Hyperventilation Syndrome

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PHAREX MEDICS

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Assessing the role of chronic hyperventilation in patients with nasal congestion: Our experience in 118 patients

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Dear Editor,

When assessing patients complaining of nasal obstruction/congestion, the possibility of a dysfunctional breathing pattern should be considered in addition to restricted nasal airflow. This has been aptly demonstrated by Bartley[1] who discovered a high prevalence of chronic hyperventilation syndrome among a group of patients in whom surgery had failed to relieve the symptom of nasal congestion. A simplified physiological definition of hyperventilation is breathing in excess of metabolic requirements, a pathophysiological process which can be acute or chronic.[2] An extrapolation of Bartley's finding is that the initial surgery may not have been performed if the chronic hyperventilation syndrome had been detected earlier. We therefore introduced the Nijmegen Questionnaire (for chronic hyperventilation syndrome) to our initial assessment of patients whose main presenting complaint was nasal obstruction or congestion. Of course, chronic hyperventilation could coexist with other inflammatory and structural nasal problems. Ogata *et al.*[3] found 25% of patients with allergic rhinitis to have a positive Nijmegen score. In such cases, the clinician has to make a subjective judgement about the extent to which the nasal obstruction can be attributed to chronic hyperventilation. Over a period of 1 year we audited not only how many patients had a positive Nijmegen score, but also the number of cases in which this lead to a significant change in diagnosis and/or treatment.

Method

A prospective audit was performed for 1 year after the introduction of the Nijmegen Questionnaire for the routine assessment of new patient referrals with nasal blockage at a general ENT clinic in Northern Ireland. The Nijmegen Questionnaire assesses 16 complaints related to different organ systems affected by hyperventilation and has been previously validated.[4] It has been found to be a quick, easy to administer and low-impact assessment tool for chronic hyperventilation[5] and its use in a routine ENT clinic has been previously published.[3] The questionnaire was completed either before the consultation or when waiting for nasal endoscopy. However, the questionnaire was not scored until after the history and examination were complete and the clinician had recorded a provisional diagno-

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sis and treatment plan. The Nijmegen score, age, sex and alteration to diagnosis and/or treatment were recorded. The questionnaire was used for patients aged 16 and over.

Results

Over 12 months, 118 new patients with nasal obstruction presented to a general ENT clinic. 64 were men and 54 women. The age range was 16 to 80 with a mean of 38. The Nijmegen score was positive in 28 patients (25%), 11 male and 20 female. The initial diagnosis was changed to exclusively hyperventilation syndrome in 12 patients (10%).

The proportion of Nijmegen-positive patients in the five most common diagnostic categories is shown in Fig. 1.

Allergic rhinitis was diagnosed in 22 patients on the basis of history, examination and skin prick tests. Four also had a positive Nijmegen score. This did not alter the prior diagnosis of allergic rhinitis. Therapy for hyperventilation syndrome was recommended to two patients with seasonal allergies but perennial nasal obstruction and normal-sized inferior turbinates at the time of examination.

An isolated diagnosis of septal deviation was initially reached in 28 patients. Four also had a positive Nijmegen score. In two of these patients, the septal deviation was graded as mild to moderate and hyperventilation syndrome was thought more likely to be the cause of the symptom of nasal blockage. The deviation was subsequently deemed insignificant.

Seven patients were felt to have a functional or psychosomatic illness on initial examination owing to unusual symptoms and a normal examination. Facial pain syndromes with nasal obstruction (negative Nijmegen scores) were included in this group. Four of these patients had high Nijmegen scores. One had previously undergone septoplasty in another hospital that had resulted in a straight septum but no change to his nasal obstruction. His Nijmegen score was 48. Hyperventilation syndrome was thought to adequately explain all of the symptoms in these four patients and their diagnosis was changed accordingly.

Twenty patients fitted the criteria for chronic rhinosinusitis defined by the European position paper on rhinosinusitis and nasal polyps, fourteen of whom had nasal polyposis. One patient with polyps had a positive Nijmegen score. This did not seem to be contributing significantly to the nasal symptoms and his diagnosis and management were unchanged. Four patients without polyps had a positive Nijmegen score. Again this was deemed insignificant from a rhinology perspective and did not change the diagnosis of chronic rhinosinusitis or therapy.

A diagnosis of non-specific rhinitis was reached in 26 patients. This diagnostic category was used for patients complaining of nasal obstruction who had erythema or engorgement of the nasal mucosa on examination but no other symptoms of allergic rhinitis, negative skin prick tests, no mucopus or polyps on endoscopy, no other symptoms of vasomotor rhinitis, no medications with recognised rhinitic side effects, no known hormonal manipulation and no irritant exposure that could be identified (occupational or otherwise). Nine of these patients had a positive Nijmegen score. The diagnosis was changed to hyperventilation syndrome in six. In the remaining three, hyperventilation syndrome was deemed to be a contributing factor but insufficient to explain the full clinical picture. The change in management was not only the

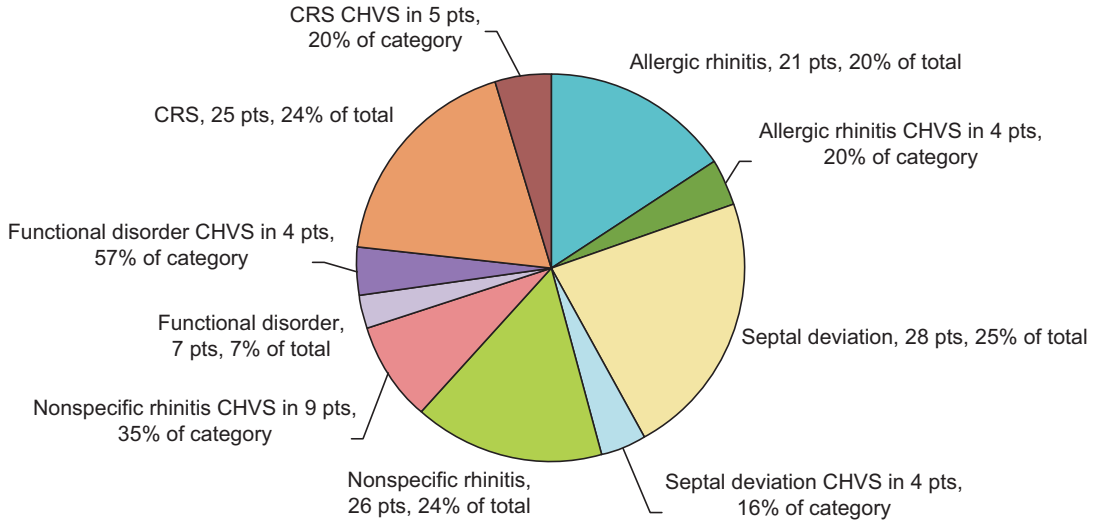

Fig. 1. Proportion of Nijmegen positive patients (CHVS) in each of the five most common diagnostic categories. CHVS: chronic hyperventilation syndrome; pts: patients; CRS: chronic rhinosinusitis.

recommendation of therapy for hyperventilation syndrome but the omission of a trial of topical steroid therapy in the six patients with a change in diagnosis.

Three patients with vasomotor rhinitis had a positive Nijmegen score and this was thought to be contributing sufficiently to nasal symptoms in one case to alter management. The diagnosis of vasomotor rhinitis was unchanged.

Three patients had rhinitis medicamentosa and one also had a positive Nijmegen score. It was thought that nasal obstruction because of hyperventilation syndrome may have lead to the abuse of nasal decongestants, and again, therapy for hyperventilation syndrome was recommended.

Of the remaining nine patients in the audit, two had alar collapse. One of these patients had a positive Nijmegen score but this was not deemed relevant to the nasal obstruction symptom and the diagnosis and management were not changed. None of the seven patients left had a positive Nijmegen score. Two were thought to have nasal obstruction as a medication side effect, two had enlarged inferior turbinates, two had acute infections at the time of clinic attendance and one had a septal perforation.

Discussion

Hyperventilation

Acute hyperventilation causes lowering of the alveolar pressure of carbon dioxide, lowering of the arterial pressure of carbon dioxide and a respiratory alkalosis. The resulting symptoms can usually be reproduced by a hyperventilation provocation test. In contrast, although chronic hyperventilation syndrome can be associated with sustained arterial and alveolar hypocapnia, patients may present with resting levels of carbon dioxide in the normal range. The respiratory rate may be elevated or the tidal volume increased, often accompanied by deep sighing respirations. It is an idiopathic fluctuating disorder which is identified by a combination of symptoms and is therefore not able to be contained within a single diagnostic measurement. The wide range of symptoms includes breathlessness, dyspnoea, light-headedness, paraesthesia, a variety of pains especially chest pains, palpitations, sweating, anxiety, excessive sighing/yawning and nasal congestion. The diagnosis was more common in the past as hyperventilation syndrome lacks a single diagnostic measure for today's era of testing technology.[6] An elaborate study by Howell comparing the hyperventilation provocation test to a placebo test has demonstrated that this test is invalid as a diagnostic test for chronic hyperventilation syndrome.[7] The Nijmegen Questionnaire has been validated. It consists of 16 complaints relating to different organ systems in which their frequency is indicated on 5-point ordinal scale (0 = never, 4 = very frequently). The maximum score is 64 and a score of >23 is considered diagnostic for chronic hyperventilation syndrome.[4]

Implications of chronic hyperventilation syndrome

This audit demonstrated that a significant proportion of patients presenting with nasal obstruction or congestion who would otherwise be diagnosed with a functional disorder or non-specific rhinitis can be reclassified as hyperventilation syndrome according to the Nijmegen Questionnaire. But what is the benefit? The therapy we recommended was breathing awareness and retraining via a self-help programme. In Bartley's study, breathing retraining was partially successful with two of five patients enrolled having relief of their nasal congestion. We did not audit the results of the self-help therapy. Perhaps the greater benefit is the avoidance of trials of medical therapy. When the diagnosis is uncertain, the clinician may prescribe a trial of topical steroid which can cause epistaxis and, if it ultimately fails, may reduce the patient's confidence in the clinician. Perhaps more importantly, when the role of a mild to moderately deviated septum is uncertain, the significance of the patient's nasal congestion in the context of hyperventilation syndrome may reveal that a septoplasty is not indicated. The patient is spared an unnecessary and unhelpful procedure and the overall success of surgery is improved through better patient selection. Only a small proportion of patients with allergic rhinitis were recommended self-help breathing exercises because of nasal congestion persisting beyond the allergen exposure season and not accounted for by hypertrophied inferior turbinates. In general though, the Nijmegen Questionnaire was not a beneficial exercise in patients with chronic rhinosinusitis or allergic rhinitis.

Chronic hyperventilation syndrome and non-specific rhinitis

The diagnostic category of non-specific rhinitis used in this audit illustrates the challenge that the clinician faces when forced to reach a diagnostic decision. Some of these patients were subsequently reclassified as hyperventilation syndrome. We do not know if the mild nasal erythema and congestion found in these patients was a variation of normal or a consequence of the hyperventilation syndrome. The Mayo Clinic described an inverse relationship between nasal resistance and Pco2 levels and presumably the elevated resistance was achieved by vascular engorgement/congestion.[8]

Conclusion

Although the interpretation of the significance of the results of the Nijmegen Questionnaire is subjective, we propose that it is useful for those patients with mild to moderately deviated septums and those who appear to have a functional disorder or non-specific rhinitis.

Key points

- Hyperventilation syndrome has been demonstrated to cause the symptom of nasal congestion/obstruction and to be a reason for failed nasal surgery.
- Routine use of the Nijmegen Questionnaire to detect hyperventilation syndrome in all new patients attending a general ENT clinic produced positive results in a significant proportion of patients (25%).
- Determining when the hyperventilation syndrome was contributing significantly to a patient's nasal congestion was a subjective clinical decision reached in 10% of the patients in this audit.
- The Nijmegen score was deemed useful for achieving a more accurate diagnosis in a significant number of patients who would otherwise have been diagnosed as a functional disorder or non-specific rhinitis.
- The Nijmegen Questionnaire was also deemed to have improved patient selection for septoplasty.

Conflict of interest

None to declare.

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The down-up bone bridge approach for cochlear and middle ear implants: Our experience in 34 patients

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Dear Editor,

Over the last few years, different authors in various countries[1–4] have proposed several minimal invasive approaches for the fashioning of the bony recess and fixation of cochlear and middle ear implants. The above-mentioned approaches offer reduced surgical morbidity related to wound complications and reduced hospital stay as compared to wider access operations[5]. However, disagreement still exists between authors about the best way to secure the implants, either with a tie-down ligature[1–3] or just by closure of the overlying periosteum[4], particularly in teenage patients.

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Contribution

Breathing pattern disorders, motor control, and low back pain

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Abstract

Motor control is a key component in injury prevention. Loss of motor control involves failure to control joints, commonly because of incoordination of the agonist-antagonist muscle co-activation. Three subsystems work together to maintain spinal stability: The central nervous subsystem (control), the osteoligamentous subsystem (passive), and the muscle subsystem (active).

There is evidence that the effects of breathing pattern disorders, such as hyperventilation, result in a variety of negative psychological, biochemical, neurological and biomechanical influences and interferences, capable of modifying each of these three subsystems. Breathing pattern disorders (the extreme form of which is hyperventilation), automatically increase levels of anxiety and apprehension, which may be sufficient to alter motor control and to markedly influence balance control. Hyperventilation results in respiratory alkalosis, leading to reduced oxygenation of tissues (including the brain), smooth muscle constriction, heightened pain perception, speeding up of spinal reflexes, increased excitability of the corticospinal system, hyperirritability of motor and sensory axons, changes in serum calcium and magnesium levels, and encouragement of the development of myofascial trigger points – all or any of which, in one way or another, are capable of modifying normal motor control of skeletal musculature.

Diaphragmatic and transversus abdominis tone are key features in provision of core stability, however it has been noted that reduction in the support offered to the spine, by the muscles of the torso, may occur if there is both a load challenge to the low back, combined with a breathing challenge. It has been demonstrated that, after approximately 60 seconds of hypercapneoa, the postural (tonic) and phasic functions of both the diaphragm and transversus abdominis are reduced or absent. Smooth muscle cells, now known to be widely embedded in connective tissues (including spinal discs, and lumbar fascia) constrict during periods of respiratory alkalosis, with as yet undetermined effects on joint stability and fascial tone. Breathing rehabilitation offers the potential for reducing the negative influences resulting from breathing pattern disorders.

Keywords: breathing pattern disorder, hyperventilation, respiratory alkalosis, motor control, musculoskeletal pain

INTRODUCTION

Motor control is a key component in injury prevention and loss of motor control involves failure to control joints, commonly because of incoordination of the agonist-antagonist muscle co-activation[1]. According to Panjabi[2] three subsystems work together to maintain spinal stability:

- the central nervous subsystem (control)
- the osteoligamentous subsystem (passive)
- the muscle subsystem (active).

Anything that interferes with any aspect of these features of normal motor control, may contribute to dysfunction and pain.

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An increased rate of ventilation, such as prevails with hyperventilation, during which the rate of carbon dioxide (CO_2) exhalation exceeds the rate of its accumulation in the tissues, produces respiratory alkalosis, characterised by the decrease in CO_2 and an increase in pH. This induces vascular constriction, decreasing blood flow, as well as inhibiting transfer from haemoglobin, of oxygen, to tissue cells (due to the Bohr Effect).[3]

The Bohr effect states that an increase in alkalinity (decrease in CO_2) increases the affinity of haemoglobin (Hb) for oxygen (O_2). The Hb molecule is therefore less likely to release its oxygen in tissues that have become increasingly alkaline due to overbreathing.[4] Increased O_2-Hb affinity also leads to changes in serum calcium and red cell phosphate levels.[5] Additionally there is a loss of intra-cellular Mg^{2+} as part of the renal compensation mechanism for correcting alkalosis.[4,5] Muscles affected in this way inevitably become

prone to fatigue, dysfunction (e.g. cramp), and trigger point evolution.[6]

Acute episodes of hyperventilation represent only approximately 1% of all cases, far outnumbering chronic patterns.[7] Chronic hyperventilation leads to hypocapnoea (reduced levels of carbon dioxide), and can present with a myriad of respiratory, cardiac, neurological or gastrointestinal symptoms, without any clinically apparent overbreathing by the patient. In the United States as many as 10% of patients in a general internal medicine practice are reported to have HVS as their primary diagnosis.[7,8]

Studies show that, relative to men, women have a higher rate of respiration and a greater tendency to respiratory alkalosis, which is exaggerated during the luteal (progesterone) phase of the menstrual cycle.[9] Hyperventilation syndrome (HVS) and breathing pattern disorders (BPD) are therefore female dominated, with a female:male ratio ranging from 2:1 to 7:1. Women may be more at risk because of hormonal influences, since progesterone stimulates respiration, and in the luteal (post ovulation/pre-menstrual) phase, CO_2 levels drop on average 25%. Additional stress can subsequently, "increase ventilation at a time when carbon dioxide levels are already low".[10]

Lum[11] points out that there are many people with BPD who have been labelled as asthmatics. "Thirty percent of cases of asthma are known to be induced by emotion or exercise, and many symptoms are common to hyperventilation and to asthma: intermittent, labored breathing; relief from bronchodilators (transient in hyperventilation); exercise; cough; fear, anxiety and panic. It is thus a matter of individual preference whether the clinician calls such cases asthma or hyperventilation. The distinction is important. Treatment of hyperventilation cures the patient. The asthmatic is condemned to a life of medication."

While investigation as to the precipitating causes of episodes of hyperventilation may help with both the diagnosis and choice of treatment, Nixon[12] suggests that there are often attacks where there is no preceding stressful event. In chronic hyperventilators the respiratory centre may have been reset to tolerate a lower than normal partial pressure of arterial carbon dioxide ($PaCO_2$). In such patients a single sigh, or one deep breath, may reduce the $PaCO_2$ sufficiently to trigger symptoms.

Lum[7] has discussed the reasons for people becoming hyperventilators: "Neurological considerations can leave little doubt that the habitually unstable breathing is the prime cause of symptoms. Why they breathe in this way must be a matter for speculation, but manifestly the salient characteristics are pure habit."

Respiratory alkalosis and its effects

Discussing hyperventilation syndrome and its links to vasospasm, Castro et al[13] observe that both the acute and chronic forms of the syndrome are characterized by hypocapnoea and respiratory alkalosis. "The chronic form has a blood pH closer to the normal range, and is usually more symptomatic, in that only mild hyperventilation is necessary to produce a substantial increase in the degree of hypocapnoea … The underlying mechanisms of the syndrome are cerebral vasoconstriction, due to hypocapnoea and a decrease in the delivery of oxygen by haemoglobin."

Respiratory alkalosis leads to an accumulation of incompletely oxidised products of metabolism, due to the activation of anaerobic energy pathways. The products of the anaerobic pathway are acids such as lactic acid. and pyruvic acid.[14] This acidification is more extreme in deconditioned individuals. When ATP production is supplemented by anaerobic glycolysis, lactate accumulates in muscle cells and the bloodstream – reducing pH. Relative acidosis then encourages bicarbonate retention, resulting in increased CO_2 production, stimulating a more rapid breathing rate, leading to the respiratory threshold being breached. In a deconditioned individual this threshold is lower, resulting in dyspnoea and fatigue early in aerobic activity. The deconditioned individual relies more on anaerobic metabolism for energy supply.

Outcomes of deconditioning include:

1. Loss of muscle mass

2. Decreased ability to use energy substrates efficiently

3. Decreased neuromuscular transmission

4. Decreased efficiency in muscle fibre recruitment with indications of disruption of normal motor control being apparent.[15]

Nixon and Andrews[16] have summarised the emerging symptoms resulting from hypocapnoea in a deconditioned individual, as follows: "Muscular aching at low levels of effort; restlessness and heightened sympathetic activity; increased neuronal sensitivity; and, constriction of smooth-muscle tubes (e.g. the vascular, respiratory and gastric-intestinal) can accompany the basic symptom of inability to make and sustain normal levels of effort."

Lum[7] notes, "Alkalosis alone cannot fully explain the symptoms [of chronic hyperventilation]. Altitude adaptation allows residents of high altitudes to remain well, despite chronic respiratory alkalosis. In symptomatic hyperventilation however, the PCO_2 fluctuates, often wildly, causing constantly changing pH in nerve cells and tissue fluid to which no adaptation is possible…significant amounts of CO_2 can be lost in a few minutes of overbreathing, immediately causing respiratory alkalosis. Compensation, by excretion of bicarbonate, is relatively slow and may take hours or days."

Low back pain, balance and anxiety

Anxiety and apprehension are closely associated with altered breathing patterns, and breathing pattern disorders are in turn exaggerated by anxiety and apprehension.[17,18] Maintaining body balance and equilibrium is a primary role of functionally coordinated muscles, acting in task specific patterns, and this is dependent on normal motor control.[19]

Balaban and Theyer [20] have examined the neurological basis of links between balance control and anxiety, based upon neural circuits that are shared by pathways that mediate autonomic control, vestibulo-autonomic interactions, and anxiety: "The core of this circuitry is a parabrachial nucleus network, consisting of the parabrachial nucleus and its reciprocal relationships with the extended central amygdaloid nucleus, infralimbic cortex, and hypothalamus. Specifically, the parabrachial nucleus is a site of convergence of vestibular information processing, and somatic and visceral sensory information processing, in pathways that appear to be involved in avoidance conditioning, anxiety, and conditioned fear."

Klein[17] reports that hyperventilation, and resultant alkalosis, is capable of triggering anxiety and/or panic (and associated balance control changes) when (as is commonly the case) it is interpreted by the individual as representing a danger of suffocation.

Abnormal breathing patterns such as hyperventilation lead to elevated reports of somatic symptoms, including disorientation. There is evidence that the central changes that accompany hyperventilation may influence balance system functioning. Healthy individuals exhibit a substantial increase in sway following voluntary hyperventilation, and this postural instability may be linked to peripheral and central changes in somatosensory function.[21]

Low back pain often involves altered muscle length relationships, postural changes, muscular imbalances, variations in location of the centres of mass and of pressure.[22,23] Unsurprisingly, in the presence of such changes, associated with chronic low back pain, the speed and intensity of muscular contractions are commonly altered[24] with deep segmentally related muscles losing both contraction speed and intensity, while over activity and tonic contraction occurs in the larger multi-segmental muscles.[25,26] All these changes lead to low back pain patients moving differently, compared to healthy individuals.[27]

Increased anxiety levels, caused or aggravated by disordered breathing patterns, such as hyperventilation, are capable of amplifying many of these changes. Put simply, the responses of the motor system alter under conditions of pain and anxiety, due to modified cerebral processing.[28] The amygdala appear to play a pivotal role in the transmission and interpretation of fear and anxiety. The neuronal interactions between the amygdala enable the individual to initiate adaptive behaviours to threat, based upon the nature of the threat and prior experience. There is mediation between the efferent pathways involving the amygdala, locus coeruleus, hypothalamus, and autonomic, neuroendocrine, and skeletal-motor responses associated with fear and anxiety.[29]

Anxious, apprehensive thoughts have been shown to have an effect on the functioning of muscles. Lotze et al[30] using functional MRI scans have demonstrated that the cortical activity involved in thinking about a movement is similar to the cortical activity associated with the movement itself. It appears that simply talking about painful experiences increases activity in associated muscles in chronic low back pain patients.[31] Therefore, there is ample evidence that anxiety regarding movement, pain and re-injury can all modify motor behaviour.[32,33]

Anxiety and other emotions have also been shown to encourage recruitment of a small number of motor units that display almost constant, or repeated, activity when influenced psychogenically. In one study, low amplitude myoelectric activity (measured using surface electromyography) was evident even when muscles were not being employed in situations of mental stress.[34] "A small pool of low-threshold motor units may be under considerable load for prolonged periods of time…motor units with Type 1 [postural] fibres are predominant among these. If the subject repeatedly recruits the same motor units, the overload may result in a metabolic crisis." This aetiology parallels the proposed evolution of myofascial trigger points, as suggested by Simons et al.[6]

Neuronal excitability

There appear to be both biochemically induced, as well as psychological effects, deriving from breathing pattern disorders. Mogyoros[35] states: "The thresholds of human sensory and motor axons are altered during hyperventilation. Hyperventilation does not alter conduction velocity, refractoriness or super-normality, implying that the hyperventilation-induced increase in excitability is not the result of conventional depolarization, as seems to occur during ischaemia. These results suggest that hyperventilation has a rather selective action on the threshold channels... The greater expression of threshold channels in sensory [rather] than in motor fibres, can explain why hyperventilation induces paraesthesiae before fasciculation, and why only paraesthesiae occur during ischaemia." [35]

Seyal et al[36] note that hyperventilation increases the excitability of both cutaneous and motor axons, and that in experimental animals, HVS increases excitability of hippocampal neurons. Their research, involving healthy humans, demonstrates that hyperventilation increases the excitability of the human corticospinal system.

Respiratory alkalosis, resulting from low $PaCO_2$, which is almost always the result of hyperventilation, automatically lowers calcium ion levels in the plasma, precipitating hyperirritability of motor and sensory axons [37] Lum [38] reports,: "During moderate hyperventilation, loss of CO_2 ions from neurons stimulates neuronal activity, causing increased sensory and motor discharges, muscular tension and spasm, speeding of spinal reflexes, heightened perception (photophobia, hyperacusis) and other sensory disturbances. More profound hypocapnoea, however, increasingly depresses activity. This parallels the clinical state: initial alertness with increased activity, progressing through decreased alertness, to stupor and coma."

Combinations of inflammatory mediators, together with altered tissue pH, effectively induce sensitisation more markedly than chemical mediators alone.[39] Fluctuations in $PaCO_2$, resulting from overbreathing, can have a

destabilising effect on the autonomic nervous system, leading to sympathetic dominance, with patients often in a state of arousal.[40] Mean urinary excretion of adrenaline in hyperventilators may up to three times greater than normal.[41]

Influence of myofascial trigger points

Myofascial trigger points are commonly a source of pain and dysfunction in the low back.[42,43,6] There appear to be a variety of possible influences operating:

Simons and Travell[6] have noted that ischemia is a precursor to the evolution of myofascial trigger points (MTrPs). Persistent ischemia, such as prevails with respiratory alkalosis, seems to account for reduced O_2 tension at MTrP sites[44] They further report that, "a muscle that contains an active trigger point shows electromyographic activity 'at rest' when it is stretched to, or beyond, the point of pain."

Baldry[45] observes that hyperventilation induced hypoxia, is a potent stimulator of bradykinin release, encouraging perpetuation of MTrP sensitisation, and persistence of pain.

Using a novel microdialysis technique Shah et al[46] have shown that at the nidus of an active trigger point, bradykinin levels are significantly higher (as were substance P, calcitonin gene-related peptide, norepinephrine, tumor necrosis factor-alpha, and IL-1) compared with latent trigger points and normal tissue.

An altered pH in the local chemical environment of peripheral nociceptors, such as occurs with respiratory alkalosis, helps to induce mechanical sensitisation and ischaemic pain.[47,48]

Bengtsson[49] has suggested that a combination of circulatory stasis and hypoxia is probably responsible for the presence of 'ragged red' fibres in the vicinity of MTrPs. Such tissues, found in both MTrP pain syndrome and fibromyalgia, apparently result from hypoxia induced alteration in ATP production[50]

Brucini et al[51] have shown that trigger points, "increase motor unit activity of muscles in both the pain and reference zone"

More recently Lucas[52] has shown that the presence of latent trigger points alters activation (firing) sequences in entire kinetic chains, for example involving latent trigger points in upper trapezius, on abduction at the shoulder joint.

A relevant question might be posed as to whether trigger points can at times be functional (to induce stabilisation of hypermobile structures, for example) in local and/or target tissues[53] since they represent an energy efficient means of assisting sustained increased contracture, a chemical rather than action potential-mediated shortening of the muscle fibers?[54]

The diaphragm

It seems likely that habitual, chronic, breathing pattern disorders interfere with normal function of key stabilizing muscles such as transversus abdominis and the diaphragm.

Hypercapnoea (increased levels of CO_2) can be induced by having the subject inhale through a long tube, increasing the dead space in the lungs, or by having the subject breath air containing higher than normal levels of CO_2. Either method appears to be preferable to voluntary hyperventilation which can have unpredictable outcomes. Hypercapnoea triggers an artificially rapid breathing rate, the effects of which can then be studied.

Using a 10% CO_2 gas mixture to elevate breathing, McGill[55] noted that reduction in the support offered to the spine, by the muscles of the torso, may occur if there is both a load challenge to the low back, combined with a breathing challenge (shovelling snow is given as an easily understood example in real-life rather than under research conditions). "Modulation of muscle activity needed to facilitate breathing may compromise the margin of safety of tissues that depend on constant muscle activity for support".

Hodges[56] demonstrated (using a long-tube breathing method) that after approximately 60 seconds of hypercapneoa the postural (tonic) and phasic functions of both the diaphragm and transversus abdominis are reduced or absent. "The present data suggest that increased central respiratory drive may attenuate the postural commands reaching motoneurons. This attenuation can affect the key inspiratory and expiratory muscles, and is likely to be co-ordinated at a pre-motoneuronal site." Hodges further hypothesises: "Although investigation of spinal mechanics is required to confirm the extent to which spinal control is compromised by increases in respiratory demand, it is hypothesised that such a compromise may lead to increased potential for injury to spinal structures and reduced postural control. During strenuous exercise, when the physical stresses to the spine are greater, the physiological vulnerability of the spine to injury is likely to be increased."

Fascial considerations

Staubesand and Li[57] studied fascia in humans using electron photomicroscopy and found smooth muscle cells (SMC) widely embedded within the collagen fibres. They describe a rich intrafascial supply of capillaries, autonomic and sensory nerve endings, and concluded that these intrafascial smooth muscle cells enable the autonomic nervous system to regulate a fascial pre-tension, independently of muscular tonus.

There is increasing interest on the possible effects that active SMC contractility may have in the many fascial/connective tissue sites in which their presence has now been identified, including ligaments, [58] menisci,[59] spinal discs[60] and, as suggested by the research of Yahia et al,[61] on the lumbodorsal fascia, which has been shown by Barker and Briggs[62] to extend from the pelvis to the cervical area: "Both superficial and deep laminae of the posterior layer are more extensive superiorly than previously thought."

One result of respiratory alkalosis, with an as yet unspecified degree of impact on low back pain and function, as pH rises markedly, involves the potential for increased contractility of SMC. The research of Yahia et al[59] suggests the possibility of (smooth) muscle cells in fascia offering a protective role, although at the time there was no histological proof of their

presence in these tissues. They have demonstrated a progressive stiffening of lumbar fascia (human cadaver specimens) when subjected to repetitive isometric strain forces. Yahia et al[59] also cite research[63,64,65] into the effects of alterations in pH on modification of the viscosity of connective tissue (the 'swelling rate'), another phenomenon with a possibly protective, and certainly an influential, role in low back stability.

SMC contractility directly impacts on circulation to muscle and brain tissues, by reducing blood vessel diameter and therefore oxygenation, leading to increased likelihood of fatigue.[66]

A further connective tissue consideration involves hypermobility which has been shown to be a major risk factor in the evolution of low back pain.[67] Breathing pattern disorders have been found to be much more common in hypermobile individuals (where fascial stability is most needed) -often associated with chronic pain syndromes.[68,69,70]

A pertinent question arises: In a hypermobile individual who hyperventilates, is the altered breathing pattern functional – a means of increasing tone and stability in lax connective tissue structures, via the effect of respiratory alkalosis on contractile smooth muscle cells?

Breathing retraining

Reducing levels of apprehension, anxiety and fear may be seen to have the potential for allowing a variety of features, including motor control, to improve. Breathing retraining is one way of achieving this objective. There is good evidence that breathing rehabilitation is a useful method for achieving reduced anxiety/panic levels and for improving postural control and somatic complaints, such as low back pain.[16,71,72,73]

Nixon and Andrews[16] suggest that recovery from BPD depends upon: "Due attention to the restoration of proper sleep, the modulation of arousal, the recovery of natural breathing, a salutary balance of rest and effort, and the subject's achievement of self-regulation and autonomy".

Breathing retraining has been used to successfully correct hyperventilation. In one study[7]more than 1000 anxious and phobic patients were treated using a combination of breathing retraining, physical therapy and relaxation. Symptoms were usually abolished in one to six months with some younger patients requiring only a few weeks. At 12 months 75% were free of all symptoms, 20% had only mild symptoms and about one patient in twenty had intractable symptoms.

In another study[72] breathing therapy was evaluated in patients with HVS in which most of the patients met the criteria for an anxiety disorder. The diagnosis was based on the presence of several stress related complaints, reproduced by voluntary hyperventilation, patients with organic diseases having been excluded. Therapy was conducted in the following sequence:

1. Brief, voluntary hyperventilation to reproduce the complaints in daily life
2. Reattribution of the cause of the symptoms to hyperventilation
3. Explaining the rationale of therapy—reduction of hyperventilation by acquiring an abdominal breathing pattern, with slowing down of expiration
4. Breathing retraining for 2 to 3 months by a physiotherapist

After breathing therapy, the sum scores of the Nijmegen Questionnaire[74,75] were markedly reduced. A canonical correlation analysis relating the changes of the various complaints to the modifications of breathing variables showed that the improvement of the complaints was correlated mainly with the slowing down of breathing frequency. The Nijmegen questionnaire provides a non-invasive test of high sensitivity (up to 91%) and specificity (up to 95%).[75] This easily administered, internationally validated[74] diagnostic questionnaire is the simplest, kindest and to date most accurate indicator of acute and chronic hyperventilation. The questions enquire as to the following symptoms, and their intensity:

- constriction in the chest,
- shortness of breath,
- accelerated or deepened breathing,
- inability to breathe deeply,
- feeling tense,
- tightness around the mouth,
- stiffness in the fingers or arms,
- cold hands or feet,
- tingling fingers,
- bloated abdominal sensation,
- dizzy spells,
- blurred vision,
- feeling of confusion or losing touch with environment.

Breath work can also be seen to offer prophylactic benefits. Aust and Fischer[73] investigated whether psychophysical breath work influences postural control. The method used involved optical patterns being projected onto a video screen, the test subjects having been instructed to shift their centre of gravity according to the patterns projected. The patterns consisted of a line which had to be followed in the anterior-posterior and lateral plane, and a circle to be followed clockwise and counter-clockwise. The results showed that those participants with some experience of breath training had significantly better results in the posturographic test with visual feedback. Additionally, the posturographic results immediately following one hour of breath work demonstrated clear improvements in body equilibrium suggesting that breath work leads to a general improvement in maintaining equilibrium, which remains stable over time.

There is also evidence of a degree of entrainment between active movement and respiratory rate, suggesting that

rhythmic slow movements (such as performed during Tai chi exercise) can assist in reducing respiratory rate.[76] Jasinskas[77] reports that, "results strongly support the existence of entrainment, and provide evidence for neurogenic input to ventilatory control during steady state work."

The respiratory (and cardiovascular) effects of rosary prayer ('Ave Maria' in Latin) and recitation of a yoga mantra have been assessed.[78] Results were similar for both methods, showing a slowing of respiration to approximately 6cpm, and synchronisation of all cardiovascular rhythms, Traube-Hering-Meyer oscillations, representing blood pressure, heart rate, cardiac contractility, pulmonary blood flow, cerebral blood flow and movement of cerebrospinal fluid). This positive influence on autonomic activity, may offer great benefits toward normalisation of sympathetic arousal and abnormal neural function resulting from BPD.

Biochemical influences on BPD, including allergy and pseudo-allergy

Lum[79] reports that more than one third of patients suffering from chronic hyperventilation have associated conditions that frustrate efforts to correct breathing. He reports that:

- "Allergies (e.g. hay fever) may keep patients sniffing and coughing for half the year, perpetuating irregular thoracic inspirations"
- Food intolerance, with bloating after meals, may 'splint' diaphragmatic movement. Such cases need an expert in dietary management.
- "Pseudo-allergy is common; many patients falsely attribute symptoms to an allergy to particular foods. In two-thirds of such cases of pseudo-allergy, the symptoms have been shown to be due to a conditioned reflex of hyperventilation on exposure. A similar mechanism is common in allergy to perfumes, and industrial gases."[80]
- Progesterone is a respiratory stimulant, making patients with BPD most vulnerable during the post-ovulation phase of the menstrual cycle.[10]
- Blood sugar levels are, "clinically the most important of these non-ventilatory factors. When blood glucose is below the middle of the normal range (i.e. below 4.4 mmol/L) the effects of overbreathing are progressively enhanced at lower levels." [81]

SUMMARY POINTS

- Chronic BPD such as hyperventilation is widespread, more frequent in females, and leads to respiratory alkalosis, constriction of smooth muscles, and a variety of neurological, cardiac, gastrointestinal and emotional symptoms.
- Reduced CO_2 levels (hypocapnoea), involving respiratory alkalosis, causes smooth muscle constriction, reduced blood, and therefore reduced oxygen, delivery to tissues, and this is more pronounced in deconditioned individuals.
- Breathing pattern disorders are associated with anxiety, and anxiety is associated with altered neuronal (including motor) function, muscular imbalances, disturbed postural balance, and the enhanced evolution of myofascial trigger points.
- BPDs, such as hyperventilation, induce biochemical changes that increase neuronal excitability, enhance sensitisation processes, and destabilize the autonomic nervous system.
- BPDs encourage trigger point evolution, and trigger points can have a profound influence on motor function and pain.
- Core stabilising muscles are compromised by hypercapnoea – an induced rise in breathing rate that leads to respiratory alkalosis – compromising key core muscles involved in spinal stability.
- SMC contractility, and its widespread presence in connective tissues, appears to have a relevance to stability, however the precise relationship with conditions such as low back pain remains to be established, as does the connection between hyperventilation and hypermobility.
- Breathing retraining can have a positive effect in normalising BPD as well as associated neural dysfunction.
- There appears to be an overlap between functional, habitual BPD and breathing pattern disorders associated with allergy.

CONCLUSION

It seems very likely that chronic BPD negatively influences motor control, neurological sensitisation, muscle behaviour, pain threshold and balance. There is evidence that breathing rehabilitation can reverse these tendencies and restore more normal breathing patterns in many individuals. As with most features and functions not directly associated with the symptoms, unless BPDs are looked for and evaluated, they are unlikely to be recognized in a manual medicine setting. While seldom causative, BPD can be seen to potentially be a major factor in encouraging and maintaining musculoskeletal dysfunction in general, and back pain in particular.

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Discussion Paper

Breathing pattern disorders and physiotherapy: inspiration for our profession

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Background: Breathing pattern disorders (BPDs), historically known as hyperventilation syndrome, are being increasingly recognized as an entity of their own. Breathing patterns reflect the functioning of the respiratory system and the biomechanical system as well as the cognitive state.
Clinical relevance: It is essential, therefore, that physiotherapists from all areas of specialty consider the assessment and treatment of a patient's breathing pattern. New literature is emerging which underpins the relevance of BPD in patients with lung disease, anxiety, and also in the comparatively new area of sport performance. Physiotherapists are well placed to treat people with disordered breathing because of their clinical skills and comprehensive knowledge base. Current treatment is briefly reviewed in this paper, and trends for future treatment are also addressed.
Conclusion: The potential for improving the patient's state, by optimizing their breathing pattern in all their activities, is an important development in physiotherapy. It is a developing area of knowledge which is pertinent to physiotherapy practice as it develops in a biopsychosocial model.

Keywords: Breathing dysfunction, Breathing exercises, Breathing pattern disorders, Breathing retraining, Hyperventilation syndrome

Introduction

Breathing is a central aspect of our whole being and is one of our most vital functions. A disordered breathing pattern can be the first sign that all is not well, whether it be a mechanical, physiological or psychological dysfunction. It is essential, therefore, that breathing is considered in all physiotherapy assessments.

Breathing practices historically span many centuries, philosophies and cultures. Since the turn of the century, Western medicine has been acknowledging the role of the breath in wellbeing,[1–3] and more recently research has been critically evaluating the role of the breath in both wellness and illness.[4–6] The concept of dysfunctional breathing, or breathing pattern disorders (BPDs) has developed, to describe the presentation of a poor breathing pattern that produces symptoms.[7] Defining BPD is an evolving process, and various disciplines are providing unique perspectives which give a multi-dimensional understanding of the multi-faceted function that is breathing.[4,8,9] Research is providing new knowledge which underpins the comprehensive role physiotherapy can provide in optimizing the breathing pattern, reducing/eliminating symptoms and facilitating wellbeing.[10–12] To date the physiotherapy literature on the topic of breathing pattern disorders and breathing re-education is sparse. Breathing pattern disorders are fast becoming recognized within the speciality area of musculoskeletal and sports physiotherapy[11] and private practice,[13] whilst still having a significant role in the more likely areas of lung disease[5,6] and of anxiety.[9,14]

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A Developing Understanding of Breathing Pattern Disorders

The symptoms of BPD first appeared in medical literature in 1871 when DaCosta,[1] noted a set of symptoms predominately in American civil war soldiers that were similar to those of heart disease: fatigue upon exertion, palpitations, sweating, chest pain and a disabling shortness of breath. DaCosta's syndrome became known as Soldier's Heart (chest pain).[15] As early as 1876 the suggestion of a mechanical origin was considered. Surgeon Arthur Davy attributed the symptoms to military drill where 'over-expanding' the chest caused dilatation of the heart, and so induced irritability.[16]

Haldane and Poultons[2] produced a paper linking the symptoms to overbreathing. This gained further support when Solely and Shock[3] reported that symptoms could be relieved by increasing partial pressure of carbon dioxide (CO_2), reinforcing an underlying respiratory disorder as the cause. It was the discovery of the role of hypocapnia in hyperventilation syndrome (HVS), which placed it firmly in the

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medical, biological framework, and subsequently, research has focused on the phenomena of hyperventilation, hypocapnia and symptoms.[17–19]

The term 'hyperventilation' was first used by Kerr *et al*. [18] and has been frequently used since this time, and more recently defined as, 'breathing in excess of metabolic demands, resulting in hypocapnia'.[20,21] Although the syndrome was given various names, the term inferred an anxiety state concurrent with cardiovascular and emotional symptoms, hence patients were considered neurotic and their condition not appropriate for serious medical consideration.[22] More recent psychology literature, however, focuses on the symptoms relating to a broad range of psychological influences on breathing, including anticipation, suppressed emotion, association and conditioned responses.[23,24] Another recent development is the significance of the musculo-skeletal aspect of breathing patterns. Chaitow[8] suggests that function and structure are so closely interconnected, that change in one aspect will lead to change in the other. He cites structural inadequacies, such as poor posture, as key factors causing BPD.

All these aspects of BPD are succinctly summarized by van Dixhoorn[25] who described breathing as having three functions, namely (1) gas exchange and respiratory function – and with this the communicative properties of smell and speech, (2) musculoskeletal movement – including moving body fluids, enhancing organ function, and maintaining musculoskeletal mobility and trunk stability, and (3) connecting conscious awareness with the state of the body.

Definition of Breathing Pattern Disorders

BPD is a complex syndrome, and a concise definition is evasive.[26] Gardner[27] questions whether HVS is an appropriate term when it is the underlying cause of the hyperventilation that needs diagnosis. He also suggests that low arterial pressure of carbon dioxide (Pa CO_2) may not necessarily be pathological and therefore indicative of HVS. Other authors have noted symptoms may occur without hypocapnia, suggesting there are other mechanisms involved.[24,28,29] Vickery[11] refers to breathing patterns disorders as long term abnormal respiratory mechanics. Also, BPD is a distinct syndrome, that is, BPDs are not an inevitable result of pathologic changes due to illness/disease.[19] Discussion at an international level as well as a local level has failed to provide a succinct definition which all parties support.[30]

A working definition by Rowley[7] based on the above perspectives, defines BPD as 'Inappropriate breathing which is persistent enough to cause symptoms, with no apparent organic cause'. Symptoms may not interrupt daily life but may impact on specific tasks, e.g. elite athletes and their performance, singers and voice production, or the child playing Saturday morning sport.

Mechanisms Underlying Breathing Pattern Disorders

The mechanisms underlying disordered breathing involve physiological, psychological and biomechanical components, and these cannot be completely separated.[27] At a physiological level, hyperventilation has been thought to be driven by central and peripheral chemoreceptors, and cortical drive.[19,31,32] Physiologically every cell in the body requires oxygen to survive yet the body's need to rid itself of carbon dioxide is the most important stimulus for breathing in a healthy person. CO_2 is the most potent chemical affecting respiration.[33]

Hyperventilation results in altered (CO_2) levels, and this is most commonly seen as lowered end tidal CO_2 (PET CO_2), or fluctuating CO_2 levels, and a slower return to normal CO_2 levels.[34] The exact mechanism by which CO_2 influences BPD symptoms remains under debate.[29,35] Research into levels of CO_2 in the HVS/BPD population has produced disparate results, therefore it may be that the effect of hypocapnia appears highly dependent on the individual.[21]

Common understanding is that the resulting respiratory alkalosis creates a state of sympathetic dominance, which invokes a 'fright-flight' response throughout the body. This includes heightened psychological and neuronal arousal, which leads to increased muscle tone, parasthesia and altered rate and depth of breathing.[36,37] Respiratory alkalosis also affects hemoglobin uptake of oxygen (O_2), coronary artery constriction and cerebral blood flow.[38] These changes in physiological, psychological, and neuronal states affect the musculo-skeletal system.

Musculo-skeletal imbalances may exist, as a result or as a pre-existing contributing factor, and this can be seen in areas such as loss of thoracic cage compliance, constant overuse and tension in the accessory respiratory muscles, and dysfunctional postures. These may impede normal movement of the chest wall, and exacerbate poor diaphragmatic descent.[8] The inefficient respiratory pattern and the increased sympathetic drive contribute further to muscle pain and fatigue, as well as psychological traits such as anxiety.[39]

Psychological factors both influence and are influenced by breathing patterns.[40] Ley states breathing should be examined as an independent variable affecting the psychological process. For example Ley[41] calls dyspnoea a 'harbinger of suffocation' and believes that it is the fear of the dyspnoea that

plays a major factor in panic attacks. Anxiety is the commonest factor thought to influence breathing, and it has been noted to cause increased inspiratory flow rate, breathing to become faster and shallower, and/or involve breath holding.[23,42] Subjects with BPD have been observed to have higher anxiety levels than the normal population.[43] Tasks involving prolonged or intense concentration have also been shown to alter breathing patterns.[44]

Aetiological Factors in Breathing Pattern Disorders

There is an extensive, perhaps exhaustive list of factors thought to trigger disordered breathing. The broad range of triggers is due to both the variable nature of BPD, and the variation in an individual's response to environmental and psychological factors. Factors that initially cause a BPD may be different from the factors that perpetuate it.[38] Once a pattern is established, however,[21,45] the breathing pattern disorder becomes habituated, and thus a disorder of its own.[19]

Table 1 shows a list produced from a range of sources.[8,18–21,23,32,38,46–49]

Common Symptoms of Breathing Pattern Disorders

The symptoms most commonly reported are respiratory. These include dyspnoea, frequent yawning and sighing, unable to get a deep enough breath, and 'air hunger'.[50] The irregularity of the breathing pattern is a common feature, and ironically breathing may appear normal at times, which makes diagnosis and observation difficult.[51] Other common symptoms are dizziness, chest pain, altered vision, feelings of depersonalization and panic attacks, nausea and reflux, general fatigue and difficulty concentrating. A large range of neurological, psychological, gastrointestinal and musculoskeletal changes can occur, and over 30 possible symptoms have been described.[52] Assessment of BPD needs to consider this range of manifestations.

Breathing Patterns

Faulty breathing patterns present differently, depending on the individual. Some patients are more inclined to mental distress, fear, anxiety and coexisting loss of self-confidence. Others may exhibit musculoskeletal and more physical symptoms such as neck and shoulder problems, chronic pain and fatigue. Many are a combination of both mental and physical factors.[53] The key focus of this paper is the musculo-skeletal aspect of BPD. Lung disease and anxiety will be covered, but to a lesser degree as these have been covered in previous physiotherapy literature reviews.

Breathing patterns and the musculo-skeletal implications

'If breathing is not normalized no other movement pattern can be'.[54,55]

Respiration and stability

Respiratory mechanics play a key role in both posture and spinal stability. Research by Hodges *et al.*[56–58] examines the relationship between trunk stability and low back pain. It supports the vital role the diaphragm plays with respect to truck stability and locomotor control. The diaphragm has the ability to perform the dual role of respiration and postural stability. When all systems are challenged, however, breathing will remain as the final driving force.[59]

In other words 'Breathing always wins'.[60]

Respiration is integral to movement as well as stability.[56,57] The diaphragm, transversus abdominus, multifidius and the pelvic floor muscles work in

Table 1 Aetiological factors in breathing pattern disorders

Biomechanical factors
Postural maladaptations
Upper limb movement
Chronic mouth breathing
Cultural, for example, 'tummy in, chest out', tight waisted clothing
Congenital
Overuse, misuse or abuse of musculo-skeletal system
Abnormal movement patterns
Braced posture, for example, post-operative
Occupational, for example, divers, singers, swimmers, dancers, musicians, equestrians
Physiological/biochemical factors
Lung disease
Metabolic disorders
Allergies – post-nasal drip, rhinitis, sinusitis
Diet
Exaggerated response to decreased CO_2
Drugs, including recreational drugs, caffeine, aspirin, alcohol
Hormonal, including progesterone
Exercise
Speech/laughter
Chronic low grade fever
Heat
Humidity/heat
Altitude
Psychological factors
Anxiety
Stress
Panic disorders
Personality traits, including perfectionist, high achiever, obsessive
Suppressed emotions, for example anger
Conditioning/learnt response
Action projection/anticipation
History of abuse
Mental tasks involving sustained concentration
Sustained boredom
Pain
Depression
Phobic avoidance
Fear of symptoms/misattribution of symptoms

unison to establish intra-abdominal pressure. All structures add to stability and allow efficient respiration, movement and continence control. Should there be a deviation away from a normal recruitment pattern, then pressure, ventilation volumes and ultimately work of breathing is affected.[59] Research by O'Sullivan[60] and Falla *et al.*[61] further supports Chaitow's[8] claims with respect to position/postures and activation of muscle groups.

When considering total body pressure control, the vocal folds and the surrounding musculature control the top of the system, the diaphragm which sits in the middle plays a key role in pressure generation, and the pelvic muscle group support at the base.[62] The primary purpose of the human larynx is to function as an exchange valve, controlling the flow of air in and out of the lungs.[63] This system adds to not only to structural support but also contributes to motility of fluid based systems within the body, i.e. gastrointestinal, lymphatic drainage, arterial and venous circulation. It also creates phonation and voice production.[64] When a system is under load respiration will dominate at the expense of voice and locomotion and postural control.

It is important to consider how these diverse functions are inter-related and can be co-ordinated into physiotherapy treatment regimes, for example, treatment regimes utilizing all systems, breath, movement and voice.

Length–tension relationship

Pressure determines the length–tension relationship. If a BPD is present respiratory accessory muscles shorten, and the diaphragm is unable to return to its optimal resting position, thus potentially contributing to dynamic hyperinflation, causing pressure changes and further compounding the disorder. Not only is accessory muscle load increased, but the muscles are also working from a shortened disadvantaged position. Shortened muscles create less force, hence the muscle length tension relationship is altered.[65] Patients with neck pain commonly have faulty breathing patterns.[66]

It is advantageous to keep this in mind, musculoskeletal techniques will not address an altered length tension ratio unless the driving BPD is addressed. It is also important to note that sustained muscular contraction may occlude local vasculature, momentarily impeding blood flow to activated muscle; this can lead to trigger point development in these muscles.[67]

Dynamic hyperinflation

Dynamic hyperinflation can occur due to a phenomenon known as breath stacking. Traditionally thought to occur in asthma, this also occurs significantly during exercise, when incomplete exhalation can result in residual air adding to the volume of the next inhalation with eventual over-inflation of the lungs. Airflow can become limited and the amount of O_2 reaching the alveoli decreases as dead space volume increases. Inefficient ventilation and dyspnoea are the end result.[65] The supporting musculature also work in less than optimal positions.

The concept of addressing dynamic hyperinflation is not new in the physiotherapy literature: this has been identified and clearly addressed regarding the asthma patient. The idea of decreasing the dynamic hyperinflation of the rib cage is based on the assumption that this intervention will decrease the elastic work of breathing and allow the inspiratory muscles to work over a more advantageous part of their length–tension relationship. There are several treatment strategies that aim to reduce chest wall hyperinflation.[5] Similar strategies could be considered when treating dynamic inflation with no organic lung disorder present.

Motor pattern changes

Dynamic hyperinflation can result due to habitual motor patterns; e.g. increased resting tone of the abdominal muscles in particular the oblique muscles at rest. This can have a 'corset' effect preventing diaphragm distension, resulting in the breathing pattern changing to one of upper chest (apical); this leads to over use of the respiratory accessory muscles, pectoralis minor tightens lifting the chest apically, their action opposed by the trapezii muscles which work harder.[68] Forward head posture occurs, and temporomandibular joint compression may occur, and potentially mouth breathing.[69] The tension relationship is altered, and consequently the diaphragm cannot return to optimal resting point, so dynamic hyperinflation occurs. At rest the work of breathing has exceeded the normal values. Unbeknown to the fashion conscious or 'fab ab' seeker, there is a host of serious physiological and mechanical, as well as psychological changes taking place. This process challenges the deep motor patterns that control trunk stability. The expiratory reserve volume is increased where tidal volume may remain the same but inspiratory reserve volume decreases, suggesting a dynamic hyperinflated pattern. If hypocapnia is present, this can further alter the resting muscle tone and ultimately motor pattern changes via the increased excitability in the nervous system and muscular system.[70–73]

Sport/the Athlete

Vital capacity and oxygen delivery

Little attention has been paid to the breathing pattern of the athlete until recently. Historically this area of research has been dominated by sports physiologists

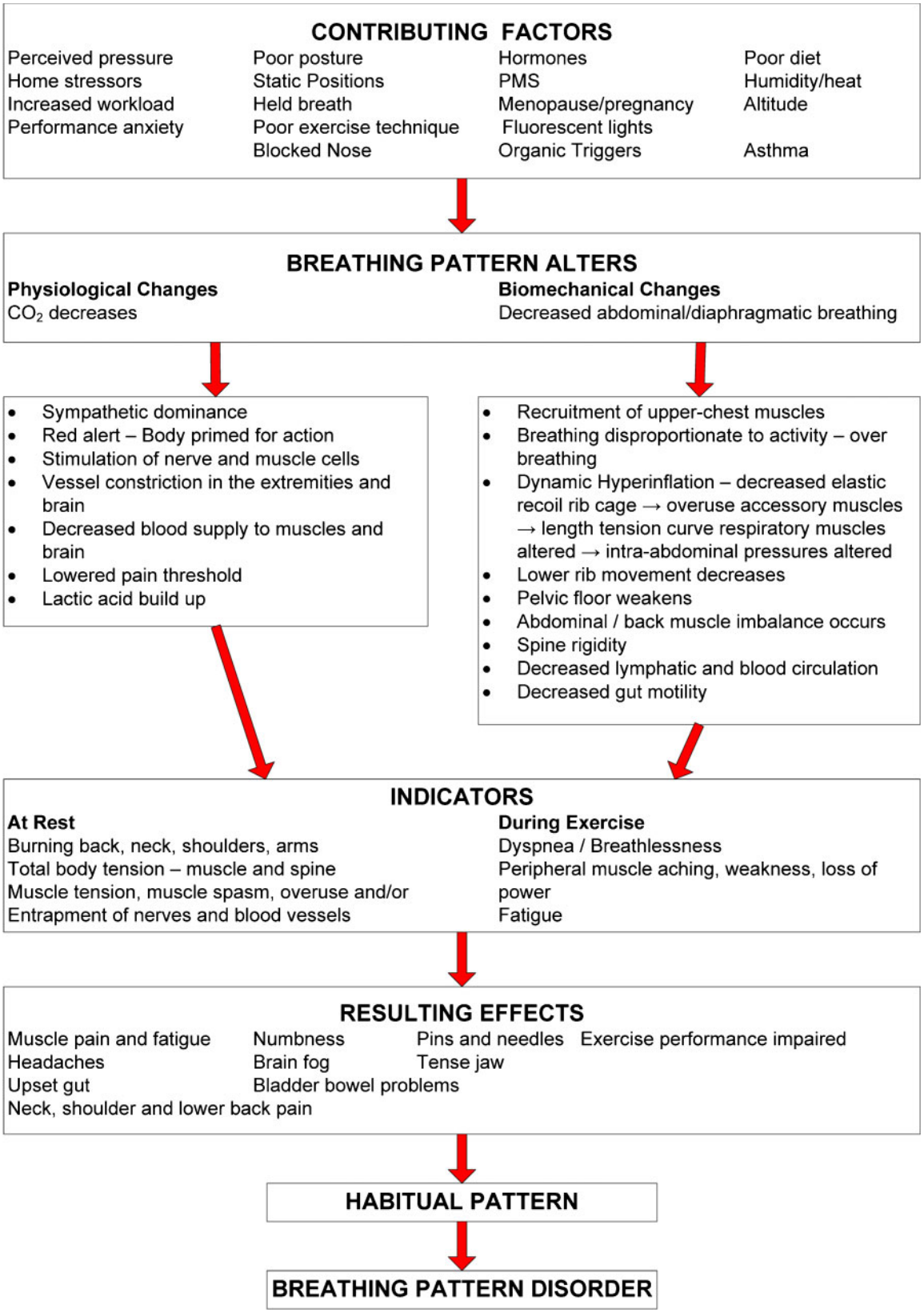

Figure 1 Breathing and the musculoskeletal connection (Tania Clifton-Smith[122]).

who have focused on ventilation and the delivery of oxygen. Research is now beyond the capacity of ventilation and starting to look at the muscles of respiration and breathing patterns.[11] The fundamental goal of our system is the protection of oxygen delivery to the respiratory muscles, thus ensuring the ability to maintain pulmonary ventilation, proper regulation of arterial blood gases and pH and overall homeostasis.

Harms *et al.*[74] identified that the work of breathing during maximal exercise resulted in marked changes in locomotor muscle blood flow, cardiac output and

both whole-body and active limb O_2 uptake. They identified the compromised locomotor blood flow was associated with noradrenaline (norepinephrine) suggesting enhanced sympathetic vasoconstriction. This concept has been referred to as blood stealing, a novel idea that literally the muscles of respiration steal O_2 rich blood from the lower limbs. Further work by Sheel[75] and St Croix[76] provide evidence for the existence of a metaboreflex, with its origin in the respiratory muscles. They believe this reflex can modulate limb perfusion via stimulation of sympathetic nervous system vasoconstrictor neurones.

Breathing pattern retraining

Vickery[11] conducted ground breaking research assessing the effect of breathing pattern retraining on performance in competitive cyclists. Results supported that four weeks of specific breathing pattern retraining enhanced endurance performance and incremental peak power and positively affected breathing pattern and perceived exertion. It appears that our system has the potential to become sensitized in its protective role and fire too early resulting in premature dyspnoea. Perhaps this is the phenomenon that is occurring in some cases of exercise induced bronchospasm?

Exercise-induced bronchoconstriction has a high prevalence in athletes and in particular elite athletes, predominately affecting endurance athletes, winter athletes and swimmers.[77] However, exercise-induced bronchoconstriction also occurs in up to 10% of subjects who are not known to be atopic or asthmatic.[78]

Breathing Pattern Disorders and Lung Disease

Breathing pattern disorders and asthma

The altered breathing pattern that occurs with acute asthma is similar to the hyperinflated, rapid upper chest, shallow pattern common in BPD, and therefore it appears reasonable that chronic asthma may contribute to a habitual disordered breathing pattern, as well as a habitual poor breathing pattern exacerbating the symptoms of asthma.[52,79] Thomas *et al.*[80] noted an incidence of hyperventilation of 29% in a sample of 219 known asthmatics in their clinic. Martinez-Moragon *et al.* [81] similarly observed 36% (n=17/157) of asthmatics at a pulmonary outpatient clinic had a BPD. A higher correlation is seen in studies assessing patients with known hyperventilation. Saisch *et al.*[82] noted asthma was certain or probable in 78% (17) of patients attending an emergency department with acute hyperventilation, including asymptomatic asthma. Similarly, Demeter and Cordasco[83] recorded 80% (38/47) of patients with hyperventilation, at a private pulmonary clinic, also had asthma. More accurate assessment and including mild/asymptomatic asthma is the likely reason the studies retrospectively assessing for asthma show a higher correlation.

BPD, asthma and exercise

Exercise is commonly thought to be a trigger for asthma, and whilst it is true for some, for others the anxiety-inducing breathlessness they attribute to asthma may be due to hyperinflation and excessive respiratory effect due to faulty breathing patterns. Kinnula and Sovijarvi[84] using cycle ergometry, noted consistent hyperventilation in all the female asthmatics, despite no evidence of bronchospasm at one minute after exercise or differences in exercise capacity. The findings are similar to a study by Hammo and Wienburger[85] which assessed 32 patients diagnosed with exercise-induced asthma, for hyperventilation. Of the 21 patients who experienced asthma symptoms, 11 had no significant decrease in FEV1, but demonstrated the lowest $PETCO_2$, suggesting hyperventilation, rather than asthma, was responsible for their symptoms. Hibbit and Pilsbury[86] observed their asthmatic subject began hyperventilating prior to exercise, with slightly lowered peak flow (470 L min^{-1} versus 500–660 expected norm). A marked decrease in PCO_2 occurred during exercise and following exercise peak flow dropped to 385 L min^{-1}, with the subject feeling anxious and distressed. After two months of breathing retraining and increased physical activities, the exercise test was repeated, with the same initial peak flow, but with considerably less PCO_2 changes during exercise, no decrease in PEFR afterwards, and no need for treatment.

A Cochrane review by Holloway and Ram[87] reported a trend for improvement in asthma symptoms after breathing retraining. More consistent improvements related to quality of life markers rather than changes in lung physiology.[10,88] The authors[87] conclude that it is the lack of consistent, robust data with a clear description of the retraining method that limits the conclusions that can be made, rather than necessarily the effectiveness of the breathing retraining itself.

People with chronic asthma may also have lower resting $PeCO_2$ making them more vulnerable to the sympathetic arousal hypocapnia can induce – which they will feel as anxiety.[82,89]

Breathing pattern disorders, anxiety and COPD

A review by Brenes[90] indicates a higher rate of anxiety in people with COPD than the general population. Other studies have linked anxiety in this population to negative quality of life status and lower functional status.[91,92] Supporting this, Livermore *et al.*[93] observed a correlation between higher anxiety in COPD patients and lower threshold for perceived dyspnoea when breathing against a set resistance

increasing the exertion of breathing, compared to perceived dsypnoea in matched subjects with COPD and a normal control group.

For these populations, correcting the breathing pattern to an efficient steady diaphragmatic pattern can help reduce perceived dyspnoea by reducing the inspiratory effort and anxiety, helping clarify symptoms attributable to actual lung disease rather than functional factors.

Breathing pattern disorders and anxiety

Anxiety may be driven by negative thoughts, but also by physiology, for example autonomic disregulation, and/or abnormal lung biomechanics causing a sensation of dyspnoea, not related to actual insufficiencies. The factors surrounding anxiety are too complex and interconnected to suggest there can be a simple causal effect.[94]

Studies report greater changes in respiratory patterns in subjects reporting high anxiety levels, when completing a stressful task, with marked increases in tidal volume and respiratory rate and decreased expiratory time with significant drop in $FETCO_2$ in the high trait anxiety group.[95,96] Similar changes are seen with anticipatory anxiety.[97] Conditioned respiratory responses have also been shown to occur prior to starting a computer task.[98,99]

In people with a confirmed diagnosis of an anxiety disorder, such as panic disorder or post traumatic stress disorder, there appears to be a loss of homeostasis, in particular regarding persistent hyperarousal of the sympathetic control.[100,101] Interestingly, Blechert *et al.*[102] noted the changes in firing of vasoconstrictor fibers in panic disorder patients were similar to those in subjects with increased muscle sympathetic outflow induced by inhaled breath hold and obstructive sleep apnoea, again reinforcing the overlap between breathing pattern disorders and a wide range of causes and symptoms.

Treatment of BPD in Physiotherapy

Assessment

Physiotherapy treatment of BPD begins with assessment. The lack of a definitive assessment tool for BPD does make diagnosis difficult and sometimes it is achieved only by a process of elimination.[103] Assessment includes gaining an accurate clinical history, observation of the person's breathing and musculo-skeletal status, and 'hands on' assessment of breathing and muscle tension.[4,104,105] Assessment tools commonly used include the Nijmegen Questionnaire, breath hold test, peak expiratory flow rate, and pulse oximetry.[4] Spirometry and capnography may be used, depending on the clinic resources.[6] Treatment can then focus on areas of dysfunction identified during assessment.

Treatment

The role of breathing exercises in patients with pulmonary disorders was documented as early as 1915.[106,107] By 1919 it was recommended that many medical and surgical patients be given breathing and physical exercise as accessories to medical and surgical treatment.[108]

The first literature referring to BPDs and breathing re-education within the physiotherapy profession was in the 1960s in cardiorespiratory physiotherapy. At this time physiotherapists advocated breathing retraining for BPD.[105,109] The Papworth method of breathing retraining evolved from the collaboration of chest physician Claude Lum and physiotherapists Diana Innocenti and Rosemary Cluff. This focused on education, and a nose/abdominal breathing pattern.[45,105,109] Other key aspects in the physiotherapy literature treatment are education, reassurance, and breathing retraining.[104,110–115]

Most physiotherapy treatment protocols appear to have the following basic principles in common.[4,6,105,112,115]

1. Education on the pathophysiology of the disorder
2. Self-observation of one's own breathing pattern
3. Restoration to a basic physiological breathing pattern: relaxed, rhythmical nose–abdominal breathing.
4. Appropriate tidal volume
5. Education of stress and tension in the body
6. Posture
7. Breathing with movement and activity
8. Clothing Awareness
9. Breathing and speech
10. Breathing and nutrition
11. Breathing and sleep
12. Breathing through an acute episode

Education

Education is broader than breathing pattern alone. Education includes the effects of abnormal versus diaphragmatic breathing, and reassurance that HVS/BPD symptoms have a physiological basis, and are treatable. Education also involves identifying the factors that initially caused the BPD, and/or may trigger the poor breathing pattern in the future.[4] Lifestyle issues are addressed, such as level of activity, relaxation (both as a technique and as a recreational activity), and sleep. Work issues, such as sustained computer work, extended periods of intense concentration and speech are also addressed, as these areas have been shown to impact on breathing patterns.[116–118]

For the public domain, physiotherapists have written and co-written books on hyperventilation/BPD. 'Asthma and Your Child' by Thompson[119] highlights many techniques to assist with breathing pattern disorders and asthma treatment. In 1991 Bradley[120] wrote the first patient handbook on the subject of hyperventilation syndrome/breathing pattern disorders. More recently, in collaboration with

CliftonSmith, they have produced dynamic breathing for asthma,[121] and breathe stretch and move.[122] All these books place emphasis on self-management.

Breathing retraining

The terms breathing exercises, breathing retraining and breathing pattern training are used interchangeably in the physiotherapy literature. There is variation, even within the physiotherapy discipline, of what parameters of normal breathing are. Cluff[105] states the rate should be 8–12 average sized breaths per minute at rest, with gentle, silent, rhythmical diaphragmatic (tummy) breathing, with little upper chest movement. West[123] reports breathing rate for an adult at rest is 10–14 breaths per minute.

The treatment of BPD is under recognized. Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient have been recently published.[124] These guidelines represent an extensive amount of work collating and analyzing research to support current physiotherapeutic management in the area of cardiorespiratory, neuromuscular diseases and musculoskeletal. Breathing pattern disorders were not mentioned during the review, except used in the context as a historical reference when referring to the treatment by physiotherapists in the management of disordered breathing.[125,126] Breathing retraining was only used in reference to asthma and secondary disordered breathing.

The BradCliff Method® looks at breathing dysfunction as an indicator of physiological and mechanical imbalances and psychological stress in the human body. It is structured on current physiotherapy research assessing and treating individuals from children with asthma to elite athletes.[127]

We are now able to have a better informed approach however, no longer assuming an adequate breathing pattern at rest is necessarily an optimal breathing pattern for all the activities our client is involved with. Diaphragmatic breathing remains the foundation of our treatment, but it is no longer the only aspect of our treatment.

Musculo-skeletal component

Musculo-skeletal issues are addressed which are impeding an effective breathing pattern. Alongside the mechanical validation of respiratory muscle contribution to motor control, research into the training of respiratory muscle strength has gained momentum,[128,129] Much of the research was initially surrounding dyspnoea and organic respiratory disorders and it is well established that the respiratory muscles could be strengthened.[130] There is evidence supporting the role of inspiratory muscle trainers to strengthen the inspiratory muscles, to reduce dyspnoea and improve function, whether it is for activities of daily living or high performance sport.[131–134]

Massery has successfully incorporated breathing, respiratory control and re-education into rehabilitation covering many neurological conditions such as cerebral palsy, complex paediatric cases, spinal cord injuries, as well as respiratory and bio-mechanical disorders. Massery utilizes a multi-system approach with breathing/respiration as an integral part. Massery remains adamant breathing is the first step of all rehabilitation.[135] Massery incorporates breath and movement into her treatment regimes at all levels of functioning and views breathing retraining and postural control strategies as simultaneous interventions. 'Motor impairments are never just a musculoskeletal problem or just a neuromotor problem. We are born with systems that interact to give us the control we need for health and participation.[136]

An extensive list of Mary Massery's publications can be viewed: http://www.masserypt.com/html/pub.html[137]

Research addressing treatment efficacy for BPD

The variability of treatment regimes and poor description of the regime details have made it difficult to gain a cohesive understanding of what the research to date has shown. Despite this variation, the authors report improvements are achieved, suggesting key elements are covered within the treatment programme.[138,139] The Papworth method has shown favourable outcomes, significantly reducing respiratory symptoms and improving health-related quality of life in a group of patients with asthma.[140,141]

Other papers from the UK also support breathing re-education/training within physiotherapy practice.[142,143]

Singh[144] reviewed the literature with respect to physiotherapy treatment and hyperventilation. The review concluded that the definition and diagnosis of hyperventilation is difficult; however, once identified physiotherapy intervention can provide an effective intervention to significantly reduce the symptoms and improve quality of life. The query over diagnosis was the hyperventilation versus breathing pattern disorder debate. It has been shown clearly in studies that breathing retraining has a positive effect on improving symptoms where the subject does not exhibit low levels of CO_2—highlighting that not only do we see people with chronic hyperventilation (lowered CO_2) but perhaps a bigger group who present with symptoms due to mechanisms directly related to other pathways.[145]

A 2004 Cochrane review of breathing exercises for asthma concluded that, due to the diversity of breathing exercises and outcomes used, it was impossible to draw conclusions from the available

evidence.[146] Thomas *et al.*[147] randomized participants into a group to receive the Papworth breathing re-education method or to see an experienced respiratory nurse providing asthma education. There were significant improvements in asthma-related quality of life in both groups after 1 month, but at 6 months a large difference between groups was found, in favour of the breathing retraining group, in asthma quality of life, anxiety and depression, Nijmegen score and a trend for an improvement in asthma control.[147]

Vickery[11] investigated the effect of breathing pattern retraining on 20-km time trial performance and respiratory and metabolic measures in competitive cyclists.

The results supported the performance enhancing effect of four weeks of breathing pattern retraining in cyclists. They suggested breathing pattern can be retrained to exhibit a controlled pattern, without a tachypnoeic shift (increased respiratory rate leading potentially to breath stacking and an irregular pattern that may impair alveolar ventilation) during high intensity cycling. Results also showed that respiratory and peripheral perceived effort was diminished. This research could open avenues of practice not yet proven before within the field of sports physiotherapy, emphasizing the importance of breathing patterns and ultimate performance.

Future trends for physiotherapy treatment

Currently in western medicine, a fundamental push is to encourage healthy life style skills. Education in one of the most fundamental tools, and yet breathing has not been emphasized enough as part of this healthy lifestyle package.

Looking to the future the consensus of health in the twenty-first century in the public domain, there appears to be a move away from the twentieth century biomedical model to a more global initiative, promoting projects and programmes that reach all human beings in a worldwide commitment to health as a global public good.[148] Keeping this in mind, there is a push from within our professions to run with this idea of 'health for all' and in particular involvement in the management, rehabilitation education and prevention of the epidemic of lifestyles diseases we are currently seeing, such as obesity, ischemic heart disease, cancer, smoking related conditions and pulmonary conditions.[149,150] There is scope within this framework to explore the concepts of breathing re-education within the profession. Breathing re-education is drug free, appealing to the new paradigm of health for all, and a practice that requires little or no machinery so a low running cost, and initial set-up is minimal for the therapist.

Conclusions

For the clinician the observation of breathing can provide insight into many systems, including biomechanics, biochemistry/physiology, and psychology reflecting the consideration of a multisystem approach.

Everyone is a complex integration of musculo/neurological/respiratory systems, which combined with individual personalities and lifestyles, reminds us that these are never distinct groups, and everyone we meet or treat works best when all systems are in homeostasis as supported by an appropriate and efficient breathing pattern.

There is a lack of robust evidence surrounding breathing pattern disorders. Ongoing research is needed that clearly describes treatment regimes and assesses outcomes that are compatible with other research and remains clinically relevant.

As a profession our diversity is an asset. The key points of breathing pattern disorders are common to whomever we treat. Our expertise is in our unique assessment and treatment skills, which enable us to develop specific programmes relevant to the individual cases whether it is the child with asthma or the elite athlete. The diversity of our profession enables us to approach breathing pattern disorders from different perspectives, yet allows us a cohesive informed approach, as physiotherapy aims to treat the whole person not just the system.

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Master class

The functions of breathing and its dysfunctions and their relationship to breathing therapy

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ABSTRACT

Breathing is unquestionably a key function of the human body; it sustains life by providing oxygen needed for metabolism and removing the by-product of these reactions, carbon dioxide. Breathing, however, has other functions apart from the ventilation of air and the maintenance of oxygen and carbon dioxide. Breathing affects motor control and postural stability and plays several roles in physiological and psychological regulation. Breathing can influence homeostatic functions in other system including the autonomic nervous system, the circulatory system, chemical regulation and metabolism.

Breathing becomes dysfunctional when the person is unable to breathe efficiently or when breathing is inappropriate, unhelpful or inefficient in responding to environmental conditions and the changing needs of the individual.

Impairment of the functions of breathing affects people's lives, challenging homeostasis, creating symptoms and compromising health. The efficiency with which breathing fulfills its various functions can be diminished because of musculo-skeletal dysfunction, disease, chronic psychological stress or other factors that affect respiratory drive and respiratory control. The neurological control of breathing shows high levels of neuroplasticity as shown by its ability to adapt to a wide range of internal and external conditions.

Breathing therapy generally aims to either correct dysfunctions of breathing or enhance its functions. Breathing, unlike most physiological functions, can be controlled voluntarily and it can serve as an entry point for physiological and psychological regulation.

1. The functions and dysfunctions of breathing

There is a developing interest in impact of dysfunctional breathing in common conditions such as asthma, chronic back and neck pain, postural stability, cardiovascular disease, anxiety and depression. Also breathing therapies are being increasingly used as components of treatment strategies for these conditions. Osteopaths have long recognized that breathing is a commonly disturbed function in the body, which if not addressed has far reaching effects on structure and function.[1] Others have also argued that while dysfunctional breathing (DB) is common, it is often overlooked and when untreated results in unnecessary suffering.[2–7] The prevalence rate of DB in the general population has been suggested to be as high as 5–11% in the general population[2,8,9] around 30% in asthmatics[10] and up to 83% in anxiety sufferers.[11]

Understanding the true prevalence of dysfunctional breathing (DB) and its impact on health is difficult because the parameters of DB are not clearly defined. Clinicians and breathing therapists argue about the perimeters of DB and its definition and the correct approaches to use in its clinical assessment. A practical approach to DB that has heuristic value is to define it as breathing which is unable to perform its various functions efficiently and is inappropriate for the needs of the individual at that time.

To evaluate the significance of breathing dysfunctions in health and to develop and refine the use of breathing therapy require further understanding of the functions and dysfunctions of breathing. This article explores some of the key functions of breathing and discusses the multi faceted nature of breathing dysfunctions and some of their consequences on mental and physical processes.

1.1. The respiratory pump and the movement of air

The 21,000 breaths per day taken by the average person come about as the breathing muscles attached to the chest wall act to change its shape. As dimensions and form of the chest wall are

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altered, resulting changes in pressure within the intrapleural and alveolar spaces drive the movement of air.[12]

In its normal relaxed state the 2 compartments of the chest wall, the rib cage or thorax and the abdomen, create an effective respiratory pump which moves in response to co-ordinated actions created by the diaphragm, scalenes, intercostals, abdominals and accessory muscles of respiration.[13,14] However under particular circumstances this co-ordinated action is lost.

This pump becomes impaired and or distorted in various diseases such as kyphoscoliosis, neuromuscular diseases, obesity, emphysema and asthma.[14] Its function can also change in response to psychological stress.[15–17] The changes in breathing pattern that occur in response to psychological states or various disease states may be appropriate responses to increased ventilatory or metabolic needs or helpful compensations for pathology. Inappropriate habits of muscle use may however be retained after the psychological, physiological or environmental conditions that initiated their development have passed. In this case they are dysfunctional and can complicate disease conditions and increase symptoms.

2. Dysfunctions of the biomechanics of breathing

2.1. The diaphragm

The diaphragm is the key to the function of other respiratory muscles and the primary driver of respiration. If the diaphragm is dysfunctional then the other respiratory muscles will change their function, often becoming overloaded. The normal phasic respiratory action of this large domed shaped muscle is to descent and flatten during inhalation, lifting and widening the lower 6 ribs. In most cases this action is accompanied by slight anterior motion of the abdomen. When the diaphragm is functioning normally, forward displacement of the abdomen is accompanied by lateral expansion and elevation of the lower 6 ribs. The extent of contribution from abdominal or lower rib cage motion can vary and still remain functional. The abdomen can displace anteriorly during inhalation or not move at all.[18] Decreased anterior motion of the abdomen can be compensated by more expansion in the lateral rib cage and vice versa enabling the decreases in intra thoracic pressure necessary for inspiratory airflow through a combination of abdominal and lower rib action.[14]

2.2. Asynchronous and paradoxical motion between rib cage and abdomen

Typically in the case of a dysfunctional diaphragm the abdominal muscles will alter their pattern of respiratory activity.[14,18,19] Paradoxical or asynchronous motion of abdomen, where the dimensions of the abdomen decrease during inspiration can be a sign of diaphragm dysfunction, weakness or paralysis.[18,20,21] However paradoxical inward motion of the abdomen during inspiration is not always dysfunctional. In fact inward abdominal motion during inspiration can be a normal and functional response to increased lung volume, physical activity, rapid respiratory maneuvers or standing posture that maintains abdominal pressure and helps the diaphragm to maintain a more ideal length and curvature.[21,22] During inhalation, paradoxical breathing is clearly dysfunctional when it is not adequately compensated by lateral motion of the rib cage and it is observed that the lower rib cage narrows instead of widening during inspiration.[22]

2.3. Upper body muscle dysfunctions

In the case of increased ventilatory demand or when breathing is inefficient the respiratory muscles of the upper rib cage, such as the scalenes, sternomastoid, upper trapezius and other anterior neck muscles such as hyoid and long colli increase their activity.[19,23,24] This results in increased vertical motion of the rib cage and elevation of the shoulders during the inspiratory phase of breathing.

A tendency to carry the head forward of the body with anterior rotation of the cranial base is a postural change commonly associated with breathing difficulty. Forward head posture is a well-known response to obstructed breathing and is common in children with chronic nasal allergy and mouth breathing because this head position opens the upper airways. Forward head posture can also indicate the presence of short flat diaphragm and weak abdominals due to the fact that positioning the head in front of the body increases the resting length of diaphragm.[19,25] This head posture while facilitating breathing has several adverse effects on the biomechanics of the head, neck and jaw and is associated with temporal mandibular joint syndrome, neck pain and headache.[19]

Shoulder problems may also result because hypertonic trapezius muscles contract during the initial stages of shoulder movement rather than towards the end.[25] This altered pattern of scapulo humeral motion is associated with shoulder pain and rotator cuff dysfunction.

3. Factors affecting efficiency of biomechanics of breathing

3.1. Hyperinflation and lung volumes

End expiratory lung volume is an important influence on the power of the diaphragm affecting its ability to act efficiently on the rib cage. Conditions like COPD, asthma and other conditions associated with increased inspiratory drive and inefficient expiration can lead to trapping of air in the lungs or hyperinflation. When this occurs the diaphragm becomes shorter and loses its curvature, as it is forced to take a lower resting position in the thorax. This shortening of the diaphragm fibers decreases the power and efficiency of the diaphragm due to the laws of length, tension relationships which apply to all contracting muscles.[26] It is also associated with loss of the curvature or doming of the diaphragm and a reduction of the zone of apposition. In this case the diaphragm fibers, which are attached to the lower 6 ribs, become orientated transversely rather than vertically. When the diaphragm contracts, it is ineffective in lifting and widen the lower rib cage. Instead there is a tendency for the diaphragm to pull the rib the lower lateral rib cage inward, decreasing the transverse diameter of the lower rib cage during inhalation.[14,27,28]

The more lung volume increases, the more the zone of apposition is reduced. When the lungs are at 30% of inspiratory capacity the costal diaphragm no longer expands the rib cage, and above 30% inspiratory capacity the costal diaphragm has a rib cage deflating action. At enlarged volumes there is also a tendency for the motion of the abdomen to reverse its timing so that inspiration is accompanied by inward motion of the abdomen and expiration is accompanied by outward motion of the abdomen.[21]

Reducing lung volumes can improve the function of the diaphragm. This is clearly demonstrated in COPD patients who experience reductions in lung volume after undertaking surgery to remove sections of their lungs. Lung reduction surgery has been shown in several studies to improve neuromechanical coupling of the diaphragm and individuals who receive this surgery consistently report increased exercise tolerance and reduced symptoms of dyspnea.[29–31]

3.2. Abdominal weakness

Abdominal muscle weakness aggravates diaphragm dysfunction.[1,19] Both tonic and phasic contraction of abdominal muscles

assist the function of the diaphragm during inspiration and expiration and can to some extent compensate for diaphragm dysfunction.[22,26,32] Contraction of the abdomen during inspiration prevents the diaphragm from shortening excessively during standing posture and during rapid and large volume respiratory maneuvers.[22,33] During expiration contraction of the abdomen assists diaphragm doming, increasing its length and curvature in preparation for effective contraction during inspiration. People with dysfunctional diaphragms, such as many individuals with COPD, can become more breathless and develop more abnormal breathing if tonic contraction of the abdomen is reduced.[34] On the other hand, increasing abdominal tone artificially using abdominal binding can assist these individuals.

3.3. Rib cage stiffness

During hyperinflation the ribs shift from their normal oblique position to a more horizontal position, impairing inspiratory action of rib cage muscles and making the rib cage stiff and difficult to expand.[35] Restrictions of the rib cage then further inhibit diaphragm function.[36]

3.4. Respiratory drive

When respiratory control centres in the brain receive messages from the cortex, limbic system, chemoreceptors or mechanoreceptors that ventilation is inadequate, the respiratory muscles adjust their functions to increase ventilation. If respiration is stimulated for prolonged periods, the diaphragm and accessory muscles of breathing may become chronically hypertonic.[13,21,37] Typical changes in breathing pattern that reflect increased respiratory drive include, upper chest breathing with decreased lateral expansion of the lower rib cage and tendency to asynchronous and paradoxical breathing.

Disease processes can increase ventilatory needs, stimulate respiratory drive and alter respiratory control often creating characteristic changes in breathing pattern. This is seen in respiratory conditions such as asthma and COPD and in heart disease.[38–40] Psychological and emotional states also alter respiratory control and respiratory rhythm generation.[41–44] Subsequently changes in breathing pattern which can be dysfunctional are very common in people with respiratory and cardiovascular disease and under psychological stress.

4. Breathing in postural and motor control

The use of breathing muscles during respiration affects how these muscles are used for non-breathing movement and for postural support. Muscles such as the diaphragm, transverse abdominus and pelvic floor muscles are important for motor control and postural support as well as for breathing. If their function is compromised there is an increased susceptibility to back pain and injury.[45–48] The respiratory functions of these muscles need to be integrated with their many other functions, such as swallowing, speech, valsalva maneuvers, spinal stabilisation and movement of the trunk and limbs. This need for integration of often unrelated functions places considerable demands on mechanism of motor control.[49,50]

In situations where respiratory drive is increased such as stress, disease or physical exercise, the ability of the respiratory muscles to perform their postural tasks is reduced. Interestingly the presence of respiratory disease is a stronger predictor for lower back pain than other established risk factors.[51] A study by McGill showed that artificially stimulated respiration led to decreased support of the spine during a load challenge.[52] Hodges in a subsequent study showed that the postural functions of the diaphragm were significantly reduced and in some cases abolished when respiration was stimulated.[53]

Respiratory muscles that are responding to increased respiratory drive due to stress or disease produce different breathing patterns to those seen in normal subjects.[33,54] The respiratory muscles in these situations can become shortened or hypertonic and subsequently less powerful and less efficient.[26] They also lose their normal co-ordinated function and one would expect this to result in increased demands on motor control mechanisms. These factors compromise the ability of respiratory muscles to create the fine tuning adjustment required for postural support. The relationship between dysfunctional breathing and postural stability, motor control and back pain has not been studied extensively however clinical observation supports the notion that patients with poor breathing muscle co-ordination are more prone to chronic back pain and neck pain.[56,57]

5. Biomechanical influences on hemodynamics and the lymphatic system

A functional respiratory pump creates rhythmic pressure fluctuations between the thorax and the abdomen that are important for the movement of body fluids such as blood and lymph. Normal pressure development during the respiratory cycle is characterized by a decrease in intra thoracic pressure during inhalation and an increase in intra abdominal pressure during expiration.[58,59] Paradoxical motion of the abdomen and dysfunction of the diaphragm alters normal pressure relationships between the thoracic and abdominal compartment during inspiration and expiration. In paradoxical motion of the abdomen during inspiration, abdominal pressures can decrease rather increase during inspiration.[21]

Osteopaths have long considered that restoration of lymphatic function and treatment of oedema and infection was related to proper function of the diaphragm, rib cage and abdomen.[1,60,61] Miller, one of the early Osteopathic developers of manual pump techniques for lymphatic drainage, noted that thoracic and abdominal pump techniques were exaggerations of respiratory movements.[62]

Respiration is one of the important extrinsic influences on lymphatic flow, interacting with intrinsic motility of lymph vessels and organs to either enhance or dampen their activity.[63] The pressure differentials created by respiration create fluctuations in central venous pressure which directly affect lymph drainage from the lungs and abdomen[64,65] and affect transmural pressure in lymphatic vessels which modulate the function of intrinisic pacemakers in the lymphatic system. Recent research also shows that the lymphatics in the diaphragm itself form a specialised system for draining fluid from the peritoneal cavity and returning it to the vascular system.[66] This suggests that breathing patterns which alter normal respiratory pressure dynamics have detrimental effect on the function of the cardiovascular and lymphatic systems.

6. The role of breathing in physiological regulation

Breathing also affects physiological regulation because of its ability to entrain respiratory oscillations to oscillations in other systems and its role in maintaining homestasis of oxygen, carbon dioxide and pH.

7. Oxygen, carbon dioxide and pH

Breathing, by exchanging carbon dioxide (CO_2) for oxygen (O_2), controls the fundamental gaseous fuels of life's energy and assists in maintaining optimal conditions for the biochemical aspect of the

internal milieu. Oxygen concentrations are generally well maintained by anyone who does not have severe pathology of the lungs, heart or central nervous system. Functional breathing disorders do not generally affect O_2 however even relatively healthy people can over breathe sufficiently to become depleted in CO_2.

Low CO_2 levels can develop quickly because of the very high solubility of CO_2 (twenty times more soluble than oxygen). Its ease of excretion means that increased ventilation resulting from non-metabolic stimuli, for example stress, anxiety or increase sensations of dyspnea, can result in depletion of CO_2. Breathing in excess of metabolic demands is called hyperventilation. The effects of hyperventilation and carbon dioxide depletion are far reaching and include inhibiting the dissociation of oxygen from hemoglobin in the blood, resulting in low oxygen concentration in tissues. The effects on the brain and the nervous system of hypocapnia are particularly pronounced and include reduced cerebral blood flow and increased neuronal excitability. Regulation of cerebro spinal fluid pressure, intracellular pH and cellular metabolism are impaired. Hypocapnia produces bronchoconstriction in the lungs and vasoconstriction in the blood vessels. Blood pressure, myocardial contractility and cardiac blood flow can also be adversely affected as can pH regulation and electrolyte balance.[67,68]

8. Hyperventilation and hypocapnia

Given the large number of physiological effects of hypocapnia it is not surprising that until the 1990s scientific literature primarily linked breathing dysfunction with hyperventilation syndrome (HVS). The diagnosis of HVS was generally made on finding an assortment of symptoms believed to be caused by either acute or chronic hypocapnia or the consequences of respiratory alkalosis.[2,5,70]

8.1. History of hyperventilation syndrome

Since the beginning of the nineteenth century it has been known that symptoms such as numbness, dizziness, muscle hypertonicity and tingling sensations could be brought on by overbreathing[71] and that these symptoms could be attributed to hypocapnia and respiratory alkalosis.[72] The idea of a hyperventilation syndrome characterized by a larger number of psychological and somatic symptoms that could be related to either acute or chronic hyperventilation began to develop after Kerr reported his findings on the effects of hyperventilation challenge on 35 patients with unexplained symptom. His patients were able to reproduce their symptoms by voluntary and prolonged hyperventilation.[3] The name Hyperventilation Syndrome began to be used at around this time and was considered to exist mostly in neurotic patients and to be a relatively rare condition.[4] The range of symptoms attributed to Hyperventilation Syndrome gradually increased until a large number of symptoms of central and peripheral neurovascular, muscular, respiratory, cardiac, gastrointestinal origin were attributed to this syndrome.[6] Dr. Claude Lum diagnosed 700 patients with medically unexplained symptoms such as palpitations including chest pain, dizziness, parasthesia, breathlessness, epigastric pain, muscle pain, tremor, tetany, dysphagia, tension and anxiety as suffering from hyperventilation syndrome. The diagnosis seemed to be confirmed when the majority of these patients recovered from most of their symptoms after 7 weeks of intensive breathing training.[2] Later studies such as those by Han, however, were to show that individuals with the symptoms generally attributed to HVS who received benefit from breathing retraining did not necessarily improve because of changes in their carbon dioxide levels.[73]

8.2. Doubts about the role of chronic hypocapnia in hyperventilation syndrome

From the late 1980s scientists began to question the role of chronic hypocapnia in HVS. Symptoms which were produced by voluntary hyperventilation were assumed to be elicited by acute hypocapnia, but on closer investigation could not always be consistently linked with chronic carbon dioxide deficit. Howell measured PCO_2 levels in 31 patients with disproportionate breathlessness and other symptoms of hyperventilation and found that they had mostly normal levels of carbon dioxide.[74] Han in comparing 399 symptomatic hyperventilators with 347 normals found no difference in ETCO2.[75] In a major review of hyperventilation Hardonk and Beumer found in their own and other studies that $ETCO_2$ levels were not significantly different in symptomatic or normal controls when measured in the laboratory. By the mid 1990s Gardener in a review of HVS described the " uncertainty and lack of consensus about the boundaries and even existence of this syndrome". He reported that patients could have low carbon dioxide but no symptoms, while other people could have relatively normal carbon dioxide levels but still exhibit the symptoms of HVS.[76]

Acute hypocapnia can be induced by the hyperventilation provocation test (HVPT) and the onset of symptoms in HVS patients after performing the HVPT was believed to be due to the acute hypocapnia produced by this voluntary overbreathing.[77] A debilitating and almost fatal blow to the hyperventilation syndrome came from Hornsveld and Garssen whose research appeared to indicate that acute hypocapnia was not the mechanism of the gold standard of HVS diagnosis, the HVPT. In their study 115 patients believed to have HVS were given the Hyperventilation Provocation Test (HVPT). 74% of their subjects were positive on the test and reported the onset of their symptoms after hyperventilation. However 65% of these responders were also positive on a placebo test, during which CO_2 levels were kept stable through manual titration. A second stage of this study, involving transcutaneous monitoring of CO_2 levels of patients in their daily lives, showed that patients suffering from attacks of the HVS symptoms suffered only a very slight drop in CO_2 levels at the onset of their symptoms and this usually followed rather than preceded the onset of symptoms.[78] As their study, and others, found that neither chronic or acute deficiency of CO_2 could be experimentally linked to HVS these authors recommended that the term hyperventilation syndrome be discontinued.[8] In recognition of the fact that causes of breathing related symptoms were unclear and often associated with psychological disturbance, researchers proposed that the term hyperventilation syndrome be replaced with behavioral breathlessness[74] or unexplained breathing disorder (UBD) or chronic symptomatic hyperventilation.[79] Subsequently the term hyperventilation syndrome is used infrequently and the terms dysfunctional breathing[10] breathing pattern disorder[80] have become more common.

However the door on hyperventilation and hypocapnia may have been shut prematurely. Hypocapnia may not be the prime suspect in HVS symptoms but an accomplice whose contribution varies according to individual susceptibility and exact symptoms. Recent studies indicate that carbon dioxide functions as one contributing factor to symptoms and its influence is probably moderated by neurological and other factors that influence symptom perception.[81] Not all symptoms of HVS appear to be equally related to carbon dioxide levels, a greater relationship exists for neurovascular symptoms than for uncomfortable respiratory sensations.[82]

The physiological effects of hypocapnia have been too well documented to be irrelevant.[67,68] Modern day researchers need to

interpret the finding of Hornsveld et al. while still keeping in mind Haldanes experiments in 1908 which clearly shown that hyperventilation caused central and peripheral neurovascular symptoms of dizziness, sensations of numbness and tingling and tetany in healthy people and the long history of studies on symptomatic individuals which repeatedly showed that voluntary acute hyperventilation caused the recurrence of patients primary and secondary complaints which could not be explained in other ways.[70] Also worth remembering are the studies which demonstrated that administration of carbon dioxide either through rebreathing or by administration of CO_2 enriched gas mixtures was able to eliminate the symptoms of hyperventilation that either came on spontaneously or were brought on by hyperventilation provocation tests.[4,5]

Chronic hypocapnia when found can and should be normalised, particularly in symptomatic individuals and individual responses to acute hypocapnia. Clinical experience also suggests that the hyperventilation provocation test may indeed be relevant to diagnosis and treatment if used in conjunction with other investigations.

9. Breathing, homeostasis and oscillations

Breathing, by creating fluctuations in the chemical composition of the blood, circulation and vascular pressure and by its effects on autonomic reflexes acts as an extrinsic influence on other oscillating physiological systems. Oscillations, which are defined as systematic rhythms in physiological variables, are found in most living system including those of the human body. Oscillations in single systems and synchronisation between oscillating systems help physiological control systems to maintain homeostasis and appropriate and rapid responsiveness to the continual changing needs of the body. When oscillations of two or more systems are synchronised it increases physiological efficiency by enabling the functions of these systems to be co-ordinated. This prevents energy being wasted on non productive functions.[85,86] Cyclic activity also allows systems to rest and renew themselves during cycles of decreased activity.

One aspect of breathing functionality is the ability of breathing oscillations to interact with oscillations in other physiological systems in ways that optimise their functions. Breathing oscillations interact with oscillations of heart rate and blood pressure,[87,88] the lymphatic system[63] the digestive system,[89,90] brain waves[91] and probably the rhythmic fluctuations occurring in cellular metabolism.[92] When respiratory oscillations entrain other oscillating systems it can enhance the physiological function of both systems. A well-known example is the phenomenon of respiratory sinus arrhythmia (RSA), where heart rate variability is entrained to respiratory frequencies. RSA improves the efficiency of gas exchange by coupling increased heat rate to the inspiratory phase of respiration.[93]

9.1. Breathing pattern dysfunctions and resonant frequencies of breathing

Breathing can be consciously manipulated to increase its ability to entrain other oscillations and increase physiological regulation. When breathing frequency is slowed to between 4 and 6 breaths per minute (0.06–0.1 Hz) oscillations in blood pressure, heart rate and autonomic nervous system tend to synchronise at this frequency and be amplified due to resonance effects between these systems.[94–96] These resonance effects between cardiorespiratory oscillations and autonomic function are important for homeostasis and maintenance of health as evidence by the fact that training the bodies ability to increase them assists people with a range of conditions including asthma, COPD, depression, hypertension and irritable bowel syndrome.[97–100] Individuals with paradoxical breathing and thoracic dominant breathing have a decreased ability to achieve resonance effects between oscillators (unpublished data), indicating that dysfunctions of breathing pattern impair the body's ability to regulate itself through co-ordinating homeostatic cardiorespiratory oscillations.

10. Breathing, stress, emotion and the autonomic nervous system

Chronic emotional stress and increased mental load can alter respiratory regulation in several ways: 1) with regard to drive; 2) breathing pattern and timing; and 3) metabolic appropriateness of the respiratory response.[42]

Breathing is particularly sensitive to states of hyperarousal, during which signs of increased respiratory drive are evidence of the body's readiness for action. Hyperarousal brought on by mental and emotional processes contributes to allostatic load and affects the capacity of the body to maintain its stability and response to change.[101] Anticipation of coming physical and emotional events has the distinct effect of increasing respiratory rate, reducing time of exhalation and changing respiratory pattern.[44,102] Breathing irregularity is a common feature of patients with anxiety and panic disorder, indicating dysregulation of normal breathing control mechanisms in these individuals.[75,103] Specific effects on the diaphragm are also seen. Fluroscopic studies show that in situations of emotional stress, the diaphragm shows signs of hypertonicity becoming flattened and immobile.[15,16]

Breathing which is responding to feelings and thoughts, rather than metabolic cues from chemoreceptors, may not be aligned to the actual physical needs of the body or its metabolic requirements.[44,88] When mental and emotional factors such as fear, grief, anxiety or depression drive breathing regulation, homeostatic and biomechanical functions of breathing can be disturbed.[42,43] Emotions are drives to particular types of action or expression. Repeatedly frustrated ability to act on strong emotional drives can lead to physiologically and biomechanically inappropriate breathing, tuned to the anticipation of action that does not occur.

A fundamental survival function of increased respiratory drive is to prepare the body for fight and flight. However homeostasis is best served through the functions of the parasympathetic nervous system, whose activity is associated with a relaxed, slow and abdominal breathing pattern.[104] Rapid, shallow and thoracic dominant breathing with high levels of tonic contraction of respiratory muscles as found in situations requiring high levels of ventilation probably indicates a system that is having difficulty returning to a state of rest. In this situation energy is wasted and homeostatic functions needed for repair and renewal are impaired.

Controlled respiration can help the system to return to a physiological rest state. It appears to act on the brain and the autonomic nervous system, synchronising neural elements in the brain and autonomic nervous system and creating a state of pycho-phsyiological coherence.[105,106] The changes induced by controlled breathing appear to order and regulate neurological function, improving psychological and emotional states.[107,108] The regulatory effects of breathing on the autonomic nervous system have been investigated from several perspectives. Several studies have shown that in the short term controlled breathing can decrease sympathetic nervous system activity and increase parasympathetic nervous system and with continued, regular practice can create long term improvements in autonomic balance and increased vagal tone.[109–113]

11. Breathing as a therapeutic tool

There are a large number of breathing therapies utilizing a wide range of techniques and several of these appear beneficial. The main rationales for breathing therapies are that they: 1) correct some aspect of dysfunctional breathing; 2) support one or several of the functions of breathing and thus stimulate healing; or 3) provide a means for regulation of mental and emotional states. The territory covered by breathing therapies is large covering a broad area ranging over psychology, physiology, spirituality and biomechanics. The evidence for the ability of breathing therapies to correct breathing dysfunctions and support the functions of breathing is relatively sparse as research has tended to focus on disease or psychological outcomes rather than investigating effects on breathing parameters.

There are several breathing therapies that aim to correct hyperventilation and restore normal carbon dioxide tension. Breathing biofeedback using a capnometer to monitor end-tidal carbon dioxide levels during breathing training is one approach to treating hypocapnia. Biofeedback training that employs the use of a capnometer aims at normalizing end-tidal CO_2 at approximately 5%. There are various systems for capnometry biofeedback available to the practitioner and in recent years these have become increasingly available.[114,115] Other breathing therapists use no instrumentation and rely on a combination of slow controlled breathing, breathing pattern correction and relaxation strategies.[116,117] The Buteyko Breathing Technique (BBT) is yet another technique whose primary aim is the correction of acute and chronic hypocapnia. It uses a unique set of breathing techniques in which breath holding is combined with reduced volume breathing. BBT exercises aim to increase carbon dioxde and reset chemoreceptor thresholds however they may also be useful in reducing hyperinflation.[118]

The practice of controlled breathing as a means of self-regulation and restoration of mental and emotional balance is a part of Indian and Taoist Yoga and is also in the domain of modern respiratory psychophysiology. Modulation of the breath and mindful attention to the breath are important parts of many meditation techniques.[119] Ancient systems such as Indian Yoga pranayama and the breathing techniques of Qi Gong teach that specific types of breathing exercises can direct vital force or energy and through this benefit the health of the mind and body.[120–123]

Respiratory psycholphysiology uses a scientific approach to understanding the physiological processes that link mental and emotional states to breathing. Practitioners of respiratory psychophysiology utilize evidence based breathing techniques including resonant frequency breathing to promote emotional self regulation and to achieve efficient physiological states that promote healing.[95]

Another interesting breathing therapy used mostly to enhance athletic performance in athletes is Intermittent Hypoxic Training (IHT).[124] This therapy exposes individuals to carefully controlled levels of hypoxia interspersed with rest periods during which they breathe normal atmospheric air or oxygen enriched air. IHT has the effect of enhancing adaptation to the specific stress of hypoxia but also results in a general increase in stress tolerance. Other benefits of IHT include enhanced antioxidant capacity, improved metabolism and increased aerobic capacity. IHT is believed to enhance mitochondrial function as it has been shown to increase the efficiency with which the body uses oxygen. In Russia IHT has been studied extensively for over 30 years and is used to treat a large number of diseases.[125]

There is a growing body of scientific evidence for the effectiveness of breathing therapies in a range of diseases including asthma, heart disease, anxiety and depression, and they are being increasingly included in therapeutic protocols. Research into Buteyko Breathing Techniques has focused on asthma and there have been at least five published clinical trials on BBT for this condition.[126–132] These clinical trials indicate that people learning the Buteyko Method are able to substantially reduce medication with no deterioration in their lung function or asthma control, although no studies have demonstrated objective changes in lung function. The quality of evidence of the Buteyko Method according to an Australian Department of Health report is stronger than any other complementary medicine treatment of asthma.[133] Recent studies indicate that several other types of breathing therapies also help asthma including resonant frequency breathing biofeedback,[97] capnometry biofeedback[134] and breathing rehabilitation.[116,135]

Breathing therapy has also been found to be very helpful for cardiovascular disease. In a study comparing patients who received standard cardiac rehabilitation with those receiving additional training in breathing therapy after myocardial infarction (MI), it was found that the breathing therapy group had about a 30% decreased in cardiac events at 5 year follow-up.[136] Another study showed that exercise training in patients with MI was not always successful in preventing future cardiac events, however the risk of treatment failure was reduced by half when relaxation and breathing training was added to exercise training.[137] Other breathing therapy based on yoga breathing was also found to improve hemodynamics and various cardiorespiratory risk factors in cardiac patients.[138,139]

The effectiveness of breathing therapies in psychological conditions and chronic stress has also been shown in several studies. In major depression, both resonant frequency biofeedback and yoga based breathing techniques appear to be effective.[99,139,140] People with anxiety and panic disorder also show beneficial response to capnometry and other breathing therapy protocols.[73,141,142] The effects of breathing on the autonomic nervous system have been demonstrated in several studies on yoga pranayama. Regular and prolonged practice of several brief breathing protocols combining slow breathing, long breath retentions and nostril breathing have the effect of increasing resetting autonomic balance and amplifying parasympathetic nervous system function.[109]

This sampling of the literature on breathing dysfunction and breathing therapies, while not exhaustive, strongly suggests that breathing therapies have the potential to be of benefit to patients with many types of conditions. It appears that use of breathing therapies is not proportional to the level of evidence supporting their efficacy. One reason for this may be the lack of coherent models for explaining the mechanisms of breathing therapies. Understanding of these mechanisms needs to be developed to refine and direct the use of breathing interventions. I propose that there are likely to be a range of mechanisms for breathing therapies and these should be sought within the various functions of breathing and its dysfunctions.

Part two of this paper will elaborate on the role of breathing dysfunction in various diseases and present some diverse approaches to evaluation of various aspects of breathing dysfunction.

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Synonyms
Hyperventilation; Neurocirculatory asthenia; Soldier's heart; Soldier heart

Historical note and nomenclature

According to 1 consensus definition, "hyperventilation syndrome is a syndrome characterized by a variety of somatic symptoms induced by physiologically inappropriate hyperventilation and usually reproduced in whole or in part by voluntary hyperventilation" (Lewis and Howell 1986). Acute hyperventilation with obvious tachypnea accounts for about 1% of all cases of hyperventilation (Lum 1975). The other 99% of cases are due to chronic hyperventilation where there may be a modest increase in respiratory rate or tidal volume, which may not even be apparent to the patient or a medical observer.

The symptoms of hyperventilation syndrome have been recognized for at least 125 years. In 1871, Da Costa published a paper, *On Irritable Heart; a Clinical Study of a Form of Functional Cardiac Disorder and its Consequences*, describing 300 Union soldiers in the American Civil War with a mysterious illness (Da Costa 1871). He felt the condition could be seen in private practice as well. Symptoms included palpitations, chest pain, shortness of breath or oppression on exertion, indigestion, abdominal distention, and diarrhea. Headache, giddiness, disturbed sleep, and dizziness were "all indicative of disturbed circulation in the cerebro-spinal centres." Da Costa reasoned that "the heart has become irritable, from its over-action and frequent excitement...." During World War I, similar symptoms often associated with fatigue were also attributed to cardiovascular dysfunction and described as "soldier's heart" (Lewis 1919) or "neurocirculatory asthenia" (Levine 1965). In contrast, Gowers used the terms "vagal" and "vaso-vagal" for these symptoms, which could include numbness and tingling of the extremities (Gowers 1907).

In 1922, Goldman was the first to make the connection between "forced ventilation" and tetany and postulated that the tetany was due to alkalosis (Goldman 1922). Kerr and colleagues introduced the term "hyperventilation syndrome," and they described the variety of symptom complexes caused by physical phenomena associated with anxiety states, which could often be reproduced in the examining room with the "hyperventilation test" (Kerr et al 1937; 1938).

Lewis contended that acute and chronic hyperventilation syndrome occurred frequently and described the common and atypical presentations, pathophysiology, and therapy (Lewis 1953). He reported that paresthesias were occasionally asymmetrical and could even be unilateral. Tavel described patients with hyperventilation syndrome presenting with unilateral paresthesias at times associated with subjective unilateral weakness that involved the left side of the face and body more commonly than the right (Tavel 1964).

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Clinical manifestations

The manifestations of hyperventilation syndrome are listed in Table 1. Patients with different symptoms may see different specialists. Cardiologists may see those with complaints of chest pain, palpitations, and shortness of breath. Neurologists frequently see patients describing dizziness and paresthesias (Pincus 1978; Perkin and Joseph 1986).

Table 1. Symptoms and Signs of Hyperventilation Syndrome

General

- Fatigability, exhaustion, weakness, sleep disturbance, nausea, sweating

Cardiovascular

- Chest pain, palpitations, tachycardia, Raynaud phenomenon

Gastrointestinal

- Aerophagia, dry mouth, pressure in throat, dysphagia, globus hystericus,
- Epigastric fullness or pain, belching, flatulence

Neurologic

- Headache, pressure in the head, fullness in the head, head warmth
- Blurred vision, tunnel vision, momentary flashing lights, diplopia
- Dizziness, faintness, vertigo, giddiness, unsteadiness
- Tinnitus
- Numbness, tingling, coldness of face, extremities, trunk
- Muscle spasms, muscle stiffness, carpopedal spasm, generalized tetany, tremor
- Ataxia, weakness
- Syncope, seizures

Psychological

- Impairment of concentration and memory
- Feelings of unreality, disorientation, confused or dream-like feeling, déjà vu
- Hallucinations
- Anxiety, apprehension, nervousness, tension, fits of crying, agoraphobia
- Neuroses, phobias, panic attacks

Respiratory

- Shortness of breath, suffocating feeling, smothering spell, inability to get a good breath or breathe deeply enough, frequent sighing, yawning

The most common cause of distal symmetrical paresthesias is hyperventilation syndrome (Macefield and Burke 1991). Although physicians generally recognize bilateral paresthesias of the face, hands, and feet as due to hyperventilation syndrome, many neurologists are not aware that hyperventilation can cause unilateral paresthesias. In 2 studies of volunteer groups, hyperventilation produced predominantly unilateral paresthesias in 16%, and these involved the left side in over 60% (Tavel 1964; Evans 1995; 2005). Of those with hand numbness, often only the fourth and fifth fingers are involved. Unusual patterns of numbness reported include 1 side of the forehead, the shoulders, and 1 side of the abdomen. Unilateral paresthesias more often involving the left side have also been reported (Tavel 1964; Blau et al 1983; Perkin and Joseph 1986; Brodtkorb et al 1990; O'Sullivan et al 1992).

Patients may report a variety of psychological complaints, commonly including anxiety, nervousness, unreality, disorientation, or feeling "spacy." Impairment of concentration and memory may be described as part of episodes or alternatively as symptoms of an

underlying anxiety neurosis or depression. A patient's concern about the cause of the various symptoms of hyperventilation may result in feelings of impending death, fear, or panic, which may accentuate the hyperventilation. Patients with hyperventilation syndrome have a mean group profile very similar to patients with pseudoseizures: a neurotic pattern where patients respond to psychological stress with somatic symptoms (Brodtkorb et al 1990). Other complaints such as déjà vu or auditory and visual hallucinations are rare (Allen and Agus 1968; Evans 1995; 2005).

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Clinical vignette

A 47-year-old woman presented with a few-week history of daily episodes of lightheadedness, nervousness, and feelings of weakness, coupled with numbness of the left arm, left leg, and perioral area. The numbness was associated with chest tightness and difficulty inhaling and lasted minutes at a time. She denied any recent stress or depression. She had normal blood and treadmill tests. Past medical history was unremarkable. General physical and neurologic examinations were normal. The hyperventilation test resulted in numbness and tingling periorally, as well as in the left upper and lower extremities. These symptoms were associated with chest tightness.

A MRI scan of the brain with MRA was normal. She was advised to slow her breathing or breathe into a paper bag if additional spells occurred. On followup, the episodes had resolved.

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Etiology

Hyperventilation syndrome is frequently associated with anxiety or stress, although some patients have no detectable psychiatric disorder and develop a habit of inappropriately increased ventilatory rate or depth (Bass and Gardner 1985).

Common triggers of acute hyperventilation syndrome include anxiety, nausea and vomiting, and fever due to the common cold (Hirokawa et al 1995).

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Pathogenesis and pathophysiology

Acute hyperventilation reduces arterial pCO2, resulting in alkalosis. Respiratory alkalosis produces the Bohr Effect, a left shift of the oxygen dissociation curve with increased binding of oxygen to hemoglobin and reduced oxygen delivery to the tissues. The alkalosis also causes a reduction in plasma Ca2+ concentration. Hypophosphatemia may be due to intracellular shifts of phosphorus caused by altered glucose metabolism (Brautbar et al 1980). In chronic hyperventilation, bicarbonate and potassium levels may be decreased because of increased renal excretion (Pearson et al 1986). Finally, stress can produce a hyperadrenergic state that may trigger hyperventilation through beta-adrenergic stimulation (Magarian 1982).

Central and peripheral mechanisms have been postulated for production of neurologic symptoms during hyperventilation (Beumer and Bruyn 1993). Voluntary hyperventilation can reduce cerebral blood flow by 30% to 40% (Gotoh et al 1965; Jibiki et al 1992). Symptoms and signs such as headache, visual disturbance, dizziness, tinnitus, ataxia, syncope, and various psychological symptoms may be produced by diminished cerebral perfusion.

The precise cause of generalized slowing of brain waves during hyperventilation is not certain. This response is most common and pronounced in children and teenagers, diminishes in young adults, and is rare in the elderly. A brainstem-mediated response to hypocarbia has been proposed (Patel and Maulsby 1987). The response may be due to metabolic rather than just hemodynamic factors (Kraaier et al 1992). Hypoglycemia can accentuate the generalized slowing or buildup.

There have been additional postulates to explain the manifestations of hyperventilation. Muscle spasms and tetany may be due to respiratory alkalosis and hypocalcemia. The

finding that there is no relationship between the rate of fall of pCO2 and the onset of dizziness and paresthesias suggests that symptoms may be due to hypophosphatemia (Rafferty et al 1992). Hypophosphatemia can result in symptoms such as tiredness, dizziness, poor concentration, disorientation, and paresthesias. A hyperadrenergic state may result in tremor, tachycardia, anxiety, and sweating. Hypokalemia can cause muscle weakness and lethargy.

The cause of bilateral and unilateral paresthesias is not certain; evidence exists for both a central and peripheral mechanism. A reduction in the concentration of extracellular Ca2+ may increase peripheral nerve axonal excitability, resulting in spontaneous bursting activity of cutaneous axons, perceived as paresthesias (Macefield and Burke 1991). Lateralization of symptoms might be explained by anatomic differences in the peripheral nerves and their nutrient vessels (Galin et al 1977).

Alternatively, symmetrically decreased cerebral perfusion could account for bilateral paresthesias and asymmetrically decreased perfusion for unilateral paresthesias. O'Sullivan and colleagues reported nonspecific, asymmetric slowing of brain waves in the hemisphere opposite to the side of unilateral paresthesias in hyperventilators and normal bilateral somatosensory evoked potentials (O'Sullivan et al 1992). Although anatomic differences in the cerebral vasculature might explain the unilateral paresthesias, normal magnetic resonance angiographic findings in 2 cases argue against this (Evans 1995). Additionally, there is a single report of asymmetrically decreased cerebral blood flow with decreased flow in the right parietal area with left-sided symptoms (Evans 1995).

It is not known why unilateral paresthesias occur more often on the left side of the face and body. One hypothesis is that psychosomatic symptoms are associated with right hemisphere psychic processes. During stress and emotional arousal, the right hemisphere is activated more than the left (Tucker et al 1977). Symptoms of conversion or hyperventilation are more likely to occur on the left side of the face and body (Galin et al 1977; O'Sullivan et al 1992). However, this hypothesis does not explain the increased frequency of left-sided paresthesias in normal subjects who are asked to hyperventilate.

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Epidemiology

Hyperventilation syndrome occurs in about 6% to 11% of the general patient population (Brashear 1983). In a clinic that evaluated patients with dizziness, hyperventilation syndrome accounted for 24% of the cases (Drachman and Hart 1972). Most studies have reported hyperventilation syndrome occurring 2 to 7 times more frequently in women than in men, with most patients ranging in age between 15 and 55 years (Garssen and Rijken 1990). One large study reported that patients with acute hyperventilation syndrome ranged in age from 5 to 85 years and was particularly prevalent in women in their late teens (Hirokawa et al 1995). The prevalence of chronic hyperventilation is highest in middle-aged women (Hirokawa et al 1995). In studies of patients with neurologic symptoms of hyperventilation syndrome, the percentage of females ranges from 50% (Blau et al 1983) to 67% (Perkin and Joseph 1986; Brodtkorb et al 1990; O'Sullivan et al 1992) to 87% (Pincus 1978).

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Prevention

For psychogenic cases of hyperventilation syndrome, avoidance of triggers is a preventative measure.

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Differential diagnosis

Hyperventilation syndrome has organic and physiological as well as emotional and habitual causes. Less than 5% of hyperventilation has a solely organic cause, 60% has a psychogenic (emotional and habitual) basis, and the remainder has varying combinations (Brashear 1984). The variety of organic disorders that can result in hyperventilation

include: (1) effects of salicylate, caffeine, topiramate (Laskey et al 2000), and other drugs; (2) cirrhosis and hepatic coma; (3) acute pain such as that accompanying a myocardial infarction; (4) splenic flexure syndrome, cholecystitis, fever, and sepsis; and (5) dissecting aortic aneurysm, respiratory dyskinesia, pulmonary embolism, pneumothorax, interstitial lung disease, asthma, and heat and altitude acclimatization (Brashear 1983; Block and Szidon 1994).

Neurologic disorders that may cause hyperventilation include Rett syndrome, Joubert syndrome, Reye syndrome, pyruvate dehydrogenase deficiency, biotin-dependent multiple carboxylase deficiency, malignant hyperthermia, brainstem tumor, primary cerebral lymphoma, encephalitis, brainstem strokes, thalamic hemorrhage, syringobulbia, and neurogenic pulmonary edema due to intracranial hypertension (Beumer and Bruyn 1993). Severe hyperventilation can occur in the absence of psychiatric, respiratory, neurologic, or other organic abnormalities (Bass and Gardner 1985).

In patients diagnosed with hyperventilation syndrome by neurologists, the misdiagnoses of referring physicians have included epilepsy, migraine, multiple sclerosis, arteriovenous malformation, cerebrovascular disease, vertebrobasilar insufficiency, brachial neuritis, angina, malingering, vasovagal attacks, functional illness, hypoglycemia, and cerebral tumor (Blau et al 1983; Perkin and Joseph 1986). Hyperventilation might also contribute to some of the manifestations of migraine such as syncope.

Cardiac abnormalities should certainly be considered in those patients with chest pain. The distinction between angina and hyperventilation syndrome at times is difficult because hyperventilation can produce electrocardiogram changes including T-wave inversions, systolic time-segment depression, and systolic time-segment elevation in patients without coronary artery disease (Heckerling and Hanashiro 1985). Some patients with angina may hyperventilate in response to their pain and anxiety. The symptoms of mitral valve prolapse and hyperventilation syndrome overlap. In some patients, symptoms may be due to hyperventilation (Tavel 1990).

The symptoms of panic attacks greatly overlap with hyperventilation syndrome, and the differential diagnosis is quite similar (Tesar and Rosenbaum 1993; Stahl and Soefje 1995). The pathophysiology of panic attacks is controversial; hyperventilation syndrome has been suggested as a cause (Ley 1985; Nutt and Lawson 1992; Folgering 1999). Patients diagnosed with panic attacks that report brief episodic unilateral paresthesias or weakness may have the neurologic symptoms reproduced with the hyperventilation test (Coyle and Sterman 1986).

Tonic spasms (paroxysmal dystonia) of multiple sclerosis can be somewhat similar to the muscle spasms, tetany, and paresthesias of hyperventilation syndrome. The episodes consist of brief, recurrent, often painful abnormal posturing of 1 or more extremities without alteration of consciousness, loss of sphincter control, or clonic movements. They last for 10 seconds to 3 minutes and recur as often as 30 times daily. Some patients may experience brief sensory disturbances in the involved extremity before or during the attack. Because the episodes can be the initial presentation of multiple sclerosis (Heath and Nightingale 1982) and can be triggered by hyperventilation (Shibasaki and Kuroiwa 1974), diagnostic confusion might result.

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Diagnostic workup

The acute form of hyperventilation syndrome is easily recognized. However, the chronic form is less easily recognized because the breathing rate is not reported as rapid or does not appear rapid and because the symptoms may appear to be atypical. For example, a respiration rate of 18 per minute combined with an increased tidal volume of 750 mL per minute may lead to overbreathing that is not easily detectable. Because the chronic disorder is intermittent, spot arterial pCO2 or end tidal volume pCO2 results can be normal. The diagnosis depends on reproducing some or all of the symptoms with the

hyperventilation provocation test and excluding other possible causes by either clinical reasoning or laboratory testing when indicated. Patients frequently report only 1 or 2 symptoms but, on performing the hyperventilation provocation test, report other symptoms that appear during their typical episodes that they had forgotten.

The hyperventilation provocation test can be performed with either an increased ventilation rate of up to 60 per minute or simply deep breathing for 3 minutes (Lum 1987). Based on a study of healthy subjects, a minimum duration of 3 minutes and end-tidal pCO2 decreasing to at least 1.9 kPa or dropping well over 50% of baseline should elicit symptoms in most people (Hornsveld et al 1995). Dizziness, unsteadiness, and blurred vision commonly develop within 20 to 30 seconds, especially with the patient in the standing position; paresthesias start later (Lum 1987). Chest pain is reported by 50% of patients after 3 minutes of hyperventilation and by all by 20 minutes (Evans and Lum 1977). For clinical purposes, measurement of end tidal volume pCO2 is not necessary. In addition, there is no clear correlation between paCO2 and neurologic signs (Stoop et al 1986). The hyperventilation provocation test should not be performed in patients with ischemic heart disease, cerebrovascular disease, pulmonary insufficiency, hyperviscosity states, significant anemia, sickle cell disease, or uncontrolled hypertension (Brashear 1983).

For some patients with hyperventilation syndrome, symptoms cannot be reliably reproduced during the hyperventilation provocation test or even on consecutive tests (Hirokawa et al 1995). In some cases, the hyperventilation provocation test lacks test-retest reliability (Lindsay et al 1991). For others, antecedent anxiety and stress, not present during the test, may predispose to symptom formation, perhaps because of a hyperadrenergic state (Magarian 1982; Perkin and Joseph 1986). Different patterns of hyperventilation with different respiratory rates, tidal volumes, and durations may induce different symptoms (Grossman and De Swart 1984; Hornsveld et al 1995). Finally, as a response to a change in body position from supine to standing, patients with hyperventilation syndrome have an accentuated increase in ventilation that can be calculated with noninvasive measurements of pulmonary gas exchange, and that distinguishes them from healthy subjects (Malmberg et al 2000).

A double-blind, placebo-controlled study found the hyperventilation provocation test to be invalid (Hornsveld et al 1996). Because hyperventilation seemed a negligible factor in the experience of spontaneous symptoms, Hornsveld and colleagues even recommended avoiding the term "hyperventilation syndrome." However, the study may be flawed because of the method of patient selection. Patients were referred because of a suspicion of hyperventilation syndrome and not based on reproduction of symptoms on a hyperventilation provocation test. Moreover, the presenting symptoms of subjects were not provided. Because the symptoms of hyperventilation syndrome can indeed be vague and nonspecific and because symptoms sometimes occur only with certain types of anxiety or stress, their conclusion may not apply to different population subsets (Naschitz et al 1996). The subjects' symptoms may have been due to chest wall pain or panic attacks.

Alternatively, the Nijmegen questionnaire (a list of 16 symptoms rated on a 5-point scale from never to very often) can be used to screen for hyperventilation syndrome. The efficacy of this questionnaire has been evaluated, revealing the sensitivity to be 91% and the specificity to be 95% (when using the clinical diagnosis based on the pattern of complaints as the gold standard) (van Dixhoorn and Duivenvoorden 1985). In a consecutive series of 100 patients in a neuro-otology practice, 23% of patients seen for vestibular assessment were diagnosed with hyperventilation syndrome; 74% of these would have potentially remained undetected had the Nijmegen questionnaire not been used (Humphriss et al 2004).

From my experience with patients with predominantly neurologic complaints, the concept of hyperventilation syndrome is valuable and the hyperventilation provocation

test, despite its recognized shortcomings (Gardner 2000), is useful. In the individual case, if the hyperventilation provocation test fails to reproduce the symptoms but clinical suspicion persists, treatment such as breath holding, slow breathing, or breathing into a paper bag can certainly be suggested on a trial basis.

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Prognosis and complications

In a followup study of children and adolescents, 40% were still hyperventilating as adults and many suffered from chronic anxiety (Herman et al 1981). One half of patients with acute hyperventilation recover without treatment (Hirokawa et al 1995). In 10% of those with chronic hyperventilation, symptoms may persist for more than 3 years (Hirokawa et al 1995). With proper management, about 70% to 90% of adults become symptom-free (Lum 1976; Campernolle et al 1979).

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Management

The various treatments for hyperventilation that have been proposed include patient reassurance and education, instructions to hold the breath, breathe more slowly, or breathe into a paper bag, along with breathing exercises and diaphragmatic retraining, biofeedback, hypnosis, psychological and psychiatric treatment, and medications such as beta blockers, benzodiazepines, and antidepressants (Beumer and Bruyn 1993). A study of nonpharmacologic treatments found efficacy for educational sessions, breathing techniques and retraining, and progressive relaxation; the greatest improvement occurred in the group given an explanation and 8 sessions of breathing retraining (Monday et al 1995). A small pilot study found benefit from acupuncture (Gibson et al 2007). There is a lack of well-controlled treatment trials comparing these approaches (Herxheimer 1991).

In my experience, most patients respond to reassurance, education, and instructions to hold the breath, breathe more slowly, or breathe into a paper bag. Providing the patient with written materials such as those used by Lance may be worthwhile (Lance and Goadsby 2005). If significant symptoms of stress, anxiety, or depression are present, use of appropriate medication and psychological or psychiatric referral may be helpful.

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Pregnancy

Although hyperventilation syndrome has often been seen during pregnancy, studies on the incidence are not available.

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Anesthesia

Not applicable.

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ICD codes

ICD-9:
Hyperventilation: 306.1

ICD-10:
Hyperventilation: R06.4

Top

Associated disorders

Acute hyperventilation
Anxiety
Chronic hyperventilation
Distal symmetrical paresthesias
Panic attacks

Raynaud phenomenon

Top

Related summaries

Dizziness
Psychophysiological vertigo (psychogenic vertigo)
Syncope
Tension-type headache

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Differential diagnosis

epilepsy
migraine
arteriovenous malformation
cerebrovascular disease
vertebrobasilar insufficiency
brachial neuritis
angina
malingering
vasovagal attacks
functional illness
hypoglycemia
cerebral tumor
cardiac abnormalities
mitral valve prolapse
panic attacks
multiple sclerosis

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Demographics

For more specific demographic information, see the Epidemiology, Etiology, and Pathogenesis and pathophysiology sections of this clinical summary.

Age

06-12 years
13-18 years
19-44 years
45-64 years
65+ years

Population

None selectively affected.

Occupation

None selectively affected.

Sex

female>male, >2:1
female>male, >1:1

Family history

None

Heredity

None

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SPECIAL ARTICLE

The role of hyperventilation - hypocapnia in the pathomechanism of panic disorder

O papel da hiperventilação - a hipocapnia no patomecanismo do distúrbio de pânico

Andras Sikter,[1] Ede Frecska,[2] Ivan Mario Braun,[3] Xenia Gonda,[2] Zoltan Rihmer[2]

Abstract

***Objective**: The authors present a profile of panic disorder based on and generalized from the effects of acute and chronic hyperventilation that are characteristic of the respiratory panic disorder subtype. The review presented attempts to integrate three premises: hyperventilation is a physiological response to hypercapnia; hyperventilation can induce panic attacks; chronic hyperventilation is a protective mechanism against panic attacks. **Method**: A selective review of the literature was made using the Medline database. Reports of the interrelationships among panic disorder, hyperventilation, acidosis, and alkalosis, as well as catecholamine release and sensitivity, were selected. The findings were structured into an integrated model. **Discussion**: The panic attacks experienced by individuals with panic disorder develop on the basis of metabolic acidosis, which is a compensatory response to chronic hyperventilation. The attacks are triggered by a sudden increase in (pCO_2) when the latent (metabolic) acidosis manifests as hypercapnic acidosis. The acidotic condition induces catecholamine release. Sympathicotonia cannot arise during the hypercapnic phase, since low pH decreases catecholamine sensitivity. Catecholamines can provoke panic when hyperventilation causes the hypercapnia to switch to hypocapnic alkalosis (overcompensation) and catecholamine sensitivity begins to increase. **Conclusion**: Therapeutic approaches should address long-term regulation of the respiratory pattern and elimination of metabolic acidosis.*

***Descriptors**: Acidosis; Catecholamines; Hyperventilation; Hypocapnia; Panic disorder*

Resumo

***Objetivo**: Os autores apresentam um modelo de transtorno do pânico que se baseia nos efeitos da hiperventilação aguda e crônica, característicos do subtipo respiratório de transtorno do pânico. O modelo é generalizado a partir desses efeitos. Ele integra três características da hiperventilação: a hiperventilação é uma resposta fisiológica à hipercapnia; a hiperventilação pode induzir ataques de pânico; a hiperventilação crônica representa um mecanismo protetor contra os ataques de pânico. **Método**: Revisão seletiva da literatura a partir da base de dados Medline. Foram selecionados relatos referentes à inter-relação entre transtorno do pânico, hiperventilação, acidose, alcalose, liberação de catecolaminas e sensibilidade a catecolaminas, sendo os achados estruturados de modo a formar um modelo integrado. **Discussão**: Os ataques de pânico do transtorno do pânico desenvolvem-se com base numa acidose metabólica, que é uma resposta compensatória à hiperventilação crônica. Os ataques são desencadeados por um súbito aumento da pressão parcial de dióxido de carbono (pCO_2), quando a acidose (metabólica) latente se manifesta pela acidose hipercápnica. A condição acidótica induz liberação de catecolaminas. A simpaticotonia não pode manifestar-se durante a fase de hipercapnia, pois o baixo pH diminui a sensibilidade às catecolaminas. As catecolaminas podem provocar pânico quando a hipercapnia comuta para uma alcalose hipocápnica devido à supercompensação pela hiperventilação, situação na qual a sensibilidade às catecolaminas liberadas começa a aumentar. **Conclusão**: As abordagens terapêuticas deveriam voltar-se para a regulação em longo prazo do padrão respiratório e a eliminação da acidose metabólica.*

***Descritores**: Acidose; Catecolaminas; Hiperventilação; Hipocapnia; Transtorno de pânico*

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Introduction

Although the correlation between the respiratory panic disorder (PD) subtype and hyperventilation is well established in the literature, the active role of hyperventilation in the pathomechanism of PD is less understood. Although Wilhelm et al. provided a thorough review of the three main theories on the role of hyperventilation in PD,[1] they identified contradictions among them and did not offer a synthesis of the current concepts. The increase of tissue H^+ ion concentration, which is regulated promptly and effectively by respiration-induced changes in pCO_2, is a strong stimulus of catecholamine release. However, acidotic conditions decrease the catecholamine sensitivity of target organs (the inverse of what occurs in alkalosis). In a panic attack, these events occur in rapid succession. Therefore, understanding the timing and the time constant (how quickly a change develops) of physiological variables is crucial for resolving the apparent contradictions and establishing a coherent model.

The role of hypocapnia in the pathomechanism of PD has been largely overlooked in the literature.[2] During the late 1930s, hyperventilation played a central role in the diagnostic formulation of hyperventilation syndrome.[3-4] Shortly after the conceptualization of PD in the DSM III (1980), it became evident that there had been an overlap between symptoms of hyperventilation syndrome and PD.[5] The article written by Klein in 1993 represented an important step toward settling the long-standing debate on the role of hyperventilation.[6] Klein denied the importance of acute or chronic hyperventilation in the generation of panic attacks. Although he described a positive correlation between chronic hyperventilation and panic attacks, he used this observation in order to put forth the idea that chronic hyperventilation is protective against panic.

The aim of this study was to review the literature on PD, with a special focus on the role of hyperventilation and hypocapnia in the pathomechanism of PD. Special attention was paid to studies investigating the interrelationships between panic, pH, pCO_2, tissue catecholamine sensitivity, and catecholamine elimination, as well as their temporal characteristics.

Method

We conducted a selective review of the literature in the Medline database, limiting our searches to articles published between 1937 and 2006. Our approach was to discuss the available literature on PD in order to show that it is not only a psychiatric disorder but also a regulatory disorder. Our first search included the terms “panic” and “hyperventilation”, and/or “hypocapnia” and/or “hypercapnia”. This search strategy yielded a total of 317 articles, from which we selected 33 for analysis. In selecting these articles, our principal aim was to represent all major opinions and trends. Within this context, we selected articles written by the most prominent authors. Therefore, these articles and their main arguments present a logical progression. In addition, we reviewed the most controversial papers. Furthermore, 17 of the articles included deal with the physiology and pathology of catecholamine homeostasis in relation to panic. These articles were identified by adding the search terms “acid-base disorder”, “acidosis”, “alkalosis”, “hypocapnia”, “hypercapnia”, “catecholamine”, “noradrenaline”, “adrenaline”, and “sympathetic nervous system”. In this step of the selection process, we focused on articles investigating the relationship between acidosis/alkalosis and catecholamine production, as well as on those investigating the catecholamine sensitivity of brain and other tissues in relation to pH. We also included 10 articles on psychiatric topics presenting borderline relationships with PD. The search of the literature and the article selection were carried out by András Sikter, who has been researching this topic for decades and therefore has profound insight into the issue. The author notes on the articles evaluated have been arranged into a logical order so that they can be integrated into a coherent model.

Discussion

Maintaining the homeostasis of intracellular and extracellular pH is a crucial regulatory task for the organism. A couple of deep breaths can substantially decrease CO_2 concentration, increasing extracellular pH to 7.4-7.7. Since CO_2 readily passes through cell membranes, intracellular pCO_2 decreases to the same degree. Therefore, altering respiration can produce marked changes in intracellular pH, the consequences of which are outlined below.[7] Acute hypocapnia has a progressive effect on membrane permeability, metabolism, oxygen consumption, and cardiac function,[8] as well as exciting the nervous system through the hypopolarization of neurons.[9-10] In contrast, hypercapnia results in decreased cell membrane permeability,[11] metabolic depression,[12] reduced muscle contractility[13], and hyperpolarization of neurons. In short, acute hypocapnia elicits effects similar to those seen when the sympathetic nervous system is stimulated, whereas acute hypercapnia evokes parasympathetic effects. The latter occurs despite the fact that hypercapnia causes increases in the levels of serum adrenaline and noradrenaline.[14] There are conflicting data in the literature regarding serum adrenaline and noradrenaline levels in acute hypocapnia, some authors reporting no alterations[14] and others demonstrating significant decreases.[15] Hypoxia is a disturbing variable in most investigations.[16] Catecholamine sensitivity decreases in hypercapnic acidosis and increases in hypocapnic alkalosis.[7] These changes in catecholamine level and sensitivity affect target organs. Lower intracellular pH is the trigger for noradrenaline release from the locus coeruleus during panic attacks.[17-18]

Chronic hypocapnia elicits a cascade of changes due to compensatory mechanisms for the restoration of intracellular and extracellular physiological pH. Renal reabsorption of chlorine ions and excretion of bicarbonate is increased in sustained hypocapnia.[19] In an experimental model of hyperventilation in dogs, it was shown to take five days for the kidneys to reestablish the equilibrium.[20] In humans, the role of intracellular buffer mechanisms is more important, and adaptation to chronic hyperventilation or hypoventilation is therefore less dependent on renal function.[21] The process of adaptation is similarly slow: to regain equilibrium can take five to seven days.[7] It takes equally as long to reverse the changes after the occurrence of eucapnia. Buffer mechanisms include the release of hydrogen ions, which shifts pH toward the physiological level, although this process also occurs only after a delay.

Various authors have downplayed the role of hyperventilation in PD and have recommended that the term ‘hyperventilation syndrome’ no longer be used.[21-24] However, in another review article, Gardner argues for the preservation of the term.[25] Other authors have stated that chronic hyperventilation is a common cause of both hyperventilation syndrome and PD.[5,25-26] Recently, Nardi addressed the role of hyperventilation in PD and tried to

clarify it, stating that it is considered to be "...a cause, a correlate, or a consequence of panic attacks." According to Nardi, acute hyperventilation might play a role in the pathomechanism of the respiratory PD subtype.[27]

In a study using transcutaneous monitoring, no relationship was found between PD and hyperventilation.[28] This method is outdated due to its high inertia (slow decay) in monitoring changes in arterial pCO_2.[2] It is widely accepted that the respiratory PD subtype, which accounts for approximately 50% of all PD cases, is closely related to hyperventilation and represents a hyperventilation syndrome comorbidity.[2,5,25-26]

There are three views in the literature regarding the role that hyperventilation plays in the pathomechanism of PD. In the first, panic is triggered by elevated CO_2 levels, and hyperventilation follows as a physiological response.[1,29] In this model, the hyperventilation is a consequence, an epiphenomenon observed during naturally-occurring and drug-induced panic attacks. In the view of other authors[30-31] – a view shared by followers of the cognitive-behavioral theory of PD[1] – hyperventilation-induced hypocapnia plays a central role. The opinion of psychotherapists can be summarized as follows: individuals with PD can misinterpret the bodily sensations caused by hyperventilation as being indicative of life-threatening danger.[32]

However, the most widely accepted view is that detailed by Klein[6]: hyperventilation is a protective mechanism against panic reactions. In his thorough study, Klein demonstrated that patients with PD are hypersensitive to increases in pCO_2, and that panic attacks are triggered by a relative increase in the level of CO_2. Such individuals present chronic hyperventilation as a means of avoiding the panic-inducing increase in CO_2 levels.

We agree with Klein that chronic hyperventilation has some defensive effects against panic attacks in individuals with PD, since a sudden increase of pCO_2 (e.g. CO_2 challenge) has been shown to provoke such attacks.[33] However, chronic hyperventilation is always accompanied by compensatory metabolic acidosis. In an individual with chronic hyperventilation, life events (i.e., relaxation, sleep, premenstrual phase, etc.) can cause pCO_2 to rise to the normal baseline or above.[6] The latent metabolic acidosis then appears, and the elevated concentration of H^+ increases CO_2 sensitivity of the respiratory center. It can be assumed that the chronic hyperventilation itself is responsible for the increased CO_2 sensitivity observed in individuals with PD.

The best supporting evidence is provided by Klein himself, who found chronic hyperventilation to correlate positively with lactate-induced panic and CO_2 sensitivity.[6] Hypophosphatemia, which is an indicator of chronic hyperventilation, has been found to be predictive of lactate-induced panic attacks.[34] Decreased plasma bicarbonate is also a marker of chronic hyperventilation and sensitizes to the onset of panic attacks.[35] However, chronic hypercapnia accompanied by metabolic alkalosis has been shown to correlate negatively with the development of panic attacks.[6]

Various researchers have been successful in using hyperventilation to provoke panic attacks.[27,36-39] Nardi addressed the role of hypocapnia and hypercapnia in PD with equal focus and equal importance in the pathogenesis.[27,38-39] However, the overall effect of hyperventilation on panic was significantly less than that of CO_2 inhalation. Respiratory challenge tests (CO_2 and breath-holding) can provoke panic attacks in individuals presenting the respiratory PD subtype.[39] Cerebral hypoxia, chronic hyperventilation, and anxiety persist in the interim between panic attacks.[26] Although individuals with PD are prone to continue hyperventiling,[1,32] the hyperventilation facilitates panic attacks.

Caldirola stated that an irregular breathing pattern is predictive of PD, and that similar irregularity can be found in generalized anxiety disorder.[40] The similarity can explain the high comorbidity of these two conditions.[26] In individuals with generalized anxiety disorder, the irregularity of breathing is less pronounced than in those with PD.[41] Various studies have shown that, in individuals with PD, there is a strong correlation between the degree of respiratory irregularity and the frequency of panic attacks, as well as between such irregularity and CO_2 vulnerability.[1,41-42] Irregular respiration occasionally causes elevated pCO_2, which can trigger a panic attack.

The hypothalamic-pituitary-adrenocortical axis model of hypercapnia induced panic is generally accepted in the literature,[17,43] although it was recently questioned by Gorman,[44] who discovered inconsistencies and pointed out that, during CO_2 challenge, actual pCO_2 values correlate negatively with signs and symptoms of panic. This indicates that panic develops not during hypercapnia but during the subsequent hypocapnic phase. The way Gorman puts it: "...in panic disorder patients, we have found that elevated cortisol, fear and hypocapnia are intercorrelated in the few minutes before actually experiencing an acute attack."

As previously mentioned, higher pCO_2 leads to increased noradrenaline release.[18] However, in human plasma, noradrenaline has a half-life of only a few minutes.[45-46] In the rebound phase of hypocapnia, cells present increased sensitivity to residual catecholamines.[7] Strong catecholamine stimuli are known to induce panic attacks.[47] Individuals with PD present normal catecholamine levels between panic attacks.[48] It is therefore possible that, in addition to the hypercapnia-related increase in catecholamine levels, the hypocapnia-induced catecholamine sensitivity plays a significant role in the induction of panic.[49]

Borelli et al. conducted electrophysiological studies in animals[50] and concluded that panic attacks represent a pathological manifestation of 'freezing behavior' (low-arousal condition), rather than the high-arousal condition of the 'fight-or-flight' response.[51] 'Freezing behavior' initially manifests as immobility, bradycardia, and hypoventilation but can transform into the flight response, which is characterized by vigorous locomotion, tachycardia, and hyperventilation.[52] The sudden change in the respiratory pattern that precedes the flight response indicates the similarity with panic attacks. It is quite probable that the role the brainstem plays in the pathomechanism of PD is more important than previously suggested.

We can build a profile of PD that integrates the three hyperventilation theories. Individuals with the respiratory PD subtype present chronic hyperventilation. The chronic hyperventilation results in a compensatory decrease in intracellular and extracellular pH due to renal secretion of bicarbonate and due to the tissue buffer mechanisms. A balanced steady-state is established between the hypocapnic alkalosis and the metabolic acidosis. Multiple factors can lead to a sudden increase in CO_2 levels. In individuals with PD and presenting sustained hypoventilation episodes, irregular breathing causes abrupt changes in pCO_2. In the prelude to a panic attack, an abrupt increase of pCO_2 occurs, which leads to unusually high intracellular H^+ concentrations, thereby triggering the release of noradrenaline in the locus coeruleus. This sudden increase in intracellular acidosis elicits hypocapnia by compensatory

hyperventilation. In addition, individuals with PD overcompensate for hypercapnia.[53] The consequence is severe sympathicotonia, since the higher catecholamine level resulting from the previous hypercapnia overlaps with the increased catecholamine sensitivity caused by the hypocapnic alkalosis. The adrenergic/noradrenergic tonus results in fear mediated by the limbic system, and the expectation of threat can create a vicious circle. Long after the chemical component phase of a panic attack is over, the cortical excitation persists, leaving the individual with a lingering, subjective feeling of anxiety. Hyperventilation pushes the individual toward progression of the panic attack.

The profile is supported by various observations. Gorman noted that, in the case of CO_2 challenge, signs and symptoms of panic correlated inversely with pCO_2.[44] One dose of biperiden (an antimuscarinic agent) can prevent panic attacks induced by CO_2 inhalation, since it eliminates the rebound hyperventilation response mediated via the muscarinic receptors of the ventral medulla.[54] Therapies proven to be effective in PD, such as cognitive therapy, biofeedback, and antidepressant pharmacotherapy, seem to also be useful in hyperventilation syndrome.[55-57] Successful pharmacotherapy of panic attacks normalizes blood gas parameters, i.e. it eliminates hyperventilation as well as the increased CO_2 sensitivity characteristic to PD.[58]

Conclusion

Taken separately, each of the three hyperventilation theories can correctly interpret one step in the pathological dynamics of panic attacks. Chronic hyperventilation predisposes an individual to PD, since compensatory mechanisms (such as alterations in renal function and tissue buffer capacity) lead to chronic metabolic acidosis, which remains latent until it is activated by chronic hypocapnia. The acidosis manifests when hyperventilation decreases or hypercapnia develops[6] (metabolic + respiratory acidosis). Acidosis induces catecholamine release, and the activity of locus coeruleus increases. Therefore, panic attacks can be triggered by the mitigation or elimination of chronic hyperventilation, with a consequent elevation of pCO_2. Due to the decreased tissue catecholamine sensitivity developed during acidosis, the catecholamine release does not cause an abrupt increase in sympathetic activity during this phase. Hypercapnia is compensated for – frequently overcompensated for – by acute hyperventilation.[29] Sympathicotonia develops when the acute hypocapnia makes the tissues sensitive to the circulating catecholamines, the elimination of which has a time lag measured in minutes. Patients with PD react with panic to extreme sympathicotonia, a reaction that involves cognitive mechanisms.[59] When chronic hyperventilation is followed by acute hypoventilation (hypercapnia) and this hypoventilation is followed by (over)compensatory hyperventilation (hypocapnia), acute hyperventilation can provoke panic.

The pathogenesis of panic attacks can include defensive mechanisms resembling 'freezing behavior', since prolonged hypercapnia induces strong catecholamine release. However, but the sympathetic response arises when tissue catecholamine sensitivity increases due to subsequent hyperventilation.[50]

The respiratory PD subtype can be explained by the different time constants of chemical processes: pCO_2 and pH changes are immediate, the elimination of catecholamines from blood takes only minutes, and the clearance of metabolic acids can require several days. Chronic hyperventilation, together with the corresponding metabolic acidosis, is a predisposing factor for PD. Therefore, therapeutic approaches should address long-term regulation of respiratory patterns[60] and elimination of metabolic acidosis.

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