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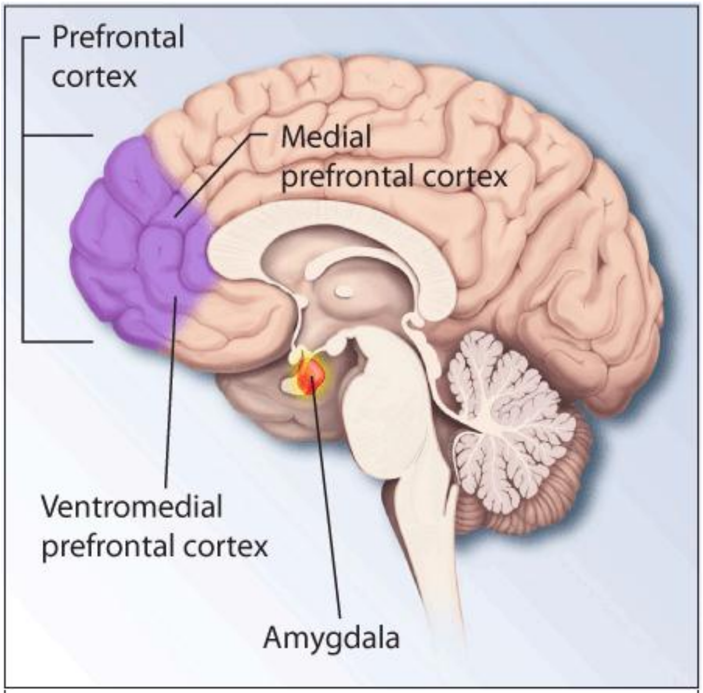
Stress

Stress affects even the most seemingly tranquil lives. We all experience it - during exams, competing in sports, or when falling out with friends and enemies alike. Why does it occur and what causes its unpleasant sensations? Is it good for anything? What happens when it goes wrong? Neuroscientists are beginning to understand how the brain generates a coordinated chemical response to stress.



Brain Structures Involved in Dealing with Fear and Stress

What is stress and why do we need it?

Stress is tricky to pin down. It isn't just being under pressure - for this is not always stressful - but some kind of mismatch between what the body and brain anticipate and what challenges we actually experience or feel. Many challenges that we face are psychological - reflecting the difficulties of interacting with others as we work towards academic success, compete for a place in the school team or, later in life, for a job. Other stresses are physical such as an acute illness or a broken leg in a car accident. Most stressors are mixed: the pain and other physical afflictions of an illness are coupled with worry and concern. Stress is a fundamental process. It affects all organisms, from the simplest bacterium and protozoan, to complex eukaryotes such as mammals. In single-celled organisms and in the individual cells of our bodies, molecules have evolved which provide a series of emergency systems that protect key cellular functions from unexpected external challenges and their internal consequences. For example, special molecules called heat-shock proteins guide damaged proteins to where they can be repaired or harmlessly degraded, thus protecting cells from toxicity or dysfunction. In complex organisms such as ourselves, stress systems have evolved as highly sophisticated processes to help deal with out-of-the-ordinary challenges that may afflict us. These use the cellular protection mechanisms as building blocks in a larger network of stress protection.

Stress and the brain

Stress is perceived and the response coordinated by the brain. Our cognitive appraisal of a situation in the brain interacts with bodily signals in the blood stream such as hormones, nutrients, and inflammatory molecules, and with information from peripheral nerves monitoring vital organs and sensations. The brain integrates these to produce a series of specific and graded responses. Our understanding of how it does this has come from the study of neuroendocrinology. Circulating hormones in the blood are monitored by the brain to enable the body to cope with stress.

Fight or Flight?

The easiest response to recognize is the immediate activation of what is - endearingly - called the sympathetic nervous system. After receiving a stressful challenge and computing the right response, the brain rapidly activates nerves originating from control centers in the brainstem.

These cause the release of noradrenalin in a variety of structures and of adrenaline from the adrenal glands (situated just above the kidney). Their release underpins the fight or flight response - the classical, immediate reaction that has to be made in response to danger. We all recognize the initial tingling sensation, sweating, heightened awareness, rapid pulse rate, higher blood pressure and general feelings of fear that we all feel in the moments immediately after a stressful challenge. These changes happen because of receptors that are found on blood vessels, causing them to constrict and so our blood pressure to shoot up, and in the heart, causing it to accelerate and produce the pounding sensation in the chest known as palpitations. There are also receptors in the skin causing hairs to erect (goosebumps) and in the gut causing those disconcerting abdominal sensations that we all sense as stress. These changes are there to prepare us to fight or to flee - and to concentrate blood flow to vital organs, the muscles and the brain.

The hypothalamic-pituitary-adrenal (HPA) axis

The second major neuroendocrine response to stress is activation of a circuit linking the body and brain called the HPA axis. This links together the hypothalamus, pituitary gland, adrenal cortex and hippocampus by a bloodstream highway carrying specialized hormones. The hypothalamus is the key brain area regulating many of our hormones. It has strong inputs from areas of the brain processing emotional information, including the amygdala, and from regions of the brainstem controlling sympathetic nervous responses. It integrates these to produce a coordinated hormonal output that stimulates the next part of the circuit - the pituitary gland. In turn, this releases a hormone called adrenocorticotrophin (ACTH) into the blood. ACTH then stimulates a part of the adrenal gland to secrete cortisol. Cortisol is a steroid hormone that is the key to understanding the next phase of the stress response. It raises blood sugar and other metabolic fuels such as fatty acids. This often occurs at the expense of proteins that are broken down into fuels required immediately - instant 'chocolate bars' for the muscles and brain. Cortisol also helps adrenaline to raise blood pressure and, in the short term, makes you feel good. Faced with the challenge of singing a solo at the school concert, the last thing you want to do is dwell on worrying things. You just want to do it right with as little self-consciousness as possible. Cortisol also turns off growth, digestion, inflammation, and even woundhealing - clearly things that can be better done later on. It also turns off sex. The last step of the circuit is cortisol feedback to the brain. The highest density of cortisol receptors is in the hippocampus, a key structure for learning and memory, but cortisol also acts on the amygdala, which processes fear and anxiety. The net effect is to turn on the amygdala - to allow learning of fear-related information; and to turn off the hippocampus - to ensure that resources are not wasted on more complex but unnecessary aspects of learning. Cortisol is focus juice.

A tale of two cortisol receptors and the shrinking hippocampus

The hippocampus has high levels of the two receptors for cortisol - let's call them the low MR and the high GR receptor. The low MR receptor is activated by the normally circulating levels of cortisol in the bloodstream highway of the HPA axis. This keeps our general metabolism and brain processing ticking over nicely. However, as cortisol levels begin to rise, particularly in the morning, the high GR receptor becomes progressively more occupied. When we become stressed, cortisol levels become very high indeed, activation of this receptor is sustained and the hippocampus is then shut down by a genetically controlled program. Put all this together and you have what is called a bell-shaped curve. This is the classical curve relating stress to brain function - a little bit is good for you, a bit more is better, but too much is bad!

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