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Review Article

Cerebral Hypoxia can lead to Personality Changes: A Review

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Introduction

The term 'Cerebral hypoxia' refers to reduced supply of oxygen to the brain tissues. If a brain cell becomes completely deprived of oxygen, the condition is referred to as cerebral anoxia. Since brain needs constant supply of oxygen for its vital functioning, cerebral hypoxia can have major impact of cerebral hemispheres, leading to cognitive, behavioural as well as personality changes including anxiety, depression and memory loss [1]. In simple words, it is condition wherein brain does not get sufficient oxygen to meet its energy demands and its functioning is adversely affected. There are several causes which may lead to cerebral hypoxia; including sudden exposure to high altitudes (wherein the barometric pressure is low resulting in lowered partial pressure of oxygen), inhalation of smoke, poisoning due to carbon monoxide, strangulation and chocking. Supply of oxygen to brain in sufficient amounts could also be interrupted or stopped during medical conditions such as overdose of drugs and anaesthesia, during cardiac arrest and stroke, drowning and low blood pressures. Acute brain injury can occur as a result of cerebral ischemia or hypoxic ischemia after an incidence of stroke, cardiac arrest, vasospasm or cerebral edema.

Cerebral damages due to hypoxia

Mammalian brain is highly oxidative organ and has high demands for oxygen. Although, brain only weighs 2% of the total body weight, approximately 20% of the entire oxygen output of the body is used by neurons in the brain. These neurons are extremely sensitive to changes in the oxygen levels. Thus even brief periods of cerebral hypoxia can cause severe damage to brain tissues [2]. A large number of enzymes which have high affinity for oxygen and are actively involved in the process of oxidative phosphorylation and ATP production (such as cytochrome C oxidase) ensure the maintenance of low partial pressure of oxygen in brain. When the supply of oxygen to brain tissues becomes

low, the process of oxidative phosphorylation is adversely affected [3,4], thereby decreasing ATP production and affecting functioning of ion channels. Free oxygen radicals thus generated further contribute to the oxidative injury of brain [5], leading to disruption in transmission of electrical impulse. If the brain is not supplied with oxygen for just few minutes, a large number of cells in the brain begin to die. The most oxygen sensitive areas of brain include cerebral cortex (including parietal and occipital lobes), the hippocampus, basal ganglia and cerebellum [6]. Hypoxia leads to oxidative stress and neuronal damage as the redox cycle is disturbed. Neurons of hippocampus region are amongst the first ones to lose their electrical activity in a hypoxic event [6]. Hypoxia related cerebral damages include various neurological disorders which affect personality, behaviour and motor skills of a person.

Personality changes due to cerebral hypoxia

Personality of an individual, which is marked by patterns of emotional and motivational behavior, is highly dependent on cognitive responses [7]. In case of effect on cerebellum, loss of coordination and balance is seen. In severe conditions, cranial nerve reflexes, apnea, coma and even brain death occurs. Initial exposure to low concentration of oxygen may lead to headache, dizziness, sweating and increase in rate of breathing. In case of brief cerebral anoxia, a person can experience the loss of concentration, coordination, speech difficulty and short term memory loss. However, most of these short term changes are reversible in nature, as the oxygen supply to brain resumes. Long term exposure to lowered oxygen levels may lead to irreversible damages. Cerebral hypoxia may also result in confusion, hallucinations, decreased memory, attention problems, disorientation, lowered consciousness and eventually death.

Constant supply of glucose and oxygen to the nervous tissues is required to perform various physiological tasks. Personality of an individual is controlled by frontal lobe of the brain. A remarkable change in the behavior of a person can be noticed when the neurons in the frontal lobe are affected due to lower oxygen availability. Oxygen supply positively affects cognitive behavior and it has been demonstrated in various studies [8-12]. In such cases, cognitive performance as well as memory is improved by supply of concentrated oxygen [13]. The supply of concentrated oxygen not only improvises cognitive performance but also increases blood oxygen saturation (SpO_2) and maintains a lowered heart rate during the process [14]. Thus the speed and accuracy of cognitive performance largely depends on oxygen flow to brain tissues [15-17].This is the precise reason why cognitive ability is compromised at high altitudes. Since cognitive tasks are highly energy demanding and requires continuous supply of ATP, increase in ATP production enhances cognitive ability [9].

However, brain requires more and more oxygen to metabolize this fuel during cognitive processing. In absence of sufficient oxygen supply, cognitive performance is compromised to a variable extent. Insufficient oxygen supply to neurons results in influx of sodium and calcium ions which cause the cells to swell and produce free oxygen radicals. Since, these free oxygen radicals are extremely reactive they cause cell injury. [18] reported changes in psychomotor performance, reaction time, vigilance, overall mental skill, memory and logical reasoning in individuals ascending to altitudes above 3,000 m (9,843 ft). Long term exposures to low oxygen levels may lead to permanent damages. Synthesis of several neurotransmitters is highly oxygen dependent. Changes in the concentration, utilization and metabolism of these neurotransmitters also attribute to behavioural changes [19,20]. Neurotransmitter systems which get highly affected due to hypoxic changes are cholinergic system and acetylcholine (ACh)

[19]. Other lesser oxygen sensitive neurotransmitters are dopamine and serotonin. These neurotransmitters play a crucial role in regulating physiological and emotional responses, mood changes, controlling pain and memory functions. Personality changes are evident after damage to specific areas of brain like frontal and temporal lobes, hippocampus and amygdala. In such cases, a person may show changes in mood by behave agitated, may show volatile emotions or even physical aggression and verbal attacks apart from memory impairment. Mood changes are often visible in the form of increased irritability, depression and anxiety. A person may get more addicted and may show sexually inappropriate compulsions.

In case of memory loss, a person may find difficult to recall names and recognize faces. Sometimes, one is unable to respond to pain signals. Struggle in walking, writing and other coordination is seen in case of changes in motor skills. Hypoxic exposure in early stages of brain development may lead to behavioural abnormalities [21]. Little data is available on changes in endocrinological parameters such as TSH, prolactin, cortisol or somatomedin in relation to hypoxic brain damage. Few studies report hormonal changes like somatotropic, gonadotropic and thyroid hormone disturbances in patients of brain injury and subarachnoid haemorrhage [22,23]. Many arginine rich peptides such as CARP's (cationic arginine-rich peptides) have been recently demonstrated as potent neuroprotective agents. They have shown the capacity to reduce reduce neuronal calcium influx [24,25] by down-regulating calcium channels and TNF receptor proteins [26,27] and thus reduce neuronal death.

Treatment

Neuro-imaging along with other clinical, biochemical and neurophysiological data are helpful in determining the extent of hypoxic brain damage. With advances in medical facilities and intensive care, more and more patients receive good neurological care and early treatment in rehabilitation facilities [28]. In case of temporary damage such as hallucinations, paralysis, memory loss etc. oxygen therapy using hyperbaric oxygen therapy (HBOT) is extremely helpful in recovery of lost abilities. This therapy has shown success in cases of global cerebral ischemia/anoxia, head injury and coma patients and has been practiced since several decades [29-33]. It makes breathing easier, reduces anxiety and quality of life is restored. This treatment strategy has been very popular as it is painless and non-invasive. Study has been conducted on rehabilitation of hypoxic-ischemic patients which emphasized on recovery of consciousness during rehabilitation [34], and prognosis of hypoxic brain damage during early neurological rehabilitation [35]. Other treatment plans may include exercise therapy, which increases the flow of blood to the brain; physical therapy, to regain lost motor skills; speech therapy; psychotherapy etc.

Summary

Personality or behavioral changes in an individual largely depends on supply of oxygen to the brain tissues. Insufficient or interrupted oxygen flow to the neurons in the brain may lead to impairment of cognitive functioning which in turn causes changes in overall personality! Rapidly changing environmental conditions and lifestyle of people are causing increase in incidences and severity of brain damage due to hypoxia. Thus this area needs to be explored and studied in more details to find out the pathophysiological causes of hypoxic brain damage for its early detection, prevention and treatment. Studies should aim towards identification of effective neuroprotective compounds and new therapeutic targets.

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