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EDITORIAL

Stress Research: Bridging Sociology and Biology

Stress is a common phenomenon in modern life. In academic institutions students encounter stressful situations with a fixed frequency, when they are compelled to write examinations. In the final years of school the pressures build, as competitive entrance examinations, requiring intense preparation, loom ahead. Research students who have generally put the hurdles of examinations behind them face an unfamiliar pressure; the need to obtain research results of an adequate quality and quantity to successfully complete a Ph D thesis. Research is often an uncertain enterprise, requiring several years of effort to put together a dissertation; a long haul involving close interaction with a supervisor. The relationships between students and mentors in research institutions can at times be strained; a not uncommon situation in human interactions. Supervisors are often under pressure to produce results and publications to obtain grants to further their own research careers. This pressure is often transferred to students, who are the true workforce in research laboratories. It is therefore common in academic institutions to encounter a fair number of unhappy individuals, who appear to be finding it difficult to cope with pressures and stress. Having done more than my fair share of amateur counselling for distressed individuals, I was pleasantly surprised to be invited to the opening of a web-based 'chat site', which would facilitate quick, easy and anonymous counselling by experienced counsellors. Being able to seek help without attracting undue attention can be a source of comfort to distressed individuals. Stress and strain are terms often used and readily understood by physicists and engineers. Stress is a term that is hard to define and even harder to measure in studies of human behaviour. Some individuals find it difficult to handle even mildly uncomfortable situations, while others display remarkable resilience, coping even with situations which appear catastrophic to most people. Modern life, especially in crowded urban centres provides an environment that promotes stress. Research on the factors that contribute to stress and strategies for creating environmental conditions for reducing stress has largely been the preserve of sociologists. Is human behaviour determined by our genetic make-up or is it entirely shaped by our environment? This is an old question, which has often

been asked triggering a debate that appears to pit sociologists against biologists – 'nature or nurture'.

A special section in the October 11 issue of *Nature* presents a wonderfully readable overview of the growing recognition that severe and prolonged stress does indeed leave a physiological imprint, with biochemical changes triggering a cascade of events that influence gene expression. Intriguingly, some current research appears suggestive of aberrant physiology being transmitted to the next generation. The prefatory editorial reminds readers of the origins of the sociology–biology divide, quoting Francis Galton: 'Nature is all that a man brings himself into the world; nurture is every influence which affects him after his birth.' The advance of modern biology over a century has ensured that 'biological determinism' is not an idea that is any longer tenable. Neuroscientists are comfortable with the idea that the environment can profoundly influence brain activity. In contrast, sociology has often sought to distance itself from scientific research that probes the causes of human behaviour. At times, this stubborn distancing from science has served a valuable purpose. As the *Nature* editorial notes, by 'energising the debate' sociologists 'did a service to both academia and society by keeping scientific arrogance and influence in check' (*Nature*, 2012, 490, 143). Stress can be caused by a myriad factors. However, individuals can differ widely in their responses to stress; an observation that suggests that it might indeed be rewarding to understand the 'roots of resilience' (Hughes, V. A., *Nature*, 2012, 490, 165).

Most readers will relate immediately to a feature that highlights the role of urban decay in promoting stress and all the attendant consequences. Alison Abbot cites a study in a London suburb, that revealed a doubling of schizophrenia cases 'from around 11 per 100,000 inhabitants per year in 1965 to 23 per 100,000 in 1997 – a period in which there was no such rise in the general population'. With populations in cities growing alarmingly, and India's cities are amongst the fastest growing, public health issues relating to mental illness may assume disturbing levels. Can the effects of stress on the brain be measured? It has long been known that the immediate physiological response to stress results in a surge of the levels of the hormones adrenaline and cortisol. These

hormones are released in response to signals from the brain, a complex process involving both chemical and electrical events. Once introduced into battle, adrenaline and cortisol direct blood flow and enhance sugar levels, providing the burst of energy that animals and humans need both for fighting and fleeing. The reserves of energy that we summon arise from an instinctive response of the brain to stress. Can these responses be monitored and are there methodologies that permit an assessment of the long term consequences of these sudden and dramatic chemical events triggered by stress? Brain imaging techniques now allow an unprecedented view of the workings of different regions of the brain. The *Nature* article draws attention to a study published last year that 'clearly showed that people who grew up in cities process negative emotions such as stress differently from those who move to the city as adults' (Abbot, A., *Nature*, 2012, **490**, 162). The study by F. Lederbogen *et al.* (*Nature*, 2011, **474**, 498) was cleverly designed to probe the effects of 'social stress' on two groups of volunteers, with distinctly different backgrounds. Interestingly, the regions of the brain activated by stress appeared to be different in volunteers with a history of city dwelling, as compared to the group who had only recently moved to urban surroundings. These studies appear to provide a connection between environmental factors, the province of sociologists, and neurobiology and neurochemistry, which undoubtedly lie in the domain of hard science. A mounting body of evidence suggests that there is a distinct genetic predisposition to psychiatric illness, with environmental stresses hastening the descent into disease. Ongoing research attempts to pull together functional magnetic resonance imaging studies and large scale analysis of genes correlated with the occurrence of schizophrenia. Stress appears to activate regions of the brain that process negative emotions to a much greater extent in those bred in cities as compared to their compatriots from non-urban backgrounds. The *Nature* report provides interesting previews of planned research, which attempts to delineate the most stressful regions of a city; a project that draws together a curious combination of physicists, geoscientists and neuroscientists.

The biochemical markers of stress are now becoming more and more evident. Elizabeth Blackburn, the 2009 Nobel laureate in Physiology or Medicine, provides a clear warning that chronic stress and disease may be linked by the observed shortening of 'telomeres', in diverse examples of stress over prolonged periods. Telomeres are long stretches of up to a few thousand DNA bases, which shorten each time a living cell divides. While enzymatic mechanisms exist to extend telomeres, aging results in shortening. The finding that pronounced shortening is also correlated with stress suggests that stress induced premature onset of age related disease is a distinct possibility (Blackburn, E. H. and Epel, E. S., *Nature*, 2012, **490**, 169). Recent work underscores the

connection between shorter telomeres and stress in groups ranging from 'kindergarten-aged children to adults as old as 80; from small clinical samples of less than 100 people to large population-based samples of thousands'. Blackburn and Epel note that there are 'three pairwise links involving three factors: stress with telomere shortness; stress with disease risks; and telomere shortness with risks for these diseases. It is hard to avoid the inference that at least one of the ways stress causes chronic diseases is by shortening telomeres'. Do these research findings hold promise for 'practical ways to improve human health'? One approach would of course be to propose a search for drugs to boost telomerase activity (the process by which cells lengthen eroding telomeres), 'without inducing unwanted side-effects'. This is a strategy that will require a formidable investment of effort, with no guarantee of quick success. Are there any alternatives? Blackburn and Epel point the way towards an approach that might find favour with social scientists. They suggest: 'More feasible approaches to alleviating telomere shortening could involve mitigating the conditions that lead to chronic stress and helping people change certain behaviours.' The warning signs of shrinking telomeres appear to be evident in children subjected to abusive treatment and in infants born to stressed mothers. Blackburn and Epel conclude on a sombre note: 'Telomeres send one or more signal – from the tips of our chromosomes – that unmanageable social and psychological stress, especially during early life, is as insidious as smoking or too much fast food.'

Are there other connections between our genes and our environment? Recent research suggests that epigenetic processes may hold the key. In attempting to explain how 'trauma affects people differently', E. J. Nestler highlights work that suggests a role for 'experience-dependent molecular alterations to DNA or proteins that alter how genes behave without changing the information they contain' (*Nature*, 2012, **490**, 171). In hunting down biochemical markers of stress response, there is a need to distinguish changes that are adaptive in nature from those that are deleterious. Nestler surveys controversial work suggesting that animals can 'inherit epigenetic vulnerability to stress'. Animal models are becoming available to determine whether maternal stress can be transmitted to offspring. Nestler is cautious in pointing out that 'epigenetics is in vogue'. There is indeed an understandable haste in identifying 'correlations between behaviour and molecular alterations in cells without establishing a causal link'.

Stress and the mental disorders that often follow pose a difficult challenge. As the connections between biology and the environment are better understood it may be possible to search for solutions. This will need sociologists and biologists to work in tandem. Stress research may indeed bridge the two cultures.

P. Balaram