Public release date: 1-Jul-2008

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Relaxation response can influence expression of stress-related genes

Genomic study finds common biological basis for effects of mind/body practices

How could a single, nonpharmacological intervention help patients deal with disorders ranging from high blood pressure, to pain syndromes, to infertility, to rheumatoid arthritis? That question may have been answered by a study finding that eliciting the relaxation response – a physiologic state of deep rest – influences the activation patterns of genes associated with the body's response to stress. The collaborative investigation by members of the Benson-Henry Institute for Mind/Body Medicine at Massachusetts General Hospital (MGH) and the Genomics Center at Beth Israel Deaconess Medical Center (BIDMC) appears in the open-access journal *PLoS One*.

"For hundreds of years Western medicine has looked at mind and body as totally separate entities, to the point where saying something 'is all in your head' implied that it was imaginary," says Herbert Benson, MD, director emeritus of the Benson-Henry Institute and co-senior author of the PloS One report. "Now we've found how changing the activity of the mind can alter the way basic genetic instructions are implemented."

Towia Libermann, PhD, director of the BIDMC Genomics Center and the report's co-senior author, adds, "This is the first comprehensive study of how the mind can affect gene expression, linking what has been looked on as a 'soft' science with the 'hard' science of genomics. It is also important because of its focus on gene expression in healthy individuals, rather than in disease states."

More than 35 years ago Benson first described the relaxation response, which can be elicited by practices including meditation, deep breathing and prayer; and his team has pioneered the field of mind/body medicine. Over the years, studies in many peer-reviewed journals documented how the relaxation response not only alleviates

symptoms of psychological disorders such as anxiety but also affects physiologic factors such as heart rate, blood pressure, oxygen consumption and brain activity. While it became evident that the relaxation response was the opposite of the well documented fight-or-flight response, the mechanism underlying these effects was still unknown.

The current study was designed to investigate if changes in gene expression – whether specific genes are activated or repressed – were behind the wide-ranging effects of the relaxation response. The first phase compared gene expression patterns of 19 long-term practitioners of different relaxation response techniques with those of 19 individuals who had never engaged in such practices. Those control participants then went through an 8-week training program to investigate whether initiating relaxation response practice would change gene expression over time.

Both phases of the study indicated that the relaxation response alters the expression of genes involved with processes such as inflammation, programmed cell death and how the body handles free radicals – molecules produced by normal metabolism that, if not appropriately neutralized, can damage cells and tissues. To validate those results, both phases were repeated in 6 different relaxation response practitioners and 5 non-practitioners, resulting in significantly similar changes in gene expression.

Jeffery Dusek, PhD, co-lead author of the study notes, "Changes in the activation of these same genes have previously been seen in conditions such as post-traumatic stress disorder; but the relaxation-response-associated changes were the opposite of stress-associated changes and were much more pronounced in the long-term practitioners." Formerly with the Benson-Henry Institute, Dusek is now at Abbott Northwestern Hospital in Minneapolis.

Benson explains, "People have been using these culturally determined mind/body techniques for millenia. We found that no matter which particular technique is used – different forms of meditation and yoga, breath focus, or repetitive prayer – the mechanism involved is the same. Now we need to see if similar changes occur in patients who use the relaxation response to help treat stress-related disorders, and those studies are underway now."

Libermann notes that the sensitive genomic analyses conducted in this study are at the cutting edge of efforts to unravel the genetic aspects of complex disorders. "There are a lot of differences in gene

expression between one healthy person and another, so it is challenging to analyze the kinds of subtle changes we are seeing and identify what changes are significant and what are just background noise. Our approach uses the latest bioinformatics tools to identify potential gene functions, generating hypotheses that can then be tested in laboratory or clinical studies."

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Benson is the Mind/Body Medical Institute Associate Professor of Medicine at Harvard Medical School, where Libermann is an associate professor of Medicine. Hasan Otu, PhD, of BIDMC Genomics Center is co-lead author of the *PLoS One* study. Additional co-authors are Ann Wohlhueter, Benson-Henry Institute; and Manoj Bhasin, PhD, Luiz Zerbini, PhD, and Marie Joseph, BIDMC. The study was supported by grants from the U.S. Centers for Disease Control and Prevention and the National Institutes of Health.

Massachusetts General Hospital (www.massgeneral.org), established in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of more than $500 million and major research centers in AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, human genetics, medical imaging, neurodegenerative disorders, regenerative medicine, systems biology, transplantation biology and photomedicine.

Beth Israel Deaconess Medical Center (www.bidmc.harvard.edu) is a patient care, teaching and research affiliate of Harvard Medical School and consistently ranks in the top four in National Institutes of Health funding among independent hospitals nationwide. BIDMC is a clinical partner of the Joslin Diabetes Center and is a research partner of the Dana-Farber/Harvard Cancer Center. BIDMC is the official hospital of the Boston Red Sox.