Reaction to stress traced to genetic differences

April 5 2009

Can people's differing reactions to situations of stress be attributed at least in part to genetic differences and do those differences affect men and women in different ways - with the edge seemingly favoring the women? Research conducted at the Hebrew University of Jerusalem would seem to indicate that the answer to both questions is yes.

Some people appear to be resilient to difficult conditions, whereas others react adversely to such challenges, incurring a range of physical and mental disorders. Much research has shown that the way in which the brain and body adapt to acute and chronic stress are critical for physical and mental health. Further, according to a recent report by the World Health Organization (WHO), stress will be the second leading cause of mortality worldwide over the next 20 years.

It is generally believed that the genetic code plays a prominent role in different responses to stress. It has been estimated that the heredity factor determines by some 62 percent the level of the stress hormone (cortisol) in our bodies. However, only a handful of investigations so far have documented the role of specific genetic variants on shaping the stress response among individuals.

In an effort to reveal a genetic basis for coping with stress, the Hebrew University researchers devised a laboratory-based social stress test. The trials were carried out on students at the Hebrew University Department of Psychology and at the Aaron Beare Research Laboratories at Herzog Hospital by Idan Shalev, a doctoral student of Hebrew University

Psychology Prof. Richard Ebstein, and in collaboration with Dr. Marsha Kaitz of the Department of Psychology. The results were published recently online in the journal Psychoneuroendocrinology.

In the test, the researchers examined the salivary cortisol response in 97 university students via the Trier Social Stress Test (TSST) devised at Trier University in Germany. The TSST measures changes in salivary cortisol to assess stress reactivity to challenging social situations.

The students were told that they would play the role of an interviewee for a job and had five minutes to convince the interviewers to hire them. The interview was carried out with a microphone and camera in front of a panel of three straight-faced judges. Additionally, in a second phase of the interview, subjects were tested in a mental arithmetic task in which they were asked to count backwards (out loud) from 1,687 in multiples of 13 as quickly and accurately as possible. If the subject made a mistake he or she was asked to start the series again.

In addition to testing the cortisol level, mouthwash samples were taken and subjects were genotyped for the brain-derived neurotrophic factor (BDNF) gene, which is involved in supporting the growth and differentiation of brain cells. Importantly, animal studies show that BDNF expression is reduced in chronic stress and restored by antidepressant treatment.

The BDNF gene is characterized by a variant that codes for either the valine (Val) or methionine (Met) amino acids. Individuals carry two copies of each gene, with the Val variant being more common. In the study, subjects carrying two copies of the VAL variant (Val/Val), were compared in their cortisol response to those carrying one copy of the Val and one of the Met (Val/Met).

When looking at the responses of the subjects in the stress testing, it was

seen that the Val/Met men and women carriers had nearly equal cortisol levels. However, the men with the Val/Val variant had a higher cortisol response (and therefore a higher reaction to social stress) than the men carrying the Val/Met variant. For the women, surprisingly, the opposite was found: the Val/Val women had a lower cortisol response than the Val/Met women. Why the Val/Val variant produces opposite stress reactions (raising it for the males and lowering it for the females) remains an enigma.

Because of the predominance of the Val/Val type for both sexes, the males showed overall greater stress in the testing than the females.

The Hebrew University researchers point out that their investigation shows the importance of genotyping as an aid in helping to resolve paradoxical observations related to stress-related sex differences and also in providing new insight into understanding how depression and other psycho-neurological illnesses may be the result of a combination of stressful life events and genetic factors.

In conclusion, say the researchers, the study specifically indicates that women with the BDNF Val/Met genotype and men with the Val/Val may be particularly vulnerable to social stress mediated by brain stress system activity.

Source: Hebrew University of Jerusalem

provided for information purposes only.