Mapping the mind under pressure: Can brain imaging research tell us anything new about stress and physical health?

Professor Peter Gianaros
University of Pittsburgh

Thursday 10 May 2011
St Andrew's in the Square

Glossary

MRI: Magnetic Resonance Imaging is a medical imaging technique used in radiology to visualize detailed internal structures of the human body. Structural MRI reveals the form and structure of the brain.

fMRI: functional Magnetic Resonance Imaging: a type of specialized MRI scan used to measure the change in blood flow related to neural activity in the brain or spinal cord of humans. fMRI has come to dominate the brain mapping field due to its relatively low invasiveness, absence of radiation exposure, and relatively wide availability.

Stroop Test: is a measure of attention, cognitive flexibility and processing speed. It is used in the evaluation of executive functions of the frontal areas of the brain. The test requires subjects to inhibit the dominant tendency to read the name of a visually presented colour word (e.g. blue) and instead state the colour in which the word is printed (e.g. the word 'blue' printed in green ink would require the response 'green'). The naming of the colour of the word takes longer and is more prone to errors than when the colour of the ink matches the name of the colour. This creates stress and its neural and physiological correlates can be measured. The score is the time taken to complete the task.

Dendrites, **dendritic tree**: the branching process of a neuron that conducts impulses toward the cell. A single nerve may possess many dendrites.

Limbic system: is comprised of four main structures: the amygdala, the hippocampus, regions of the limbic cortex and the septal area. These structures form connections between the limbic system and the hypothalamus, thalamus and cerebral cortex. The amygdala plays a role in the processing and memory of emotional reaction, the hippocampus is important in memory and learning, while the limbic system itself is central in the control of emotional and stress responses.

Cingulate: an integral part of the limbic system, which is involved with emotion formation and processing, learning, and memory, and is also important for executive function and autonomic respiratory control.

Paralimbic system: the paralimbic cortex lies close to the limbic structures, and is directly connected with it. It is a group of interconnecting brain structures that are involved in emotion processing, goal seeking, motivation and self-control. Paralimbic brain areas have a dual role in processing emotional information and regulating physiology which supports adaptive behaviour.

Intramedia thickness: is a measurement of the thickness of artery walls, usually by external ultrasound, to detect the presence and track the progression of atherosclerotic disease in humans.

Overview

This lecture outlines the relationship between the stresses of everyday life and the incidence and distribution of cardiovascular disease. It describes the various neural and physiological pathways through which the stresses of everyday life differentially affect individuals and groups in the premature expression of cardiovascular disease.

Summary

In seeking to answer the question: "*How do stress processes instantiated in the brain translate into premature expression of cardio vascular risk?*" the lecture falls into three parts.

Firstly it describes the broader context in which research on this question has been conducted.

Secondly, it outlines the key aspects of brain imagery research investigating this phenomenon.

Thirdly it outlines which questions will be explored next based on the results so far.

Each of these three parts is summarised below.

The Broader Context

Peter began by saying that in investigating pathways between stress and the brain, he is especially interested in the behavioural and biological processes of such pathways which translate into disease risk.

In one line of enquiry, Peter and his colleagues use functional Magnetic Resonance Imaging (fMRI) to track areas of the brain which are involved in acute changes, occurring over minutes, to brain function and cardiovascular function during stressful episodes, for example increase in blood pressure and changes in heart rate.

In a second line of research they use structural Magnetic Resonance Imaging (sMRI) to explore longer term changes in the form and structure of the brain related to more chronic forms of stress occurring over weeks months and years. This lecture concentrates more on fMRI and acute responses.

Peter observed that in most instances of cardiovascular disease (CVD), most attention concentrates on late stage events like heart attacks which lead to sudden death. However, CVD is a progressive disease characterised by the build up of material (e.g. cholesterol) in arteries which cause the blockages in arteries associated with heart attacks.

Peter's research investigates the processes of everyday life that lead to these stress responses which are often expressed in increased risk for premature expression of acute cardiovascular events like heart attacks.

How do these stress responses which begin in the brain relate to the premature expression of CVD through cardiovascular reactivity?

Cardiovascular reactivity in stressful conditions is characterised by an acute rise in blood pressure, heart rate, the contractive force of the heart and an increased constriction of the blood vessels. In the short term this reactivity is helpful in supporting adaptive response to stress – the well known flight or fight response. In the longer term, repeated and elevated stress and physical stress responses can create or exacerbate health problems. The neural regions responsible for invoking these changes are well known, though the extent of reactivity varies widely according to individual psycho-social factors, e.g. socio economic status and individual differences. Those whose reactivity is higher tend to be those who are at a greater risk from CVD later in life.

What are the pathways which link acute stress processes instantiated in the brain to this CVD reactivity?

Key aspects of Brain imagery research

To study these phenomena, study subjects are asked to complete a stressful test (in this case a Stroop Test designed to make it impossible to score more than about half right), while undergoing fMRI and blood pressure measurements. This research highlights that across individuals, a distribution of blood pressure response to stress exists. Some individuals react more strongly than others and this difference is stable over time. This correlates with other markers of preclinical risk for CVD.

The research focuses on Paralimbic brain structures which process emotional experience AND mediate endocrine (stress) response. Of these areas, Peter concentrated on their research on the amygdala, a cell complex in the brain which assigns emotional importance to environmental events. It also plays a role in regulating blood pressure.

Peter then went on to illustrate, using some research undertaken with colleagues that, in humans, those subjects who show a greater increase in amygdala activity under stress also have greater increase in blood pressure reactivity to stress.

In subsequent research they showed that increased amygdala activity and associated blood pressure is both stable over time and associated with intima-media thickness in the carotid artery (cIMT), controlling for other variables, indicating higher risk of CVD. This research indicates that acute physiological response, particularly to threatening changes in the environment, is associated with increased CVD risk in the longer term.

Next Steps

To date, the research described above has been investigating how the brain is linked to physiological stress which might predispose people to increased premature risk of CVD.

It is well known that a gradient exists between socioeconomic status (SES) and CVD.

Social deprivation is associated with increased incidence of a number of chronic illnesses, including CVD. How might one investigate the neural correlates of stress and socio economic status?

This is a complex question as the relationship between SES and health has multiple dimensions e.g. neural physiological, social, economic, cultural and at the level of individual, group and nation.

One aspect of this complex is perceived socioeconomic status. With his colleagues, Peter has been investigating the relationship of brain morphology and function to subjective dimensions of SES such as perceived SES.

In this research, perceived SES is shown to be related to a number of health outcomes e.g. self reported health (positive relationship) and intensity of acute response to stress and metabolic syndrome, obesity and intima media thickness (inverse relationship).

In the research subjects are asked to place themselves on the MacArthur Ladder of perceived status. These rankings are then correlated with the subject's brain structure. Those who perceive their SES to be lower have differently structured cingulates than those whose perceived SES is higher. Here he referenced Elizabeth Gould's work (described in a previous GCPH seminar) which indicates that chronic stress causes the dense connections with other parts of the brain which support better function to atrophy. Dendrites wither; cells die off leading to a loss of brain tissue volume.

In a hundred otherwise healthy adults, those who thought themselves to have lower SES also showed lower grey matter volume in the anterior cingulate cortex, controlling for many other variables.

This was followed up by further research investigating the role of the amygdala in development to adulthood. How does perceived childhood SES relate to amygdala activity under stress? Does increased threat sensitivity associated with perceived low childhood status predict increased risk for CVD? Peter and others undertook research which compared amygdala response to stress with perceived SES in young adults. They found that when subjects thought their childhood SES was lower amygdala reactivity to stress was higher.

The team is now conducting research which tires to correlate amygdale reactivity to acute stress with preclinical markers of CVD over time. Is it possible to predict who will develop risk and so address risk early? They are also trying to trace a pathway between SES, brain function and changes in physiology in individuals and preclinical risk, again with a view to early intervention.