Review article

Effects of diving and oxygen on autonomic nervous system and cerebral blood flow

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Abstract

(Winklewski PJ, Kot J, Frydrychowski AF, Nuckowska MK and Tkachenko Y. Effects of diving and oxygen on autonomic nervous system and cerebral blood flow. *Diving and Hyperbaric Medicine*. 2013 September;43(3):148-156.)
Recreational scuba diving is a popular leisure activity with the number of divers reaching several millions worldwide. Scuba diving represents a huge challenge for integrative physiology. In mammalian evolution, physiological reflexes developed to deal with lack of oxygen, rather than with an excess, which makes adaptations to scuba diving more difficult to describe and understand than those associated with breath-hold diving. The underwater environment significantly limits the use of equipment to register the organism's functions, so, in most instances, scientific theories are built on experiments that model real diving to some extent, like hyperbaric exposures, dive reflexes or water immersion. The aim of this review is to summarise the current knowledge related to the influence exerted by physiological conditions specific to diving on the autonomic nervous system and cerebral blood flow. The main factors regulating cerebral blood flow during scuba diving are discussed as follows: 1) increased oxygen partial pressure; 2) immersion-related trigemino-cardiac reflexes and 3) exposure to cold, exercise and stress. Also discussed are the potential mechanisms associated with immersion pulmonary oedema.

Key words
Scuba diving, cerebral blood flow, oxygen, autonomic nervous system, neurogenic pulmonary oedema, immersion pulmonary oedema

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Introduction

Recreational self-contained underwater breathing apparatus (scuba) diving is a popular leisure activity. It is not easy to provide any estimates related to the number of scuba divers worldwide; however, some diving portals state 3–6 million; obviously, it is a large and growing population. When conducted within recreational limits (concerning depths, times, types of breathing mixtures, decompression burden, and environmental factors), the risk for injury or death is quite low. The annual per capita fatality rate ranges from 1.7 to 16.4 deaths per 100,000 persons per year depending on surveillance programmes, which is no higher than the rate for jogging or motor vehicle accidents (13 and 16 deaths per 100,000 persons per year, respectively).[1] Divers Alert Network (DAN) is a dive organization that publishes annual accident reports:
<http://www.diversalertnetwork.org/medical/report/>.

There are many reports describing the consequences of diving injuries, decompression illness and the high pressure neurological syndrome.[2,3] Some extreme environmental factors, like cold water and deep scuba diving, may have long-term negative effects on cerebral blood flow (CBF) and neurological function with consequent intellectual deterioration.[4] The possible neuropsychological effects of deep diving have been highlighted by other authors.[5,6] In this review, we will focus mainly on uneventful dives and their effect on the pathophysiology of the human body, concentrating on the autonomic nervous system (ANS) and CBF.

The main factors affecting the ANS and CBF during scuba diving include: increased oxygen partial pressure (PO_2), immersion-related trigemino-cardiac reflexes and exposure to cold, exercise and stress. All of these act through different physiological pathways, but they are cross-linked with variations and imbalances in ANS activity. The exact role that the ANS plays in the regulation of CBF remains a matter of scientific discussion, even outside the diving world. It is interesting to present how diving-related factors influence the ANS and consequently its contribution to the regulation of CBF during uneventful recreational diving. With the increasing popularity of scuba diving in populations with less than optimal health status (i.e., age, physical unfitness and mild cardiovascular disturbances) or autonomic imbalance (e.g., adolescents), such knowledge is of even greater importance. A better understanding of the role that the ANS and oxygen play during scuba diving may help to develop more efficient strategies in the treatment of several life-threatening diseases that are not related to diving activities, such as stroke, brain trauma or pulmonary hypertension.

ANS in the regulation of CBF

Before discussing the main factors affecting the ANS and CBF during scuba diving, we provide a brief summary of

the current knowledge with respect to the role of the ANS in CBF regulation in other conditions. This is a large subject and readers are referred to two review articles for more detailed information.[7,8]

The sympathetic (SNS) and parasympathetic (PNS) nervous systems function in opposition to each other. The SNS typically functions in actions requiring rapid responses, whilst PNS functions with actions that do not require immediate reaction. The SNS is often considered the "*fight or flight*" system, while the PNS is often considered the "*rest and digest*" or "*feed and breed*" system. Therefore, the SNS is activated by exercise, cold and anxiety to divert blood flow away from the gastro-intestinal tract and skin (via vasoconstriction) to brain, heart, skeletal muscles and the lungs. In addition, SNS activation increases heart rate and myocardial contractility, further enhancing blood flow to brain and skeletal muscles.

Brain blood vessels are richly innervated with parasympathetic fibres.[9,10] Acetylcholine, the postganglionic neurotransmitter of parasympathetic neurons, interacts with endothelial muscarinic receptors to facilitate vasodilation.[11,12] The release of acetylcholine from the animal cerebral cortex contributes to the exercise-induced increase in CBF.[13] Muscarinic receptors are present in human cerebral arteries, including the middle cerebral artery, and acetylcholine induces vasodilation in human cerebral arterioles by stimulating the brain subtype of these receptors.[11,14] Evidence for vasodilation of cerebral vessels by nerves releasing acetylcholine has been reported recently in humans, with an increase in CBF velocity during exercise being abolished with muscarinic receptor blockade.[15] Atropine, an acetylcholine antagonist, decreases pial artery pulsation in humans (unpublished observations).

The cerebral arteries, arterioles and, to a lesser extent, veins are richly innervated with sympathetic nerve fibres.[16,17] However, the role of the SNS in regulating cerebral circulation remains a matter of controversy.[18–20] Adrenergic receptors have been found in human cerebral vessels, including the middle cerebral artery, and their activation leads to contraction of human pial artery segments.[21,22] Only recently has it become possible to assess pial arteries in intact animals and humans. Infusion of noradrenalin (the SNS neurotransmitter) constricts pial arteries in animals, while static exercise exerts similar effects in humans.[23,24] There is accumulating evidence that the SNS might be an important element in brain protection against excessive increases in perfusion pressure and flow.[25–28] Moreover, recent studies employing techniques based on infrared light have suggested an increase in cerebral venous blood volume following sympathetic stimulation.[29]

Increased oxygen partial pressure (hyperoxia)

Oxygen partial pressure (PO_2) depends on the fraction of oxygen in the inspired gas mixture and ambient pressure (diving depth). In recreational diving, PO_2 is kept below 162.6 kPa (1.6 ATA) in order to avoid its toxic effect on the central nervous system (CNS). The ANS response to increasing PO_2 is biphasic, with the PNS predominating initially.[30] Massive sympathetic discharge originating from the CNS is seen only at very high PO_2, usually leading to acute intoxication and, while it has been described in animals, it has not been reported during conventional recreational scuba dives.[31–33]

It remains controversial whether or not, during the initial response to oxygen, the SNS is also activated. Interesting data comes from outside diving-related research, namely from a functional magnetic resonance imaging study in children aged from 8 to 15 years. Two minutes of hyperoxic ventilation at sea level (101.3 kPa inspired O_2) produced pronounced responses in the central autonomic and hormonal control areas, namely the posterior hypothalamus, insula, hippocampus, cerebellum, caudate, and thalamic regions, which are brain structures that are usually recognised as intertwined with the central SNS.[34] This clearly showed that even very short exposure to hyperoxia may affect several structures in the CNS. However, this study should be interpreted with caution because the CNS in children is less mature than that of adults and may respond differently to hyperoxia. Also, it is not known if activation of these regions resulted in any peripheral changes, i.e., SNS efferent firing, changes in hormone levels or cardiovascular alterations. Several studies in adults report a decrease in SNS activity in the PO_2 range below 162 kPa or lack of relevance of SNS activity on peripheral changes.[35–37]

Breathing oxygen-enriched gas mixtures under normobaric conditions (PO_2 less than 101.3 kPa) leads to peripheral vasoconstriction, and decreased heart rate, stroke volume and cardiac output, changed baroreflex sensitivity, reduced carotid artery diameter and CBF, and increased brain tissue oxygen saturation.[37–42] Peripheral blood pressure either does not change or increases.[31,37,42] Based on animal research, it is suggested that hyperbaric oxygen may exert different effects on the left and right ventricles.[42] While function of the left ventricle is depressed, the right ventricle may be less affected, which in turn may lead to pulmonary hypertension and increased pulmonary arterial wedge pressure.

Hyperoxia induces peripheral vasoconstriction. Several different explanations have been proposed for this, including inhibition of the local release of nitric oxide (NO) from cysteine-binding in the haemoglobin molecule (S-nitrosothiol) by increased venous PO_2 and superoxide anions and inactivation of endothelium-derived relaxing factor by hyperoxia.[43,44] Several other factors may be involved, but this vasoconstriction seems not to be associated with increased SNS activity.[36]

Decreases in heart rate, stroke volume and cardiac output occur as a result of two overlapping factors: 1) lowering of the heart rate, triggered by an increase in PNS activity;

and 2) impairment of left ventricular diastolic function.[42,45] Oxidative stress due to exposure to an oxygen-rich environment is well-documented in humans and animals.[46,47] On returning to normoxic conditions, the time course of recovery is different for various cardiovascular variables. Heart rate is the first to return to baseline, while the vascular resistance, cardiac output and stroke volume changes persist for longer. Such a sequence of events supports the above reasoning: 1) the recovery of cardiovascular function is not controlled solely by baroreflex activity but there are two distinct phenomena: central negative chronotropic action and local vasomotor control; and 2) cardiac output and stroke volume reduction could be strongly attributed to the impairment in left ventricle function.[30]

Hyperoxia-induced alterations in cardiac function need further consideration with respect to brain perfusion. The clinical and experimental literature suggest a close link between the function of the left ventricle and brain perfusion.[48–50] The CBF response to a rapid decline in systemic blood pressure in healthy volunteers was closely related to unloading of the arterial baroreceptors, which suggests cardiac output involvement in the regulation of CBF.[49] In that study, during full cardiac autonomic blockade, an attenuated tachycardia response exacerbated the cuff release-induced reductions in mean systemic blood pressure, and consequently evoked a greater transient decrease in mean CBF velocity. These findings indicate that the baroreflex-induced tachycardia response following acute hypotension regulates the reduction in systemic blood pressure, thus acting to minimise decreases in CBF.[49]

Data coming from our lab indicated direct interactions, independent of systemic blood pressure, between cardiac output and brain microcirculation, at least in animals.[50] To the best of our knowledge, there have been no studies assessing brain and heart interdependence during hyperoxia and the time course of recovery. If we hypothesise that such interdependence exists, the initial activation of the PNS may be seen as a regulatory mechanism to preserve brain homeostasis, i.e., it protects the CNS from O_2 intoxication.

Hyperoxia per se induces a decrease in CBF.[38,40] This was elegantly shown in a study in which healthy subjects were exposed to various ambient pressures (101.3 kPa, 202.6 kPa and 405 kPa) while breathing either air or 100% oxygen.[38] Oxygen inhalation reduced middle cerebral arterial blood flow velocity while ambient pressure per se did not seem to influence it. Unfortunately there was no comparison between lower and higher ambient pressures (101.3 kPa versus 405 kPa) while breathing the same and normoxic PO_2 (20 kPa). Therefore, PO_2 remains the main factor regulating CBF, but the effects of other confounders, including ambient pressure, need to be further elucidated.

The mechanism of oxygen-induced cerebral vasoconstriction is based on an interruption in NO-mediated basal relaxation of cerebral vessels.[51,52] Hyperoxia leads to the generation of reactive oxygen species like superoxide ($\cdot O_2$), which can react with NO to generate the strong oxidant peroxynitrite, resulting in transient reduction in its perivascular concentration.[51] The equilibrium between $\cdot O_2$ and NO is regulated by superoxide dismutase-3.[51] Superoxide dismutase-3 is present in high concentrations in vessels where NO is important for vascular relaxation. Inactivation by $\cdot O_2$ interferes with NO-dependent basal tone and vasorelaxation. Therefore, scavenging of $\cdot O_2$ by superoxide dismutase-3, plays a critical role in regulation of NO-dependent CBF.[53] As a result, the reduction in CBF caused by hyperoxia protects the brain against an excess of oxygen.

When hyperoxia persists after an initial fall in CBF, the production of NO appears to compensate and may result in an increase of CBF and, as a consequence, the delivery of toxic amounts of oxygen to the brain. Such secondary CBF increase always precedes O_2-induced manifestations of brain poisoning, both in animals and in humans.[51–55] However, the secondary increase in CBF and O_2-induced seizures were reported at very high oxygen doses (283 kPa and 506.5 kPa of inspired O_2 in humans and animals, respectively), therefore, significantly exceeding even the most liberal limits set for recreational scuba diving.

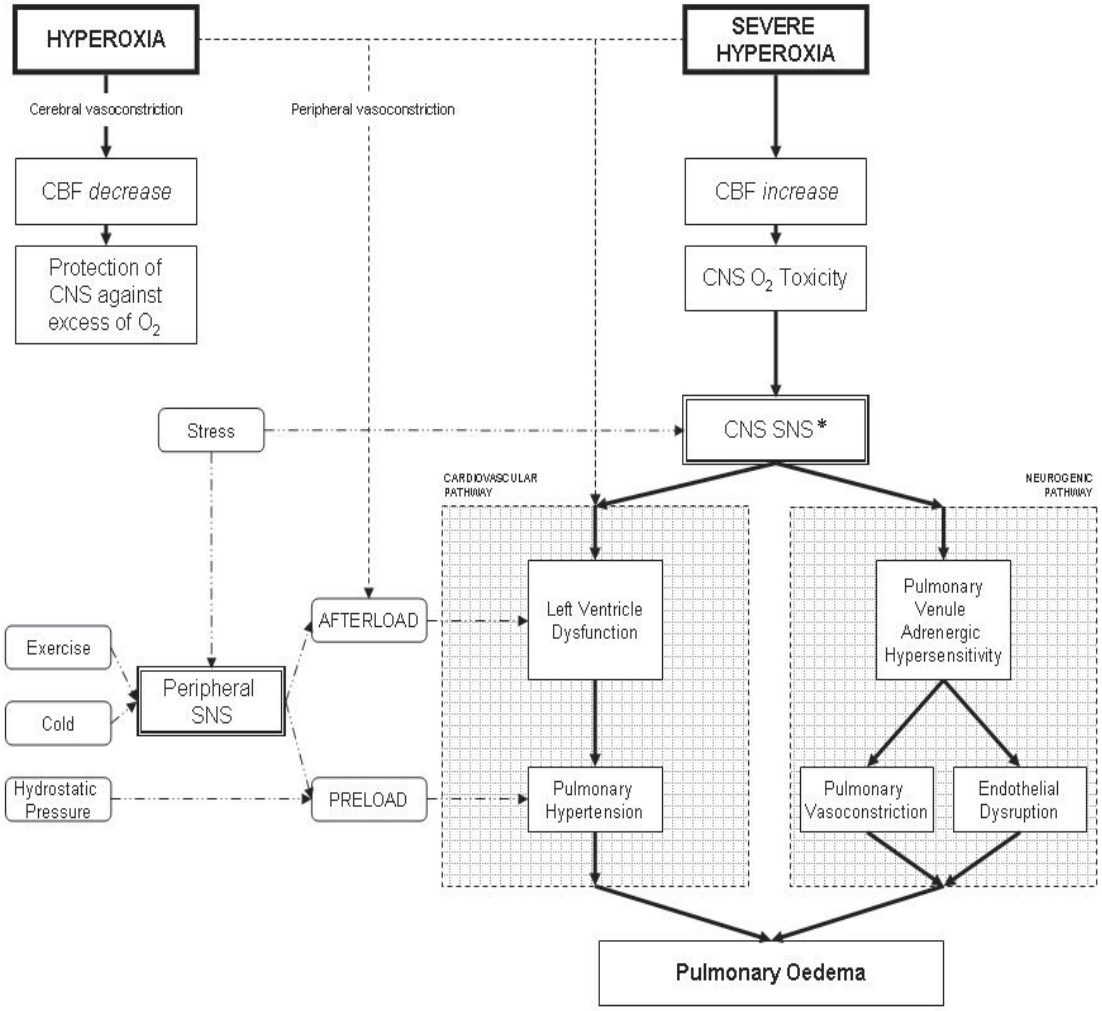
Nevertheless, doses of oxygen that induce CNS oxygen toxicity also activate the SNS. Intense SNS discharge and the release of catecholamines have been reported in brain insult irrespective of the causality, in particular, in neurologic conditions that cause abrupt, rapid and extreme elevations in intracranial pressure.[56,57] It is hypothesised that massive SNS discharge following CNS injury, for example, directly affects the pulmonary vascular bed via α- and β-adrenergic receptors, leading to isolated pulmonary venoconstriction and/or endothelial disruption. This theory of "*pulmonary venule adrenergic hypersensitivity*" can explain neurogenic pulmonary oedema.[58]

In diving, the CNS symptoms of oxygen toxicity (generalised convulsions) and pulmonary damage induced by hyperbaric O_2 have long been considered to be separate entities, with oxygen acting directly on the CNS in the first case and on the alveolar region of the lung in the second.[59] Involvement of the SNS, as a link to both events, was initially proposed in animal models, but has not been seen in human studies.[32,60,61] It remains unclear why oxygen brain poisoning leads to neurogenic pulmonary oedema in small animals, but not in humans.[31,32,60,61]

Immersion pulmonary oedema

Immersion pulmonary oedema (IPE) represents a different mechanism of lung injury than neurogenic pulmonary oedema caused by a significant CNS insult. Whilst the ANS is involved in both syndromes, in the case of CNS oxygen toxicity, lung inflammation and possibly Takotsubo cardiomyopathy (a form of acute left ventricular dysfunction

Figure 1
Pathways of oxygen and SNS involvement in development of pulmonary oedema;
* extrapolated data from animal studies



characterized by normal contraction of the apex, and dilatation of the remainder, with a fancied resemblance of the left ventricle to a Japanese octopus pot – 'takotsubo'), this is mediated by massive sympathetic discharges originating from the CNS.[58] On the other hand, in IPE, this is owing to an increase in central venous (preload), pulmonary arterial and pulmonary wedge pressures. This phenomenon is mediated by the cardio-endocrine-renal axis, with immediate translocation of blood to the heart and slower autotransfusion of fluid from the cells to the vascular compartment.[62] The question of whether central SNS activation may facilitate development of IPE during some dives with strenuous exercise in cold water remains unanswered. Figure 1 provides a graphical summary of the various pathways of oxygen and SNS involvement in the development of pulmonary oedema. Note that the SNS pathway leading directly to neurogenic pulmonary oedema has been confirmed only in small animals.

In 22 healthy divers who suffered from IPE after dives involving strenuous exercise, physiological and/or mental stress, the common feature was the occurrence of respiratory symptoms during the ascent.[63] Most of the dives were deep (37 metres' sea water, (msw) on average) and in cool water (15°C).[63] The average inspired PO_2 was 100 kPa, thus within the range that potentially may activate brain structures that are associated with the central SNS.[34] Some divers reported an unpleasant cold sensation, hard effort and/or anxiety. Anxiety is another potential trigger for central SNS activation.[64] It was proposed that the development of lung oedema was associated with decreased heart rate and ventricular contractility and peripheral vasoconstriction due to high oxygen exposure. In five divers, increased troponin levels were found within 24 hours after immersion and, in nine divers, elevated natriuretic peptide levels were considered to reflect congestive heart failure.[63] Both markers (troponin and natriuretic peptide) might have indicated left ventricle dysfunction due to central sympathetic hyperexcitation, but it is not possible to differentiate this from left ventricle dysfunction caused by the direct effect of hyperoxia.[64] IPE in scuba divers in cold waters, first described by Wilmshurst, is probably of haemodynamic

origin.[65–67] Immersion-induced increases in pulmonary blood volume and pulmonary hypertension due to exertion most likely have an additive effect.[68] Interestingly, breathing with hyperoxic gas attenuates high pulmonary pressure evoked by exercise in thermo-neutral water but not in cold water.[69] This suggests that SNS involvement triggered by cold-water immersion promotes pulmonary hypertension. Owing to the complexity of interrelated factors like temperature, exercise, anxiety, PO_2 and probably several other components, interaction between the peripheral and central SNS on the cardiovascular system during diving remains unclear.

Immersion-related trigemino-cardiac reflexes

The trigemino-cardiac reflex, or "*dive reflex*", represents the most powerful of the so-called oxygen-conserving autonomous reflexes in mammals.[70–74] Apnea with bradycardia is associated with a slightly smaller reduction in arterial oxygen saturation than apnea without bradycardia or with less pronounced bradycardia. The trigemino-cardiac reflex was first reported during surgery in the cerebellopontine angle.[75] It was observed that electrical, mechanical or chemical manipulation of the trigeminal nerve on its intra- and extra-cranial course provoked a drop in mean arterial blood pressure and bradycardia.[75,76] The exact mechanism of the trigemino-cardiac reflex is far from clear. In fact, it consists of many sub-reflexes, for example the dive reflex, nasopharyngeal reflex and oculo-cardiac reflexes, which are well described and frequently observed during diving. It seems that the trigemino-cardiac reflex is dominant and the efferent effects can strongly affect human physiology.[77,78]

During immersion, the trigemino-cardiac reflex is elicited by contact of the face with cold water and involves breath-holding, intense peripheral vasoconstriction, bradycardia and increased mean arterial pressure, thus maintaining adequate oxygenation of the heart and brain at the expense of organs less sensitive to hypoxia.[79] Within seconds of the initiation of such a reflex, there is a powerful and differentiated activation of the SNS and PNS with subsequent elevation in CBF. This increase in CBF is independent of the partial pressure of carbon dioxide.[80]

The increase in CBF, with no changes in the cerebral metabolic rate of oxygen or the cerebral metabolic rate of glucose evoked by the dive reflex, is most likely a neuroprotective adaptation or a type of preconditioning strategy.[78] Reticulospinal neurons of the rostral ventrolateral medulla oblongata are critical for detecting and initiating the vascular, cardiac and respiratory responses to hypoxia and ischaemia.[80] The systemic response to excitation of these neurons includes projections to spinal preganglionic sympathetic neurons and cardio-vagal motor medullary neurons, which results in blood redistribution from the viscera to the brain in response to a challenge to cerebral metabolism.[77,80] Excess blood flow to the brain allows diving mammals to survive for a relatively long time underwater.[81] Owing to their physiological function in diving mammals, the oxygen-conserving autonomous reflexes are gaining increasing attention as a potential preconditioning therapeutic strategy in various neurological conditions associated with neuronal death.[77,78]

Human bradycardia resulting from apneic face immersion is inversely proportional to water temperature within a range determined by the ambient air temperature. Face immersion in cold water after exposure to a high ambient air temperature induces the most pronounced bradycardia.[82] The question of whether face-only breath-hold immersion is a good model for investigating the changes that occur during scuba or even real breath-hold diving remains unanswered. The subject is usually requested to hold their breath, and then immerse their face in a tub of water, and to persist in such a position for a certain period of time.[83] The oxygen-conserving effect of the dive reflex in the immersed diver is the same as that observed in the dry, horizontal simulated diving model.[84] However, in scuba diving, the CBF increase seen in the dive reflex is most likely overridden by exposure to inhaled oxygen during the course of immersion and CBF is reduced to protect the brain from hyperbaric hyperoxia. Furthermore, the nasopharyngeal reflex and oculo-cardiac reflexes are supressed by the use of a diving mask. Nevertheless, simultaneous occurrence of trigemino-cardiac reflex and increased PO_2 in the breathing-gas mixture expose the diver to contradictory influences with respect to CBF and powerful, non-physiological and conflicting ANS stimulus. Moreover, the dive response might be partially involved in the mechanism described above for IPE.[85]

Exposure to cold, exercise and stress

When allowed to breathe, immersion in warm and cold water results in different responses with respect to cardiovascular parameters.[85] Warm-water, whole-body immersion (29–31^{o}C) produces increases in cardiac output, and pulmonary arterial, wedge and central venous pressures, while systemic arterial pressure and heart rate remain unaltered. Cold-water, whole-body immersion (18–20^{o}C) leads to systemic arterial pressure and heart rate increases, while cardiac output, and pulmonary arterial, wedge and central venous pressure increases were more pronounced in comparison to warm water.[85] Face-only immersion in cold water reduces apneic time and stimulates ventilation, predominating over the potential oxygen-conserving and apnea-prolonging effects of the diving response.[86] Sudden, whole-body immersion in ice water is linked to the so-called cold shock response consisting of respiratory gasps, hyperventilation, tachycardia, hypertension and decreased CBF during the first 2–3 minutes.[87] A significant reduction in CBF may be associated with signs of imminent syncope, such as drowsiness, blurred vision and loss of responsiveness, and may be a possible cause of drowning.[87] Adaptation to the response is possible and requires repeated cold immersion. However, even without

Table 1

Summary of changes in heart rate, cardiac output and systemic and pulmonary arterial, central venous and wedge pressures after immersion in warm (29–31OC) and cold (18–20OC) water and exposure to normoxia and hyperoxia at 476 kPa in warm water (29–31OC). * compared to baseline (before immersion); † compared to immersion in warm water; ‡ compared to immersion at 476 kPa (PO2 20 kPa); § at 476 kPa stroke volume was measured, not cardiac output; + increase, - decrease, +/- no change
(summary derived from references 40 and 60)

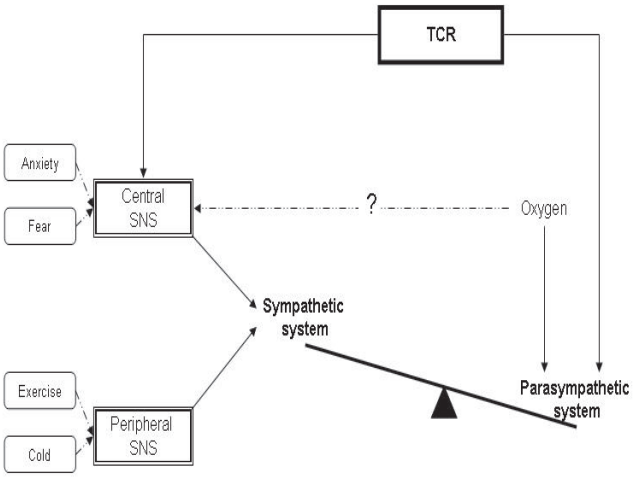
	Warm immersion at rest *	**Cold immersion** at rest†	**476 kPa** (PO_2 20 kPa) during exercise†	**476 kPa** (PO_2 172 kPa) during exercise‡
Heart rate	+/-	+	+	-
Cardiac output §	+	++	++	+/-
Systemic blood pressure	+/-	+	+	-
Pulmonary arterial pressure	+	++	not measured	not measured
Central venous pressure	+	++	++	-
Wedge pressure	+	++	not measured	not measured

prior cold-water experience, subjects, if properly educated, are able to suppress reflex hyperventilation following ice-water immersion and maintain their CBF at a level that is not associated with impaired consciousness.[88] Actually, in experienced scuba divers, noradrenaline and adrenaline blood concentrations may decrease after immersion, most likely because of orthostatic release caused by the external hydrostatic pressure on the peripheral vasculature.[89] This is in line with the fact that novice scuba divers tend to hyperventilate, particularly in stressful conditions, while more experienced divers are able to better control their underwater breathing depth and frequency. The cold-shock response is usually considered with respect to a change from a warm ambient temperature to immersion in cold water. However, a significant temperature change may also occur underwater, when a diver crosses a thermocline and/or swims into a cold current. In experimental conditions, temperature switches from 29–31^{O}C to 18–20^{O}C during immersion at sea level result in increased systemic and pulmonary arterial pressures, while heart rate, central venous pressure, stroke volume and systemic arterial resistance remain unchanged.[85] Unfortunately, there are no reports on the effect of temperature changes on CBF during diving, but it seems that, in such circumstances, the sudden, significant decrease in temperature may induce changes similar to cold shock with all of its consequences, including additional SNS activity.

Diving is usually associated with exercise. The typical response to exercise at the surface consists of tachycardia, hyperventilation, increased cardiac output and elevated CBF.[90] Exercise during immersion at sea level increases heart rate, cardiac output, and pulmonary arterial and wedge pressures, while central venous pressure remains unchanged, both in warm (29–31^{O}C) and cold (18–20^{O}C) water.[85] Responses to exercise at 476 kPa depend on the inspired PO_2. Exercise at 476 kPa with normoxic PO_2 (20 kPa inspired PO_2) in warm water increases heart rate, blood pressure, central venous pressure, stroke volume and systemic vascular resistance, while hyperoxia at 476 kPa (176 kPa inspired PO_2) in warm water decreases the heart rate, blood pressure and central venous pressure response

Figure 2

Autonomic conflict during uneventful scuba diving
TCR – trigemino-cardiac reflex



to exercise, whilst systemic vascular resistance and stroke volume are not significantly altered versus 20 kPa inspired PO_2.[68] As mentioned before, concomitant hyperoxia does not attenuate the increase in pulmonary vascular pressures associated with cold-water immersion.[69] A summary of changes in heart rate, cardiac output and systemic blood, pulmonary arterial, central venous and wedge pressures after immersion in warm and cold water and exposure to normoxia and hyperoxia at 476 kPa in warm water is provided in Table 1. Face cooling with mist water increases CBF during exercise.[91]

Concluding remarks

Taking into account all of the factors discussed, it is obvious that recreational scuba diving represents an effort for humans and activates both the sympathetic and parasympathetic components of the ANS. To further complicate the picture, there is a strong and conflicting relationship between the SNS and PNS. In fact, the phenomenon of 'autonomic conflict' described for cold-water immersion is most likely significantly exacerbated during scuba diving.[92] Figure 2

provides a graphic summary of this conflicted relationship. Furthermore, increased PO_2 diminishes while the trigemino-cardiac reflex and exercise elevate CBF, exposing the diver to contradictory or conflicting stimuli with respect to brain perfusion. PNS activation and related decreases in cardiac parameters seem to protect the brain from oxygen excess, but at the same time impair the ability of the left ventricle to cope with increased afterload and preload, and increases the probability of IPE. This could be of considerable importance for those individuals who are not physically trained or lack physical activity in their everyday life. Moreover, hyperoxia, exercise, cold and stress present during scuba diving may actually reveal or exacerbate existing but undiagnosed medical conditions.

While individual reflexes and responses to oxygen and immersion have been studied, the overall changes to CBF and the ANS during exposures to a combination of pressure, immersion and hyperoxia such as those seen during typical recreational scuba dives have not been well documented and require further study. Scuba diving represents a huge challenge for integrative physiology. During the evolutionary process, physiological reflexes that have developed to deal with the lack of oxygen underwater, rather than an excess make adaptations to scuba diving more difficult to describe and understand.

In this review, we have summarised the current knowledge related to the selected physiological factors exerted by scuba diving on CBF, with particular emphasis on the role of oxygen and the ANS. We have not addressed here one important issue: given the complex interactions between environment and ANS resulting in a myriad of effects (some contradictory) on CBF and cardiac performance, what will be the effects of many of the medications that our divers of increasing age are now taking, particularly those affecting the renin-angiotensin and cardiac systems?

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