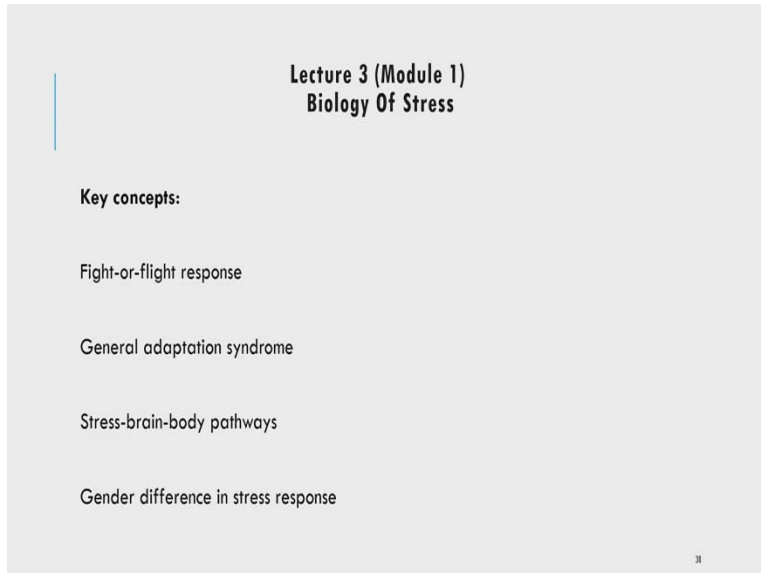


Psychology of Stress, Health and Well-being
Professor Dr. Dilwar Hussain
Department of Humanities and Social Sciences
Indian Institute of Technology, Guwahati
Module 1
Lecture 3: Biology of Stress

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Lecture 3 (Module 1)
Biology Of Stress

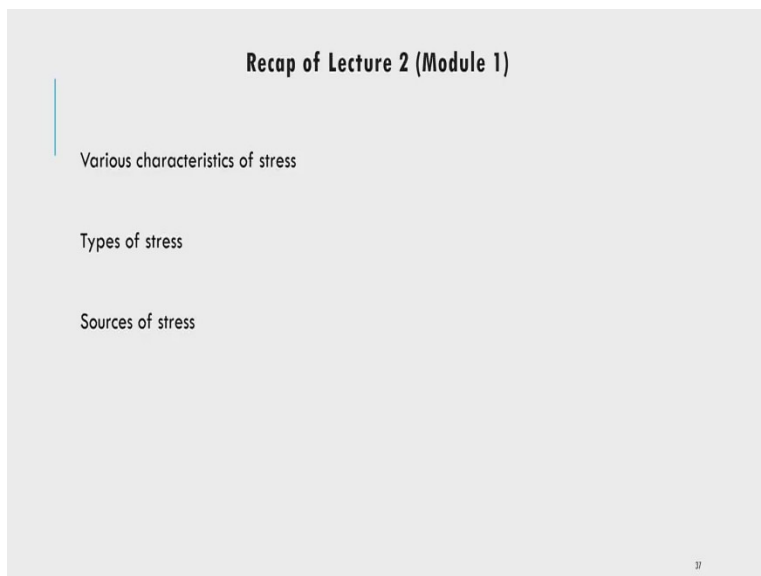
Key concepts:

- Fight-or-flight response
- General adaptation syndrome
- Stress-brain-body pathways
- Gender difference in stress response

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I welcome you all to the third lecture of module one. The title of today's lecture is "Biology of Stress". Before we talk about today's lecture, let me have a brief recap of the lecture two, which is the previous lecture.

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Recap of Lecture 2 (Module 1)

- Various characteristics of stress
- Types of stress
- Sources of stress

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So, in the last lecture, we discussed various characteristics of stress. We have discussed that stress is subjective and it can be self-created. We have also discussed that stress is an everyday phenomenon as we experience it daily. So it is not something that exclusively happens only on certain occasions.

We have also discussed that stress can have additive or cumulative effects, which basically means when we have multiple stressful events in a day and all may have a cumulative effect on our system, mind, and body. We have also discussed that stress can be influenced by culture, primarily because culture influences our thought processes, interpretation processes, so in that sense, culture can also influence how we interpret a situation.

We have also discussed that stress can have a spillover effect, with the idea that stress can get transferred from one domain of life to another domain of life, like workplace to family life. So that is called as a spillover effect.

We have also discussed that stress can be contagious because stress can transfer from one person to another person, particularly people who are close to us. So it is kind of contagious in that sense. We have also discussed different types of stress, such as acute stress versus chronic stress; distress versus eustress. So there can be different ways of categorizing stress.

We have also discussed various sources of stress such as frustrations in life can be a source of stress, conflicts in different situations of life can also lead to stressful experiences.

Specific life changes can be very stressful, and also, we have discussed the pressure to perform in a situation or pressure to conform to norms can also be stressful. So these are some of the central concepts that we have discussed in the last lecture. Today, we will discuss the biology of stress or the physiological aspects of stress.

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Lecture 3 (Module 1)
Biology Of Stress

Key concepts:

- Fight-or-flight response
- General adaptation syndrome
- Stress-brain-body pathways
- Gender difference in stress response

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So, the key concepts that we will discuss in today's lecture include fight or flight response, general adaptation syndrome, stress-brain-body pathways and lastly, gender differences in stress response. So let us discuss one by one.

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The physiology of stress

Stressful experiences are associated with various physiological changes in the body. Some of these include the following-

The Fight-or-Flight Response

Walter Cannon (1932) was the first person to describe body's reaction to stress in terms of fight-or-flight response.

It refers to physiological reaction of the body as a result to threat or stressor. It mobilizes and prepares body either for the fight (stand) or flight (run away) when confronted by a threat.

The Fight-or-Flight Response reaction occurs in the sympathetic division of the autonomic nervous system.

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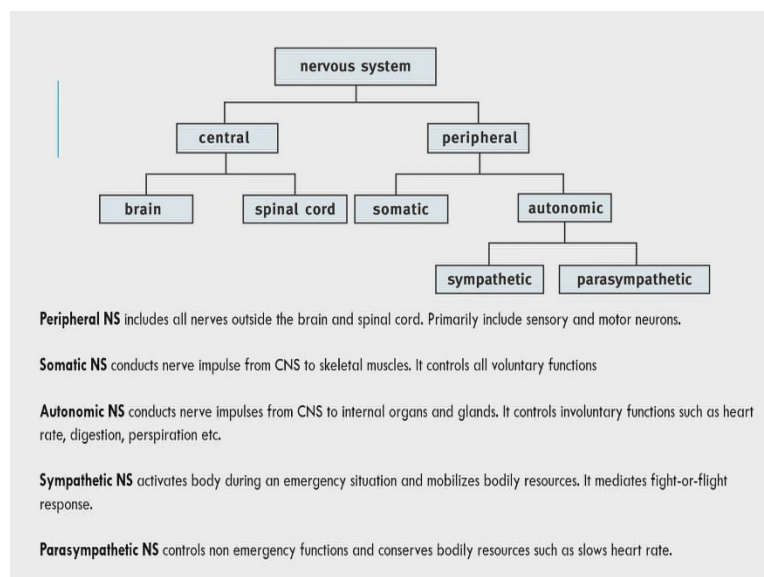
Stressful experiences are always associated with certain physiological changes in the body. So we have already tried to understand the mental experiences of stress. We will also look into more detail about the mind-body interactions. So, the mental experiences of stress directly influence your physiology or the body. Stress is always associated with specific changes in the body level.

So some of these physiological changes we will discuss which are commonly associated with stressful experiences.

So, one physiological response which is very commonly associated with stress is called a fight or flight response. This was coined by a scientist known as Walter Cannon in 1932, who first described the body's reaction to stress in terms of fight or flight response. This is also called the acute stress response. Whenever we experience acute stress, our body responds with the fight or flight response. It is a kind of physiological reaction of the body due to any threat or stressful situations.

The fight or flight response mobilizes and prepares the body either for fight (to stand and fight with the situation) or flee, which is called flight (if it is not possible to fight) when confronted by a threat. So, this is a typical physiological reaction that happens. Body prepares you to fight or run away from the situation. This response is mediated by the autonomic nervous system, specifically one part of the autonomic nervous system called the sympathetic nervous system. Let us briefly talk about the structure of the nervous system to understand the autonomic nervous system and sympathetic nervous system.

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So, if you look at the human nervous system, it is divided into two parts. One is called as the central nervous system, and the other is called as the peripheral nervous system. So central nervous system includes the brain and spinal cord. All the remaining nervous system is called as

the peripheral nervous system, which includes all nerves outside the brain and spinal cord and it includes sensory and motor neurons.

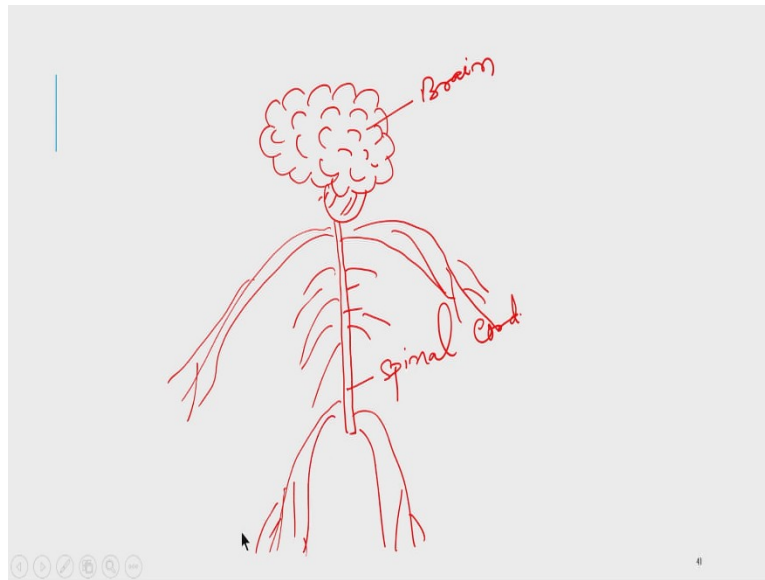
So, apart from the brain and spinal cord, all the other aspects of the nervous system are collectively called as the peripheral nervous system. The peripheral nervous system is again divided into two parts. One is called the somatic nervous system, and the other is called the autonomic nervous system. The somatic nervous system basically conducts nerve impulses from the central nervous system to skeletal muscles. So, it conducts nerve impulses from the central nervous system to the skeletal muscles and it primarily controls all the voluntary function. For example, I am moving my hand; I am walking with my legs; all these voluntary functions are done mainly by the somatic nervous system.

The other part is called the autonomic nervous system. It conducts nerve impulses from the central nervous system to various internal organs and glands such as the heart, glands like the thyroid gland, pancreas, etc. So, all the internal organs and glands are connected and controlled by the autonomic nervous system, and it controls mostly involuntary functions such as heart rate, digestion, perspiration, etc. The autonomic nervous system is again divided into two parts. One is called the sympathetic nervous system, and the other is called para-sympathetic nervous system. The sympathetic nervous system activates, arouses, or stimulates the body by mobilizing all the resources.

The sympathetic nervous system activates or stimulates the body and provides necessary energy when we encounter a stressful or threatening situation. So, the fight and flight response is primarily controlled by the sympathetic nervous system. Whenever we encounter a stressful situation, the sympathetic nervous system gets activated, and it activates all the physiological aspects such as the increase in the heart rate plus perspiration, etc.

The parasympathetic nervous system, on the other hand, does the opposite of the sympathetic nervous system. When the body gets aroused by the sympathetic nervous system, parasympathetic nervous system tries to maintain balance by decreasing the arousal of the body system. So, it tries to conserve bodily resources such as by slowing heart rate. So, let me draw a human brain.

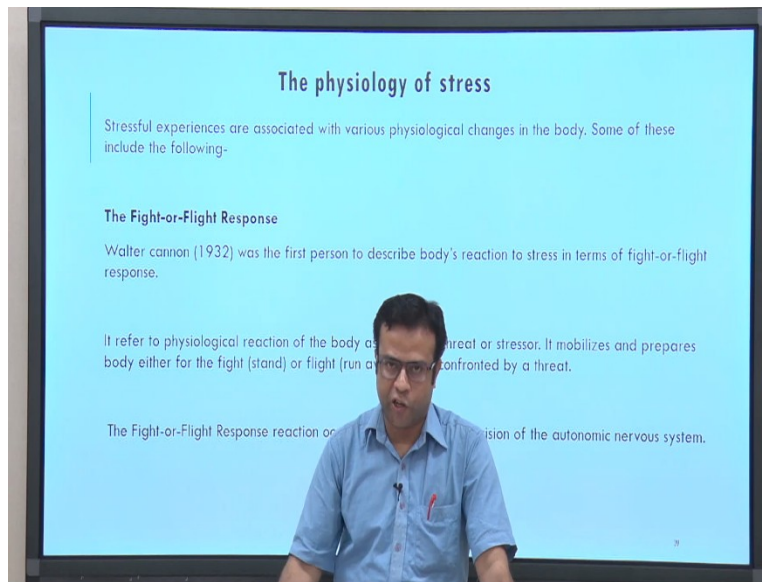
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Let us consider this as the human brain. So, the central nervous system includes the brain and spinal cord. The peripheral nervous system goes from brain and spinal cord to all the other parts of the body. So nerves will connect our hands, legs and other body parts. So it will go to our hands, so different nerves will go to different internal organs. Then it will go to different parts of our leg. So all these branches are part of our peripheral nervous system.

So, if we make an analogy of our brain with the electric grid system, then the central nervous system is like a power house that gives you power. The peripheral nervous system is more like cables that connect the power house with the different parts of the city. Similarly, brain and spinal cord are the power house, and they connect with the different parts of the body and internal organs using the peripheral nervous system.

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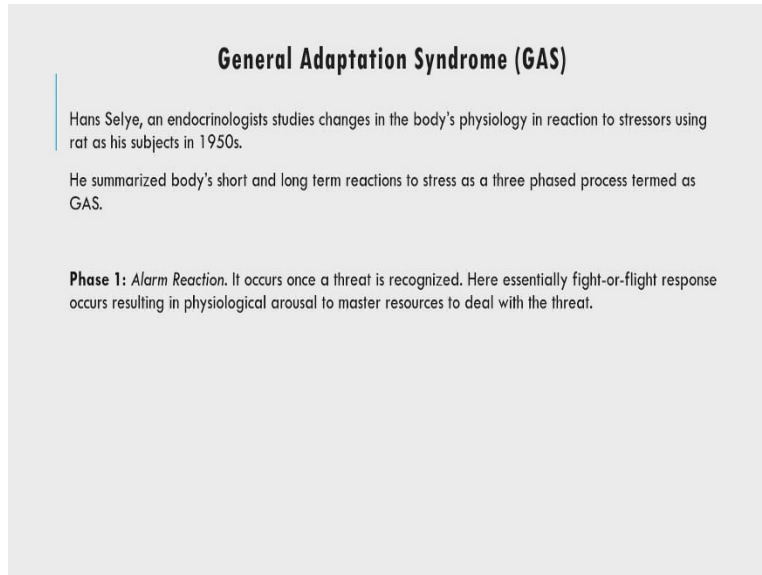
So, fight and flight response is a kind of survival mechanism. It is the body's way of dealing with a threat. It helps us to survive in a threatening situation, in a stressful situation and this is a very rapid process. It happens very unconsciously. We may not be consciously aware, but whenever there is a threat in front of us, the body automatically activates the sympathetic part of the nervous system, and it mobilizes and distributes energy to the different parts of the body wherever it is required.

Physical symptoms of the fight and flight response include an increase in heartbeat, tensed muscle, dry mouth, dilation of the pupil of the eye, sweating of the palms, and so on. Once the threat is over, we have discussed that para-sympathetic nervous system tries to return the body to normal, relaxed as the body cannot stay in that aroused state for a long time because it can be very exhausting. So, the parasympathetic nervous system tries to bring the body to a normal relaxed state. Walter Cannon used the term 'homeostasis' to connote the idea that the body always tries to maintain its equilibrium by bringing it back to a normal state. Our body will not be able to survive for a long time if it is in an aroused state for a long time. So, parasympathetic nervous system tries to maintain that balance.

Another important thing is that fight or flight response can happen in the face of actual danger, such as, let us say, you suddenly see a snake in front of you, or to an imagined threat also. Let us say you want to appear for a public speech or a presentation. One may get stressed just by

imagining this task if you interpret it as a threat. Our brain cannot make a difference between the actual and imagined threat. The body will react in a very similar fashion.

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General Adaptation Syndrome (GAS)

Hans Selye, an endocrinologist, studies changes in the body's physiology in reaction to stressors using rat as his subjects in 1950s.

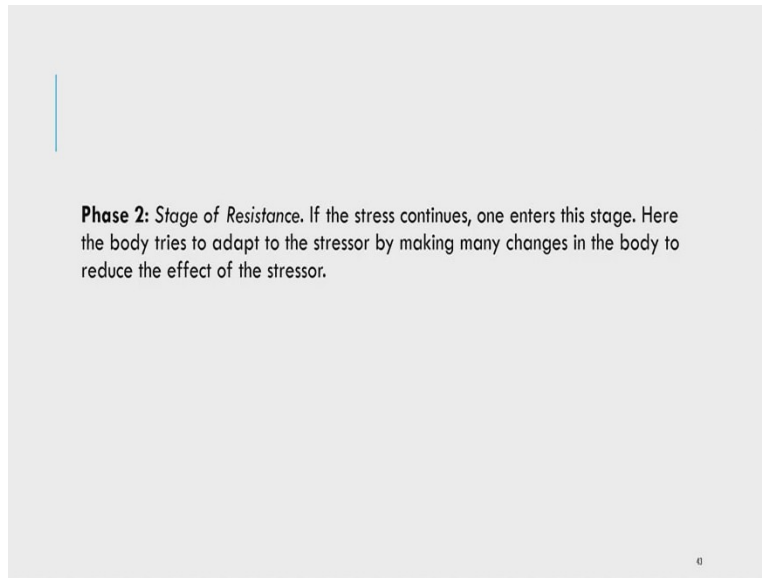
He summarized body's short and long term reactions to stress as a three phased process termed as GAS.

Phase 1: Alarm Reaction. It occurs once a threat is recognized. Here essentially fight-or-flight response occurs resulting in physiological arousal to master resources to deal with the threat.

Another physiological response of the body is called general adaptation syndrome or, in short, GAS. This was proposed by the endocrinologist Hans Selye who was one of the founding researchers in the field of stress. He studied changes in the body's physiology as a reaction to the stress while studying rats. He was interested in the body's short and long-term reactions to stress. So fight and flight happens for the short term or acute stress. But what happens when stress persists for a long time? What are the stages that our body goes through? So general adaptation syndrome tries to explain that.

So, Hans Selye summarized body's short and long-term reaction to stress in three staged or phased processes called the general adaptation syndrome. The first stage is called Alarm Reaction. The alarm reaction happens when we first encounter stress or threat. This stage is typically a fight or flight response that we have discussed earlier. So, the alarm reaction generally is a fight and flight response.

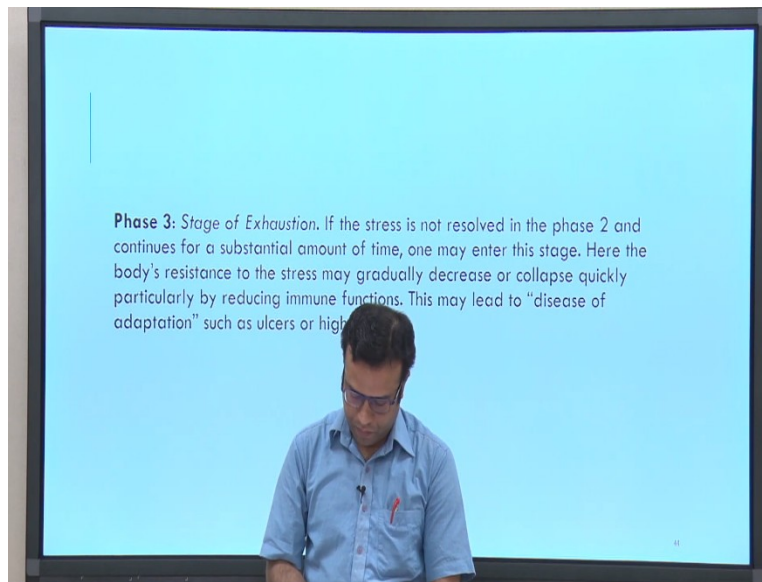
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The next phase is called the stage of resistance or resistance stage. After the initial alarm reaction, the body begins to repair itself, and the parasympathetic nervous system tries to cool down the body and bring it back to the normal state. The body tries to enter into the recovery phase for a while, but it remains in a very vigilant state.

So, in this stage, if you overcome stress, then everything may go back to normal functioning. However, if the stress continues beyond fight and flight response, the body enters into the stage of resistance. Here, the body tries to adapt and learns how to live with the higher stress level or continued stress level. The body makes various changes and adaptations to reduce the effect of stress. For example, the body secretes various stress hormones (stress hormones will be discussed after some time) and tries to maintain high blood pressure. The symptoms of the resistance stage may include irritability, frustrations, low concentration etc. So, the body tries to resist to higher stress level by mobilizing various resources and by secretion of stress hormones.

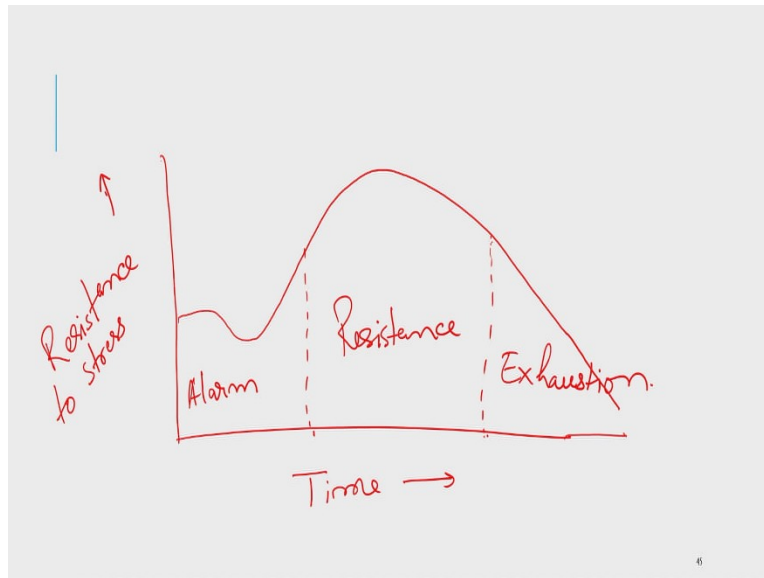
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The next stage is called the exhaustion stage. If the stress is not resolved in the second stage and continues for a long time, one may enter into the stage of exhaustion. Here, the body's resistance to stress gradually decreases and may even collapse very quickly and reduce our immune functions. We will look into all these other aspects also when we talk about the influence of stress on our health. In the exhaustion stage, various diseases, physical diseases may appear in our body because of the collapse of resistance. For example, people may experience symptoms of ulcers, high blood pressure, etc. So this is the most dangerous stage. That is why, we have discussed earlier that chronic stress is the most problematic stress because when stress continues for a long time, the body enters the stage of exhaustion and may lead to diverse physical diseases. The symptoms of this stage may include fatigue, burnout, a decrease of stress resistance, etc. Our body's immune system may also decrease. So we will look into the mechanism of immune system and stress in the upcoming lecture. These are some of the stages that our body goes through when we experience stress.

So it may start with the alarm reaction stage, then the body enters into the resistance stage if the stress continues. However, if the body is not able to resolve stress at that stage, it may enter into the exhaustion stage, where the body may exhaust all its energy and resources and may experience physical diseases. So diagrammatically, this can be shown like this.

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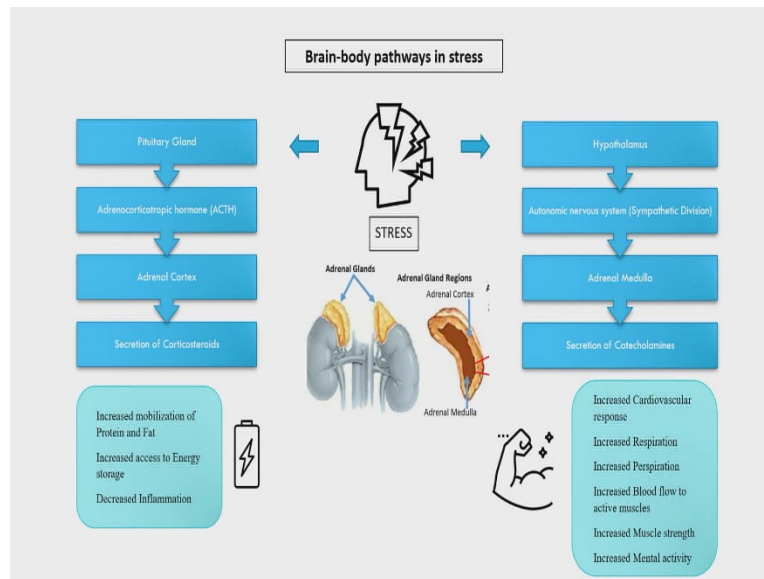
So, graphically we can present these three stages like this. So this is one side we are showing the resistance to stress and the other side the progress of time. So initially, we have the alarm stage; there is not much resistance at this stage; the body starts showing the symptoms of fight and flight. Then slowly, the resistance increases as time passes and then after a certain time, the resistance begins decreasing, and sometimes it may collapse very quickly. So this is the phase of exhaustion where the resistance may go down very quickly or slowly. So, graphically, we can present these stages like this.

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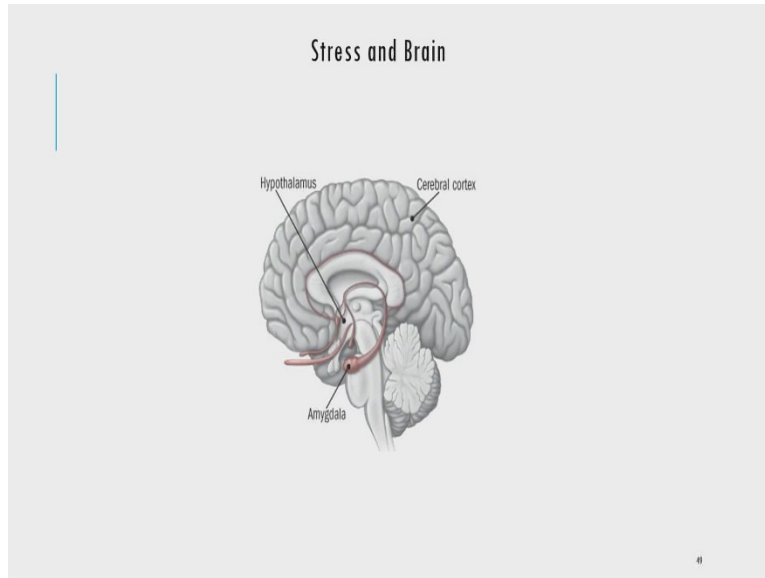
Now, let us talk about how stress is connected to the brain and body. We will discuss detailed pathways throughout which stress influences our body and brain.

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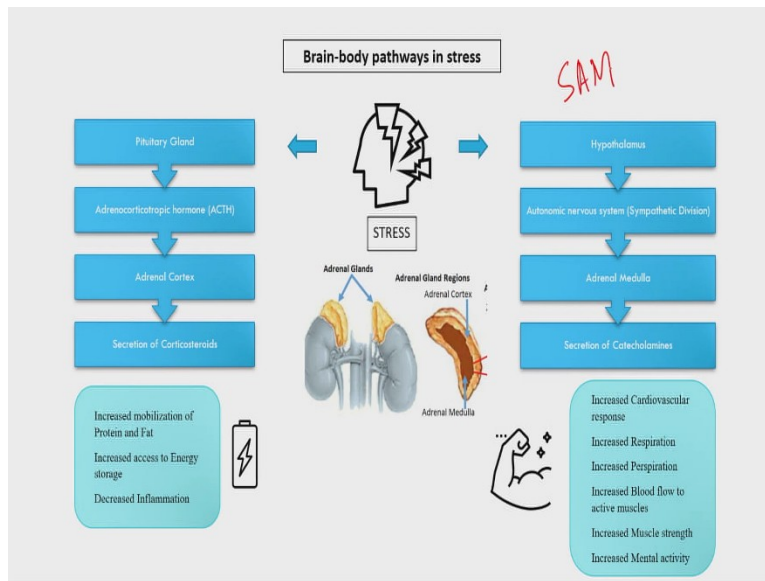
So, this is a diagrammatic representation of how stress is connected to our brain and body. When someone experiences stress, one part of our brain, a small part of our human brain called the amygdala, gets activated (the amygdala is primarily responsible for emotional processing). The amygdala then sends a signal to the hypothalamus, another part of the human brain, which is the control center in the brain.

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So, if you see in the diagram, the amygdala will be somewhere here and the hypothalamus is somewhere here. So during the stress, the amygdala gets activated, and then it sends a signal to the hypothalamus. The hypothalamus then activates two pathways. One pathway is called as SAM system. And the other is called HPA system.

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The hypothalamus is the center of the brain in the context of stress response. It activates two pathways leading to release of stress hormones. These are-

- The sympathetic adrenal medullary (SAM) system**, which leads to the secretion of the two catecholamines-adrenaline (epinephrine) and noradrenaline (norepinephrine).
- The hypothalamic pituitary adrenocortical (HPA) system**, which leads to the secretion of corticosteroids such as cortisol.

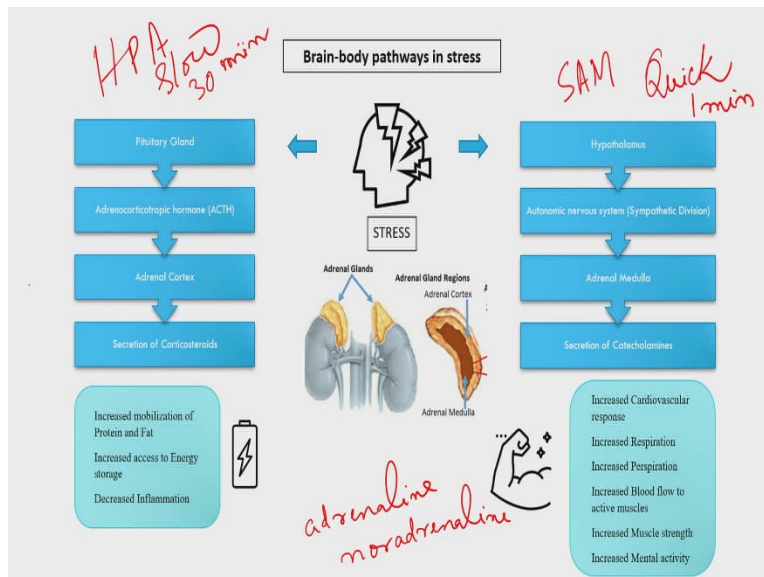
In the SAM pathway, the Sympathetic NS activates adrenal medulla, which secretes the stress hormones catecholamines (adrenaline and noradrenaline) in the blood stream. Their release increases heart rate, blood pressure, release of glucose and fatty acids from the liver thus increasing energy in the body. This is a quick reaction (within a minute) and is significant for coping with acute stress.

In the HPA pathway, the hypothalamus activates anterior pituitary, which secretes adrenocorticotropic hormone (ACTH) in the blood stream which reaches the adrenal cortex which releases cortisol in the blood stream. Cortisol influences metabolism, storage of the fats and immune functions. This process is much slower (may take 30 minutes) and is significant for coping with chronic stress.

The bodily consequences of chronic stress response is different from the acute stress response. The chronic stress response adversely affects our physical health.

So, the SAM pathways mean the sympathetic adrenal medullary system.

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Here, the hypothalamus activates the autonomic nervous system, particularly the sympathetic part of the nervous system, and the sympathetic nervous system then activates the adrenal medulla. The adrenal gland is located near the kidney, and the medulla is the inner layer of the gland. So, you can see here in the diagram, these are the two glands which are called as adrenal glands. So they are just above the kidney. These are small, two small structures above the

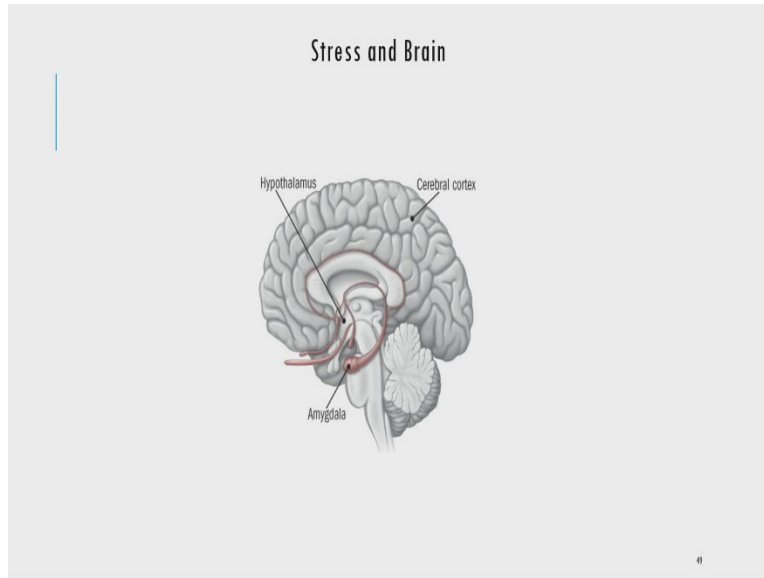
kidney. They are called adrenal gland. So sympathetic nervous system activates adrenal medulla. Medulla basically is the inner part of the gland.

So, the autonomic nervous system activates the inner part of the adrenal gland called the adrenal medulla. This inner part of the adrenal gland secretes a group of hormones called catecholamines, which basically includes hormones such as adrenaline (also called epinephrine) and noradrenaline (also called norepinephrine). Adrenaline is a very commonly known hormone. The word adrenaline rush is used when we get highly activated and energized. These hormones, when released in the blood, do some functions such as increase cardio-vascular response, increase respiration rate, increase our perspiration rate, increase blood flow to active muscles, and increase muscle strength increases mental activities. This is one pathway by which stress releases hormones in the body and ultimately influences our body.

Another pathway is called HPA, which means the hypothalamic pituitary adrenocortical pathway. In addition to activating the sympathetic nervous system, the hypothalamus also activates the pituitary gland, a small gland located just below the hypothalamus. It is called the master gland as it controls all the other glands. So, the pituitary glands, once it is activated, release a hormone called adrenocorticotrophic hormone (ACTH). This hormone activates the adrenal cortex, the outer layer of the adrenal gland. The sympathetic nervous system activates the medulla or inner part, and adrenocorticotrophic hormone or ACTH activates the adrenal gland's outer layer or cortex. The adrenal cortex, once activated, releases a group of hormones called corticosteroids such as cortisol. The cortisol activates certain functions in the body, such as increased mobilization of protein and fat, increased access to energy, storage, decreased inflammation.

The SAM pathway is quick and very fast and activates within one minute of perception of a threat, that is, mainly in response to acute stress. HPA pathway is relatively slow. It may take about 30 minutes to get activated, that is, mostly under chronic stress conditions. So, depending on the stress conditions, both slow and quick pathways may get activated. Both the pathways release stress hormones in the blood and mobilize the body to give energy and resources to deal with the situation.

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Next, we will see how stress is connected to the brain.

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Stress and Brain

Stress, hippocampus, and pre-frontal cortex

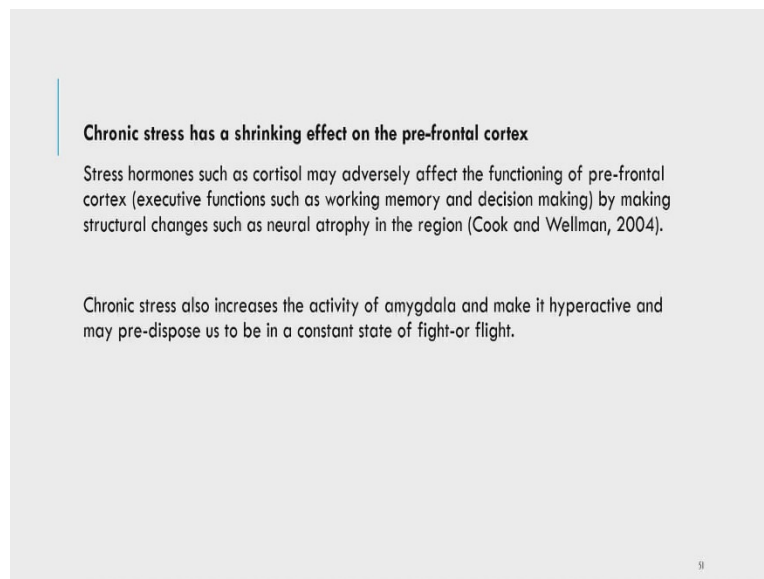
Chronic release of stress hormone such as cortisol adversely influence two major areas of the brain i.e. pre-frontal cortex (executive functions such as working memory and decision making, regulating thoughts and emotions) and hippocampus (important in learning memory and emotions).

In a study by Justin B. Echouffo-Tcheugui and colleagues (2018) found that high level of blood cortisol was associated with poorer memory and cognitive functioning particularly for the women. It was also associated with lower total cerebral brain volume.

Now, stress influences two major parts of the human brain. One is called the pre-frontal cortex, and the other is the hippocampus. The pre-frontal cortex is the frontal part of the outer cortex of the brain. The hippocampus is another small organ in the human brain which is responsible for learning, memory, and emotions. The pre-frontal cortex is responsible for executive functions such as memory, decision making, regulation of thoughts and emotions, and the hippocampus is responsible for learning, memory, and emotions.

Chronic stress particularly leads to the release of cortisol which adversely influences both the pre-frontal cortex and hippocampus and thus adversely influences all the functions related to these parts. Stress by influencing our brain will adversely affect various functions or disrupt various functions such as emotions, memory, learning, decision-making, regulation of thoughts and emotions, etc. A study by Justin B and colleagues in 2018 found that a high level of blood cortisol was associated with poorer memory, cognitive functioning, particularly for women. It was also associated with lower total cerebral brain volume. So, Justin B and his colleagues collected data from 2231 healthy, middle-aged people, and they kind of collected their cortisol level from the blood and various cognitive functions. They reported that high blood cortisol is associated with poorer memory and cognitive functions. Another study showed that chronic stress may even shrink in terms of the physical volume of the brain, particularly the pre-frontal cortex of the brain.

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So, chronic stress has a shrinking effect on the pre-frontal cortex which means chronic stress may actually reduce the physical volume of the pre-frontal cortex. This shrinking effect may take place by a phenomenon called neural atrophy, that is, by killing or removing some of the neurons in the brain.

So, cortisol can adversely affect the functioning of the pre-frontal cortex by making even structural changes such as neural atrophy in the region. So it can actually physically shrink the pre-frontal cortex of the brain by killing neurons in that region.

Chronic stress also increases the activity of the amygdala, which is primarily responsible for emotional reactions. Chronic stress may pre-dispose people to be in the constant state of fight or flight response by making the amygdala hyperactive. So, when we are under emotional and stressful situations, all the energy goes to certain parts of the brain, particularly the amygdala which is responsible for emotional reactions. Consequently, other parts of the brain such as the pre-frontal cortex may not have much energy and may hamper higher cognitive functioning such as thinking, decision-making, etc.

So, stress can have all these impacts on the human brain, and it particularly influences certain parts of the brain. Stress can even physically kill some neurons in some parts of the brain, such as the pre-frontal cortex.

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Stress can disrupt synaptic regulation (brain cell connectivity)

It can disrupt synapse regulation (van der Kooij et al, 2014), resulting in the loss of sociability and the avoidance of interactions with others and memory.

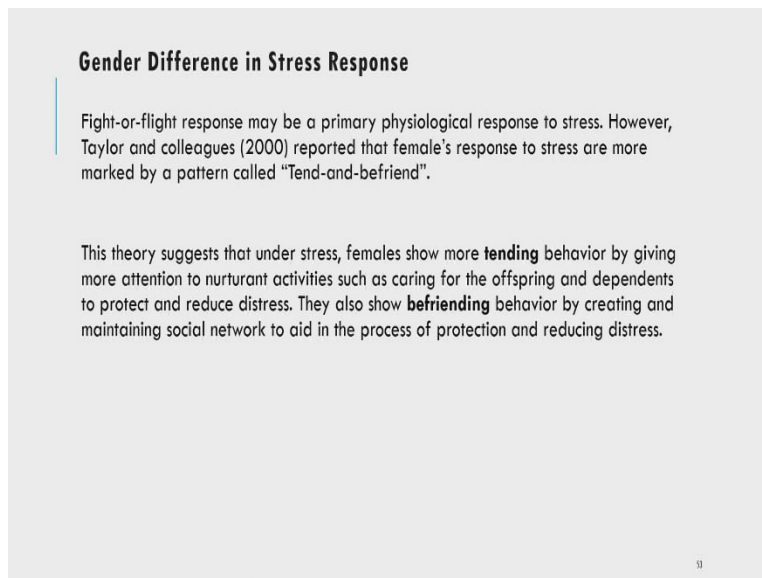
They discovered an enzyme (MMP-9), when triggered by stress, that attacks a molecule in the hippocampus which is responsible for regulating synapses. When the synapses are modified, fewer neural connections are able to be made in the area.

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Some research also shows that stress can disrupt synaptic regulation. A synapse is a junction between two neurons. Synaptic regulation means the conduction of nerve impulses in a synapse. Through synaptic regulation, messages are passed between neurons. So, stress can adversely impact synaptic regulation by disrupting brain cell connectivity.

For example, some of the research done by van der Kooij and others in 2014 shows stress can disrupt synaptic regulation, resulting in the loss of sociability and avoidance of interaction with others and may impact our memory functions. So this particular research found a particular enzyme called MMP-9 triggered by stress reaction and attacks a molecule in the hippocampus responsible for regulating synapse. So it disrupts synaptic regulation by attacking the hippocampus. So this is also another finding that shows how stress can influence our brain.

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Gender Difference in Stress Response

Fight-or-flight response may be a primary physiological response to stress. However, Taylor and colleagues (2000) reported that female's response to stress are more marked by a pattern called "Tend-and-befriend".

This theory suggests that under stress, females show more **tending** behavior by giving more attention to nurturant activities such as caring for the offspring and dependents to protect and reduce distress. They also show **befriending** behavior by creating and maintaining social network to aid in the process of protection and reducing distress.

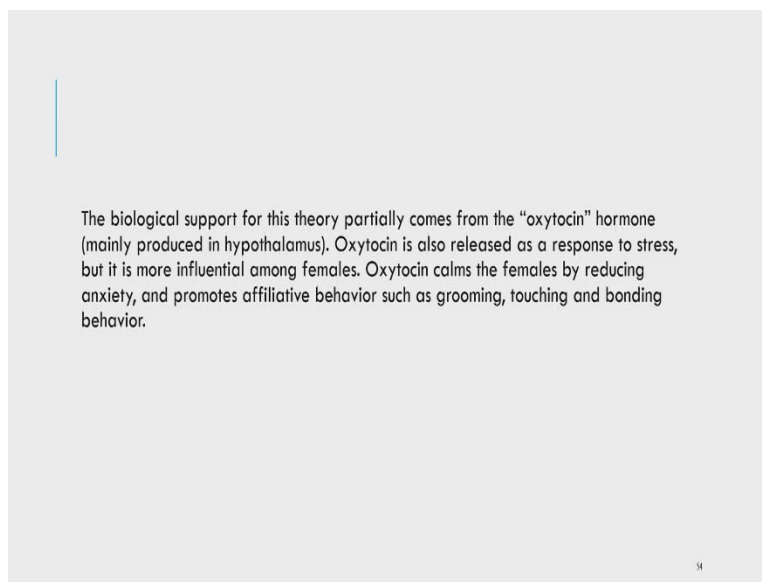
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Now, some of the research also shows there is a possibility of gender difference in the reaction of the stress response, particularly in the fight and flight response. Generally, research shows fight and flight response is a kind of primary physiological response shown by all individuals and is a kind of universal thing. However, some of the research, particularly by Taylor and colleagues in 2000, also found that the fight and flight response may be a little bit different in the case of females, and it is more marked by another phenomenon called 'tend and befriend'.

Although fight and flight response can be there, females may show more prominent tend and befriend symptoms when they encounter stress, particularly acute stress. So what is the meaning of this? This theory suggests that females show more tending behavior under stress, which basically means giving more attention to nurturing activities or nurturing activities such as caring for the offspring and dependents.

So, tending behavior gets activated in the females, particularly for offspring and the dependents, to protect and reduce stress. So, females may show tending behavior to reduce their stress levels. They may also show befriending behavior under stressful circumstances by creating and maintaining the social network to aid in the process of protection and reducing stress. So, they tend to build and maintain social networks, which can help in the process of protection. At least some biological evidence shows that it is possible that females show more tend and befriend symptoms under stress reaction compared to males.

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One evidence comes from biological support of this theory, at least partially comes from the release of oxytocin hormone, which is mainly produced in the hypothalamus. Oxytocin is also released as a response to stress, but it is more influential among females, that is, oxytocin is released more among females when under stress. It helps in calming during stress. So it helps to calm by reducing anxiety and promotes affiliative behavior such as grooming, touching, bonding behavior.

So, at least this provides partial support for tend-and-befriend theory for females under stress. Furthermore, there can also be an evolutionary reason for this theory. Throughout history, females have been primarily responsible for caring for offspring. This is one of the primary tasks that females have been doing. Therefore, fight-and-flight response may not be appropriate from the evolutionary point of view. If they fight, they may be injured and become unable to defend

their offspring. If they flee also, then their offspring are left unprotected. So for females, engaging in fight and flight response may endanger species. So, probably tend and befriend is more beneficial in protecting the offspring and maintaining the species. But fight and flight response is very much universal, and all people show it. But tend and befriend may be more prominent among females as compared to males. With this, I end today's lecture. Thank you.