and inflammatory pathways. PLoS One 2013;8:e62817.

8. Zimmerman R. Say 'Om': Researchers find gene action altered after relaxation practice. 2013. Online document at: www.commonhealth.legacy.wbur.org/2013/05/genes-altered-after-relaxation-practice

9. Bergland C. Meditation has the power to influence your genes. 2013. Online document at: www.psychologytoday.com/blog/the-athletes-way/201312/meditation-has-the-power-influence-your-genes.

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