The allocation principle has also been tested using more direct approaches, involving natural selection in the laboratory. Such experiments have a rich history, probably beginning with the experiments of Reverend William H. Dallinger, a contemporary of Darwin who was likely best known for his detailed accounts of protozoan life cycles, which helped dispel a widely held view at the time that life arose *de novo*, from nothing.

Encouraged by Darwin, Dallinger sought to test the theory of evolution via natural selection by subjecting protozoa to increasingly higher temperatures to see if they would adapt to the new conditions. To do this, Dallinger had to construct an incubation apparatus that allowed precise control of temperature (Figure 2). In an experiment that lasted seven years, Dallinger was able to show that an organism originating from an environment where the temperature is 60°F could, amazingly, become adapted to 158°F. Darwin's own reaction on hearing about the work speaks to its importance: "I did not know that you were attending to the mutation of the lower organisms under changed conditions of life; and your results, I have no doubt, will be extremely curious and valuable. The fact which you mention about their being adapted to certain temperatures, but becoming gradually accustomed to much higher ones, is very remarkable. It explains the existence of algae in hot springs." Interestingly, when Dallinger placed the adapted protozoa back at 60°F, this proved lethal, an observation that would seem consistent with the allocation principle.

The tradition of experimental evolution continued into the 20th century with work on a number of other organisms chosen in part for their relatively short generation times, such as *Drosophila*. But the Dallinger experiment has a particularly close corollary in a fruitful line of research initiated by Richard Lenski and colleagues, who have been performing a long-term evolution experiment on bacteria exposed to different, sometimes varying conditions. Initiated in 1988, the experiment has now crossed the 50,000 generation mark. The work has addressed a number of questions, but, of relevance to Dallinger and allocation theory, Bennett and Lenski placed 20 different lines of *Escherichia coli* at 20°C for 2,000 generations and then asked how they fared at 40°C [3]. In general, while fitness increased at 20°C, it became reduced at 40°C, consistent with allocation theory. But the effect was not universal as several lines showed no loss of fitness at the higher temperature and, in one case, even greater fitness.

What we can take away from these studies is that we are starting to see patterns that in some cases are consistent with tradeoffs occurring over the course of evolution, but this is certainly not a given. In some cases, there is apparently no penalty for maintaining adaptations that are no longer of use. It will be interesting to continue to gather data from more species using different stresses and selection regimes to see if these patterns hold up. And, of course, we'll want to better understand the genetic basis of adaptation to stress so that we can start to understand the mechanisms and why, in some cases, a tradeoff may be necessary as organisms adapt to stressful environments.

Coming full circle then, we can see that the term 'stress' can be broadly construed, functioning as an integral part of the life cycle but more often manifesting as an environmental insult, in response to which homeostatic mechanisms arise. Stress responses also operate at various scales, from rapid millisecond responses that restore homeostasis, to the adaptation of organisms over evolutionary timescales. The reach of stress into so many facets of biology is such that we almost take it for granted. It seems appropriate then that we devote this special issue to the topic and explore stress in its various forms. Enjoy!

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Feature

Chronic stress means we're always on the hunt

Stress responses that evolved for occasional dangerous situations can make us ill when they become chronic. But why do we perceive our relatively safe lives as stressful and what can we do to avoid the associated dangers? **Michael Gross** investigates.

Life for many mammalian species is a long string of happy days spent grazing in the savannah — brutally interrupted by short moments when a predator shows up and they have to run for their lives. Herbivores, like the horses and their relatives, have evolved a range of characteristics especially for these short moments of flight, from their fast-running legs through to the ability to keep cool by abundant sweating (shared with humans but otherwise rare in the animal kingdom).

The situation is similar for the hunters, albeit reversed. Lions spend much of their day sleeping and digesting, interrupted by short periods of hunting fleet-footed prey. Their survival also depends on this short period of exertion, as they would starve if they failed to hunt successfully.

In both cases, two systems are activated. The sympathetic nervous system prepares the body's organs for 'fight or flight' responses, increasing oxygen intake, blood pressure, heart rate, and muscle activity, while shutting down the digestive system. Additionally, a general hormone response is activated that makes extra energy available for the short-term use and sharpens the senses. Specifically, the HPA axis (hypothalamus, pituitary gland, and adrenal cortex) releases hormones including corticosteroids and the catecholamines adrenaline (epinephrine) and noradrenaline, which enhance metabolic activity (increasing blood sugar), and improve alertness and attention. These two processes, nervous and endocrine (hormonal), work together to form the physiological stress response.

Red danger: The physiological stress response is good and important in dangerous situations where rapid reactions are needed, but damaging if it becomes a chronic element of everyday life. Psychologist Catherine Franssen reports that extreme sports like sky diving or rock climbing may help to put the trivial problems of modern life into perspective. The picture shows the Red Devils Freefall Team. (Photo: ©Crown Copyright. Used with permission from The Red Devils Freefall Team (www.reddevilsonline.com).)

Humans share these very same responses with other mammals, and they can also be life-saving for us in dangerous situations. However, if the hormonal response is used too often, and stays turned on for too long, the emergency programme turns into chronic stress, and this has a wide range of damaging effects that can lead to fatal diseases, including heart failure.

We are facing something of a paradox here. As long as we don't live in war zones or engage in extreme adventures, our lives are safer than they ever were in human history and there are no predatory species left that we should fear, apart from our own. So why has stress become a defining feature of modern life and a major health concern?

Cultural history of stress

The definition of biological stress as a situation an individual can be in, as opposed to the concept from physics, which describes the external forces that might induce a strain, can be traced back to the work of the Hungarian endocrinologist Hans Selye (1907–1982).

In the 1960s, it became a widely investigated concept in psychology, and by the 1970s it spread into popular usage, along with associated terms such as burnout and midlife crisis.

Researchers investigated causes of stress in the environmental conditions of modern life, including the work environment, the commuter experience in an increasingly suburbanised society, and social discrimination. Medical research also became interested in the impact of stress on conditions such as heart disease.

It is, again, a remarkable paradox that the rapidly increasing wealth and safety in Western societies after the end of World War II should lead to increasing concerns over stress. Shouldn't people have been blissfully happy with their new peacetime lives?

As it turned out, the constant flow of minor 'threats' in a competitive work environment, such as deadlines, demands for rapid decisions, etc., were producing a situation that continuously triggers the natural stress response and thereby produces chronic stress instead of the rare emergency response that it evolved for.

It could almost appear that war, with its alternation of boredom and moments of life-threatening crisis, is better suited to fit the natural stress response. However, in response to recent changes in the nature of conflict, the military has also become involved in stress research, with a view to reduce the impact of combat stress and trauma in their personnel.

The concept of post-traumatic stress disorder (PTSD) was also popularised in the 1970s, particularly by protestors against the Vietnam war. This recognised psychiatric condition is separate from chronic stress. Typical symptoms include frequent intrusive flashbacks in which the patient involuntarily re-experiences the traumatic events they have been exposed to, as well as recurring nightmares. These can severely affect trust, confidence, concentration, sleep, and general mood. Interestingly, PTSD is more likely to be caused by man-made trauma, such as violence, than by natural disasters, such as forest fires.

Red mind

Since the problems of chronic stress started to become appreciated in the 1970s, technology has made huge progress and provided us with all kinds of devices designed to facilitate tasks, thus promising to make life easier for us. But has it worked out?

Today, somebody running late for an appointment no longer has to look for a phone booth to make a call, and motorists can rely on their electronic helpers to find the most efficient route and avoid road closures and traffic jams. And yet we appear to be no less stressed than we were in the 1970s.

On the contrary, psychologists are warning that the presence of smartphones in our pockets, making us contactable around the clock and wherever we may be, might add to the problems. While each individual contact may be easily manageable, the fact of being exposed to external demands around the clock is adding to the chronic stress.

In the 'always-on' society, it is becoming increasingly difficult to escape the emails and calls from bosses, colleagues or customers demanding immediate attention even outside office hours. In a brave attempt to swim against this tide, France has recently legislated to make it illegal to email employees out of their working hours.

An additional problem created by communications technology is the temptation to use many channels at the same time. While many people like to believe they can easily manage multitasking, psychologists and neuroscientists have warned that what

they actually do is switching back and forth between separate activities, which may mean that one of them isn't getting enough attention. This is why many countries have had to ban the use of mobile phones while driving.

The chronic stress heightened by relentless intrusion of communication gadgets into all aspects of our lives presents significant health problems in the long term, says Catherine Franssen from James Madison University at Harrisonburg, Virginia, US.

"Most of the leading causes of debilitating illness and death are correlated with, if not caused by, stress," Franssen explains. "Loads of research has provided direct links between stress and heart disease, stroke, diabetes, and suicide/self-harm. Further, stress can impact the immune system, leading to vulnerability to infectious and chronic diseases. And we need only to look at our own lives to note that more accidents happen when we are stressed. While some of those accidents are as simple as slicing a finger instead of a vegetable while preparing a meal too quickly, all too many accidents are much more severe — particularly when you add in the risks of multitasking."

As a remedy for chronic stress, she advocates giving the stress response system, which she likes to call the "red mind" (in contrast to the more relaxed "blue mind" which we will encounter below), some real work to do. From her own experience as a skydiver, Franssen knows that activities confronting the red mind with real danger in the way it evolved to operate can put the significance of everyday stressors into perspective.

"I started skydiving in graduate school and became quickly hooked not only on the adrenaline rush, but also the super-fast problem-solving challenges that sport provided," Franssen recalls. "When I returned to the trials of top-tier graduate study after a weekend of skydiving, I found myself calmer, more relaxed, and better able to put the strain of deadlines and experimental difficulties into perspective. That, at least, wasn't life or death!"

Recently, Franssen has studied the hormone responses of extreme climbers and found that their levels of stress hormones were lower than those of control subjects in comparable situations, such as taking college exams. She is continuing this work with other extreme sports enthusiasts to explore whether extreme sports might really be a scientifically viable alternative treatment for anxiety.

Blue solutions: The serenity we get from looking out across the sea or large rivers can help to restore hormonal balance and overcome stress-related problems, as Wallace J. Nichols argues in his new book, *Blue Mind*. The image shows the skyline of Frankfurt, Germany, exuding calm after a busy day for bankers and builders. (Photo: Michael Gross.)

Communications media apart, another important area that can significantly relieve or add to chronic stress is urban planning and transport. As Charles Montgomery has explained in his recent book *Happy City*, the development of car-friendly cities, such as Los Angeles and Atlanta in the US or Milton Keynes in the UK, during the second half of the 20th century has added to commuter stress and seduced people into unhealthy habits of walking less and driving everywhere.

Montgomery cites research showing that people would on average like to spend 16 minutes getting to their work place, and tend to be happier when they can walk or cycle to work. In the US, however, 90% of commuters drive, and their journey takes more than 25 minutes each way on average.

Experiments have shown that unhappy commuters stuck in their cars have unhealthy, chronically elevated levels of stress hormones in their circulation. In extremis, road rage incidents or reckless driving can be the result of this hormonal overload.

Reversing decades of planning that has made people more stressed and less happy will require interventions backed by a strong political will. Montgomery cites the city of Bogotá, Colombia, as a positive example. Back in the 1990s, motor traffic there was notoriously dangerous, and alternatives nonexistent. The introduction of car-reduction schemes and a new public transport system in the early 2000s, along with the improving political security situation, has achieved a dramatic turn-around, making the city safe and enjoyable for all road users including cyclists and pedestrians.

Blue mind

If you're suffering from chronic stress and don't have the power to redesign your city nor the courage to take up skydiving, what can you do about it? Wallace J. Nichols, a Research Associate at the California Academy of Sciences at San Francisco, California, recommends to go wherever you can find water. Nichols is an ecologist who works on conservation of sea turtles, which led him to become interested in the influence of the oceans on our emotional well-being (Curr. Biol. (2013) *23*, R501–R504).

Nichols coined the phrase "blue mind" for this interface between

Mobile madness: Electronic gadgets like smartphones and the associated culture of always being online have added to the stress of modern life. Psychologists warn that multitasking can diminish the attention we can devote to an important task, which can be particularly dangerous when driving. (Photo: Christopher J. Mills.)

our psychology and our natural environment. He organises the Blue Mind conference series, the fourth instalment of which takes place at Bedruthan Steps, Cornwall, UK, 10–12 June 2014, and will be live-streamed on the web (www.bluemind.me). As Nichols describes it: "over the past several years I've brought together an eclectic group of scientists, psychologists, researchers, educators, athletes, explorers, businesspeople, and artists to consider a fundamental question: what happens when our most complex organ —the brain — meets the planet's largest feature — water?"

He has also explained these ideas in a new book, called *Blue Mind: How Water Makes You Happier, More Connected, and Better at What You Do*, which is also due to appear in June. In his book, Nichols discusses a spate of recent psychology papers showing that the proximity of "blue nature" can improve people's physical and mental health and counterbalance the damaging effects of the chronic stress and the permanent engagement of the red mind. While the opportunity to exercise plays a part, several studies have shown that the positive effect of being near water can be separated from that aspect.

Water has also proven beneficial for people with specific problems beyond chronic stress. Nichols cites as examples organisations that offer kayaking excursions for war veterans with PTSD and/or physical injuries, such as Rivers of Recovery (ROR). Children with autism are also widely reported to have a natural affinity for water and to benefit from the calming effect of being near or on the water.

"Practising Blue Mind is no silver bullet solution," Nichols concludes, "but when understood and used in conjunction with indoor relaxation practices we find it to be widely useful. By describing and assigning the full value of the cognitive and emotional benefits and services to healthy waterways and oceans we provide a compelling additional argument for restoration, protection, maintenance and access."

Whether you decide to reduce stress by walking to work, by doing yoga on the beach, or by jumping out of planes, it all boils down to finding the natural balance between the highly alert red mind and the relaxed blue mind.

Michael Gross is a science writer based at Oxford. He can be contacted via his web page at www.michaelgross.co.uk

Primer

Stress and life history

Pat Monaghan and Karen A. Spencer

In his book on behavioural endocrinology, Randy Nelson describes 'stress' as a 'notoriously ethereal concept'. Yet, despite this lack of clarity, studies of the consequences of stress across different time scales, life history stages, taxa and levels of biological enquiry form a large part of modern biology and biomedicine. Organisms need to recognise and respond to environmental challenges. Being able to do so appropriately, and with minimal costs, is an important physiological attribute, with great adaptive value. The costs and benefits of different mechanisms that enable organisms to cope with unpredictable environmental changes can be manifest to different degrees at different life stages. Accordingly, the level of stress experienced in the environment can act as a strong selective pressure that drives the evolution of life histories.

Though tight definitions have certainly proved problematic, there is considerable consensus about what stress is and why it plays such an important part in shaping life histories. The more challenging the environment, the more important is the stress response system. The concept of stress is closely related to the concept of homeostasis. Both are best viewed as biological states, the latter representing the optimal physiological state or 'comfort zone', and the former the state that arises when homeostasis is disrupted. We can think of organisms as occupying a multi-dimensional physiological space, in which they have optimal zones or set points for key body parameters, such as temperature, metabolic activity, energy balance, blood flow, water balance and so on. When internal or external circumstances give rise to a situation that takes, or threatens to take, the individual out of its zone of tolerance for one or a number of parameters, or cause it direct harm,