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The Cardio-Respiratory Mechanisms Involved in the Diving Response Adaptation and Breath-Hold Training Effects in Freedivers

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ABSTRACT

This review aims to explore the cardiovascular and respiratory mechanisms involved in the training effects of the diving response adaptation and to determine the adaptive changes during apnoea and breath-hold training in breath-hold divers. A sounder theoretical knowledge of these critical aspects is necessary to be able to understand the oxygen-conserving mechanism of the diving response, and the apnoea-induced cardiorespiratory adjustments involved in enriching the science of respiratory physiology and the development of breath-hold training and ability. These insights may contribute to understanding the pathophysiology of respiratory abnormalities and dysfunctional breathing in humans. Furthermore, it may facilitate the development of efficacious interventions to increase breath-holding ability, and sports performance, as well as assist with the management and treatment of various physiological and psychological conditions. This review will be presented in four separate sections. Section one will describe the diving response and its physiology. Section two will explore the cardio-respiratory mechanisms of the diving response. Section three will discuss the adaptive changes associated with breath-hold training and/or apnoea training, as well as the associated cardio-respiratory adaptions. Section four will explore the clinical applications and implications of the diving response.

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Introduction

Diving Response

The Diving Response (DR) is a physiological reflex that optimises respiration, allowing humans to endure a lack of oxygen underwater. For more than a century, this reflex has been studied extensively in animals; however human studies are limited [1]. The DR is the most powerful autonomic reflex characterized by bradycardia, peripheral vasoconstriction, blood centralization, decreased cardiac output, increased arterial blood pressure, and decreased arterial oxygen saturation (SaO_2) [2-4]. These mechanisms are exaggerated in breath-hold divers and assist in increasing diving durations by temporarily reducing peripheral tissue oxygen uptake [5].

Multiple factors stimulate the diving response, although the contributions of each in eliciting the DR and the central mechanisms that control and regulate these responses have not been fully understood [6]. Factors activating the DR include, apnoea (cessation of respiration), also known as Breath-Holding (BH), Cold Facial Immersion (CFI) and tactile stimulation of receptors of the face, hypercapnic and hypoxic factors influencing chemoreceptors on the vascular bed, carotid sinuses, medulla oblongata centres (i.e., respiratory, vasomotor) [7,8]. Physiological differences between humans and aquatic mammals point to the limitations of the human response to deep breath-hold diving [9]. According to a review by Ponganis et al. several factors including baroreceptor reflexes, pulmonary stretch receptor reflexes, trigeminal/glossopharyngeal nerve stimulation, carotid body receptor responses, blood gases, volitional control and exercise may influence the exaggeration of one's diving response activation [10].

Whilst the diving reflex is involuntary, Schagatay and Andersson suggest that the DR can be trained and can have positive effects on both heart rate reduction and apnoeic duration [4]. Training effects have been observed in pearl, shell, and sponge divers as well as athletes of free diving; the sport of diving on one breath. Undoubtedly, this training has contributed to the exceptional breath-hold ability of divers, as evidenced by the world record free diving depths humans have been able to conquer. Long-term training of free diving is associated with several physiological adaptations including a more pronounced diving response, and greater lung volume, lung oxygen and carbon dioxide stores [4,11]. The heart rate of human breath-hold divers can decrease by more than 50% whilst diving [9]. This review aims to explore the cardio-respiratory mechanisms involved in the training effect of the diving response adaptation and to determine the adaptive changes during apnoea and breath-hold training in trained breath-hold divers. We aim to bring together recent advances and insights in the research of the diving response and its associated adaptive training effects. In recent years, the diving response literature has shown promising results in the reduction of panic and anxiety symptoms, depressive symptoms and in decreasing acute psychosocial stress responses and in increasing positive mood and well-being [12-15].

Cardio-Respiratory Mechanisms

The main purpose of the adaptive mechanisms of the cardio-respiratory system is to prioritize survival by conserving oxygen (O_2) and ensuring O_2 supply is provided to the vital organs including the brain and heart, as a result of anoxia. The diving response is controlled by a complex integration of neural networks incorporating the respiratory and cardiovascular systems [2,3]. The DR is mainly the respiratory system which is linked to the responses of the cardiac system [16].

The complex adaptive mechanisms of the cardio-respiratory system are a constellation of simultaneous activation of the parasympathetic and sympathetic nervous system, which leads to responses that include bradycardia, peripheral vasoconstriction, increased secretion of catecholamine and the splenic effect elicited through hormonal reaction of the adrenal glands [3,16,17].

Studies have established that the parasympathetic nervous system controls bradycardia through the vagus nerve, while the sympathetic nervous system via the stimulation of peripheral sympathetic vasomotor fibres controls peripheral vascular tone [10]. Peripheral vasoconstriction is associated with an increased sympathetic discharge, while bradycardia is the result of increased vagal activity [18].

Bradycardia

To conserve energy, breath-holding stimulates complex cardiovascular adaptations facilitated by acute cardiac autonomic changes [19]. The DR is initiated by stimulation of the trigeminal afferent fibres located predominantly in the forehead, periorbital and maxillary regions, and nasal area [2]. Stimulation of the trigeminal nerve in these facial areas causes cardiovascular responses that involve excitation of vasomotor centres and cardiac vagal motor neurons and suppression of respiration which accentuates the DR [3,8].

Consequently, the heart rate (HR) reduction is achieved by an increased output to the periphery which stimulates cardiac vagal activity associated with vasoconstriction of selected vascular beds [2].

Bradycardia frequently occurs following facial immersion in cold water with a latent time of less than 9 seconds [7]. It develops in the first 30 seconds of breath-holding, in direct response to decreased cardiac volume output, increase in Blood Pressure (BP), and contraction of peripheral vessels [4,9,20]. Efficient use of O_2 is maintained due to the lower demand for oxygen during reduced HR and subsequent decrease in cardiac minute volume [16].

According to Ferrigno et al., whilst diving, breath-hold divers can experience a drop in their HR to around 20 to 30 bpm, while arterial blood pressure can increase to as high as 280/200 mm Hg (systolic/diastolic). Marabotti et al. concluded that the diving reflex elicitation and breath-holding induced at the surface level of the water played only a minor role in inducing cardiovascular changes during breath-hold diving. In comparison, diving at depth led to a subsequent increase in hydrostatic pressure which was an essential component in inducing cardiovascular changes during BHD [21]. However contrary evidence suggests that depth does not have an effect on the degree of HR reduction during BHD, but instead, the extent of bradycardia is dependent on the duration of the breath-hold and is significant when breath-holding exceeds 50 seconds [9,16]. Until the depth of about 20m during descension, HR decreases with no observed significant changes. A critical point in the bradycardic reaction occurs at a depth beyond 20m, as an increase in water pressure leads to a decrease in lung volume to one-third of the maximal volume [16].

The decrease in HR is smaller after short submersions, which may be due to the high pressure experienced in the chest of divers as a result of deep inhalation before diving, which leads to stimulation of the sympathetic nervous system's pressure receptors and lower HR [16]. Intensified breathing increases chest pressure which disrupts venous blood circulation causing an increase in BP, reduced HR, and decreased cardiac minute volume [9,16]. This effect may be prolonged by Glossopharyngeal Insufflation (GI) techniques which increase storage for CO_2 and O_2, enabling divers to dive deeper, however, this leads to higher pressure inside the chest [20,22]. The decrease in HR and increase in BP corresponds with the start of decrease in arterial oxygen saturation (SaO_2), also due to the effects of vasoconstriction [16].

The degree of diving bradycardia is also dependent on temperature of both air and water and the difference between ambient air and water temperature. Lower water temperatures (0˚C- 10˚C) increase both minute ventilation (VE) and elicit more pronounced bradycardia as compared to warmer water [23,24]. In particular, research indicates facial cold receptors are more strongly stimulated by immersion in water with a temperature ranging from 10-15 °C [25,26]. Ferrigno et al. postulate that the lower HR values as well as the rapid onset of bradycardia in cold water as compared to thermo-neutral water suggests that water temperature is the most important factor in the elicitation of bradycardia in the DR [9]. According to Caspers et al. water is considered thermo-neutral at a temperature of 35.5˚C, however, because the thermal conductivity of water is 25 times higher than that of air, facial receptors can experience a cooling effect despite CFI in water at room temperatures. Higher bradycardic responses are to be expected from lower water temperatures, while lower bradycardic responses are to be expected from higher water temperatures [27,28].

The occurrence and mechanisms underlying bradycardia in freedivers cannot be fully explained, however, according to Lin et al. bradycardia may result from the cold moisture detected by the face receptors through the vagus nerve reaction, contraction of peripheral blood vessels due to sympathetic nervous system response, hypoxia caused by apnoea or the activity of chemoreceptors in the lungs and large blood vessels [29].

Peripheral Vasoconstriction and Blood Centralization

An increase in oxygen tension leads to vasoconstriction; this reaction manifests 15-25 seconds after the start of apnoea as a result of an increase in endogenous CO_2 and lowered O_2 availability as well as termination of ventilation [6]. During cardiovascular adjustments of the DR, blood flow is redistributed to vital organs, and moves from peripheral circulation to cerebral circulation, resulting in oxygen conservation for oxygen-sensitive organs including the brain and heart [2,3,9].

During a breath hold dive, arterial pO_2 and pH fall while pCO_2 rises, causing the chemoreceptor reflex to reinforce the DR as the heart-brain circuit utilises the use of oxygen stored in the blood that would otherwise be used up by skeletal muscle [16]. Reduced blood flow to extremities results in blood centralization which increases blood pressure [11]. Due to this effect, oxygen is consumed less by organs that are less essential in survival, as glucose metabolism and lactate production are reduced [16].

It has been well-established that the main aim of the DR is to conserve oxygen; however, the DR is also responsible for the activation of multilevel endogenous neuroprotective mechanisms suggesting that the DR may also have a neuroprotective role [30]. Peripheral vasoconstriction during heightened diving bradycardia is an important factor in the protection of cerebral perfusion and the maintenance of its pressure [9]. Redistribution of blood flow from peripheral to cerebral circulation is also supported by increased carotid artery blood flow [3]. Studies conducted on full immersion without the use of equipment have provided indirect evidence that professional divers possess enhanced mechanisms of cerebral protection against hypoxia compared to normal participants [31,32].

Cranial Blood Flow (CBF) compensates, for decreased arterial blood oxygen saturation, allowing proper oxygenation of the brain tissues to be maintained [16]. With long breath-holds, arterial oxygen saturation (SaO_2) is significantly reduced however increases in CBF as a result maintain the cerebral tissue oxygenation by potentially offsetting the reduced SaO_2 [16]. These vascular redistribution mechanisms assist in protecting the brain during hypoxia [33].

A study by Baranova et al. revealed that cold stimulation, hypoxia, and hypercapnia precipitated changes in measures of CBF which included an increase in linear blood flow and a reduction in the tone of cerebral resistance vessels [6]. This implicated that a combination of all three factors produced significantly greater changes to CBF as compared to exposures to these factors separately and the degree of contribution of these stimulating factors is largely dependent on individual sensitivity to these stimuli.

To maintain cranial perfusion, chemosensitivity of the peripheral nervous system acts as a protective mechanism in ensuring cranial perfusion and circulation of mainly blood through tissue or organs [16]. Autoregulation of CBF most likely differs between conditions of high and low pressure and the exact mechanisms regulating CBF are not clearly understood [34]. A powerful metabolic regulator of cerebral blood flow is carbon dioxide (CO_2) as increases in partial pressure of carbon dioxide elicits vascular dilation [7]. The effect of CO_2 on brain tissues is facilitated by corresponding increases in Hydrogen (H+) ions that are present as a result of the dissociation of carbonic acid that is formed [6].

Near-infrared spectroscopy studies have revealed that as a result of reduced peripheral blood flow and oxygenation, cerebral oxygenation is only slightly reduced at the end of breath-holds [35]. Blood vessels reach a state of maximal narrowing where a minimal supply of blood containing O_2 reaches the extremities due to anaerobic transformation (the process through which all other processes are maintained during this development) in the later phases of dives and during dives to greater depths [36]. High-energy phosphates are used by tissues experiencing a deficiency of oxygen to generate energy through the aerobic metabolism of oxygenated tissues and the production of lactic acid through anaerobic metabolism [11]. Metabolic regulation mediated through resistance vessels (e.g., arterioles, small arteries) that are sensitive to changes such as decrease in blood pO_2, increase in pCO_2, and increase in extracellular fluid pH, is an important factor in mediating cerebral blood supply [37].

Previously it was believed that individual Vital Lung Capacity (VC) and Residual Lung Capacity (RC) determined maximal diving depth, as it was believed that lung suppression occurred when VC decreased below the RC. However, lung suppression in such a situation does not occur as mechanisms are in place that compensate and protect the lungs from suppression [16]. The reaction mechanisms explored revealed that blood delivery to the chest increases as a result of higher external pressure; a reduction in the number of peripheral vessels leads to an increase in blood volume delivered to the chest [4,16].

The average O_2 in the tissues of an average and regular man is around 1500ml, with 280ml in the blood and 370ml located in the lungs [38]. In general, the O_2 reserve in lungs of elite divers is higher compared to non-divers, with approximately 1000ml recorded; and due to this large reserve, arterial blood is re-oxygenated upon reaching the lung alveolar, and despite sustaining at 3 minutes BH, the arterial blood O_2 saturation is still close to 100% in experienced and trained athletes [16].

Peripheral vasoconstriction also results in static lung volume changes. Blood shift or blood centralization and simultaneous peripheral vasoconstriction results in large amounts of blood delivery to the chest aimed at protecting the lungs at greater depths. Blood centralization and the resulting accumulation of blood in the thorax is a physiological mechanism through which reduction in pulmonary air is compensated, thus preventing the collapse of the rib cage protecting the lungs due to residual lung volume. Blood shift to lungs is the result of a pressure gradient formed between separate body sections responding differently to water pressure [16].

In healthy subjects under normal physiological conditions, pulmonary pressure at the base of the lungs is approximately 2,26 KPa (17mmHg) and as a result of gravity, the value is on average approximately 1,33 KPa* (10mmHg); however, during immersion, pulmonary transmural pressure at the level of pulmonary arteries, is estimated to rise over 10mm Hg. The descent of a dive leads to suppression of the lungs due to water pressure, causing the chest to sink to oppose external water which results in a balance of water pressure by the resistant force from chest elasticity and lung air pressure [16].

Slight hypotension is always present in the lungs, as with increasing depth, the chest is not able to shrink to the extent of compressed lungs, therefore while under pressure, and to compensate, blood from extremities is transferred and delivered to the blood vessels of the chest. The blood shift effect allows for a steady shift of internal organs to the chest from the abdomen, dependent on the elasticity of one's diaphragm. This effect increases with depth and protects the ribs from fracturing as the chest is filled with blood and organs which unlike air in the lungs are not compressible [16].

Trigeminal Reflexes

In exploring the cardio-respiratory mechanisms of the DR, it may be beneficial to review recent advances in understanding the trigeminal reflexes. The brain and the heart are engaged in a complex bidirectional relationship. The diving reflex is considered to be a subtype or peripheral type of the Trigeminal Cardiac Reflex (TCR), and both share several similarities that include clinical manifestation and mechanisms of action [30]. Cardiovascular adjustments following exposure to cold water stimulate the trigeminal nerve branches over the face and can lead to stimulation of the TCR resulting in a decrease in heart rate of up to 10 to 25% [30]. The diving reflex is initiated by the stimulation of V1 ophthalmic division of the trigeminal nerve activated in the

forehead, cornea, and nasal mucosa resulting in parasympathetic mediated bradycardia and apnoea and sympathetically mediated increase in blood pressure and peripheral vasoconstriction [30].

According to Schaller et al. the central circuit of the DR is fundamental to the brainstem. Alboni et al. postulated that the ventral superficial medullary dorsal horn is where the first relay of the circuit is located, as evidenced by blocked cardiac responses due to injecting either lidocaine or kynurenic into the bloodstream. It was concluded that the trigeminal system within the lower brainstem is responsible for vagally mediated bradycardia and sympathetically mediated vasoconstriction; however, the networks and association between the trigeminal system and autonomic neurons of the brainstem are still undetermined [2].

The TCR, similar to other reflexes, is made up of the afferent and efferent pathways. Receptors of the TCR are innervated by the trigeminal nerve and can be found in the neck, head, and face region. Neuronal signals are delivered to the sensory nucleus of the trigeminal nerve when any of these receptors are stimulated through mechanical, chemical, electrical, or direct stimulation, forming the afferent path of the reflex. The polysynaptic connections which are endogenously modulated by the seretogenic (5-HT), and cholinergic receptors are responsible for linking the trigeminal nerve to the reticular formation, in which the afferent pathway is connected to the efferent pathway through short internuncial fibres found in the reticular formation. Neurons located in the dorsal vagal nucleus and nucleus ambiguous, innervate the heart and other viscera through the vagus nerve, and these mainly form the efferent pathway. Further evidence that the ventral circuit of the TCR lies within the brainstem has been provided by animal studies that demonstrated that cardiac responses can be seen even in decerebrate animals [30].

Breath-Holding (BH) and Cold Facial Immersion (CFI)

CFI alone is sufficient in contributing to the oxygen-conserving effect of the diving response [24,39]. During CFI, receptors that are supplied by the trigeminal nerve transmit this information to the brain and subsequently innervate the vagus nerve which is part of the Autonomic Nervous System (ANS). The mechanisms underlying increases in BP due to CFI are likely the result of sympathetic nervous system activation; increases in sympathetic nerve activity elicit responses that include, vascular resistance in the peripheral, visceral and cerebral vasculatures, all of which contribute to increases in blood pressure [1,40-44]. The increase in sympathetic nervous activity as a result of CFI is related to multiple mechanisms through which increases in stroke volume occur [24,28,45,46].

According to Nepal et al. exposing the peripheral skin to cold stimulus is also sufficient in eliciting a diving response, further stating that stimulation of the trigeminal nerve around the facial region is not the only method in eliciting DR. A study by Andersson et al. concluded that while HR reduction and selective vasoconstriction brought about by BH without immersion were augmented by CFI, forearm immersion in water as apnoea begins had no effect on eliciting the DR. The study also revealed that cold-water immersion augmented the reduction in skin capillary blood flow, further stating that cold stimulation is an effective method in provoking reflex vasoconstriction in the skin. Regardless of the site of stimulation, cold stimulation leads to vasoconstriction in the skin vessels that are not affected or augmented by concurrent cold stimulation to another part of the body [8].

The peripheral chemoreceptors detect and respond to an increase in partial pressure of CO_2 and decreases in pH or PO_2 [2]. During apnoea, peripheral chemoreceptors are stimulated by the lack of consistent afferent stimuli directed from the pulmonary stretch receptors leading to hypoxia. The response of the cardiovascular system includes bradycardia, vasoconstriction, and secretion of suprarenal catecholamine. Conversely, during facial or whole-body immersion, the accompanying bradycardic response is not attributed to the peripheral chemoreceptors but instead is a manifestation of the DR. In this instance, the arterial partial pressure of O_2 and CO_2 are within normal range, hence, the bradycardic response is independent of chemoreceptor stimulation and is triggered exclusively via apnoea and through cutaneous cold receptors; however, findings of previous research suggest that the chemoreceptor stimulation during prolonged hypoxic dives may play a part in accentuating bradycardia [2].

Diving stimulates synergistically mediated sympathetic and parasympathetic responses responsible for the heightened cardiovascular reflexes in humans, which when compared to cold facial stimulation and breath-holding alone, produces a greater response than the sum of individual responses [1,8]. The exact mechanisms by which the parasympathetic nervous system is activated by apnoea remains undetermined, however, potential explanations include activation of baroreflex, activation of the lung inflation reflex and normalization of blood gases, as well as hypoxia and hypercapnia playing an important part in the stimulation of chemoreceptors [3,39].

Studies have demonstrated that decreases in heart rate are much greater with facial immersion while breath-holding, this can be explained by the stimulation of the trigeminal nerve around the facial and neck region [4]. The cold sensation stimulates the afferent pathway of the trigeminal nerve causing stimulation of the cardiac centre located in the medulla resulting in bradycardia. Apnoea with face immersion producing intense bradycardia and marked vasoconstriction could lead to lowered oxygen consumption and decreased carbon dioxide production [4]. Due to increased bradycardia, the metabolic demand for the cardiac muscle is lowered and marked vasoconstriction leads to reduced oxygen consumption by tissues, which during apnoea with cold facial immersion, results in smaller degree of arterial haemoglobin desaturation as compared to apnoea in air [4].

In a study by Andersson and Schagatay, the level of arterial haemoglobin desaturation observed was lower after apnoea with face immersion, than after apnoea alone suggesting that oxygen consumption was reduced due to a stronger diving response elicited during apnoea with face immersion [4]. A study measuring neural and circulatory responses during simulated diving in humans found that clear and significant bradycardia was not evident during either facial immersion or apnoea alone, suggesting the importance of both these stimuli in eliciting a combination of central sympathetic outflow and cardiac vagal outflow [1].

Ventilatory Response

Previous studies have demonstrated that divers possess larger lungs than was predicted [4,11]. Schagatay, Richardson, and Lodin-Sundstrom revealed that the mean Vital Capacity (VC) of elite divers in their study was well above normal, spanning from 5.5 to 8.9 Litres (L) which was 158% higher than that of the general adult male population reported by Chiba et al. and Laub et al. which was at a mean of 4.1L for 225 Caucasian subjects [47-49]. According to Schagatay et al. skilled divers that possess

larger lungs could be due to several factors including individual predisposition, increased chest flexibility, increases in respiratory muscle strength or lung growth as a result of training effects. Under apnoeic conditions, changes in HR are strongly influenced by the held lung volume [3].

A study by Earing, McKeon and Kubin (2014) investigating the ventilatory response to CO_2 in experienced SCUBA divers revealed that compared to controls of similar age and build, experienced divers possessed 40% lower mean ventilatory response to carbon dioxide, regardless of the measured conditions (e.g., rest, exercise), indicating a dominant adaptation of central CO_2 sensitivity.

The DR is affected by lung volume as well as intrapleural pressure, recent advances in research have demonstrated that bradycardic responses are greatest with smaller lung volumes [4]. Cessation of breathing occurring at smaller lung volumes leads to greater arterial chemoreceptor stimulation as a result of hypoxia and lower oxygen storage in the lungs, further accentuating bradycardia [3]

In a study by Schagatay, Richardson, and Lodin-Sundstrom, in the three most successful divers, the mean Vital Capacity (VC) was more than 1L, which equates to 200mL of O_2 to the total body stores which resulted in an added duration of 60 seconds of apnoea [47]. The dilution effect and a larger VC also increase CO_2 storage capacity, demonstrating that a major factor in determining the length of apnoea is lung volume. Larger VC could also assist in speeding up recovery after apnoea via reduction of relative dead space and increase of alveolar gas exchange by increasing minute ventilation at any given respiratory rate. Freedivers are capable of lowering oxygen in their lungs and reaching alveolar levels of less than 30mm Hg oxygen and are also able to withstand high alveolar partial pressure of more than 50mm Hg CO_2 [33].

Oxygen reserve is greater in the lungs of elite divers as compared to non-divers, at approximately 1000mL, and because of this, arterial blood reaching the lung alveolar can re-oxygenate leading to arterial blood oxygen saturation to be near 100% despite breath-holds of over 3 minutes [16]. During apnoea, vasomotor and cardio-inhibitive activity increases as a result of inhibition of the respiratory centres and lack of afferent input from pulmonary stretch receptors. With increasing time, the blood flow becomes less oxygenated due to oxygen consumption and subsequent decrease in its partial pressure in the lung alveolar, and while oxygen blood saturation is lower, dilation of blood vessels in the brain as a result of increased carbon dioxide concentration leads to higher blood circulation to the brain [16].

One factor enhancing the supply of O_2 to tissues when concentrations of CO_2 are high is a glycolysis product synthesized in blood and primarily induced by hypoxia called 2,3-diphosphoglycerate which reduces the affinity of haemoglobin to oxygen and increases in this product during high oxygen saturation augments tissue oxygen delivery [16].

Marabotti et al. in their study found that in-air maximal voluntary BH leads to progressive left ventricular dilation with increased stroke volume and maintained cardiac output. Less oxygen desaturation was observed for whole-body immersion which induced similar haemodynamic changes to in-air maximal voluntary BH, which suggests that despite the lack of increased hydrostatic pressure, immersion leads to an oxygen-sparing effect. In both dry and immersed conditions, a hindrance to the LV filling was observed suggesting a constrictive-restrictive effect of chest squeezing. According to Marabotti et al. the underlying mechanism of this pattern of maximal apnoea may be explained by an increase in right ventricular volume that is associated with increased venous return to the heart. Prolonged apnoea increases left ventricular systolic and diastolic volumes, reduces left ventricular ejection fraction, increases stroke volume and results in no changes in cardiac output. The hydrostatic pressure experienced during shallow immersion is mild compared to diving at depth. This low hydrostatic prevents pulmonary blood shift and reduction of chest volume that occurs at greater depth which affects ventral haemodynamic and explains the varying changes observed in left ventricle volumes during immersions at depth and shallow immersions.

Spleen Effect and Hormonal Reactions in BHD

Humans show great individual variation in spleen size and its ability to contract. In elite divers, studies have shown that both lung and spleen volume predict apnoea performance. Recent evidence suggests that splenic contractions are also part of the diving response in humans and occur without the trigger of chemical stimuli (i.e., hypoxia/hypercapnia) and transpire despite very short breath holds [2,17]. The spleen effect is associated with increases of catecholamines in blood plasma or occurs as a result of the combination of hormonal and nervous reactions and transpires simultaneously with peripheral vasoconstriction, bradycardia, and blood centralization [42,50]. Catecholamine-mediated a-adrenoreceptor response is responsible for inducing splenic contractions [51].

The human spleen contains ~200-250ml of densely packed red blood cells (RBC) [52]. Haematological observations conducted by Schagatay et al. and radionuclide measurements of spleen volume by Espersen et al. inform the conceptual understanding of splenic contractions [3,42,53]. The spleen serves as an erythrocyte reservoir and during increased activity (i.e., diving, exercise), contraction of the spleen increases levels of circulating haemoglobin in the blood, thus producing an oxygen-conserving effect [2]. Haemoglobin concentration increases by 3-4% during apnoea with face immersion [54]. A study by Bakovic et al. concluded that rapid spleen contraction and its subsequent slow recovery results in the maintenance and prolongation of consecutive, briefly repeated apnoea. The release of erythrocytes from splenic contractions assists in increasing the durations of static apnoea and in some cases repeated dynamic apnoea [35,52,55].

A study by Schagatay et al. revealed that the three of the best-performing elite divers had the largest spleen volumes averaging 538 (53) mL compared to lower-performing divers 270 (71) mL and greater vital capacity at 7.9 (0.36) L compared to lower scoring divers 6.7 (0.19) L, thus concluding that spleen and lung volume predicts apnoea performance in elite divers. Increased haemoglobin during apnoea as a result of spleen contraction, enhances CO_2 buffering capacity leading to a reduced urge to breathe and prolonging individual breaking point. Therefore, it is part of training and pre-start procedures to engage in several dozen apnoea as a warm-up before diving [53]. A more recent study by Holmstrom et al. revealed that the spleen was larger in groups that lived in high-altitude climates compared to low-altitude climates [56]. Similarly, the greater spleen volume identified in Sherpa groups that live in high altitudes compared to Nepalese lowlanders is consistent with research that long-term freedivers in the Indonesian Bajau population had a greater resting spleen when compared to the Saluan population which is a non-diving population [56,57]. Greater resting spleen volume has been a

consequence of training effects following 8 weeks of apnoea training which is consistent with what is observed in [58].

Individual Determinants in BHD

One area of conflict and debate is in establishing whether elite performance in BHD, tolerance to CO_2 and diminished respiratory drive under hypercapnia may be hereditary or the result of an adaptation due to frequent short-term exposure to hypercapnia. The world records and boundaries of breath-holding and diving depths have been challenged and "pushed further" in the last decade, exposing BHD to frequently severe hypercapnia and hypoxic conditions [22].

Ferringno et al. investigated the physiological responses to dives down to 65m in 3 elite breath-hold divers, all of whom were from the same family. Results showed that all three divers demonstrated marked bradycardia (20-25 beats per min) compared to untrained controls, however according to Ferrigno et al. physiological observations obtained from the DR may not necessarily be the result of physiological adaptation, but rather the expression of genetic factors [9]. According to Alboni et al. studies have revealed that compared to inexperienced divers, breath-hold divers demonstrate more pronounced bradycardia and states, that while these differences between groups may be the result of training; it may also be due to genetic differences between groups [2].

There are also varying levels of CO_2 tolerance and individual sensitivity to CO_2. A study by Vagin and Zelenkova exploring the physiological mechanisms of hypoxia tolerance and physical endurance in freedivers, basketball players and untrained subjects found that compared with other groups in this study, freedivers possessed the greatest tolerance to hypoxia and showed the highest physical work capacity. Freedivers also had the highest fall in SpO2 values and were the only group to perform between 3 to 8 breath-holds while still active on the cycle ergometer. In their experiment, Baranova et al. discovered that inhalation of 7% hypercapnic mixture led to variations in measures and magnitude of changes of cerebral blood flow CBF indicating varying levels of sensitivities to stimulus amongst subjects [6].

In exploring the mechanisms of the DR, recent genetic studies suggest that the intensity of vasoconstriction experienced during the activation of the DR is subject to interpersonal differences. Baronova et al. in their study investigating the genetic mechanisms of the vascular reactions in response to DR conducted a genetic analysis of the polymorphisms of renin-angiotensin, kinin-bradykinin genes, and the gene β2-adrenoreceptor (ADRB2 48) found that during DR, changes in BP and vascular tone in subjects were dependent on their genotype. More specifically, this study found that subjects with the most pronounced peripheral vasoconstriction in response to diving had BDKRB2 (C/C), ACE (D/D) and ADBR2 (G/G, G/A) genotypes. This study concluded that changes experienced by subjects in the vascular tone and BP were dependent on their genotype (i.e., different combinations of alleles of the studied genes) [7].

Individual differences such as age and diving experience influence the extent of DR. The diving bradycardia is pronounced in children between ages 4 and 12 months, as this may assist children in surviving through "hypoxic episodes proximal to birth" [20]. With advancing age, the DR weakens and is more pronounced in experienced and habitual breath-hold divers than non-divers [20]. A study by West et al. found that 11–14-year-old children exhibited a greater reduction of Heart Rate (HR) after CFI as compared to adults, further stating that with advancing age, the extent of HR reduction weakens. However, according to Ostrowski et al. unlike other sports, for freedivers, age plays a less vital role in performance, further stating that world records have been beaten by younger athletes ranging from 20 to 30 years old as well as by divers in their mid-40s. These achievements may be because of long-term training in breath-holding and diving-related skills leads to experience and enhanced adaptive abilities. While the body's efficiency may decrease with age, enhanced adaptive mechanisms through training and experience compensate for this and enable elderly divers to have an equal chance of succeeding and achieving world records [16].

Psychological and physiological factors both play a role in increased breath-holding time [4]. Prolonged BH not only elicits extensive physiological changes, but also requires exceptional psychological states and therefore BH is thought to be a unique psycho-physiological state. There are two phases of breath-holding, the easy-going phase (low levels of breathing urges) and the struggle phase determined by the physiological breaking point (arterial CO_2 reaches critical levels), thus triggering involuntary breathing movements, and a final "fighting" phase usually experienced by elite divers. The length of the easy-going phase is primarily dependent on the accumulation of arterial PCO_2 and less dependent on arterial PO_2. Besides physiological capabilities, psychological factors are important aspects of breath-hold diving, as mentally, freedivers need resiliency towards pain, physical exertion, withstanding extreme environmental conditions, and coping with dangers to health and possible loss of life [16,17].

In trained apnea divers, duration of the easy-going phase is extended due to training induced adaptations, while humans not trained in BH usually end apnea at the start of the struggle phase. In the easy-phase of breath-holding, physiological factors such as tolerance to increasing $PaCO_2$, determines duration of BH, while significant mental effort is necessary to maintain BH through the discomfort of asphyxia in the struggle phase requiring motivation, stamina, emotion regulation and cognitive factors that includes inhibition and interoception. Mental predispositions and psychological capacity to tolerate the discomfort and urge to breathe strongly influences breath-holding durations in the struggle phase [12].

Adaptive Changes during Breath-Hold and Apnoea Training

There have been a number of studies conducted on breath-holding (BH) over the years, many of which have focussed on the physiological aspects of BH. Yet despite constant improvements in performance of elite breath-hold divers that are capable of diving beyond 200m, and BH over 10 mins, many questions regarding these demonstrated performance increases are still unanswered. Humans are capable of such extraordinary feats; however, it is still questionable whether these abilities they possess are inherited or developed through training. This section will focus on exploring the effects of short-term and long-term Breath-Hold Training (BHT) and the adaptive changes associated with it.

Improvements in performance and age differences between previous and current world record holders point to the adaptive capabilities of humans, progress in devices, training techniques, and technical progress [16]. There have been several studies investigating the short-term and long-term training effects of DR, with many attributing short-term training effects to psychological and physiological factors, however the mechanisms behind these adaptations have not yet been completely clarified [59-65].

The most common questions posed by Tipton regarding the development of an adaptation include, "how long does it take to acquire", and more importantly, "how long does the adaptation last?". Two techniques are commonly used in inducing adaptations; the first being repeated achievement of a constant physiological strain (e.g., deep body temperature, heart level, level of exertion) or repeated exposure to a constant stimulus, while the second aims to maintain the stimulus to adapt and delivers more effective physiological adaptation. Whilst the diving reflex is involuntary, Schagatay and Andersson suggest that the DR can be trained, and it can have positive effects on both heart rate reduction and apnoeic duration [4].

It has been well established in the literature that BH divers have more of a pronounced DR. Costalat et al. attributed this to simultaneous shifts in both cardiac and peripheral hemodynamics taking place at the halfway point of the breath hold as measured by kinetics analysis [66]. Structural changes have also been identified in the heart, as evidenced by an increase in the size of heart chambers, resulting from training effects and cardiovascular adaptive changes [67]. In a study investigating cardiac autonomic activity in free diving (FD) athletes, Christoforidi et al. revealed that when compared to an untrained control group, FD exhibited higher sympathetic and enhanced cardiac paraszympathetic tone 4 days after the last breath-hold diving [19]. This was the first study to show that as a result of exercise training and repeated exposure to FD stimulus, the vagal tone and resting cardiac autonomic is significantly higher in FD athletes. There is however a gap in literature exploring long-term cardiac autonomic adaptations in breath-hold divers.

Physical and apnoea training are both vital components of active diving, however, a study conducted by Schagatay, and colleagues demonstrates that apnoea training and frequent exposure to apnoea is the most beneficial form of training in promoting bradycardia and delaying the physiological breaking point. Adaptations of the cardiovascular system to physical training result in increased oxygen delivery to the muscles enabling intense aerobic physical exercise, while adaptive changes are also exhibited at the muscular level allowing increased extraction of O_2 [17].

Short-term and long-term apnoea training and physical training have demonstrated adaptations to diving conditions and augmentation of the arterial compliance function. There are two major functions of the arterial system; the first is the delivery of nutrients and oxygenated blood to organs and the second function is to act as a buffer in softening pulsations from the heart to allow continuous capillary blood flow [68]. Arterial compliance can be defined as the relationship between changes in vessel dimension for a given change in pressure or distending pressure [69]. Several factors can alter arterial circulation after a dive such as cold-water immersion and hyperoxic exposure, and in cases of scuba diving, decompression-induced circulating bubbles [61].

Biological aging and atherosclerosis are two contributing factors towards arterial stiffness that are typically found in pathological conditions that include diabetes, chronic kidney disease, isolated systolic hypertension, and atherosclerosis [70]. Tanaka et al. investigated the effects of chronic diving manoeuvres on arterial elasticity, structure, and function of Japanese female pearl divers (Ama) and found that Ama divers possess significantly lower arterial stiffness and values in indices of arterial wave reflection, and higher subendocardial perfusion as compared to non-Ama, which point to lower cardiac activity. Based on the results of this study, it seems that regular diving manoeuvres are associated with favourable adaptations in arterial elasticity, wave reflection, and reduced risks of cardiovascular-based diseases [71].

Several studies have established that physical training leads to modification in arterial wall properties, however, the vascular modifications induced are dependent on the training modalities [61]. Increases in central arterial compliance have been observed as a result of regular endurance exercise, which is attributed to changes in vascular endothelium-derived factors [61,71]. According to Gole et al. previous studies have shown that acute endothelial alteration can be induced after a single dive [61]. The endothelium plays a crucial role in maintaining vascular homeostasis by achieving a balance between endothelium-derived contracting and relaxing factors, and also through the release of paracrine factors that act on platelets, inflammatory cells, and the vessel wall. When this balance is disrupted, it predisposes the vasculature to vasoconstriction, leukocyte adherence, platelet activation, mitogenesis, pro-oxidation, thrombosis, impaired coagulation, vascular inflammation, and atherosclerosis. Ersson, Walles and Ohlsoon, found that after 2 months of diving training, plasma levels of neutrophil gelatinase-associated lipocalcin and interleukin L8 increased, indicating the activation of neutrophils and endothelial cells; therefore Errson et al. hypothesized that repeated dives could result in long-term endothelial modifications [72]. Endothelial growth factor promotes CD34* release from the bone marrow which can increase energy output and immune boosting as well as muscle fibre repair and blood cell and capillary regeneration [73].

Previous research has demonstrated a decrease in plasma concentrations of endothelin-1 (vasoconstrictor peptide) produced by vascular endothelial cells in endurance-trained individuals [61]. Endurance training has also been associated with an increase in concentrations of nitric oxide (NO) and NO bioavailability (vasodilator produced by vascular endothelial cells) that play an important role in maintaining vascular reactivity and tone. NO also contradicts the actions of endothelium-derived contracting factors (angiotensin-II and endothelin-1) and in order to maintain vascular smooth muscle in a non-proliferative state, it also inhibits white cell and platelets activation. NO is the product of synthesis from L-arginine and the enzyme NO synthase (NOS).

One of the benefits of short-term training effects of repeated apneas is prolonged breath-holding time [2]. In a variety of athletes, including elite endurance athletes and breath-hold athletes, reduced chemosensitivity has been observed to progressive hypoxia and hypercapnia [3]. According to Andersson and Schagatay reduced sensitivity to CO_2 observed in divers is not a trait that is genetically inherited; instead, it is caused by training of breath-holding diving. Studies investigating instructors working at a submarine escape training tank have demonstrated this fact.

The Hypercapnic Ventilatory Response (HCVR) which is blunted in breath-hold divers is another mechanism through which breath-hold divers can prolong breath-holding time. The HCVR curve measures CO_2 sensitivity. Ferretti and Costa postulated that the prolonged breath-holding time demonstrated by trained divers may be due to a displaced threshold and reduced sensitivity to CO_2 because of frequent exposures to hypercapnia leading to a reduced urge to breathe [11]. Schagatay et al. demonstrated that two weeks of daily apnoeic training increased both the diving response and the duration of breath-hold. In non-divers, even short-term repetitive breath-hold training has demonstrated a positive

effect on BH duration without changing the magnitude of the DR, or its oxygen-conserving effect. It has been suggested that breath hold training builds greater tolerance to CO_2 as demonstrated by trained synchronized swimmers who can sustain a normoxic BH for approximately twice the breath hold time as compared to non-diving controls [74].

Trained breath-hold divers will endure the human diving response during a breath-hold until PaO_2 has fallen to 35 mmHg and $PaCO_2$ has increased to 50 mmHg whereas non-divers when engaging in breath-hold activity, can generally reduce their arterial PaO2 as low as 60 mmHg and their $PaCO_2$ as high as 45 mmHg [11]. Foster and Steel determined that trained breath-hold divers have reduced chemosensitivity to progressive hypoxia and hypercapnia and that the resultant decrease in respiratory drive increases the magnitude of the cardiovascular responses and enables longer breath-hold times [3].

Studies have shown that only long-term exposures to hypercapnia result in blunted HCVR, while short-term training has no effect. A study by Schagatay and Andersson investigating whether short-term training reduces the HCVR found that reduced CO_2 sensitivity was not a contributing factor to the observed short-term apnea training effects. The time course for the development of this adaptation to BH, which includes how many and how frequent these exposures are needed has not yet been investigated.

A study by Nygren-Bonnier et al. investigating whether 6 weeks of training in Glossopharyngeal Pistoning (GP) increased vital capacity in healthy women found that vital capacity increased in the training group by 0.13 litres and the increase in vital capacity persisted for 12 weeks post-training [75]. The mean vital capacity increase in the training group was by 3% after the 6-week training period. Divers that have undergone long-term specialized training in BH have also demonstrated increases in the respiratory system's functional parameters, which during prolonged breath-hold diving, assist in delaying respiratory muscle fatigue [76]. Bavis et al. draws on hypoxia research to suggest that the human respiratory of breath-hold divers have plasticity on several levels, including increased lung capacity, diaphragmatic changes, and biochemical shifts. Joulia et al. postulated that apnoea training provides hypoxic preconditioning and hence it may be potentially used to optimise hypoxia protection in various conditions such as hypobaric hypoxia exposure, COPD, and asthma [31]. This may be further extended to respiratory abnormalities that involve a higher sensitivity to carbon dioxide, including panic disorder and sleep apnoea. The exact underlying mechanism explaining increases in VC is undetermined; however, this phenomenon may be the result of an increase in pulmonary compliance as a result of stretching experienced, thereby allowing inspiratory respiratory muscles to inhale to a larger lung volume [77].

BHT has also been shown to induce adaptive metabolic responses to repetitive periods of hypoxaemia. A longitudinal study by Joulia et al. investigating the benefits of a 3-month training program of dynamic apnoea found that as a result of training, static apnoea lengthened in duration along with accentuated bradycardia. A decrease was also found in venous blood pH and an increase in lactic acid concentration post-apnoea. The study also demonstrated that the training suppressed oxidative stress following both static and dynamic apnoea, and increased tolerance to hypoxemia independent of any genetic factor. The study also revealed that exposure to intermittent asphyxia even in the short-term, causes a sympathetic activation that continues after the removal of the chemical stimuli, serving as an explanation as to why the DR was accentuated after BHT. Results from this study suggest that exposure to intermittent asphyxia during BHT has enhanced the mechanisms protecting against membrane lipid peroxidation and reduced oxidative stress. The adaptive mechanisms responsible for the protection of tissues against the harmful effects of reactive oxygen species at rest require prolonged exposures to hypoxemia. According to Joulia et al. the tolerance to lengthened apnoea duration can be explained by post-training effects resulting in the reduction of lethal cellular consequences of blood acidosis and oxygen free radicals' production.

In a study by Andersson and Schagatay, prolonged breath-holding time observed as a result of short-term apnea training was attributed to changes in hematocrit and hemoglobin concentrations, suggesting that changes in hematocrit and hemoglobin concentration levels caused by splenic contractions could contribute to the short-term training effects observed further stating that the changes concentration levels of hematocrit and hemoglobin lead to a delay of the physiological breaking point of apnea [52].

Physical and apnoea training are both vital components of active diving performance; a study by Schagatay et al. demonstrated that of the two modes of training, frequent exposure and performance of apnoea assists in increasing BH time by delaying the physiological breaking point and enhancing bradycardia. Longitudinal changes observed in divers by Carey et al. lead to the suggestion that training may be responsible for increases in lung volumes [78]. Frequent exposure to swimming or high altitudes may also be responsible for an increase in lung volumes; however, this effect has not been demonstrated in other sports. Specific training protocols and complex training programs developed by elite divers have also demonstrated benefits in increasing lung volume. According to Schagatay et al. similar to the concept of specificity, training effects that are expressed are training-specific and dependent on the type of training that was performed.

Clinical Application of DR

This review is intended to further explore and support the clinical application of DR and BH training in treating patients with panic disorder and other respiratory abnormalities. While changes in physiology produced by activation of the DR have been extensively explored and investigated, its use as a tool for treating panic symptoms has never been investigated.

BH task has frequently been used as a measure of distress (in) tolerance and self-regulatory strength. Distress tolerance implies a process of actively overcoming an unpleasant experience. "If the breath-holding task indeed involves an active and effortful withstanding to aversive stimuli, breath-holding duration should be associated with performance on neuro behavioural tests loading on cognitive/or behavioural inhibitory resources". It is plausible that the inhibition of respiratory musculature requires the involvement of a higher cognitive-control network. This control network would integrate the perception of homeostasis including air hunger and the related emotional states while simultaneously sustaining the motivation for approaching the goal (i.e., long BH).

Breathing irregularity is a common symptom in patients suffering from panic disorder and other anxiety disorders. Dysregulation of normal breathing patterns is observed, and specific diaphragmatic changes are noted. Fluoroscopic studies demonstrated that the diaphragm becomes flat and is immobile in situations of emotional

stress. When a fight/flight response is activated rapid, shallow, and thoracic breathing dominates where high levels of tonic contraction of respiratory muscles expend a lot of energy and homeostatic functions needed for repair and renewal are impaired [79].

In most anxiety and panic treatment approaches the reversal of the fight and flight response is achieved by breathing training, which involves practicing controlled slow breathing as well as various relaxation techniques such as progressive muscle relaxation. Breathing techniques are becoming increasingly popular given the impact of dysfunctional breathing in common conditions including asthma, chronic pain, cardiovascular disease, anxiety, and depression. The prevalence rate of dysfunctional breathing in the general population has been as high as 5-11% [80-82]. In asthma sufferers it is as high as 30% and in anxiety sufferers as high as 83% [83]. For some time now, it has been known that PD symptoms such as numbness, tingling sensations, dizziness, and muscle hypertonicity could be brought on by hyperventilation and that these symptoms could be attributed to hypocapnia and respiratory alkalosis [79].

According to Walterspacher et al. breath-hold training led to a distinct pattern of blunted ventilatory response to elevated CO2 concentrations indicating this phenomenon is trained rather than inherited [22]. Similarly, Roecker et al. found that trained divers had a blunted ventilator response to elevated carbon dioxide [84].

According to Andersson and Schatagay, frequent long-term exposures to hypercapnia may reduce the sensitivity of the central chemoreceptors, thereby reducing the hypercapnic urge to breathe. Furthermore, Andersson and Schagatay postulated that future studies should investigate the time course for the development of this adaptation to breath-hold cold facial immersion and or diving, i.e., how many exposures and how frequent exposures are needed to reduce CO_2 sensitivity [4].

To date, there have been a large number of breathing techniques that are effective in regulating mental and emotional states. The evidence for the ability of breathing therapies to correct breathing dysfunctions is relatively sparse as research has largely focused on psychological outcomes rather than examining the efficacy of breathing parameters. Free divers are known to have exceptional breathing control as well as mental control and draw on a range of techniques to assist them in attaining greater depths underwater. The rising concentration of CO_2 in the blood is what drives the need for a free diver to end their breath hold. The breaking point can be postponed by changing the physiological conditions in the blood or by increasing the individual tolerance to such conditions.

The DR makes it possible for humans to dive to depths beyond imaginable, thought potentially fatal by the medical profession for the human body to survive. In particular, some of the breathing techniques used in free diving have been effective in activating the parasympathetic system and slowing down the heart rate. Long-term apnoea training is associated with several physiological adaptations including longer breath-holding dives, a more pronounced diving response, and larger vital capacities than untrained control subjects [4,11,78].

In many ways the physiological adaptations experienced whilst free diving is the opposite of those triggered when an individual encounters a panic attack. Given that the key factors in both freediving and panic attacks are exceptional mental and breathing control, it is plausible that the diaphragmatic breathing techniques already used to treat panic may benefit from drawing on the physiological adaptions and techniques used in the sport of free diving.

Elevated heart rate is one of the typical constitutional responses seen during a variety of psychological states. Specifically elevated heart rate is well known to accompany anxiety and panic states and indeed can be associated with much of the physical distress associated with these states. Further, it has been established that effecting reductions in heart rate can provide substantial acute symptomatic relief for persons in such states. Physiologically such reductions in heart rate can be affected by the activation of facial cold, baroreceptors and chemoreceptors. Typically, this has involved the immersion of the face in cold water.

The DR has been used in the treatment of Paroxysmal Supraventricular Tachycardia (PVST). While the clinical application of the diving response in managing Paroxysmal Supraventricular Tachycardia (PVST) has gained acceptance in the medical community when applied within international resuscitation guidelines, evidence in the literature regarding its effectiveness is limited and results between studies vary greatly [85]. According to Smith et al. the diving reflex elicits a bradycardic response and accompanying increase in myocardial refractoriness which is regarded as a non-invasive manoeuvre for the termination of Paroxysmal Supraventricular Tachycardia (PVST) [85]. The diving response has also been utilized as a therapeutic procedure for children, to interrupt paroxysmal supraventricular tachycardia after catheter ablation introduction, through facial immersion and is effective in 60-80% of cases [2].

It can be difficult to distinguish between PVST and panic attacks as both are characterised by similar clinical symptoms, specifically both PVST and panic attacks present with rapid heart rate [86]. In discriminating between PVST and panic attacks, ECG taken exactly during the attack can help make the diagnosis simple, as in addition to rapid heart rate of about 160 to 180 beats/min, activation of the heart is no longer normal, with a P wave followed by the QRS complex. While in patients with a panic attack, the rapid heart rate is attributed to an increase in sympathetic drive causing an increase in sinus rate, and the maintenance of the P and QRS sequence [86].

A study by Yadav et al. comparing the effectiveness of airflow and facial cooling stimulation versus controlled breathing exercises (i.e., diaphragmatic exercises) to reduce dyspnoea in patients with Chronic Obstructive Lung Disease (COPD) concluded that facial cooling and airflow stimulation were more effective in relieving dyspnoea [87]. Dyspnoea or shortness of breathing is characterized by impaired breathing that requires increased effort for breathing against increased resistance and in 85% of cases is the result of asthma, pneumonia, chronic obstructive lung disease, congestive heart failure, or psychogenic causes (i.e., panic disorder, anxiety) [87-95]. Kyriakoulis et al. in their study found that activating the DR reduced panic symptoms and panic cognitions in panic participants [12].

Conclusion

Research about the training effects of the DR appears to be in its infancy. Whilst the cardiorespiratory mechanisms involved in the activation of the DR, remain largely unknown, its application and utility in terms of general well-being and in improving both physical and mental health is showing some promise in a wide number of areas including sports performance, respiratory

conditions, mental health, well-being, and general health. Hence, further research is needed to provide further insights into the psychophysiological mechanisms and the application of the diving response in assisting with the development of evidence-based interventions.

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