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NEUROLOGICAL COMPLICATIONS ASSOCIATED WITH SCUBA DIVING (WITH AN EMPHASIS ON TAU PROTEIN)

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ABSTRACT

Scuba diving is practised as a recreational sport and for commercial and military purposes. Divers breathe gas mixtures at partial pressure and are subjected to stress from the hyperbaric environment. Decompression illness (DCI) is a serious risk for divers and can affect the nervous system. Cerebral white matter (WM) lesions and cognitive impairment have been identified in divers, and although some cases are linked with DCI, others showed no apparent connection. It has been proposed that the act of diving may have negative neurological consequences regardless of history of DCI, but studies have been inconclusive and hard to interpret. Further research is needed, and blood tau protein levels could be a promising tool to assess neuronal stress associated with diving, in order to determine the long-term neurologic consequences related to scuba diving.

KEYWORDS: *scuba, diving, decompression, neurological, brain, lesion, cognitive, DCI, DCS, AGE*

INTRODUCTION

Scuba diving is practiced by commercial divers, military members, professionals, and recreational sports divers worldwide. Every year in the United States alone, approximately 3 million people practice diving recreationally, and the sport is gaining in popularity (1). Divers breathe a mix of gases at partial pressure and are subjected to changes in hydrostatic and atmospheric pressure that is exerted on the body as they descend and ascend.

There are certainly benefits for those who practice diving, such as the physical activity, social interaction, and stress reduction it can provide, as well as the opportunity to immerse in nature and open blue spaces of water (2). However, the human body is very sensitive to changes in ambient pressure, with hyperbaric conditions producing pulmonary, circulatory, and cardiac changes during the compression and decompression stages of immersion in water. There are serious risks as well, and apart from drowning, cold temperatures, and possible equipment failure, physiological changes can lead to complications such as oxygen toxicity, nitrogen narcosis, barotrauma to the lungs and sinuses, and decompression illness (DCI).

DCI can affect the nervous system, and some studies have indicated that diving itself, even in the case of undocumented DCI, may cause alterations to cerebral white matter (WM) and affect cognitive functions. However, results have been conflicting and hard to interpret, with some showing CNS lesions without a clear cause. Currently, no definite consensus has been reached and further research is necessary to validate the investigations presented.

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This review will look at the correlation between neurological complications and cerebral damage that has been presented as of now, and the importance this may have for the long-term health outcome of those who partake in scuba diving.

Decompression illness

DCI is caused by the formation of intravascular or extravascular gas bubbles as a result of decompression. This term encompasses both decompression sickness (DCS) and arterial gas embolism (AGE), the two main decompression pathologies that afflict scuba divers (3). Both DCS and AGE are caused by bubbles; In DCS gas bubbles are formed in venous blood and tissue, and in AGE the bubbles enter the arterial circulation. Each causes damage to the particular afflicted tissue by ways of different mechanisms (4). DCS tends to have a delayed onset, and progressively worsen after the dive, whereas that of AGE is sudden (5).

Scuba divers breathe a mixture of gases that include oxygen, nitrogen, and sometimes helium. During descent, the increase in ambient pressure causes nitrogen to become dissolved in bodily fluids and tissues, and the amount of nitrogen bubbles that is accumulated depends on the bottom time (time at reached depth) and the level of depth, in addition to numerous individual factors of variability. During ascent, the change from a high to a lower-pressure environment draws the dissolved inert nitrogen out of these fluids and tissues. A slow, controlled ascent can allow nitrogen to be eliminated safely, but a critical amount of buildup with an uncontrolled or rapid ascent can cause it to revert to a gas and form bubbles in the blood or tissues, causing DCS (6). DCS is a multisystem disorder and symptoms can vary greatly, ranging from harmless joint pains to serious complications such as cerebral gas embolism and death (7).

The extent of bubble formation, the gas load, predicts the severity of DCS, which can be classified as two types. Type I DCS, the milder form, involves the musculoskeletal system and skin, causing joint and limb pain, and rashes or itching (8). Type II DCS, the serious form, involves the central nervous system (CNS) and the thoracic level spinal cord is commonly affected. Although the spinal cord can be affected by Type II DCS, it is rare to have cerebral injury in addition to spinal cord injury (9). Although rare, cerebral DCI is very serious and can be life-threatening (10). Nitrogen is far more soluble in fat when compared to blood. It is five times more soluble in lipids and adipose tissue, and fat will act as a nitrogen reservoir, suggesting that obesity could be a risk factor for DCS (11). The WM of the spinal cord is particularly sensitive as nitrogen is highly soluble in myelin (9).

AGE occurs when bubbles enter directly into arterial circulation, possibly due to an overexpansion injury such as pulmonary baurotrauma, where they can result in emboli in distal arterioles and cause tissue or organ damage (12). Usually, the lungs can filter small bubbles in the venous system, and they are unnoticeable. However, pulmonary baurotrauma can be caused by breath-holding during ascent, uncontrolled ascent, or by lung diseases such as asthma or bronchitis, and leads to lung hyperexpansion, which allows gas bubbles to enter directly into the blood stream (13).

The brain is predominantly affected by arterial bubbles, as it receives a large proportion of blood flow (5,14). If gas bubbles are arterialized into the brain, it can cause stroke-like symptoms and a transient embolism, and the diver will typically lose consciousness within 10 minutes of surfacing. Embolism will occur in multiple areas, with different lesions causing crossed neurological deficits. Neurological symptoms can appear minor, such as tingling or numbness, motor weakness, or difficulty in thinking, or include paralysis, sensory loss, visual disturbances, and convulsions (14).

"Right-to-left" cardiac or pulmonary shunts could allow otherwise asymptomatic vascular gas bubbles to enter the arterial circulation and cause AGE. An increased risk has been associated with the presence and size of patent foramen ovale (PFO) of the heart, which acts as a "right-to-left" shunt where bubbles can cross into arterial circulation (15,16).

An AGE in the brain stem causes blood pressure to increase and dilatation of cerebral arterioles, leading to cerebrovascular autoregulation, cardiac arrhythmias, and possibly cardiac arrest and respiratory depression (13). Immediate death can result if the gas bubbles in the brain stem are large enough to block blood flow (13).

Both DCS and AGE, enveloped within the term DCI, follow the same course of treatment. Mild symptoms after diving may tend to be ignored or be attributed to other causes initially, but treatment must be initiated as soon as possible to improve the likelihood of a good outcome (14). The first course is breathing 100% oxygen by mask, followed by recompression with hyperbaric therapy (5). Treatment has high rates of success, although serious cases require more recompression sessions and there can be residual deficits and brain damage (3).

Proper dive safety procedures have been implemented to control the slow release of N during the ascent phase to minimize the risk of DCS (17), but apart from accidents and failure to adhere to protocol, there are numerous individual factors that are risks for the development of DCS. Some of the potential risk factors include alcohol consumption, dehydration, overexertion, obesity, injury and fatigue, thermal stress, and performing multiple ascents, and consecutive dives and days of diving (13).

CNS involvement in decompression illness

DCS includes many different symptoms, ranging from mild to severe, but neurological symptoms are well-documented and considered the hallmark of serious cases (9,18). Neurological symptoms usually appear one hour after resurfacing and may include confusion, difficulty in concentration and coordination, paresthesia and dysesthesia, lethargy, vertigo, motor weakness, bowel and bladder disfunction, and paralysis (8,19). Entrapped vascular bubbles may cause cellular injury, increased permeability of the blood-brain barrier (BBB), cerebral edema (20), and stroke-like symptoms (3). There is also a greater risk of neurological DCS for divers with PFO, especially if it is large (15).

Recreational divers breathe compressed air, which is commonly 79% nitrogen. In the CNS, nitrogen could be accumulated by myelin, the lipid-rich substance produced by glial cells, under hyperbaric conditions, although myelin alterations have not been studied in divers as of yet (21). Nitrogen is highly soluble in fat and due to the high amount of blood flow to the brain, and in the presence of hyperbaric conditions, the gas is carried and dissolves in the myelin sheaths of neurons, where the bubbles may cause mechanical disruption and affect the functioning of WM (21,22).

A recent study by Coco et al. of 54 professional divers utilized Diffusion Tensor Imaging and neuropsychological testing to study the effects of diving on brain WM and cognitive abilities. Anterior WM alterations were present, as well as impaired attention and memory functions of the prefrontal cortex, suggesting that repeated dives may build-up micro-lesions in the CNS, presumably affecting the myelin sheet of neurons (21).

Different theories have been proposed to explain how bubbles damage the CNS. Arterial occlusion, venous infarction, and in situ nitrogen toxicity have been proposed as the cause. The presence of cerebral lesions from AGE similar to those of stroke, the fact that cerebral blood flow can be obstructed by bubbles, the higher risk of DCI in those with a PFO, and hypoperfused areas identified by single-photon emission computed tomography (SPECT) give support for damage by arterial occlusion (10,23,24). Microvascular damage may progress over time by "silent embolism", when inert gas bubbles cause slight damage that can accumulate with repeated dives. The "silent" bubbles could cause subclinical cerebral vasculopathy, without the presence of DCI, and lead to some unexplained findings in some studies (25). Venous infarction may also be a cause and has been supported by different radiologic and histopathologic findings (26-28). And finally, the theory regarding in situ nitrogen toxicity claims that bubbles can alter nerve conduction and be toxic to neurons, leading to cytotoxic edema and cell death (29). But these mechanisms appear to be interlaced in patients and the complexity of neurological DCI has yet to be elucidated.

Cognitive impairment and white matter damage

Numerous studies have been conducted to identify the neurological effects of diving. Neuropsychological and neurobehavioral tests, electroencephalograms (EEGs), and SPECT scans have been used in studies to determine the neurological function and extent of effects, and magnetic resonance imaging (MRI) has been used to assess areas where WM damage has occurred.

It has been seen that DCI can lead to nervous system damage, which could have possible long-term neurologic effects. One study by Bast-Pettersen et al. found no long-term neuropsychological effects in recreational divers after a 12-year follow-up, but impaired memory and neuropsychiatric symptoms were shown to affect divers who had a history of DCI (30). EEG has also shown abnormalities in the temporal regions of commercial saturation divers, which was exacerbated by a history of DCI (31). However, another study by Murrison et al. found no abnormalities in EEG in divers who had experienced DCI, and no evidence to support involvement of the brain (32).

The presence of a PFO, especially a large one, is a risk factor in diving, as it has been linked to higher rates of DCI and brain lesions (33), likely caused by an AGE that enters the arterial circulation through the PFO. A study by Reul et al. found a high percentage of brain lesions, and multiple lesions, came from a subgroup of 27% of studied divers, which could suggest the involvement of the PFO, which is present in 10-30% of the general population (34). Knauth et al. were able to link multiple brain lesions with the presence of a large PFO, despite the absence of DCI (33). Still, another study by Balestra et al. showed that divers with PFO showed no greater prevalence of WM lesions when compared to non-PFO divers (16).

However, most dives are asymptomatic, meaning that DCI does not occur, and it is still unclear how the act of asymptomatic diving itself could affect the nervous system in the long-term, as studies have shown mixed results. MRI and EEG have provided conflicting results, and it could be that these methods are not sufficiently sensitive to detect cerebral changes associated with diving (35).

Different studies have shown negative effects in asymptomatic diving (21,25,36-43).

A study of 113 military divers by Erdem et al. investigated the prevalence of lesions in divers with similar parameters (blood pressure, smoking, alcohol consumption, history of head trauma or migraine) against a non-diving control group. They found a higher incidence of cerebral WM lesions, which was not affected by age or dive history (39). An MRI study

by Gempp et al. in military divers showed a higher prevalence of brain hyperintense spots and WM changes in divers when compared to a control group, and especially in divers with right-to-left shunting (40).

Very deep dives, usually performed by commercial saturation divers, could exacerbate the damage and repeated deep diving can have more severe effects (41,42). Long-term effects may be influenced by extreme conditions, number of dives, and deep depth (38,44-46). While engaging in dives to depths of 50 meters or more, during the compression phase bottom time, and immediately after resurfacing, neurological and neurophysiologic effects have been shown in divers (43).

Some studies have shown a correlation between impaired cognitive function and higher number of dives (21,25). Coco et al. found that WM alterations and mild associated cognitive impairment increased with a high number of dives, independent of the age of divers, when compared to a non-diving control group (21).

In contrast to these studies, others have shown little neurologic effects associated with asymptomatic diving (47-50).

An experimental rodent study investigated the effects of severe decompression, such as that experienced by commercial saturation divers, on the brain. It was seen that there were circulatory changes in the brain during the acute phase of decompression, but structural or cellular injury to brain tissue was not present, even after 2 weeks follow-up (47). A 2000 study with MRI showed no differences in WM damage between a group of experienced elderly divers and a control group of non-divers (48). Another study of the same year by Cordes et al. found no abnormal neurologic findings with neuropyschometric test results, and no increased prevalence of cerebral lesions in military divers (49). Finally, interesting research by Hemelryck et al. compared the cognitive functioning of scuba divers with a healthy control group as well as to professional boxers, who are at high risk of brain damage. The divers showed memory deficits when compared to the control group, but performed much better than the boxers, who had the lowest results and showed the most cognitive function deficiency (50).

In summary, as to the relationship of diving having negative long-term effects on the brain, affecting cognitive function, and causing lesions, studies until now have provided conflicting results and have so far been inconclusive.

Tau protein

Some recent research to determine the harmful effects of the hyperbaric environment on the CNS has begun to focus on tau protein levels, as tau may be an indicator of neuronal stress in diving.

Breathing partial pressures of oxygen and nitrogen at depth could increase reactive oxygen species (ROS) production and oxidative stress, which could cause neuronal damage (51), and could be observed by biochemical markers such as tau.

Tau protein is a microtubule-associated protein (MAP) found in the neurons of the CNS, and their dysfunction, and successive formation of neurofibrillary tangles, is linked to different neurodegenerative diseases such as Alzheimer's disease and chronic traumatic encephalopathy (52). It can be released after axonal damage and increased neuronal activity in response to stress. Increased tau levels in the blood have also been seen in association with traumatic brain injuries (53) and in contact sports where concussions are common, such as boxing (54,55). High intensity interval training and breath-hold diving have been seen to raise tau levels after activity (56,57), and tau seems to be unrelated to DCI (58), which could prove useful for focusing on CNS damage inflicted by the act of diving itself.

Studies by Rosén et al. have found increased blood tau protein levels after diving, with no identified correlation between absolute tau concentrations and venous gas loads in divers. A small, 2019 pilot study of 10 divers, who performed repeated deep dives between 52 and 90 meters over four days, found serum tau concentration was increased after diving by 2.5 times (59). In another recent study, Rosén et al. measured the blood tau levels of 32 divers in a water-filled hyperbaric chamber, for a time of 10 minutes, to simulate a dive pressurized to 42 meters. Blood was sampled from the divers before diving and two intervals afterwards at 35-40 and 120 minutes. Tau levels were seen to increase after diving at the 35-40 min, and were further increased at 120 min, and the study was repeated with uniform results (60).

Future research using blood biomarkers such as tau could be useful for investigating neuronal damage from scuba diving.

Significance

Scuba diving is a relatively new activity and has been growing in popularity as a recreational sport. Because of this, the long-term effects of continuous diving are now being investigated and, considering the growing number of people who are participating in diving globally and the aging population of divers, it is becoming increasingly important to determine the neurological health effects that may be associated with it.

As discussed, studies have provided conflicting results, with some showing the potential neurologic damage that could be incurred by diving and others being unconclusive. Some have shown that cognitive impairment and WM lesions have

been linked to diving in people with a history of DCI and even in those without. It may be possible that the higher prevalence of cerebral lesions seen in some studies of divers without a history of DCI could be due to cumulative, subclinical injury to the neurological system caused by inert nitrogen gas bubbles during diving (39).

WM lesions are a common characteristic seen by MRI in adults (61), especially in the aging brain, with 90% prevalence in people 65 years of age and older (62). Lesions have been associated with dementia, depression, Alzheimer's Disease, and cognitive decline (63-65). They may be non-specific, but sources of lesions are many, and can include vascular diseases, untreated chronic hypertension, migraine, inflammatory disorders, infectious diseases, alcohol abuse, metabolic disorders, and traumatic brain injuries, amongst others. Just because lesions are revealed in divers by MRI does not mean they are the direct consequence of diving.

And the presence of brain lesions does not correlate directly with reduced cognitive functioning, although it has been shown there may be a relationship in some studies. More research combining MRI and neuropsychological testing is needed to define the relationship of these brain lesions to neurologic performance.

Causation and correlation must be established in further studies by limiting for the various independent factors and methodological consistency. Numerous independent factors can interfere with results, including age, the presence of a PFO, prior head injuries and brain damage, and cardiovascular diseases including high cholesterol and hypertension.

Many studies conducted as to date have methodological flaws and biases, which could explain the inconclusive results between similar studies. Selection biases, varying degrees of age, of diving experience, and number of dives, and insufficient detection sensitivity of MRI are all factors that could be responsible for the conflicting results from studies (16). Furthermore, these studies are methodologically diverse, each reaching an independent conclusion instead of a collective result. Finally, psychometric function testing should be correlated to imaging-detected cerebral points of interest for verification (16).

Tau protein levels may be a useful tool for indicating neuronal stress caused by diving, and research should be continued to provide further insight. More studies are needed to elaborate the correlation of WM damage with diving, establish the causation, and determine the significance of lesions for the long-term neurological health outcome of divers.

CONCLUSIONS

The commercialization of diving has led to high safety standards and diving today is considered relatively safe when safety protocol is followed (66). However, DCI is a great risk for divers, even when depth and time regulations are followed, due to accidents, rapid ascent, and a high variability of independent factors that are associated with its occurrence. DCS and AGE can have serious health consequences for divers, but the risk can be minimized by attentively following safety protocol.

Studies on the possible neurological effects related to diving have been conflicting, with some showing WM lesions and cognitive impairment in divers, and others showing no evidence of this. Overall, the causation of such research cannot be clearly related to diving, as those studies regarding the neurological consequences of diving have not yet been able to prove a direct correlation between cerebral damage and asymptomatic diving. Numerous variables must be accounted for to determine the underlying cause of WM damage and related cognitive deficits. Further research is needed to clarify the long-term, cumulative neurological effects that could be caused by the act of diving. Biochemical markers of neuronal damage, such as tau protein, could be useful for assessing increased neuronal activity in response to stress.

Deep diving and diving in severe conditions causes a high level of decompression stress on the body and carries a higher risk of DCI, and it could also be true that this carries a higher risk for long-term health outcome, as some studies have shown possible neurological effects. Therefore, DCI should remain the biggest concern and divers should aim to practice their sport in a conscientious and prudent manner to avoid the occurrence of DCS and AGE.

Conflict of interest

The author declares that they have no conflict of interest.

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