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High ventilation breathwork practices: An overview of their effects, mechanisms, and considerations for clinical applications

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ABSTRACT

High Ventilation Breathwork (HVB) refers to practices employing specific volitional manipulation of breathing, with a long history of use to relieve various forms of psychological distress. This paper seeks to offer a consolidative insight into potential clinical application of HVB as a treatment of psychiatric disorders. We thus review the characteristic phenomenological and neurophysiological effects of these practices to inform their mechanism of therapeutic action, safety profiles and future clinical applications. Clinical observations and data from neurophysiological studies indicate that HVB is associated with extraordinary changes in subjective experience, as well as with profound effects on central and autonomic nervous systems functions through modulation of neurometabolic parameters and interoceptive sensory systems. This growing evidence base may guide how the phenomenological effects of HVB can be understood, and potentially harnessed in the context of such volitional perturbation of psychophysiological state. Reports of putative beneficial effects for trauma-related, affective, and somatic disorders invite further research to obtain detailed mechanistic knowledge, and rigorous clinical testing of these potential therapeutic uses.

1. Introduction

1.1. High ventilation breathwork defined

Breathwork is defined by the Oxford English Dictionary as "*any of various exercises, techniques, and therapies that involve manipulating the manner in which one breathes*" (OED, 2023). This broad definition of breathwork encompasses myriad different practices, reflecting its multifaceted historical origins and inspirations, and is currently receiving increased interest as an alternative (or adjunct) therapeutic to pharmaceuticals for the alleviation of psychological distress and physical discomfort. A body of clinical research has been published over the past decade, which uses empirical methods of clinical research to reassess traditional healing practices for their repurposing as therapies within conventional Western health settings. This 'paradigm shift' includes the medical 'renaissance' of psychedelics (George et al., 2022; Hadar et al., 2022), and the rigorous enquiry into the neurobiological underpinnings of integrative mind-body practices – notably mindfulness meditation (Brewer et al., 2011; Tang et al., 2012). The growth in scientific interest into breathwork parallels its explosion in public visibility in the media and popularity across the general population: while it is hard to estimate precisely how many people regularly practice breathwork techniques, there are likely to be tens of millions of breathwork practitioners worldwide, since just one breathwork program—Sudarshan Kriya Yoga—is recorded to have been taught to over six million people in 152 countries (Zope and Zope, 2013).

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All breathwork practices invariably require a controlled pattern of volitional breathing. However, large variations between breathing practice modalities and their underlying principles must be acknowledged. One key distinction is between slow breathing techniques, previously operationalised as < 10 breaths/min (Zaccaro et al., 2018), versus fast breathing techniques, where the rate and/or depth of ventilation is increased – in other words, hyperventilation. Throughout this review, we will use the terminology and rubric of *High Ventilation Breathwork* (HVB) to define breathwork practices that employ increased ventilation, to align with both scientific and breathwork communities. In other words, breathwork practices that employ respiratory rates above the normal range are classed as HVB.

Slow-paced breathwork techniques have attracted significant research attention, not only since slow breathing typically heightens heart rate variability (cardiac parasympathetic tone), commonly interpreted as an index of reduced stress (Fincham et al., 2023; Zaccaro et al., 2018). There are, however, far fewer scientific evaluations of fast-paced breathwork practices, despite promising examples of HVB producing beneficial health outcomes. It is important to consider that these practices might possibly lead to serious health consequences for individuals with specific comorbid conditions, especially when performed alone without expert monitoring. Here, we review and describe the unique features of HVB, including its physiological effects and safety profile, to provide essential information to guide future research on its therapeutic mechanisms and clinical applications. As a note of caution, HVB is just one element of many holistic practices and rituals, and there is a risk that extracting one single component from these ancient practices may result in oversimplification of their multi-faceted aspects. However, we feel scientific and clinical characterisation of HVB as a stand-alone component is a valuable approach to guide scientific exploration of these practices. Therefore, the main objectives of this review are: 1) to summarise the prominent types of HVB practices – their historical roots and characteristics, 2) to describe the acute subjective effects and findings from preliminary clinical applications, and 3) to identify the main neurophysiological mechanisms underlying such effects of HVB, with emphasis on their neurometabolic and autonomic effects. Our ultimate goal is to explore HVB methodically to shape future investigation and guide clinical and therapeutic applications.

1.2. History of HVB practices

HVB techniques are observed worldwide and have complex historical roots grounded in both religious and secular traditions (see Table 1 and Fig. 1). HVB techniques are likely to have been used since ancient times for spiritual and healing purposes, and are described in the rituals and practices of many cultures including Inuit, Sufi, and Native American cultures (Deepak, 2002; Grof and Grof, 2010; Puente, 2013; Raghuraj et al., 1998). Though the origins of breathwork likely date back to over 10,000 years ago (Brown and Gerbarg, 2012) from being taught by shamans, perhaps the most well-known practices originate in the context of Yoga, exemplified by Pranayama. This translates as regulation of the vital energy or breath (where *prana* means vital energy or life force, and *ayama* means regulation or control). Variants include *Kapalabhati* pranayama (or 'Skull Shining Breath' in Sanskrit) and *Bhastrika* pranayama ('Bellows Breath'). HVB associated with Buddhism is also widely known, notably *g-Tummo* yoga/meditation, wherein visualisation of inner heat accompanies the breathwork (in Tibetan, the concept of Tummo refers to 'inner fire' or 'psychic heat') (Kozhevnikov et al., 2013). These traditional forms have inspired newer forms of HVB which include: *Holotropic Breathwork* developed by Stanislav and Cristina Grof, now using the brand name *Grof® Breathwork* (and hereon referred to as GBW) (Grof and Grof, 2010), *Holorenic Breathwork* developed by Josep Maria Fericgla (Cervantes and Puente, 2014; Puente, 2013), *Rebirthing Breathwork* developed by Leonard Orr and also popularised by Sondra Ray (Albery, 1984; Orr, 1992), *Conscious Connected Breathing* (CCB), *Sudarshan Kriya®* breathing from Sudarshan kriya yoga developed by Sri Sri Ravi Shankar (Zope and Zope, 2013) (hereon referred to as SKY), and the breathing technique of the *Wim Hof Method®* (WHM) developed by Wim Hof (Kox et al., 2012) (hereon referred to as the WHbM). It has been suggested that the first prominent attempted use of hyperventilation as a therapeutic modality in the West was by psychoanalyst Wilhelm Reich (Victoria and Caldwell, 2013).

Modern instantiations of breathwork are often, but not always, led by a trained facilitator and accompanied by evocative and/or ambient music, which can guide breathing rhythms. Prominent practices, including the WHbM, GBW, rebirthing and CCB, involve deep inhalation with active mobilisation of the chest and abdomen, with a relatively more passive outbreath from relaxation of respiratory muscles and elastic recoil of the lungs. However, not all HVB practices solely involve deep inhalation – for example holorenic breathwork combines styles of both GBW (deep breaths with emphasis on active inhalation), and kapalabhati (shallower breaths, with emphasis on active exhalation and passive inhalation) (Puente, 2013). Kapalabhati involves breathing solely through the nose and comprises contraction of the abdominal muscles leading to forceful exhales and passive inhales (Ansari, 2016). The WHbM is in part derived from tummo, yet it is also influenced by yogic pranayama (Fig. 1). In contrast, in Sudarshan kriya, a practitioner engages in cyclical rhythmic breathing and alternates between rhythms, one of which (the slow cycle) can fall within the average typical resting rate for adults (Banaś-Ząbczyk et al., 2022).

Nomenclature may also prove confusing: both kapalabhati and bhastrika (up to 100 + breaths/min) may be referred to as 'breath of fire' and are also used in Kundalini Yoga. Again, the literature is ambiguous on this. Depending on teacher and/or tradition, there can be considerable overlap between kapalabhati and bhastrika or even combining of the two (Novaes et al., 2020), with the former usually being executed via fast, vigorous contraction of the (anterior) abdominal wall and latter via engaging intercostal and accessory muscles pertaining to respiration (Frostell et al., 1983; Miles, 1964). In brief, bhastrika involves both active inhales and exhales, whereas kapalabhati employs more passive inhales and active exhales (Saraswati, 1994). Both yogic pranayama techniques have been practiced extremely rapidly at over 200 breaths/min (Frostell et al., 1983), in addition to gently (Dhruva et al., 2012) and even slowly (Pramanik et al., 2009). In SKY, bhastrika may be taught at only 30 breaths/min with emphasis on forceful exhales and rapid inhales, with the rhythmic, cyclical breathing (similar to kapalabhati) being performed relatively faster during the Sudarshan kriya ('proper vision by purifying action') component (Zope and Zope, 2013). Bhastrika can also involve arm and body movements. In line with the myriad ways breathwork can be practiced in general, it is also possible for bhastrika and kapalabhati pranayama to use breath holding (*Kumbhaka*) and muscle locks (*Bhanda*) after rounds (Saraswati, 1994). This aspect of retention paired with fast breathing, and the fact that pranayama practitioners may be encouraged to take cold baths (Sivananda, 1962), reinforces the notion that the modern-day WHM has roots in yogic pranayama along with Buddhist tummo meditation. Sometimes bhastrika involves verbal exhalation and is much slower than kapalabhati. However, others state it is more intense than kapalabhati (Iyengar, 1981). Regardless, we refer to the yogic breathwork practices involving bhastrika, kapalabhati and kriya that employ respiratory rates above the normal range and are thus classed as HVB.

Similarly, CCB has been used as an umbrella term to describe analogous processes used across several HVB techniques. CCB itself has developed as a stand-alone practice and is incorporated into GBW, rebirthing, and holorenic breathwork (de Wit and Cruz, 2021; de Wit et al., 2018). Additionally, SKY primarily refers to its core cyclical, rhythmic breathwork component of Sudarshan kriya but SKY includes other practices such as bhastrika, along with slower paced breathing techniques and chanting (Brown and Gerbarg, 2005a; Zope and Zope, 2013). Most of the practice time is devoted to the core technique of Sudarshan kriya, again incorporating cyclical breathing with slow, medium, and fast cycles.

Table 1
Individual characteristics of different High Ventilation Breathwork (HVB) practices. Includes the founder or most acknowledged teacher/tradition they pertain to, their approximate ages, and the nature of the HVB (i.e., pauses, holds and apnoea, full autonomy versus restricted breathing style, approximate rate and depth, external accessory elements). *Note:* Due to the ubiquitous nature of breathing and thus breathwork, the list and descriptions are not exhaustive – there are also variations within HVB practices as well.

Breathwork technique	Teacher or tradition & time period	Brief description	Presence of interrupted ins/exp cycles	Approx. pacing & duration	Accessory elements	Potential acute effects
g-Tummo (Inner Fire; Psychic Heat) Meditation (or Yoga)	Tibetan Buddhism. ~701–800 AD (but could be much older)	'Vase' breathing technique alternating both 'gentle' & 'forceful' breathing	Yes (breath holds)	Ins is loud/longer & exp is faster. Duration varies – mins to hrs	Muscle contraction & apnoea; Visualisations; Forceful breathing is paired with sound	Increase in body temp, light-headedness, dizziness, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, anxiety, sweating, tiredness & exhaustion, ringing in ear (tinnitus), dry mouth (when mouth breathing is used)
Kapalabhati (Skull Shining Breath)	Hinduism (Yoga & Pranayama). Likely several 1000 s of years old	Nasal, abdominal breathing; Forceful exhale & passive inhale	If breath holds & muscle locks are used after HVB in form of Kumbhaka & Bhandhas, respectively, or when resting	Varies – with different rhythms & intensities. Usually 5–10 mins with short breaks. Can be slow or extremely fast	Pranayama teacher may be present	Light-headedness, dizziness, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, anxiety, changes in body temp (cold & hot flushes), sweating, shortness of breath, fatigue, laughing, eyes watering
Bhastrika (Bellows Breath)	Hinduism (Yoga & Pranayama). Likely several 1000 s of years old	Forceful inhales into chest & purposeful exhales. Can involve movement	If breath holds & muscle locks are used after HVB in form of Kumbhaka & Bhandhas, respectively, or when resting	Varies – with different rhythms & intensities. Usually up to 5 mins with short breaks. Can be slow or extremely fast	Pranayama teacher may be present; Breathing resembles sound of bellows	Light-headedness, dizziness, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, anxiety, changes in body temp (cold & hot flushes), sweating, shortness of breath, fatigue, laughing, eyes watering
Holotropic / Grof® Breathwork (GBW)	Stanislav Grof & Cristina Grof (Czech Republic & US). 1970 s	Very fast & deep breathing (essentially uses CCB style of breathwork)	No	No set pace – but advised to breathe hard/fast as one can. 3hrs of HVB. Can also be 1 hr in 1-on-1 sessions	Evocative music; Elective bodywork; Sitter in group setting (can include physical touch); Meditative art (mandala drawing) & discussion after	Light-headedness, dizziness, fainting, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, dry mouth, anxiety, body temp changes, sweating, tinnitus & exhaustion. Spontaneous movement may also occur due to alkalosis-induced tetany, including cramping of extremities. Crying & cathartic noises such as laughs, screams, groans, sighs, chants, talking in tongue, infant or animal-like noises/grunts
Rebirthing breathwork	Leonard Orr (US). 1960–70 s	Gradually increasing fast & deep breathing. No pause between inhale & exhale (i.e., CCB)	No	No set pace – but typically gradually increases. Duration varies – usually ~1 hr	Facilitator usually present to offer guidance	Light-headedness, dizziness, fainting, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, tinnitus, dry mouth, anxiety, body temp changes, sweating, exhaustion, spontaneous movements, crying, cathartic noises
Holorenic breathwork	Josep Maria Fericgla (Spain). 1980 s	Combination of Sufi & Shamanic breathing along with Kapalabhati & Holotropic breathwork	No	Hyperventilation can be 140–160 respiratory cycles/min. Duration varies — can be 2–3 hr sessions	Evocative music; Elective bodywork; Facilitator guidance	Light-headedness, dizziness, fainting, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, tinnitus, dry mouth, anxiety, body temp changes, sweating, exhaustion, spontaneous

(*continued on next page*)

Table 1 (*continued*)

Breathwork technique	Teacher or tradition & time period	Brief description	Presence of interrupted ins/exp cycles	Approx. pacing & duration	Accessory elements	Potential acute effects
						movements, crying, cathartic noises
Sudarshan Kriya® breathing from Sudarshan Kriya Yoga (SKY)	Sri Sri Ravi Shankar (India). 1981	Cyclical rhythmic breathing with different cycles of slow-medium to fast-very fast	No (but changes rhythms)	8–14 resp cycles/min, 40–50 cycles/min, 60–100 + cycles/min). Can be slower – or faster. Short Sudarshan Kriya approx. 10 mins; Long Kriya 30–45 mins	Can use guidance from tape or SKY instructor	Light-headedness, dizziness, tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, anxiety, body temp changes, sweating, exhaustion, laughing, eyes watering
Wim Hof (breathing) Method (WHbM) from the Wim Hof Method® (WHM)	Wim Hof (Netherlands). 1990–2000 s	Cyclical deep breathing from diaphragm to chest; Forceful inhale	Yes (breath holds)	Typically 3–4 sets of 30–40 deep breaths with breath holds in between. Duration dependent on rate & apnoea length but usually 10–15 + mins	Can use guidance from WHM app (with/out music) or WHM instructor	Light-headedness, dizziness, fainting (particularly on breath holds), tachycardia, visual disturbance, paraesthesia, palpitations, shakiness, tinnitus, dry mouth, anxiety, change in body temp, sweating, exhaustion, spontaneous movements, crying, cathartic noises

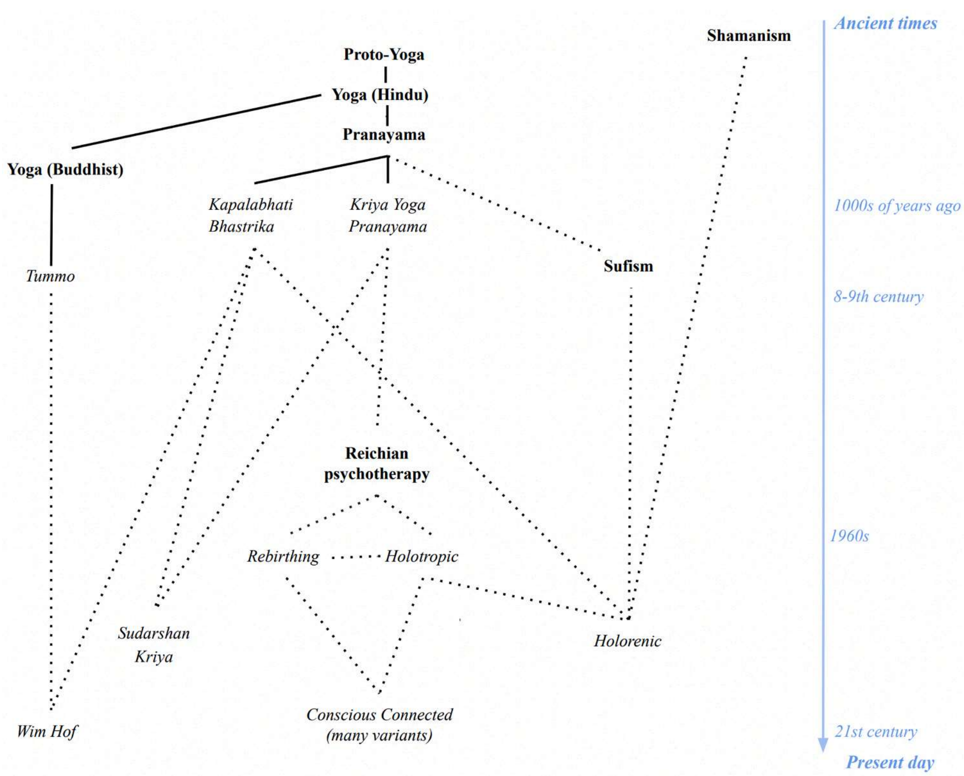

Fig. 1. Evolutionary diagram with examples of HVB techniques (in italics) and related traditions (in bold). Ancient practices are at the top, and descending are some more recent practices. Several of these techniques are gaining popularity in recent decades in line with the rise of holistic 'mind-body' practices such as Yoga, an increasing therapeutic interest in both the mind-body relationship, and the healing capacity of psychedelics via induction of altered states of consciousness. The specific age of the traditional practices included in this review from Buddhism and Hinduism are not exactly known but are believed to have originated several 1000 s of years ago – and have formed an integral part of these cultures and religions for centuries. Solid line = derived from or covered by a specific technique or tradition. Dotted line = incorporates elements of another technique or tradition. For example: Holorenic breathwork is a combination of Sufi and Shamanic breathing along with Kapalabhati and Holotropic breathwork, whereas a similar style of Conscious Connected breathing is used in Rebirthing and Holotropic breathwork. (Diagram made by the authors).

To summarise, this set of breathwork techniques share high-ventilation modalities that overlap and are often related. To satisfy the nomenclature of different communities, while attending to common underlying mechanisms, we use the rubric HVB. Moreover, throughout this review, we have prioritised our attempts to be accurate over providing an exhaustive appraisal of detailed differences, which would undoubtedly prove very challenging due to innumerable differing viewpoints and the extremely long, complex history of HVB.

2. Noteworthy HVB practices

2.1. Key distinguishing elements of techniques

Key distinguishing features of HVB techniques are summarised in Table 1. The WHbM, for instance, involves cyclic hyperventilation, incorporating periods of fast ventilation (usually 30–40 fast and deep breaths) followed by apnoea (whereby a participant alternates between the two) (Kopplin and Rosenthal, 2022). The WHM as a whole includes cold water exposure, muscle stretching and meditation, with the adoption of a 'mindset', operationalised as intention setting – to increase general stress resilience. This technique is finding favour in scientific literature (i.e., Kox et al., 2014).

GBW is a popular technique developed by psychiatrist Stanislav Grof as a non-drug alternative for inducing non-ordinary states of consciousness for psychotherapeutic applications after the drug compound lysergic acid diethylamide (LSD) was criminalised in 1968 and could no longer be used for this purpose. It usually instructs participants to breathe as fast and deep as they can for three hours with no pauses or prescribed rhythm, rate, or pattern. CCB is another technique in which a high ventilation breathing cycle is maintained with no pauses between breath – this is essentially what GBW and rebirthing also use (de Wit et al., 2018; Holotrópica and de Acción, 2014; Lalande et al., 2012; Rhinewine and Williams, 2007).

The distinct HVB techniques are associated with different subjective outcomes, suggesting dissociable underlying mechanisms. For example, g-tummo and the WHbM involve periods of breath holds/retentions, while SKY varies the speed of ventilation in a cyclical manner. CCB, GBW, rebirthing and holorenic breathwork often do not involve purposeful breath holds, but rather continuous accelerated breathing without pauses. Moreover, rituals and exercises that are performed around the time of HVB are anecdotally reported to be as important for therapeutic benefit as the breathwork component itself. For example, GBW may include evocative music, elective bodywork, a sitter being present (which can involve physical touch), meditative art in the form of mandala drawing and group discussion afterwards. Furthermore, the dynamics of being in a group setting undoubtedly influence individual and collective experience. Most HVB practices are performed in a group with a facilitator (highly recommended for inexperienced, HVB-naïve practitioners), although kapalabhati, bhastrika, CCB, and the WHbM are also frequently practiced individually (if this is the case, it must always be safe to do so – see Section 5).

The purported anecdotal psychedelic effects mentioned below in Section 2.2 may relate mostly to the more modern-day HVB practices that employ CCB (i.e., continuous, uninterrupted hyperventilation, without pauses/retention) for extended periods of time (i.e., hours as opposed to minutes). Inducing non-ordinary altered states of consciousness (ASCs) is a primary aim of these, as opposed to more traditional practices which may be geared towards the attainment of *Samadhi* or 'enlightenment'. However, several of the aforementioned HVB practices do include interrupted hyperventilation, and it is not to say that techniques involving breath holding, for example, do not induce non-ordinary ASCs. It remains imperative to honour their complex historical roots arriving from different cultures, and there are even anecdotal reports of ASCs in freediving.

Given the growth in both popularity and different varieties of HVB, this review undoubtedly omits several, as new methods continue to emerge and evolve. A full characterisation of the physiology and phenomenology of breathwork will aid its advancement as a discipline. Inconsistent definitions and nomenclature currently impede the characterisations of HVB, hence this review attempts to clarify and facilitate future HVB research. Further, HVB techniques have variable accessibility: the teaching of tummo meditation/yoga is restricted to advanced Buddhist practitioners, while the WHbM, albeit now trademarked, is open to the public via YouTube teachings. Presumably, there are additional practical, religious, traditional, and spiritual factors that can prevent individuals or groups from accessing different HVB practices. Furthermore, the commercialisation and trademark protection of some recent techniques, like GBW and SKY, might also diminish accessibility to the public. However, facilitators of these techniques may argue that such trademarking is necessary for preserving the form and quality of the practices and ensure the core teachings (religious, spiritual, or otherwise) are not attenuated.

2.2. Potential acute effects

During and after HVB, especially when prolonged, participants often experience changes in the intensity and content of thoughts, emotions, and somatic sensations. Acute effects include (but are not limited to) light-headedness, visual disturbances, watery eyes, paraesthesia, palpitations, shakiness, dry mouth, tinnitus, anxiety, hot flushes, sweating, fatigue, or exhaustion (Posse et al., 1997). Spontaneous movement may also occur, as well as cramping of the extremities, in particular the hands. Individuals often exhibit emotional behaviours in the form of crying and cathartic noises such as laughing, screaming, groaning, sighing, infant noises, animal-like grunts, chanting, or talking in tongues. For potential adverse side effects, see Section 5.2 on safety considerations for HVB practices.

Individuals that engage in HVB can experience a broad assortment of acute effects in perception, emotion, and cognition that are similar, albeit less intense, to those evoked by hallucinogenic drugs (Grof, 1988; Nichols, 2016). The following manifestations of ASCs are reported by individuals who engage in hyperventilation after approximately eight minutes: ringing/roaring in the ears, clouded vision, feelings of astonishment, and lightness (Agadzhanyan et al., 2003). Furthermore, after around 15 min, more dramatic changes in consciousness can occur, including perceptual distortions and subjective visions (Agadzhanyan et al., 2003). Manifestation of ASCs are likely to be more pronounced in HVB practices that employ continuous hyperventilation for prolonged periods (i.e., CCB, GBW, rebirthing) and do not involve breath holds (i.e., WHbM, tummo), rest (i.e., kapalabhati, bhastrika) or cycled changes in tempo back to slower breathing (i.e., SKY) (see Table 1 for presence of interrupted inspiration/expiration cycles). Such interruptions in breathing are likely to negate acute and longer lasting effects of ASCs since hyperventilation is terminated during these periods, meaning acute effects may be more short-lived or less intense. In particular, we believe continuous HVB techniques are more likely to affect the efficacy of interoceptive feedback control (explained later in Section 4.3) because sustaining hyperventilation perpetuates a state of homeostatic dysregulation, whilst breath holds would counteract this effect.

GBW has been described as inducing 'psychedelic' experiential states by over 80% of psychiatric inpatients (in a bulletin for the Multidisciplinary Association for Psychedelic Studies—MAPS) (Eyerman, 2013), and to evoke a 'complete mystical experience', assessed by The States of Consciousness Questionnaire (SCQ) (Griffiths et al., 2006), in around 10% of those participating in a day-long workshop of GBW (Puente, 2014b). Comparable rates (around 11%) of mystical experiences are described by participants after being administered a 10 mg/70 kg psilocybin dose (Griffiths et al., 2011). Serotonergic hallucinogenic compounds are commonly associated with mystical experiences, which are largely ineffable beyond their phenomenological characterisation by a sense of unity, that 'all is one', a transcendence of time and space, and positive mood (Griffiths et al., 2006; Hick, 1962; Pahnke, 1963). The sense of unity is arguably central to these experiences and reportedly experienced as a breakdown between 'the self' and 'the other' (i.e., the world around). Such a self-less state, also known as ego dissolution, is perhaps better defined as 'the experience of a compromised sense of self' (Nour et al., 2016) since metacognitive aspects of the self-as-observer appear preserved. These psychedelic experiences appear to underlie therapeutic utility: the phenomenology of psychedelic experience is shown to mediate outcome variables related to wellbeing in studies of individuals taking psychedelic drugs (Griffiths et al., 2011; Griffiths et al., 2006; Puente, 2014a; Uthaug et al., 2019; Uthaug et al., 2020).

Interestingly, while ego dissolution (assessed by the Ego Dissolution Inventory; EDI) has been reported by only a third of participants in a study of GBW (Uthaug et al., 2022), most participants still experienced an improvement in wellbeing variables. Similar effects have been reported previously for GBW (Puente, 2014a), and in studies of hallucinogenic compounds including psilocybin, ayahuasca and 5-MeO-DMT (Mason et al., 2019; Uthaug et al., 2019; Uthaug et al., 2021). EDI ratings of ego dissolution do not necessarily capture the full subjective experiential state evoked by HVB and there may be other attributable pathways toward improved wellbeing and mental health related variables. The potential relevance of the mechanisms of action of HVB in the genesis of these effects is discussed further in Section 4.3. In essence, while 'experiences' of the mystical/ego dissolution is part of what may drive therapeutic effects in psychedelic trials it is seemingly not the only factor at play. There may be other 'ingredients' that drive betterment such as psychological insight as well as emotional breakthrough (Kangaslampi, 2023), along with changes in affect attributed to non-pharmacological factors (e.g., in Ayahuasca retreat rituals) (Uthaug et al., 2021). This also includes pivotal mental states (Brouwer and Carhart-Harris, 2021) and catharsis which may also be a part of the equation of 'mechanisms of effect'. In fact, there could be a somatic equivalent of this (i.e., pivotal bodily states), resting in the premise of hormesis. The characterisation of the similarities and differences between HVB and hallucinogens in their evoked experiential states and later outcomes is still in its infancy. Nevertheless, HVB represents a promising non-pharmacological alternative to engender alterations in an individual's state of consciousness that might mediate therapeutic benefit to mental health and wellbeing.

3. Preliminary indications of therapeutic effects of HVB practices

Observational research and anecdotal reports have been used to promote interest in the therapeutic potential of HVB techniques, with authors claiming improvement of both mental and physical conditions (i.e., Grof and Grof, 2010). Anecdotally, breathwork facilitators report improved symptoms of mood, anxiety, and trauma-related disorders (e.g., post-traumatic stress disorder—PTSD) in people participating in HVB. Clinical implementation of HVB practices as therapy have been evaluated in large community samples, including people in prisons and in over 11,000 psychiatric inpatients (MAPS report) (Brewerton et al., 2012; Brown and Gerbarg, 2005b; Eyerman, 2013; Meuret et al., 2005). However, the quality of such studies is generally constrained by limited detail about methods used to deliver breathwork. The physiological effects of HVB have also been the subject of empirical studies, though the evidence base is small. One example relates to kapalabhati, where physiological effects of this fast-paced breathing practice were measured only over one-minute periods (Bellissimo et al., 2020; Bhargav et al., 2014). Despite the general scarcity of published studies on HVB practices, we summarise the existing work to indicate their therapeutic potential. The findings across various HVB practices tentatively concur with Fincham et al.'s (2023) recent meta-analysis, which identified that breathwork was associated with lower levels of subjective stress, anxiety, and depression, when compared to non-breathwork control groups. However, only around 20% of the included randomised-controlled trials (RCTs) had a primary focus on fast-paced breathwork; the remaining RCTs were mainly focused on slow-paced techniques.

3.1. Grof (holotropic) breathwork

GBW, formerly known as holotropic breathwork, is perhaps the most well-known HVB technique for inducing ASCs and involves up to three hours of hyperventilation paired with evocative music and several other components (see Table 1 for accessory elements). It was found to have beneficial impacts on character development, inferred by an increase in self-awareness and positive changes in temperament (Miller and Nielsen, 2015). Volunteers in a GBW workshop rated their experience as 'considerably meaningful' and to evoke 'increased wellbeing' (Puente, 2014a). Participants of GBW also reportedly recovered from substance abuse disorders (Metcalf, 1995), psychosomatic conditions such as asthma (Grof and Grof, 2010), as well as psychological conditions including anxiety and depression (Lalande et al., 2012). Uthaug et al. (2022) found that ratings of non-judgement of thoughts increased within 24 hours (i.e., sub acutely) following the GBW session and persisted for four weeks. Moreover, stress-related symptoms significantly decreased, while satisfaction with life significantly increased four weeks post GBW. Further, a decrease in death anxiety and increase in self-esteem was found in participants who received GBW therapy, compared to those who received verbal therapies (Holmes et al., 1996). Healthy participants also experiencing GBW for the first time reported reductions in rigidity and dogmatic thinking, with increases in capacity for connecting with others, and sensitivity towards their own needs and emotions (Binarová, 2003). Considering these are traits associated with psychological resilience, it is plausible that GBW may also have applications as a preventative measure.

3.2. Rebirthing and conscious connected breathing

Anecdotal support for clinical efficacy of these practices comes from a clinical case study reported by de Wit and Cruz (2021), who describe sustained remission of PTSD symptoms, and reduction of depression and anxiety symptoms after eight weekly breathwork sessions of around an hour. The authors theorise that the CCB-enhanced cognitive processing capacity of the traumatic experience was paralleled by shifting components of autonomous nervous system activity (de Wit and Cruz, 2021). Further benefits of CCB were found in participants who underwent 10 sessions of CCB over four months, reporting decreases in anger, anxiety, and depression, along with an increase in joy and satisfaction following CCB (Heyda, 2000).

3.3. Sudarshan kriya and yogic pranayama

SKY and Yogic-type HVB, though often combined with other pranayama (mainly slow), have seemingly received the most rigorous investigation at present in RCTs, as displayed in Table 2. Such RCTs in SKY indicate positive self-reported psychological effects pertaining to mental health, in particular PTSD. In Carter et al.'s (2013) study, patients with PTSD performed 22 hours of guided SKY. There were reports of mild psychological discomfort, featuring fleeting images from past trauma – however there were no reactions that were classed as severe. The severity of PTSD symptoms was significantly reduced and remained low when reassessed six weeks and six months post-intervention. The effect size of the difference in clinically administered PTSD scale scores from pre-intervention to six months was large (2.9) for the SKY group; while effect sizes for antidepressant trials are in the moderate 0.5 range (Carter et al., 2013). Another investigation using SKY also found a significant reduction in PTSD and anxiety symptoms and reduced respiratory rates in comparison to a control group, both immediately after the intervention, and at one-month and one-year follow-ups (Seppälä et al., 2014). In addition, administering SKY to tsunami survivors who were diagnosed with PTSD revealed that at six and 24-week follow-ups, the mean PTSD scores were significantly lower than pre-intervention levels, in this non-

randomised trial (Descilo et al., 2010).

SKY has also showed promise as a therapy for other psychiatric disorders including depression, anxiety, insomnia, substance use disorder, and has been implemented at large in programmes for individuals in imprisonment to promote decreases in violence and improve attention and wellbeing (Brown and Gerbarg, 2005b). Whilst SKY has undergone a series of rigorous research investigations, in diagnostically defined clinical cohorts, few RCTs have examined objective physiological data.

Table 2
RCTs using yogic pranayama with HVB, and their participant, intervention, control, outcome (PICOs), and brief summary of results. Studies were only included if they were RCTs which comprised a HVB component. Studies on yoga and pranayama without a HVB component were not included.

Authors	Population	Intervention (s) (*Breathwork type*)	Control (s)	Outcome type	Summary of results
(Carter et al., 2013)	Vietnam war male veterans with PTSD	SKY program adapted for veterans	Wait-list	Psychological (subjective self-report)	Significant reduction in PTSD symptoms after participating in intervention
(Janakiramaiah et al., 2000)	Hospitalised untreated melancholic depressives	SKY with supine rest	C1: Electroconvulsive therapy (ECT), C2: imipramine (IMN)	Psychological	No significant differences between the three groups, however significant reductions in depressive symptoms for all. Reductions highest for ECT
(Sureka et al., 2014)	Male prisoners with non-psychotic psychiatric disorders	Sudarshan Kriya & related practices (SK&P): 1) three staged Ujjayi breathing, (2) Bellows breath (Bhastrika), (3) Om chant, (4) Sudarshan Kriya & (5) alternate nostril breathing (Nadhi Shodhan)	Sit in armchair & pay gentle attention to breath	Psychological	Intervention group showed improvement on global assessment of functioning, anxiety, depressed mood, positive wellbeing, general health, self-control, vitality, & total positive general wellbeing. Compared to controls, change on scale scores was statistically significant (all in direction suggestive of improvement)
(Sharma et al., 2017)	Patients with major depressive disorder following inadequate response to antidepressants	SKY program featuring Yoga postures, sitting meditation & stress education, then Sudarshan Kriya home practice	Wait-list	Psychological	Significant improvement in self-reported depression & anxiety symptoms in intervention group compared to control group
(Goldstein et al., 2020)	University students	SKY Campus Happiness Program (workshop for stress management & wellness)	Wisdom on Wellness (WoW) psychoeducation stress management workshop	Psychophysiological (subjective & objective measures)	Intervention group showed greater improvements compared to WoW on: perceived stress, sleep, social connectedness, distress, anxiety, depression, conscientiousness, self-esteem & life satisfaction. Both groups improved concerning heart rate measures of stress reactivity
(Seppälä et al., 2014)	Iraq or Afghanistan war male veterans with PTSD	SKY program for veterans (several practices with periods of discussion & stretching)	Wait-list	Psychophysiological	Intervention group showed reduction in PTSD symptoms, anxiety symptoms & respiration rate, however control group did not. Immediately post-intervention, reductions in startle corresponded with decreases in symptom of hyperarousal
(Seppälä et al., 2020)	University students	SKY Campus Happiness Program (or Foundations of Emotional Intelligence—EI, or Mindfulness-Based Stress Reduction—MBSR)	Wait-list	Psychological	SKY group displayed most benefit compared to control on depression, stress, mental health, mindfulness, positive affect & social connectedness. MBSR group exhibited no change. EI showed improvement on mindfulness
(Novaes et al., 2020)	Healthy young adults	Bhastrika pranayama (classed as cycles of Kapalabhati), Nadhi Shodhan & breath hold/retention with three Bandhas	Ludic cognitive activities such as crosswords, puzzles, domino, checkers & card games, also in the presence of an instructor	Psychophysiological	Bhastrika group showed significantly reduced anxiety & negative affect. Such changes were connected to the modulation of brain area activity & connectivity involved in attention, awareness & emotion
(Vedamurthachar et al., 2006)	Inpatients with alcohol dependence following one week of detoxification management	SK&P: Ujjayi pranayama, Bhastrika pranayama, Sudarshan Kriya, followed by Yoga Nidra (lying down in quiet way / restful state). Sudarshan Kriya comprised main component	No intervention	Psychophysiological	Decreases in both groups' depression scores, plasma cortisol & adrenocorticotropic hormone but significantly more reduction in intervention group. Decreases on self-reported depression correlated with cortisol in intervention group
(Kumar et al., 2013)	Advanced stage breast cancer patients	Ujjayi breathing, Bhastrika pranayama, Sudarshan Kriya	Standard care	Psychophysiological	Significant decrease in blood cortisol levels in intervention group compared to control condition. Pain perception, according to self-reported scale, reduced in intervention group
(Subramanian et al., 2012)	Engineering students undergoing exams	Gentle stretching (asanas), breathing practices (SK&P: Ujjayi, Bhastrika, & Sudarshan Kriya), meditation with positive thinking	No intervention	Physiological (objective)	Improvements in lipid profile & haematological parameters found in intervention group
(Bayley et al., 2022)	Military veterans with PTSD	SKY (five techniques: alternate nostril breath, straw breathing,	Cognitive processing therapy (CPT)	Psychological	SKY found to be non-inferior to CPT for self-reported PTSD scores

(*continued on next page*)

Table 2 (*continued*)

Authors	Population	Intervention (s) (***Breathwork type***)	Control (s)	Outcome type	Summary of results
		Ujjayi, Bhastrika & Sudarshan Kriya, followed by meditation & rest)			post-intervention at 1-month & 1-year follow-up. SKY also non-inferior to CPT for scores on subjective depressive symptoms along with positive & negative affect at 1-month, but not 1-year
(Ravindran et al., 2021)	Outpatients with unipolar or bipolar depression	Pranayama: Ujjayi, cyclical Kapalabhati – 40–60 breaths/min, 60–80 breaths/min, 80–100 breaths/min	Psychoeducation protocol for unipolar & bipolar depression	Psychological	Intervention group showed significant reduction in depressive symptoms (for first half of study—this was a crossover trial), but there was no significant difference between groups

At present, this includes exploration of a SKY intervention using electrocardiogram (ECG) and respiration measures in non-clinical college populations, along with eye-blink startle and resting respiration in veterans with PSTD (Goldstein et al., 2020; Seppälä et al., 2014).

3.4. Wim Hof breathing method and tummo meditation

Worldwide, millions practise the WHbM, yet scientific investigations on the method and its components are scarce. However, a controlled laboratory case study on Wim Hof has examined the influence of his method on the inflammatory response to bacterial endotoxin—*E. Coli.* (Kox et al., 2012). Results showed a blunted proinflammatory response compared to a historical cohort of over 100 healthy control samples who did not practise this HVB. Kox et al. (2014) further studied the modulatory effects of the WHbM on systemic inflammatory and neuroendocrine responses upon administration of toxins *E. Coli.* and Lipopolysaccharide (LPS). This immune challenge was administered to novices who had trained in the WHM for 10 days (Kox et al., 2014). Consequently, these individuals demonstrated the same diminished pro-inflammatory responses, in comparison to controls (WHbM-naïve). The authors reported that the higher the levels of adrenaline during cyclical hyperventilation (a feature of the WHbM), the lower the inflammatory response was, and the greater the anti-inflammatory response. Furthermore, cortisol peaks were similar between both groups, however the WHM-trained condition had a faster recovery of baseline cortisol levels after cessation of HVB (Kox et al., 2012; Kox et al., 2014).

In a non-randomised observational study, researchers found eight weeks of WHM-training led to a reduction in self-reported depressive symptoms compared to the control condition (Touskova et al., 2022). Considering growing evidence that overactivation of the innate immune system is associated with mood dysregulation and depression (Beurel et al., 2020), the observed blunted response to a pro-inflammatory challenge might indirectly suggest that this type of HVB practice could confer beneficial health benefits to conditions associated with both mood disorders and systemic inflammation (Buijze et al., 2019; Zwaag et al., 2020). Recently, Zwaag et al. (2022) showed that the WHbM was associated with an increase in levels of plasma epinephrine in healthy young men, while cold exposure alone did not relevantly modulate the inflammatory response induced by LPS administration. In fact, the WHbM led to significantly attenuated and enhanced proinflammatory and anti-inflammatory cytokine levels, respectively, with the cold exposure significantly enhancing the immunomodulatory effects of the WHbM (Zwaag et al., 2022). One randomised trial related to WHbM and perceived subjective stress has been published (Kopplin and Rosenthal, 2022); the combined group (daily cold shower and the WHbM – essentially the WHM) exhibited a medium-large positive effect on perceived stress compared to a wait-list control group. The findings suggest that an application of the WHbM is associated with a statistically significant decrease in perceived stress. The overall effect size (of all three interventions – the WHM, WHbM, or cold exposure only) calculated was considered a medium effect, compared to the control group. While all intervention groups experienced this effect over time, the combined practice of HVB and cold exposure (i.e., cold shower) yielded the highest benefit (Kopplin and Rosenthal, 2022).

Regarding g-tummo (from which the WHbM is derived, along with pranayama), Kozhevnikov et al. (2013) identified increases in axillary temperature during forceful breathing and observed increases in alpha, beta, and gamma power, measured with electroencephalography (EEG). Increases in alpha power significantly correlated with increases in temperature (Kozhevnikov et al., 2013). This indicates that HVB techniques could assist people in regulating body temperature, such as poikilothermic patients (Kurz et al., 1998). Most recently, an RCT showed that five minutes of daily breathwork and mindfulness meditation for four weeks can improve mood and reduce anxiety, but breathwork practices (including a five-minute daily practice of HVB with breath retention similar to tummo and the WHbM) improved mood and physiological arousal more than the meditation group for the same duration (Balban et al., 2023).

4. Neurophysiological mechanisms of HVB practices

HVB is typically accomplished through an increase in respiratory rate, an increase in tidal volume, or both. The result is hyperventilation, i.e., 'an increase in minute ventilation in excess of the requirement for the body's oxygen consumption' (Ley, 1999). This section summarises the neurophysiological perturbations underlying sustained hyperventilation. Describing the physiological cascade of systemic and CNS events resulting from hyperventilation might help identify the aspects of HVB practices that are related to clinically relevant effects. In particular, the characterisation of these mechanisms highlights the likely downstream effects of HVB practices on neurometabolism and neuronal function, that are conducive to their acute experiential states, profile of safety and tolerability, and possibly therapeutic effects. Fig. 2 below illustrates the main neurophysiological effects of hyperventilation, focusing specifically on modulation of neurometabolism and neuronal excitability. Although hyperventilation and HVB are not interchangeable terms, extrapolating from mechanistic literature of hyperventilation is useful due to the inadequate body of literature directly investigating the physiology of HVB techniques.

The primary roles of ventilation are: 1) to acquire oxygen (O_2) to support aerobic metabolism, and 2) to eliminate carbon dioxide (CO_2) to maintain an optimal acid-base balance (i.e., pH 7.35–7.45) (Hopkins et al., 2022). The elimination of CO_2 via expiration represents a survival-oriented method for acute homeostatic regulation of pH and is proximally coupled to respiratory drive (Guyenet and Bayliss, 2015). Tight regulation of acid-base balance is critical for optimal cellular function and is orchestrated by a distributed network of CO_2-sensing chemosensors located in arguably the most phylogenetically ancient structures of the brain (Guyenet and Bayliss, 2015; Hopkins et al., 2022). Ancient gas exchange mechanisms among aquatic vertebrates predate the evolution of lung structures that support air-breathing terrestrial

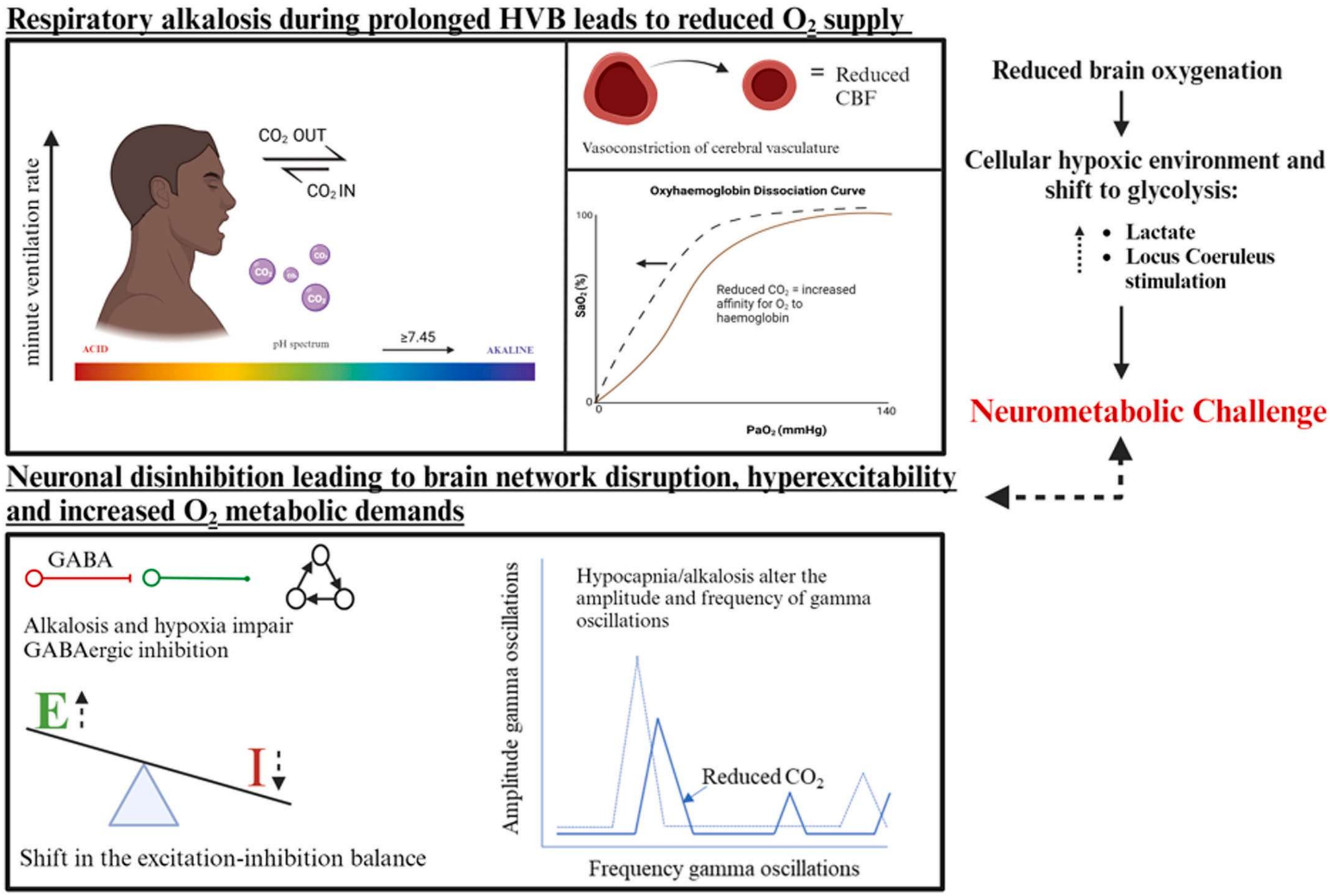

Fig. 2. Neurophysiological mechanisms of HVB practices occurring in parallel during continuous HVB. As ventilation rate/depth is increased and CO_2 is eliminated faster than it is taken up, respiratory alkalosis ensues, causing cerebral vasoconstriction and oxyhaemoglobin dissociation curve shift, resulting in reduced supply of O_2 delivery to the brain. This induces a hypoxic environment, neuronal metabolic shift towards glycolysis causing lactate accumulation and stimulation of adrenergic Locus Coeruleus. In parallel, alkalosis/hypocapnia impair GABAergic inhibition of excitatory neurons leading to disruption of gamma oscillatory networks (Stenkamp et al., 2001), hyperexcitability of neurons and increased neurometabolic demands, which cannot be matched by adequate O_2 supply (Diagram created by the authors with BioRender.com).

vertebrates, including amphibians (Ultsch et al., 2004). Evolutionary pressure enabled the development of adaptive and specialised responses to salient environmental challenges, for example the build-up of atmospheric CO_2 in response to volcanic eruptions.

The chemosensor-driven hyperventilatory response to acidosis is a primitive reflex. Nevertheless, the response is also subject to voluntary control, and hence can support the situational integration of afferent interoceptive ascending chemosignalling, with top-down motor commands. This dual voluntary and non-voluntary organisation extends to the innervation and structure of thoracic diaphragm muscle (Nakayama et al., 2004). Together, this architecture supports allostatic respiratory control, which itself can be framed within predictive coding/active inference models of behaviour. During active respiration, the primary motor cortex initiates muscular contraction by transmitting impulses down the spinal cord via corticospinal tracts, engaging the diaphragm and accessory muscles of respiration (Moutlana, 2020). Some respiratory muscles are more readily activated by volition, such as the scalenes and parasternal intercostals, due to unequal distribution of strength and corticospinal inputs to respiratory muscles (Hudson et al., 2020). When volitional control of breath is exercised, unconscious and autonomic control of breath can be overridden (descending motor ‘predictions’ suppress ascending interoceptive ‘prediction error’ signals). This is characteristic of ventilation and arguably distinguishes it from other homeostatic reflexes with equally crucial survival value, such as glucagon responses to hypoglycaemic stress (Taborsky Jr and Mundinger, 2012). The volitional ability to manipulate ventilation is linked evolutionarily to both upright gait and the support of phylogenetically modern functions such as voice control (Li and Rymer, 2011).

Volitional control enables the organism to either accumulate CO_2 through extended periods of breath-holding, or to eliminate CO_2 via hyperventilation. Breath-holding capacity is limited as volitional control is typically incapable of sustained overriding of reflex control at (partial pressure of end-tidal) $PetCO_2 \sim 54 \pm 2$ mmHg (Lin et al., 1974), although apnoea training increases both subjective tolerance and brainstem response to hypercapnia, such as in the case of experienced divers (Goossens et al., 2014). Instead, voluntary hyperventilation can be maintained for extended periods of time by healthy individuals, even without specific training. This results in (end-tidal) $ETCO_2$ levels substantially reduced below typical physiological levels – at sea level and normal body temperature, normal $ETCO_2$ is ~35 mmHg CO_2 (Godoy et al., 2017).

4.1. Autonomic and endocrine effects of hyperventilation

HVB practices affect the function of the autonomic nervous system. A state of sustained hyperventilation breaches homeostatic mechanisms maintained by involuntary respiration and requires allostatic adjustment. Physiologically, cardiorespiratory coupling is achieved at several levels. First, there are basic mechanical interactions between lung inflation, chest pressure and cardiac ventricular filling. Second, further smoothing and coordination occurs via arterial baroreflex-related control of sympathetic and parasympathetic outputs at the level of the medulla. This effect underpins respiratory sinus arrhythmia and reflects a direct action of afferent signalling from lung stretch receptors on central control of vagal tone (Eckberg, 2009; Taha et al., 1995). Thirdly, in support of allostasis, baroreflex-related cardiorespiratory coupling, including respiratory sinus arrhythmia, is frequently overridden by descending 'top-down' control. The baroreflex is inhibited usually as a stress response to enable increased cardiac output (raised heart rate and blood pressure) in support of adaptive (motoric) behaviour.

The intentional regulation of respiration is one of two main mechanisms (the other being postural/muscle control and relaxation) through which one can volitionally alter autonomic activity, which regulates usually uncontrollable inner bodily functions. Initiating HVB disinhibits sympathetic tone through both central command and cortically mediated sympathetic drive, in anticipation of, and in response to, increased muscular activity such as vigorous breathing, leading to increased cardiac output with engagement of the respiratory muscles (Kety and Schmidt, 1946; Schüttler et al., 2020). Increasing ventilation inhibits parasympathetic cardiovascular drive and amplifies accompanying effects on physiological arousal mediated by the disinhibited sympathetic nerves. The result of increased sympathetic and decreased parasympathetic tone to the sinoatrial pacemaker and myocardium is elevated heart rate, increased blood pressure and increased electrodermal (sympathetic sudomotor) activity (Kety and Schmidt, 1946; Schüttler et al., 2020).

Such cardiorespiratory arousal can intensify experiential changes: sympathetic nervous activation also accompanies administration of psychedelic compounds, and the magnitude of subjective experience is reported to be positively correlated with sympathetic activity and negatively with parasympathetic activation (Olbrich et al., 2021).

Shifts in sympathetic/parasympathetic autonomic balance are also characteristically associated with neuroendocrine function, most commonly affecting the hypothalamic-pituitary-adrenal (HPA) axis which mediates humoral stress responses (Abelson et al., 2010). This system is driven by forebrain processing of physical and emotional stressors, to shape the more homeostatic hypothalamic-pituitary release of cortisol from the adrenal cortices. HVB likely also engages, both directly and in response to hypocapnia/hypoxia these same descending influences on HPA axis activity (King et al., 2009; Lyubkin et al., 2010); voluntary hyperventilation correspondingly increases circulating adrenal stress hormones (Stäubli et al., 1988).

Though increasing the circulation of stress hormones seemingly counters the healing reputation of HVB, observations from a study assessing the effects of the WHbM might provide a possible mechanistic insight into this apparent paradoxical effect (Kox et al., 2014): the authors reported that peripheral endocrine and inflammatory response to a pro-inflammatory challenge was affected by the WHbM. After the inflammatory challenge, the WHbM practitioners were found to have higher cortisol spikes, yet a quicker recovery and stabilisation of cortisol levels after cessation of breathwork in comparison to the control group of WHbM-naïve individuals (Kox et al., 2014). These findings suggest that modulation of HPA cortisol release by HVB might contribute to beneficial and longer-term therapeutic outcomes; for instance in conditions associated with chronically raised cortisol levels such as anxiety and PTSD (Bhatt et al., 2021; Lenze et al., 2011; Yehuda, 2001). These remain speculative ideas, as the study of cortisol levels post-HVB and in recovery phases remain unexplored.

More generally, the global physiological disruption induced by HVB has been viewed as a form of 'eustress': a 'hormetic' intervention that confers beneficial health characteristics as a function of moderate stress on multiple biological systems. This was proposed to occur by reversing dysregulation or defective adaptive stress responses, resulting in increasing resilience to (future) emotional, cognitive, and biological stressors (Faye et al., 2018).

4.2. Neurometabolic effects of hyperventilation

As CO_2 is acidic in solution, lowering $ETCO_2$ by sustained hyperventilation leads to elimination of acids, and hence respiratory alkalosis. Studies in both humans and animals demonstrated that hyperventilation causes an immediate rise of blood and cerebrospinal fluid (CSF) pH (see Table 3). The pH elevation triggers a cascade of downstream effects that alter central nervous system function at several levels. Cellular alkalosis is specifically detected by central and intrinsic proton detectors, such as the TASK-2 channels that are strongly expressed by the Phox2b-expressing glutamatergic neurons of the medullary retrotrapezoid nucleus (Wang et al., 2013). Phox2b neurons are especially activated by hypercapnia, and probably reduce respiratory pattern generation by hypocapnia (Guyenet and Bayliss, 2015; Guyenet et al., 2016) as these signals are relayed to pontomedullary regions to facilitate efferent respiratory pattern generation. Alkalosis impairs GABAergic inhibition of cortical circuits at multiple levels: in an alkalotic environment, evoked GABAergic synaptic transmission is impaired, as is neural repolarisation, blocking production of sequential spikes (Sun et al., 2012). This reduced synaptic efficiency of cortical GABAergic interneurons lowers their inhibitory tone to pyramidal neurons, further enhancing their excitability (Li et al., 2012). The consequence is an overall shift in the excitation-inhibition balance, affecting both interregional cortical and efferent pyramidal neurotransmission. Moreover, a further sequela of alkalosis is a reduction in serum calcium (Ca^{2+}), which further increases cerebral neuronal excitability (Han et al., 2015). Hypocalcaemia resulting from HVB also stimulates the release of excitatory amino acids N-methyl-D-aspartate and glutamate, which further contribute to the hyperexcitability effects (Curley et al., 2010; Salvati and Beenhakker, 2019).

The widespread increased neuronal excitability is accompanied by increased metabolic demands and hence rate of cerebral oxygen consumption ($CMRO_2$). However, during sustained HVB practices, the increased cerebral neurometabolic demands are not followed by an adequately increased O_2 supply, due to the vasoconstrictive effect of hypocapnia on brain-wise cerebral haemodynamics, as CO_2 has a direct vasodilatory effect on cerebral arterioles (Brian, 1998; Curley et al., 2010; Laffey and Kavanagh, 2002; Raichle and Plum, 1972; Stocchetti et al., 2005). The positive relationship between partial pressure of CO2 in arterial blood ($PACO_2$) and cerebral blood flow (CBF), i.e., cerebrovascular CO_2 reactivity (Ainslie and Duffin, 2009; Wei and Kontos, 1999) means that alkalosis leads to a reduction in CBF (constricted cerebral vessels produce approximately a 2% reduction in CBF per 1 mmHg decline in $ETCO_2$) (Godoy et al., 2017; Raichle and Plum, 1972). These effects are presumed to preserve central pH and adaptively-attenuate the potential excitotoxic effect of sustained alkalosis (Ainslie and Duffin, 2009).

The impairment in O_2 supply may be exacerbated by low CO_2 which compromises gas exchange in the lungs, producing hypoxemia and shifting the oxygen-haemoglobin dissociation curve leftward. This results in haemoglobin having increased affinity to O_2, hence inefficient release of O_2 to cells (so-called 'high affinity hypoxia') (Curley et al., 2010; Stocchetti et al., 2005). The disproportionate cerebral O_2 utilisation relative to O_2 supply results in the development of a cellular hypoxic environment. Acute hypoxia constitutes a neurometabolic challenge and further stimulates neuronal O_2 consumption (Watts et al., 2018). In parallel, there is a progressive shift in neuronal metabolism toward increased utilisation of glycolysis (ultimately, a less efficient means of energy production which results in lactic acid accumulation), which is proportional to the decrease in $PACO_2$, and promotes arousal via stimulation of Locus Coeruleus noradrenergic neurons (Huckabee, 1958; Nariko, 1968).

Despite decades of research, the neurophysiological adaptation response to sustained conditions of prolonged hyperventilation remains contentious. Experimental observations from studies investigating the effects of prolonged passive/active hyperventilation in awake subjects

Table 3
Summary of relevant physiological studies reporting the effects of prolonged hyperventilation (HV) on haemodynamic and neurometabolic parameters, such as $CMRO_2$, CBF, pH, in awake and healthy human volunteers. Studies were included if hyperventilation was employed for longer than 20 min to investigate its effects on neurometabolic and haemodynamic parameters. Studies where hyperventilation was conducted under anaesthesia were not included, as this is known to alter haemodynamic parameters. *Note*: One study in unanaesthetised goats is included as illustrative of early (< 1 hr) and delayed (> 1 hr) compensatory mechanisms.

Authors	Methods & measures	Active or Passive HV	Duration	Effects
(Poulin et al., 1998)	Transcranial doppler US middle cerebral artery blood flow (MCA CBF)	Passive	20 mins	Rapid ↓ MCA CBF at HV onset followed by progressive ↑ in MCA CBF (return to baseline)
(Reivich et al., 1968)	Kety - Schmidt method (pO_2; pCO_2; glucose; lactate)	Passive phase I: normal breathing phase II: 6%O_2 for 10 mins phase III 100%O_2 for 10 mins	20 mins	Linear arterial ↓ pCO_2 in & CBF in HV phases ↑ anaerobic index during HV phase II from 3.5% to 15.8% ↓ anaerobic index during HV phase III (return to baseline) = cerebral excess lactate
(Ellingsen et al., 1987)	Transcranial doppler US (CBF)	Active	> 20 mins	↓ CBF, new semi-steady state within ~2 mins. ↑ CBF towards baseline within 10 mins of hypocapnia
(Kety and Schmidt, 1946)	Kety - Schmidt method (CBF; $CMRO_2$)	Active & Passive	20–30 mins	↓ arterial & venous CO_2 & H^+ ↑ in cAV, O_2 & CO_2 diff ↓ in CBF (−32% in voluntary HV, −36% in passive HV) = $CMRO_2$ (passive) or ↑ (active)
(Severinghaus and Lassen, 1967)	Kety - Schmidt method (CBF)	Active	1.5 hrs	First 30 s: ↓ CBF with a time constant of 0.3 min to 68% of baseline
(Raichle et al., 1970)	Kety - Schmidt method (CBF; pCO_2)	Active	4.5 hrs	↓ CBF at onset of HV, ↑ CBF return to 90% of baseline through HV ↑ CBF rises to 20% above baseline after end of HV
(Dempsey et al., 1975)	Arterial & CSF sampling (pH, Lactic acid)	Passive (normoxic & hypoxic)	26 hrs	↑ Arterial pH after HV onset = Arterial pH during initial 12–14hrs of normoxic HV ↓ Arterial pH during initial 12–14hrs of hypoxic HV Return to baseline levels over final 6–10hrs ↑ Arterial lactate in hypoxic HV CSF Lactate > Arterial Lactate
(Albrecht et al., 1987) *	*Study in unanaesthetised goats. CSF & cerebral venous blood sampling (pH, HCO3, lactate, pyruvate)	Passive	6 hrs	*During HV:* ↓ CBF & $CMRO_2$ after HV initiation but return to baseline within 6hrs ↑ pH (Arterial, sagittal sinus, CSF) after HV initiation but return to baseline within 6hrs ↑ Lactate & Pyruvate (Arterial, sagittal sinus) ↑ = Lactate & Pyruvate (CSF) = Lactate: Pyruvate ratio (all tissues) *Upon termination of HV:* ↑ CBF & $CMRO_2$ above baseline

are summarised in Table 3. After initial alkalinisation, pH in brain tissue and cerebral arterial and venous blood progressively fall due to lactic acid accumulation in brain and blood (Albrecht et al., 1987; Dempsey et al., 1975). It is expected that such a fall in pH should be accompanied by a parallel rise of CBF to baseline levels, however, interactions between (partial pressure) pCO_2, pH, and CBF are complex. In fact, results of studies employing different experimental paradigms indicate that prolonged hyperventilation does not result in rapid compensatory restoration of CBF; Severinghaus and Lassen (1967) found no return of CBF to full baseline levels in conscious healthy humans after 90 min of active hyperventilation. Similarly, Raichle et al. (1970) also identified in conscious healthy individuals that CBF fell immediately after hyperventilation initiation, and gradually continued to rise back 90% of baseline levels, exceeding such levels once hyperventilation stopped.

Furthermore, Albrecht et al. (1987) reported in unanaesthetised, passively ventilated goats, a progressive return of CBF to baseline levels after six hours of hyperventilation. Buffer mechanisms that are triggered by the onset of alkalosis to normalise pH changes in CSF and extracellular space also include the cellular efflux of hydrogen ions (H^+) and the exchange of extracellular bicarbonate (HCO_3) for intracellular chloride and a slower acting buffer mechanism at the proximal renal tubular level, where HCO_3 reabsorption is prevented in combination with H^+ secretion (Curley et al., 2010; Godoy et al., 2017; Stocchetti et al., 2005). Whilst this mechanism begins minutes after the onset of hypocapnia, it appears to take effect and reduce pH after approximately four hours of prolonged HVB and normalises CSF and perivascular pH after six hours of hypocapnia (Mykita et al., 1986). The resulting effect of adaptation during sustained HVB, such as that obtained by prolonged HVB practices (for example GBW), is likely a time-dependent normalisation of CBF and pH perturbations. It is not known whether repeated practice can potentially alter the time course of compensatory adaptive changes.

The evidence reviewed above suggests that phenomena impacting both specific and general higher cerebral functions might implicate the attenuation of GABAergic contributions to excitation-inhibition balance across networked brain systems – GABAergic function underpins the orchestration of gamma oscillatory rhythms: implicated in perceptual and cognitive functions ('predictions' of predictive coding) that include attention (Jensen et al., 2007), object recognition (Keil et al., 1999), learning (Sederberg et al., 2007), long-term memory formation (Axmacher et al., 2006; Van Vugt et al., 2010) and pain (Schulz et al., 2012). Gamma oscillations also are linked to the pathophysiology of mood disturbance (Pinna and Colasanti, 2021) which is relevant to the possible psychedelic effects of HVB, where their association with perceptual alterations (Baldeweg et al., 1998) suggests their role as neural substrates of dream-like states (Llinas and Ribary, 1993).

In vitro experimental work has helped elucidate the mechanisms by which alkalosis and associated hypoxia influence brain-wise gamma rhythms. Hypocapnic exposure of rodent hippocampal slices directly modulates induced gamma rhythms (Stenkamp et al., 2001). Fast-spiking hippocampal basket cells, i.e., the GABAergic parvalbumin interneurons (PV-INs) that generate and maintain gamma oscillations (Csicsvari et al., 2003; Sohal et al., 2009; Veit et al., 2017), display a unique neurometabolic vulnerability to hypoxia (Pinna and Colasanti, 2021). Across the neocortex, PV-INs constitute the largest interneuron population and have the largest share of inhibitory GABAergic boutons (Gulyás et al., 1999). Within cortical circuits, PV fast-spiking basket cells are strategically positioned to exert both feedforward and feedback inhibition and gain control (Espinoza et al., 2018; Scudder et al., 2018) to excitatory pyramidal outputs, and are constantly active across the total cycle of fast gamma oscillations. The resulting high demand for mitochondrial adenosine triphosphate (ATP) production requires a continuous and plentiful supply of oxygen (Gulyás et al., 2010; Hájos et al., 2004; Tukker et al., 2013). This makes PV-INs, and functions dependent upon gamma oscillations, exquisitely vulnerable to effects of hypoxia. The hypoxic environment putatively induced by prolonged HVB is thus likely to dysregulate the inhibitory-excitatory balance underlying the function of brain networks involved in higher-order functions (Huchzermeyer et al., 2008).

These mechanisms affecting neuronal hyperexcitability and network communication also contribute towards further understanding the bases of acute subjective experiences of HVB techniques (Section 2.2) from low level effects such as yawning and blepharospasm that are involuntary automatisms deriving from altered neuronal excitability (Lum et al., 2002; Nims et al., 1940), through to higher-order experiences of transcendence and self-dissolution. There also are parallels here with mechanisms implicated in epilepsy, where hyperexcitability of neural circuits and changes in network synchrony during seizure propagation are associated with perceptual changes and local automatisms, through to dissociative states and generalised impairment of consciousness. Practically, hyperventilation might lower the seizure threshold in patients with epilepsy, which therefore represent a contraindication to HVB practices, discussed below.

4.3. Mismatching interoceptive predictions putatively underlie HVB-induced altered consciousness states

Sustained hyperventilation evokes a combination of direct and compensatory physiological changes (a metastable state) that impact specific aspects of brain function and associated perceptual, cognitive and affective processes. We propose that the subjective ASCs – reported by expert practitioners to be a central phenomenological aspect of certain HVB – can be attributed to the selective and profound perturbation of neural circuitry responsible for the integration and regulation of interoceptive signals.

Such circuits normally support adaptive behaviours by coordinating allostatic responses for the whole organism/individual. We speculate that during prolonged hyperventilation, opponent neurophysiological states arise – on one hand, signalling via rostroventral, largely subcortical, interoceptive projections from the midbrain convey a compelling instinctual urge to inhibit the rate and volume of breathing to correct neuronal acid-base balance and restore cerebral supply of O_2 (Colasanti and Critchley, 2021). On the other hand, the engagement of volitional motor circuitry from the prefrontal cortex and primary motor cortex sustains rapid and deep breathing by driving striated accessory muscles of respiration, unchecked by interoceptive feedback. This mechanism overrides normal physiological regulation, governed by homeostatic loops that ensure a tight relationship between autonomic control of smooth muscle and interoceptive feedback. Within a predictive coding framework, attaining a desired internal state involves testing the effects of efferent autonomic drive against ascending interoceptive feedback to generate and minimise prediction errors. Typically, autonomic changes would correct for abnormalities in acid-base balance and blood gases. However, motivational and volitional behaviours can suppress responses to interoceptive prediction errors, temporarily sustaining less homeostatic internal physiological states, so that survival-related, adaptive goals can be achieved over a longer term – this is allostasis.

HVB takes this mechanism to an extreme, resulting even in a violation of principles of allostasis. Reductions in CBF, pH alkalinisation, and reduction of O_2 tension are accompanied by a progressive increase in minute ventilation as volitional behaviour becomes uncoupled from the interoceptive error signals that, through brainstem to insular-cingulate projections, evoke primordial homeostatic (motivational) feelings (Colasanti and Critchley, 2021). Such embodied feelings have high survival value and are usually so imperious that they domineer the entire stream of consciousness and assume 'plenipotentiary power over behaviour' (Denton et al., 2009). The mismatch between 1) interoceptive representation and homeostatic responses to perturbed internal physiological states and 2) the concurrent experience of motor agency accompanying wilful hyperventilation generates an interoceptive prediction error 'overload'. Putatively, there is a supraordinate metacognitive evaluation of this incompatibility between the indefinite continuation of action, while ignoring of the salient alarm associated with neurometabolic dyshomeostasis.

Stephan, Petzschner and colleagues (Stephan et al., 2016) proposed such a higher metacognitive layer of awareness for monitoring self-efficacy, i.e., the capacity for continued successful regulation of the performance of interoceptive-allostatic circuitry. In their model, a system failure in self-efficacy can trigger a behavioural shutdown, manifesting clinically as depression and/or fatigue states. These states nevertheless maintain a form of stability and the integrity of a conscious self-representation. In HVB, we theorise that the impairment of selfhood, reported by HVB practitioners as subjective feelings of 'ego-dissolution' and 'oceanic boundlessness', is consequent upon the splitting of metacognitive integrity. This arises as the sense of agency maintaining allostatic oversight of self-generated behaviour (hyperventilation) is split from interoceptive feedback control and typically negative associated motivational feelings. The consequence is a mental experience that loses its grounding in coherent interoceptive embodiment, arguably akin to dissociative states of dreaming and depersonalisation. Circumstantial evidence in support of this theory is that patients with early psychosis who are presenting with dissociative symptoms also display impairment in measures of metacognitive interoceptive awareness (Garfinkel et al., 2018). Hence, we propose that HVB impacts representational states of internal physiological agency through a profound discounting of interoceptive prediction errors and agency, which possibly accounts for its perception as a positive feeling state.

5. Clinical considerations for HVB practices

5.1. Putative therapeutic indications and general considerations

The only robust clinical research evidence in support of clinical efficacy of therapeutic applications of HVB in cohorts with well-defined psychiatric diagnoses, was obtained from studies in patients with PTSD symptoms using SKY (see Section 3 and Table 2) (Bayley et al., 2022; Carter et al., 2013; Seppälä et al., 2014). A recent non-inferiority trial by Bayley et al. (2022) found SKY to have comparable efficacy to a first line recommended treatment for PTSD, cognitive processing therapy, with a low to moderate effect size in reduction of PTSD symptoms. Considering at least a third of PTSD sufferers do not achieve remission to PTSD-targeting psychotherapies or pharmacotherapies, other treatments are urgently needed (Steenkamp et al., 2015). However, since HVB forms one of several components of SKY, the effects of this multi-component modality cannot solely be attributed to HVB. Although HVB in the form of Sudarshan kriya forms the main component of SKY there is a confound here, and therefore caution must be exercised while extracting, mechanistically explaining and linking only one component of this yogic practice to therapeutics. For other clinical indications in diagnostically well-defined groups, such as mood disorders and anxiety disorders, current support for clinical application of HVB practices is primarily based on anecdotal reports, hence controlled research trials are needed.

Though some forms of HVB can have anxiety inducing subacute effects (Table 1) it could, in fact, possibly act therapeutically as 'exposure' therapy, enabling participants to experience a volitionally induced stressor in the moment, which may then enable the reduction of anxiety (Table 2) in the long term, potentially through gradual adaptation. The key perhaps is the volitional control of ventilation. Hyperventilation that occurs reflexively has been related to anxiety, however hyperventilation performed deliberately in a controlled manner has also been shown to be therapeutic (Balban et al., 2023; Meuret et al., 2005). Therapeutic modalities like psychedelics share this experiential quality, with anxiety commonly being present initially during a psychedelic journey/trip, particularly at the beginning, and decreasing in intensity as the experience progresses.

Again, it is important to note that practitioners of HVB which consists of periodic breath holds and/or rest – in other words, frequent interruptions to hyperventilation (i.e., tummo, WHbM, yogic pranayama) – will likely return to 'normal' homeostatic states more quickly than individuals employing HVB comprising intensive, prolonged and continuous hyperventilation (i.e., CCB, rebirthing, GBW). This suggests why the latter practices are more commonly associated with non-ordinary states of consciousness and psychedelic effects, anecdotally at least.

5.2. General safety considerations

Given the widespread practice of various forms of HVB (potentially over centuries) along with current anecdotal observations, breathwork communities generally consider the practice to be safe for healthy individuals. A recent systematic review and meta-analysis on breathwork and mental health, focusing solely on RCTs, did not find reported adverse events directly attributed to fast-paced breathwork, although only around 20% of the included studies actively reported on adverse events (Fincham et al., 2023). Minor adverse reactions do not necessarily negatively impact the engagement in HVB practice: for example, patients with unipolar/bipolar depression reported incidence of hot flushes, shortness of breath and/or sweating during HVB; nonetheless, all opted to continue the breathwork (mainly kapalabhati) (Ravindran et al., 2021).

It is vital that facilitators inform practitioners of potential risks and contraindications before consenting to participate in HVB. General safety considerations include the notion that hyperventilation can have panicogenic and anxiogenic effects in vulnerable individuals (see below), including rare case reports of fully formed auditory or visual hallucinations triggered by hyperventilation (Allen and Agus, 1968). Patients with acute stress disorders appear to be more likely to experience intrusive traumatic re-experiencing symptoms in response to hyperventilation challenge than non-affected participants (Nixon and Bryant, 2005).

To ensure safety, it appears logical to recommend a cautious employment of HVB in people with cerebrovascular and cardiovascular conditions based on the well-established acute effects of prolonged hyperventilation on blood pressure and CBF. Although these effects are generally short-lived and reversible, the tolerability profile of repeat therapeutic HVB practices in people with such physical health comorbidities is unknown. At this stage caution is recommended for people with comorbid respiratory (i.e., chronic obstructive pulmonary disease), cardiovascular (i.e., severe or malignant hypertension, cardiac arrythmias, heart failure, ischemic heart disease, aneurysms), neurological (i.e., ischemic or haemorrhagic cerebrovascular disease, cerebral aneurysms), or other pre-existing pathology where acute blood pressure or vasoconstriction increase could pose increased risks of end-organ damage, such as renal failure or pheochromocytoma.

The need for physiological monitoring, including haemodynamic parameters, particularly in individuals with the above risk factors, might require restricting the potentially-too-wide application of HVB practices in non-medical contexts at present. In such cases, a clinical screening by a physician is warranted. For example, since HVB can have a significant and direct impact on blood pressure, it is important to empathise a note of caution for people with hypertension.

Furthermore, considering the acute dissociative effects that some forms of prolonged HVB may initiate, caution with HVB is advised if an individual is diagnosed/suspected to have a psychotic disorder. Specific contraindications are needed for pregnant individuals and for some clinical populations, notably patients with epilepsy, panic disorder (PD), and psychotic disorders as explained below. Lastly, it should always be made evident that any practitioners attempting to practise HVB alone must be in a safe environment, especially away from water, hard surfaces or anywhere and any situation in which HVB risks harm to oneself or others, and particularly where fainting could prove fatal.

5.3. Specific contraindications

5.3.1. Epilepsy

Converging indications on the powerful modulating effects of respiratory alkalosis on cerebrovascular function and neuronal excitability point to specific risks related to lowering epileptic threshold and ischemic conditions. Short voluntary hyperventilation is routinely used to induce a seizure in those with suspected epilepsy to confirm diagnosis (Moeller et al., 2019). This method is particularly reliable for children with absence seizures, in which the patients typically demonstrate abnormal 3 Hz EEG activities, due to impairment of thalamocortical interactions. Although hyperventilation is used to induce epileptic seizures in generalised and focal seizures, most patients in this clinical population demonstrate seizures within 90 sec of starting hyperventilation (Watemberg et al., 2015). It is proposed that the most likely mechanisms appear to be an increased sodium and potassium permeability resulting in neuronal hyperexcitability, due to respiratory alkalosis. This effect is more prominent when patients have specific pathological impairments such as mesial temporal (hippocampal) sclerosis (Leonhardt et al., 2002). Direct administration of 5% CO_2 to patients with absence seizures has an anti-convulsant effect and will suppress hyperventilation-induced seizures (Yang et al., 2014). This indicates the central trigger for a seizure may be reductions in CBF.

5.3.2. Panic Disorder

The link between panic and breathing has been well documented (Colasanti et al., 2008; Nardi et al., 2009). The notion of hyperventilation as a core feature of panic attacks symptomatology, and that there is chronically increased ventilatory rates in patients with PD, has led to postulation that hyperventilation has a central role in the pathogenesis of catastrophic cognitions of panic attacks, leading to the development of PD and agoraphobia (Ley, 1985). This theory has been later debated and followed by an alternative hypothesis that hyperventilation in patients with PD instead reflected a compensatory biobehavioural response to a hypersensitive CO_2-detector signalling a 'false suffocation alarm' (Klein, 1993). This theory had stemmed from multiple experimental observations indicating that patients suffering from PD are uniquely vulnerable to the panicogenic effects of respiratory challenges, specifically lactate infusion and CO_2 inhalation (Colasanti et al., 2012). Brief experimental hyperventilation challenges were also reported to have panicogenic effects, although these effects appear much weaker than CO_2 or lactate challenges, with only a proportion (between 16% and 51%) of patients with PD vulnerable to hyperventilation (Goetz et al., 2001; Gorman et al., 1994; Nardi et al., 2004; Papp et al., 1997; Zandbergen et al., 1991).

Additionally, PD patients have rated panic-like reactions to hyperventilation as different to spontaneously occurred panic attacks (Lindsay et al., 1991). Hyperventilation has even been suggested as a therapeutic intervention for PD (Meuret et al., 2005). Nonetheless, there are robust arguments suggesting that a diagnosis of PD should be considered a contraindication to inclusion in trials of HVB practices – i.e., that respiratory and acid-base abnormalities have been consistently reported in patients experiencing recurrent panic attacks (Esquivel et al., 2010). PD patients might display an exaggerated physiological and neurometabolic response to alkalosis and may be more vulnerable to the effects of brain hypoxia during hyperventilation, as indicated by evidence of raised brain and serum lactate levels measured with proton magnetic resonance spectroscopy (^{1}H-MRS), and in response to hyperventilation challenges (Dager et al., 1995; Ueda et al., 2009; Wilhelm et al., 2001).

More generally, significant discomfort and distress may be experienced by anxious people with a tendency to catastrophise physical symptoms due to the transient adverse physical effects of HVB, which include nausea, tetany, palpitations, light-headedness, dizziness, visual disturbance, shakiness, anxiety, and exhaustion (Posse et al., 1997).

6. Conclusions

The extent of support that HVB practices have accumulated over centuries indicates huge potential in terms of therapeutic applications. However, its popularity has not been matched by advances in clinically and mechanistically focused research investigating its neurobiological mechanisms and clinical efficacy in rigorous, controlled studies. Our review summarises the historical roots, common and distinguishing characteristics, and acute effects of the best known HVB practices. Established autonomic and neurometabolic effects of hyperventilation clearly support the notion that HVB can induce profound modulatory effects at various levels of central and autonomous nervous systems, altering their functions and reciprocal interactions, and ultimately impacting high order metacognitive functions that might be relevant to HVBs therapeutic effects. However, direct support for specific clinical application of HVB practice is scarce at present. The evidence we have reviewed could contribute to define clinical indications and contraindications for therapeutic use of HVB, and to set an agenda for future empirical clinical testing.

To advance the field of HVB research and practice, a roadmap of well-designed studies is needed. Rigorous pilot and feasibility studies are required to gauge both safety and tolerability as well as therapeutic potential. Moreover, regarding clinical efficacy, non-inferiority and superiority trials should use appropriate active control groups depending on the population being studied. Rigorous psychophysiological studies should also explore both brain and body physiological responses and phenomenological correlates to further uncover objective and subjective outcomes of HVB.

Research on breathwork is poised for an extraordinary surge in both public and scientific inquiry, much like meditation over the past few decades, and now psychedelics. Given HVBs close ties with these, we expect substantial growth in the field and, as such, encourage robust examination of HVB at the outset.

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Declaration of interest

GWF is a trained breathwork teacher with The Breath-Body-Mind Foundation, a 501(C)3 nonprofit in New York. The remaining authors declare no conflicts of interest.

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References

Abelson, J.L., Khan, S., Giardino, N., 2010. HPA axis, respiration and the airways in stress—a review in search of intersections. Biol. Psychol. 84 (1), 57–65. https://doi.org/10.1016/j.biopsycho.2010.01.021.

Agadzhanyan, N., Panina, M., Kozupitsa, G., Sergeev, O., 2003. Subjective and neurological manifestations of hyperventilation states of different intensities. Hum. Physiol. 29, 448–452. https://doi.org/10.1023/A:1024929523667.

Ainslie, P.N., Duffin, J., 2009. Integration of cerebrovascular CO_2 reactivity and chemoreflex control of breathing: mechanisms of regulation, measurement, and interpretation. Am. J. Physiol. -Regul., Integr. Comp. Physiol. 296 (5), R1473–R1495. https://doi.org/10.1152/ajpregu.91008.2008.

Albery, N., 1984. Leonard orr's rebirthing. Self Soc. 12 (5), 264–274. https://doi.org/10.1080/03060497.1984.11084641.

Albrecht, R.F., Miletich, D.J., Ruttle, M., 1987. Cerebral effects of extended hyperventilation in unanesthetized goats. Stroke 18 (3), 649–655. https://doi.org/10.1161/01.STR.18.3.649.

Allen, T.E., Agus, B., 1968. Hyperventilation leading to hallucinations. Am. J. Psychiatry 125 (5), 632–637. https://doi.org/10.1176/ajp.125.5.632.

Ansari, R.M., 2016. Kapalabhati pranayama: an answer to modern day polycystic ovarian syndrome and coexisting metabolic syndrome. Int. J. Yoga 9 (2), 163. https://doi.org/10.4103/0973-6131.183705.

Axmacher, N., Mormann, F., Fernández, G., Elger, C.E., Fell, J., 2006. Memory formation by neuronal synchronization. Brain Res. Rev. 52 (1), 170–182. https://doi.org/10.1016/j.brainresrev.2006.01.007.

Balban, M.Y., Neri, E., Kogon, M.M., Weed, L., Nouriani, B., Jo, B., Holl, G., Zeitzer, J.M., Spiegel, D., Huberman, A.D., 2023. Brief structured respiration practices enhance mood and reduce physiological arousal. Cell Rep. Med., 100895 https://doi.org/10.1016/j.xcrm.2022.100895.

Baldeweg, T., Spence, S., Hirsch, S.R., Gruzelier, J., 1998. γ-band electroencephalographic oscillations in a patient with somatic hallucinations. Lancet 352 (9128), 620–621. https://doi.org/10.1016/S0140-6736(05)79575-1.

Banaś-Ząbczyk, A., Jakubczyk, P., Pikuła, B., Sendera, A., Kopańska, M., 2022. Breathing-based meditation (Sudarshan Kriya Yoga) increases sense of coherence. No-cost stress prevention. Adv. Integr. Med. 9 (4), 214–220. https://doi.org/10.1016/j.aimed.2022.11.001.

Bayley, P.J., Schulz-Heik, R.J., Tang, J.S., Mathersul, D.C., Avery, T., Wong, M., Zeitzer, J.M., Rosen, C.S., Burn, A.S., Hernandez, B., 2022. Randomised clinical non-inferiority trial of breathing-based meditation and cognitive processing therapy for symptoms of post-traumatic stress disorder in military veterans. Bmj Open 12 (8), e056609. https://doi.org/10.1136/bmjopen-2021-056609.

Bellissimo, G., Leslie, E., Maestas, V., Zuhl, M., 2020. The effects of fast and slow yoga breathing on cerebral and central hemodynamics. Int. J. Yoga 13 (3), 207. https://doi.org/10.4103/ijoy.IJOY_98_19.

Beurel, E., Toups, M., Nemeroff, C.B., 2020. The bidirectional relationship of depression and inflammation: double trouble. Neuron 107 (2), 234–256. https://doi.org/10.1016/j.neuron.2020.06.002.

Bhargav, H., BN, G., Raghuram, N., HR, N., 2014. Frontal hemodynamic responses to high frequency yoga breathing in schizophrenia: a functional near-infrared spectroscopy study. [Orig. Res.]. *Front. Psychiatry 5*. https://doi.org/10.3389/fpsyt.2014.00029.

Bhatt, S., Hillmer, A.T., Rusowicz, A., Nabulsi, N., Matuskey, D., Angarita, G.A., Najafzadeh, S., Kapinos, M., Southwick, S.M., Krystal, J.H., 2021. Imaging brain cortisol regulation in PTSD with a target for 11β-hydroxysteroid dehydrogenase type 1. J. Clin. Investig. 131 (20) https://doi.org/10.1172/JCI150452.

Binarová, D., 2003. The effect of Holotropic Breathwork on personality. Ceská a Slov. Psychiatr. 99 (8), 410–414.

Brewer, J.A., Worhunsky, P.D., Gray, J.R., Tang, Y.-Y., Weber, J., Kober, H., 2011. Meditation experience is associated with differences in default mode network activity and connectivity. Proc. Natl. Acad. Sci. 108 (50), 20254–20259. https://doi.org/10.1073/pnas.1112029108.

Brewerton, T.D., Eyerman, J.E., Cappetta, P., Mithoefer, M.C., 2012. Long-term abstinence following holotropic breathwork as adjunctive treatment of substance use disorders and related psychiatric comorbidity. Int. J. Ment. Health Addict. 10, 453–459. https://doi.org/10.1007/s11469-011-9352-3.

Brian, J.E., 1998. Carbon dioxide and the cerebral circulation. J. Am. Soc. Anesthesiol. 88 (5), 1365–1386. https://doi.org/10.1097/00000542-199805000-00029.

Brouwer, A., Carhart-Harris, R.L., 2021. Pivotal mental states. J. Psychopharmacol. 35 (4), 319–352. https://doi.org/10.1177/0269881120959637.

Brown, R., & Gerbarg, P.L. (2012). *The healing power of the breath: Simple techniques to reduce stress and anxiety, enhance concentration, and balance your emotions*. Shambhala Publications.

Brown, R.P., Gerbarg, P.L., 2005a. Sudarshan Kriya Yogic breathing in the treatment of stress, anxiety, and depression: part II—clinical applications and guidelines. *j.. Altern. Complement. Med.* 11 (4), 711–717. https://doi.org/10.1089/acm.2005.11.711.

Brown, R.P., Gerbarg, P.L., 2005b. Sudarshan Kriya yogic breathing in the treatment of stress, anxiety, and depression: part I—neurophysiologic model. J. Altern. Complement. Med. 11 (1), 189–201. https://doi.org/10.1089/acm.2005.11.189.

Buijze, G., De Jong, H., Kox, M., van de Sande, M., Van Schaardenburg, D., Van Vugt, R., Popa, C., Pickkers, P., Baeten, D., 2019. An add-on training program involving breathing exercises, cold exposure, and meditation attenuates inflammation and disease activity in axial spondyloarthritis–a proof of concept trial. Plos One 14 (12), e0225749. https://doi.org/10.1371/journal.pone.0225749.

Carter, J., Gerbarg, P., Brown, R., Ware, R., D'ambrosio, C., 2013. Multi-component yoga breath program for Vietnam veteran post traumatic stress disorder: randomized controlled trial. J. Trauma. Stress Disord. Treat. 3 (2) https://doi.org/10.4172/2324-8947.1000108.

Cervantes, J., Puente, I., 2014. Effects of Holorenic Breathwork on anxiety and heart rate variability: preliminary results. J. Transpers. Res. 6 (1), 134–142.

Colasanti, A., Critchley, H.D., 2021. Primordial emotions, neural substrates, and sentience: affective neuroscience relevant to psychiatric practice. J. Conscious. Stud. 28 (7–8), 154–173.

Colasanti, A., Salamon, E., Schruers, K., Van Diest, R., Van Duinen, M., Griez, E.J., 2008. Carbon dioxide-induced emotion and respiratory symptoms in healthy volunteers. Neuropsychopharmacology 33 (13), 3103–3110. https://doi.org/10.1038/npp.2008.31.

Colasanti, A., Esquivel, G., J Schruers, K., J Griez, E., 2012. On the psychotropic effects of carbon dioxide. Curr. Pharm. Des. 18 (35), 5627–5637. https://doi.org/10.2174/138161212803530745.

Csicsvari, J., Jamieson, B., Wise, K.D., Buzsáki, G., 2003. Mechanisms of gamma oscillations in the hippocampus of the behaving rat. Neuron 37 (2), 311–322. https://doi.org/10.1016/S0896-6273(02)01169-8.

Curley, G., Kavanagh, B.P., Laffey, J.G., 2010. Hypocapnia and the injured brain: more harm than benefit. Crit. care Med. 38 (5), 1348–1359. https://doi.org/10.1097/CCM.0b013e3181d8cf2b.

Dager, S.R., Strauss, W.L., Marro, K.I., Richards, T.L., Metzger, G.D., Artru, A.A., 1995. Proton magnetic resonance spectroscopy investigation of hyperventilation in subjects with panic disorder and comparison subjects. Am. J. Psychiatry 152 (5), 666–672. https://doi.org/10.1176/ajp.152.5.666.

Deepak, K. (2002). The role of autonomic nervous system in rapid breathing practices. Proceedings: Science of Breath. International Symposium on Sudarshan Kriya, Pranayam and Consciousness, New Delhi: All India Institute of Medical Sciences,

Dempsey, J., Forster, H., Gledhill, N., DoPico, G., 1975. Effects of moderate hypoxemia and hypocapnia on CSF [H+] and ventilation in man. J. Appl. Physiol. 38 (4), 665–674. https://doi.org/10.1152/jappl.1975.38.4.665.

Denton, D.A., McKinley, M.J., Farrell, M., Egan, G.F., 2009. The role of primordial emotions in the evolutionary origin of consciousness. Conscious. Cogn. 18 (2), 500–514. https://doi.org/10.1016/j.concog.2008.06.009.

Descilo, T., Vedamurtachar, A., Gerbarg, P., Nagaraja, D., Gangadhar, B., Damodaran, B., Adelson, B., Braslow, L., Marcus, S., Brown, R., 2010. Effects of a yoga breath intervention alone and in combination with an exposure therapy for post-traumatic stress disorder and depression in survivors of the 2004 South-East Asia tsunami. Acta Psychiatr. Scand. 121 (4), 289–300. https://doi.org/10.1111/j.1600-0447.2009.01466.x.

Dhruva, A., Miaskowski, C., Abrams, D., Acree, M., Cooper, B., Goodman, S., Hecht, F.M., 2012. Yoga breathing for cancer chemotherapy-associated symptoms and quality of life: results of a pilot randomized controlled trial. J. Altern. Complement. Med. 18 (5), 473–479. https://doi.org/10.1089/acm.2011.0555.

Eckberg, D.L., 2009. Point: counterpoint: respiratory sinus arrhythmia is due to a central mechanism vs. respiratory sinus arrhythmia is due to the baroreflex mechanism. J. Appl. Physiol. https://doi.org/10.1152/japplphysiol.91107.2008.

Ellingsen, I., Hauge, A., Nicolaysen, G., Thoresen, M., Walløe, L., 1987. Changes in human cerebral blood flow due to step changes in PAO2 and PACO2. Acta Physiol. Scand. 129 (2), 157–163. https://doi.org/10.1111/j.1748-1716.1987.tb08054.x.

Espinoza, C., Guzman, S.J., Zhang, X., Jonas, P., 2018. Parvalbumin+ interneurons obey unique connectivity rules and establish a powerful lateral-inhibition microcircuit in dentate gyrus. Nat. Commun. 9 (1), 4605. https://doi.org/10.1038/s41467-018-06899-3.

Esquivel, G., Schruers, K., Maddock, R., Colasanti, A., Griez, E., 2010. Acids in the brain: a factor in panic? J. Psychopharmacol. 24 (5), 639–647. https://doi.org/10.1177/0269881109104847.

Eyerman, J., 2013. A clinical report of Holotropic Breathwork in 11,000 psychiatric inpatients in a community hospital setting. Multidiscip. Assoc. Psychedelic Stud. Bull. Spec. Ed. 23 (1), 24–27.

Faye, C., McGowan, J.C., Denny, C.A., David, D.J., 2018. Neurobiological mechanisms of stress resilience and implications for the aged population. Curr. Neuropharmacol. 16 (3), 234–270. https://doi.org/10.2174/1570159x15666170818095105.

Fincham, G.W., Strauss, C., Montero-Marin, J., Cavanagh, K., 2023. Effect of breathwork on stress and mental health: a meta-analysis of randomised-controlled trials. Sci. Rep. 13 (1), 432. https://doi.org/10.1038/s41598-022-27247-y.

Frostell, C., Pande, J., Hedenstierna, G., 1983. Effects of high-frequency breathing on pulmonary ventilation and gas exchange. J. Appl. Physiol. 55 (6), 1854–1861. https://doi.org/10.1152/jappl.1983.55.6.1854.

Garfinkel, S., Greenwood, K., Rae, C., Davies, G., van Praag, C.G., Seth, A., Nick, M., Critchley, H., 2018. T149. metacognitive deficits in interoception are associated with dissociative experiences in patients with first episode psychosis. Schizophr. Bull. 44 (Suppl 1), S173 https://doi.org/10.1093%2Fschbul%2Fsby016.425.

George, D.R., Hanson, R., Wilkinson, D., Garcia-Romeu, A., 2022. Ancient roots of today's emerging renaissance in psychedelic medicine. Cult., Med., Psychiatry 46 (4), 890–903. https://doi.org/10.1007/s11013-021-09749-y.

Godoy, D.A., Seifi, A., Garza, D., Lubillo-Montenegro, S., Murillo-Cabezas, F., 2017. Hyperventilation therapy for control of posttraumatic intracranial hypertension. Front. Neurol. 8, 250. https://doi.org/10.3389/fneur.2017.00250.

Goetz, R.R., Klein, D.F., Papp, L.A., Martinez, J.M., Gorman, J.M., 2001. Acute panic inventory symptoms during CO_2 inhalation and room-air hyperventilation among panic disorder patients and normal controls. Depress Anxiety 14 (2), 123–136. https://doi.org/10.1002/da.1054.

Goldstein, M., Lewin, R., Allen, J., 2020. Improvements in well-being and cardiac metrics of stress following a yogic breathing workshop: Randomized controlled trial with active comparison. J. Am. Coll. Health.: J. ACH 1–11. https://doi.org/10.1080/07448481.2020.1781867.

Goossens, L., Leibold, N., Peeters, R., Esquivel, G., Knuts, I., Backes, W., Marcelis, M., Hofman, P., Griez, E., Schruers, K., 2014. Brainstem response to hypercapnia: a symptom provocation study into the pathophysiology of panic disorder. J. Psychopharmacol. 28 (5), 449–456. https://doi.org/10.1177/0269881114527363.

Gorman, J.M., Papp, L.A., Coplan, J.D., Martinez, J.M., Lennon, S., Goetz, R.R., Ross, D., Klein, D.F., 1994. Anxiogenic effects of CO_2 and hyperventilation in patients with panic disorder. Am. J. Psychiatry 151 (4), 547–553. https://doi.org/10.1176/ajp.151.4.547.

Griffiths, R.R., Richards, W.A., McCann, U., Jesse, R., 2006. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology 187, 268–283. https://doi.org/10.1007/s00213-006-0457-5.

Griffiths, R.R., Johnson, M.W., Richards, W.A., Richards, B.D., McCann, U., Jesse, R., 2011. Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. Psychopharmacology 218, 649–665. https://doi.org/10.1007/s00213-011-2358-5.

Grof, S., 1988. The adventure of self-discovery: dimensions of consciousness and new perspectives in psychotherapy and inner exploration. State University of New York Press.

Grof, S., Grof, C., 2010. Holotropic breathwork. State University of New York Press.

Gulyás, A.I., Megıas, M., Emri, Z., Freund, T.F., 1999. Total number and ratio of excitatory and inhibitory synapses converging onto single interneurons of different types in the CA1 area of the rat hippocampus. J. Neurosci. 19 (22), 10082–10097. https://doi.org/10.1523/JNEUROSCI.19-22-10082.1999.

Gulyás, A.I., Szabó, G.G., Ulbert, I., Holderith, N., Monyer, H., Erdélyi, F., Szabó, G., Freund, T.F., Hájos, N., 2010. Parvalbumin-containing fast-spiking basket cells generate the field potential oscillations induced by cholinergic receptor activation in the hippocampus. J. Neurosci. 30 (45), 15134–15145. https://doi.org/10.1523/JNEUROSCI.4104-10.2010.

Guyenet, P.G., Bayliss, D.A., 2015. Neural control of breathing and CO_2 homeostasis. Neuron 87 (5), 946–961. https://doi.org/10.1016/j.neuron.2015.08.001.

Guyenet, P.G., Bayliss, D.A., Stornetta, R.L., Ludwig, M.G., Kumar, N.N., Shi, Y., Burke, P. G., Kanbar, R., Basting, T.M., Holloway, B.B., 2016. Proton detection and breathing regulation by the retrotrapezoid nucleus. J. Physiol. 594 (6), 1529–1551. https://doi.org/10.1113/JP271480.

Hadar, A., David, J., Shalit, N., Roseman, L., Gross, R., Sessa, B., Lev-Ran, S., 2022. The psychedelic renaissance in clinical research: a bibliometric analysis of three decades of human studies with psychedelics. J. Psychoact. Drugs 1–10. https://doi.org/10.1080/02791072.2021.2022254.

Hájos, N., Pálhalmi, J., Mann, E.O., Németh, B., Paulsen, O., Freund, T.F., 2004. Spike timing of distinct types of GABAergic interneuron during hippocampal gamma oscillations in vitro. J. Neurosci. 24 (41), 9127–9137. https://doi.org/10.1523/JNEUROSCI.2113-04.2004.

Han, P., Trinidad, B.J., Shi, J., 2015. Hypocalcemia-induced seizure: demystifying the calcium paradox, 1759091415578050 Asn Neuro 7 (2). https://doi.org/10.1177/1759091415578050.

Heyda, A., 2000. An impact of the conscious connectred breathing training on emotional states. Heal. Breath. 29.

Hick, J., 1962. The teachings of the mystics: being selections from the great mystics and mystical writings of the world. J. Philos. 59 (5), 135–136. https://doi.org/10.2307/2023306.

Holmes, S.W., Morris, R., Clance, P.R., Putney, R.T., 1996. Holotropic breathwork: an experiential approach to psychotherapy. Psychother.: Theory, Res., Pract., Train. 33 (1), 114. https://doi.org/10.1037/0033-3204.33.1.114.

Holotrópica, R., de Acción, M. d l M., 2014. Holotropic Breathwork: Models of mechanism of action. J. Transpers. Research© 6 (1), 64–72.

Hopkins, E., Sanvictores, T., Sharma, S., 2022. Physiology, acid base balance. In *StatPearls [Internet]*. StatPearls Publishing.

Huchzermeyer, C., Albus, K., Gabriel, H.-J., Otáhal, J., Taubenberger, N., Heinemann, U., Kovács, R., Kann, O., 2008. Gamma oscillations and spontaneous network activity in the hippocampus are highly sensitive to decreases in pO2 and concomitant changes in mitochondrial redox state. J. Neurosci. 28 (5), 1153–1162. https://doi.org/10.1523/JNEUROSCI.4105-07.2008.

Huckabee, W.E., 1958. Relationships of pyruvate and lactate during anaerobic metabolism. I. Effects of infusion of pyruvate or glucose and of hyperventilation. J. Clin. Investig. 37 (2), 244–254.

Hudson, A.L., Walsh, L.D., Gandevia, S.C., Butler, J.E., 2020. Respiratory muscle activity in voluntary breathing tracking tasks: implications for the assessment of respiratory motor control. Respir. Physiol. Neurobiol. 274, 103353 https://doi.org/10.1016/j.resp.2019.103353.

Iyengar, B.K.S., 1981. Light on pranayama: the yogic art of breathing. Crossroad.

Janakiramaiah, N., Gangadhar, B., Murthy, P.N.V., Harish, M., Subbakrishna, D., Vedamurthachar, A., 2000. Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine. J. Affect. Disord. 57 (1–3), 255–259. https://doi.org/10.1016/s0165-0327(99)00079-8.

Jensen, O., Kaiser, J., Lachaux, J.-P., 2007. Human gamma-frequency oscillations associated with attention and memory. Trends Neurosci. 30 (7), 317–324. https://doi.org/10.1016/j.tins.2007.05.001.

Kangaslampi, S., 2023. Association between mystical-type experiences under psychedelics and improvements in well-being or mental health–A comprehensive review of the evidence. J. Psychedelic Stud. 7 (1), 18–28. https://doi.org/10.1556/2054.2023.00243.

Keil, A., Müller, M.M., Ray, W.J., Gruber, T., Elbert, T., 1999. Human gamma band activity and perception of a gestalt. J. Neurosci. 19 (16), 7152–7161. https://doi.org/10.1523/jneurosci.19-16-07152.1999.

Kety, S., Schmidt, C., 1946. Measurement of cerebral blood flow and cerebral oxygen consumption in man. Federation proceedings.

King, A.P., Abelson, J.L., Britton, J.C., Phan, K.L., Taylor, S.F., Liberzon, I., 2009. Medial prefrontal cortex and right insula activity predict plasma ACTH response to trauma recall. Neuroimage 47 (3), 872–880. https://doi.org/10.1016/j.neuroimage.2009.05.088.

Klein, D.F., 1993. False suffocation alarms, spontaneous panics, and related conditions: an integrative hypothesis. Arch. Gen. Psychiatry 50 (4), 306–317. https://doi.org/10.1001/archpsyc.1993.01820160076009.

Kopplin, C.S., Rosenthal, L., 2022. The positive effects of combined breathing techniques and cold exposure on perceived stress: a randomised trial. Curr. Psychol. 1–13. https://doi.org/10.1007/s12144-022-03739-y.

Kox, M., Stoffels, M., Smeekens, S.P., Van Alfen, N., Gomes, M., Eijsvogels, T.M., Hopman, M.T., Van Der Hoeven, J.G., Netea, M.G., Pickkers, P., 2012. The influence of concentration/meditation on autonomic nervous system activity and the innate immune response: a case study. Psychosom. Med. 74 (5), 489–494.

Kox, M., van Eijk, L.T., Zwaag, J., van den Wildenberg, J., Sweep, F.C., van der Hoeven, J.G., Pickkers, P., 2014. Voluntary activation of the sympathetic nervous system and attenuation of the innate immune response in humans. Proc. Natl. Acad. Sci. 111 (20), 7379–7384. https://doi.org/10.1073/pnas.1322174111.

Kozhevnikov, M., Elliott, J., Shephard, J., Gramann, K., 2013. Neurocognitive and somatic components of temperature increases during g-tummo meditation: legend and reality. Plos One 8 (3), e58244. https://doi.org/10.1371/journal.pone.0058244.

Kumar, N., Bhatnagar, S., Velpandian, T., Patnaik, S., Menon, G., Mehta, M., Kashyap, K., Singh, V., 2013. Randomized controlled trial in advance stage breast cancer patients for the effectiveness on stress marker and pain through Sudarshan Kriya and Pranayam. Indian J. Palliat. Care 19 (3), 180–185. https://doi.org/10.4103/0973-1075.121537.

Kurz, A., Sessler, D., Tayefeh, E., Goldberger, R., 1998. Poikilothermia syndrome. J. Intern. Med. -Oxf. 244, 431–436.

Laffey, J.G., Kavanagh, B.P., 2002. Hypocapnia. New Engl. J. Med. 347 (1), 43–53. https://doi.org/10.1056/NEJMra012457.

Lalande, L., Bambling, M., King, R., Lowe, R., 2012. Breathwork: An additional treatment option for depression and anxiety. J. Contemp. Psychother. 42, 113–119. https://doi.org/10.1007/s10879-011-9180-6.

Lenze, E.J., Mantella, R.C., Shi, P., Goate, A.M., Nowotny, P., Butters, M.A., Andreescu, C., Thompson, P.A., Rollman, B.L., 2011. Elevated cortisol in older adults with generalized anxiety disorder is reduced by treatment: a placebo-controlled evaluation of escitalopram. Am. J. Geriatr. Psychiatry 19 (5), 482–490. https://doi.org/10.1097/JGP.0b013e3181ec806c.

Leonhardt, G., de Greiff, A., Marks, S., Ludwig, T., Doerfler, A., Forsting, M., Konermann, S., Hufnagel, A., 2002. Brain diffusion during hyperventilation: diffusion-weighted MR-monitoring in patients with temporal lobe epilepsy and in healthy volunteers. Epilepsy Res. 51 (3), 269–278. https://doi.org/10.1016/s0920-1211(02)00154-7.

Ley, R., 1985. Agoraphobia, the panic attack and the hyperventilation syndrome. Behav. Res. Ther. 23 (1), 79–81. https://doi.org/10.1016/0005-7967(85)90145-7.

Ley, R., 1999. The modification of breathing behavior: pavlovian and operant control in emotion and cognition. Behav. Modif. 23 (3), 441–479. https://doi.org/10.1177/0145445599233006.

Li, K.-X., Lu, Y.-M., Xu, Z.-H., Zhang, J., Zhu, J.-M., Zhang, J.-M., Cao, S.-X., Chen, X.-J., Chen, Z., Luo, J.-H., 2012. Neuregulin 1 regulates excitability of fast-spiking neurons through Kv1. 1 and acts in epilepsy. Nat. Neurosci. 15 (2), 267–273. https://doi.org/10.1038/nn.3006.

Li, S., Rymer, W.Z., 2011. Voluntary breathing influences corticospinal excitability of nonrespiratory finger muscles. J. Neurophysiol. 105 (2), 512–521. https://doi.org/10.1152/jn.00946.2010.

Lin, Y., Lally, D., Moore, T., Hong, S., 1974. Physiological and conventional breath-hold breaking points. J. Appl. Physiol. 37 (3), 291–296. https://doi.org/10.1152/jappl.1974.37.3.291.

Lindsay, S., Saqi, S., Bass, C., 1991. The test-retest reliability of the hyperventilation provocation test. J. Psychosom. Res. 35 (2–3), 155–162. https://doi.org/10.1016/0022-3999(91)90070-5.

Llinas, R., Ribary, U., 1993. Coherent 40-Hz oscillation characterizes dream state in humans. Proc. Natl. Acad. Sci. 90 (5), 2078–2081. https://doi.org/10.1073/pnas.90.5.2078.

Lum, L.M., Connolly, M.B., Farrell, K., Wong, P.K., 2002. Hyperventilation-induced high-amplitude rhythmic slowing with altered awareness: a video-EEG comparison with absence seizures. Epilepsia 43 (11), 1372–1378. https://doi.org/10.1046/j.1528-1157.2002.35101.x.

Lyubkin, M., Giardino, N.D., Abelson, J.L., 2010. Relationship between respiratory, endocrine, and cognitive-emotional factors in response to a pharmacological panicogen. Depress Anxiety 27 (11), 1011–1016. https://doi.org/10.1002/da.20725.

Mason, N.L., Mischler, E., Uthaug, M.V., Kuypers, K.P., 2019. Sub-acute effects of psilocybin on empathy, creative thinking, and subjective well-being. J. Psychoact. Drugs 51 (2), 123–134. https://doi.org/10.1080/02791072.2019.1580804.

Metcalf, B.A., 1995. Examining the effects of Holotropic Breathwork in the recovery from alcoholism and drug dependence. Cent. Transpers. Stud. Dev.

Meuret, A.E., Ritz, T., Wilhelm, F.H., Roth, W.T., 2005. Voluntary hyperventilation in the treatment of panic disorder—functions of hyperventilation, their implications for breathing training, and recommendations for standardization. Clin. Psychol. Rev. 25 (3), 285–306. https://doi.org/10.1016/j.cpr.2005.01.002.

Miles, W.R., 1964. Oxygen consumption during three yoga-type breathing patterns. J. Appl. Physiol. 19 (1), 75–82. https://doi.org/10.1152/jappl.1964.19.1.75.

Miller, T., Nielsen, L., 2015. Measure of significance of holotropic breathwork in the development of self-awareness. J. Altern. Complement. Med. 21 (12), 796–803. https://doi.org/10.1089/acm.2014.0297.

Moeller, J. , Haider, H.A. , & Hirsch, L.J. (2019). Electroencephalography (EEG) in the diagnosis of seizures and epilepsy. UpToDate. Garcia P. (Ed) UpToDate, Waltham, MA. Accessed January.

Moutlana, H., 2020. Physiological control of respiration. South. Afr. J. Anaesth. Analg. 26 (6), S128–S132. https://doi.org/10.36303/SAJAA.2020.26.6.S3.2557.

Mykita, S., Hoffmann, D., Dreyfus, H., Freysz, L., Massarelli, R., 1986. Protection and therapeutic effect of CDP choline in hypocapnic neurons in culture. Dyn. Cholinergic Funct. 153–163. https://doi.org/10.1007/978-1-4684-5194-8_14.

Nakayama, T., Fujii, Y., Suzuki, K., Kanazawa, I., Nakada, T., 2004. The primary motor area for voluntary diaphragmatic motion identified by high field fMRI. J. Neurol. 251, 730–735. https://doi.org/10.1007/s00415-004-0413-4.

Nardi, A.E., Lopes, F.L., Valença, A.M., Nascimento, I., Mezzasalma, M.A., Zin, W.A., 2004. Psychopathological description of hyperventilation-induced panic attacks: a comparison with spontaneous panic attacks. Psychopathology 37 (1), 29–35. https://doi.org/10.1159/000077017.

Nardi, A.E., Freire, R.C., Zin, W.A., 2009. Panic disorder and control of breathing. Respir. Physiol. Neurobiol. 167 (1), 133–143. https://doi.org/10.1016/j.resp.2008.07.011.

Nariko, T., 1968. Role of hypocapnia in the blood lactate accumulation during acute hypoxia. Respir. Physiol. 4 (1), 32–41. https://doi.org/10.1016/0034-5687(68)90005-4.

Nichols, D.E., 2016. Psychedelics. Pharmacol. Rev. 68 (2), 264–355. https://doi.org/10.1124/pr.115.011478.

Nims, L., Gibbs, E., Lennox, W., Gibbs, F., WILLIAMS, D., 1940. Adjustment of acid-base balance of patients with petit mal epilepsy to overventilation. Arch. Neurol. Psychiatry 43 (2), 262–269. https://doi.org/10.1001/archneurpsyc.1940.02280020070005.

Nixon, R.D., Bryant, R.A., 2005. Induced arousal and reexperiencing in acute stress disorder. J. Anxiety Disord. 19 (5), 587–594. https://doi.org/10.1016/j.janxdis.2004.05.001.
Nour, M.M., Evans, L., Nutt, D., Carhart-Harris, R.L., 2016. Ego-dissolution and psychedelics: validation of the ego-dissolution inventory (EDI. Front. Hum. Neurosci. 269. https://doi.org/10.3389/fnhum.2016.00269.
Novaes, M.M., Palhano-Fontes, F., Onias, H., Andrade, K.C., Lobão-Soares, B., Arruda-Sanchez, T., Kozasa, E.H., Santaella, D.F., de Araujo, D.B., 2020. Effects of yoga respiratory practice (Bhastrika pranayama) on anxiety, affect, and brain functional connectivity and activity: a randomized controlled trial. Front. Psychiatry 467. https://doi.org/10.3389/fpsyt.2020.00467.
OED. (2023). Definition: Breathwork, Noun. (1972–2019).
Olbrich, S., Preller, K.H., Vollenweider, F.X., 2021. LSD and ketanserin and their impact on the human autonomic nervous system. Psychophysiology 58 (6), e13822. https://doi.org/10.1111/psyp.13822.
Orr, L., 1992. The story of rebirthing. Self Soc. 20 (2), 10–13. https://doi.org/10.1080/03060497.1992.11085252.
Pahnke, W.N., 1963. Drugs and mysticism: An analysis of the relationship between psychedelic drugs and the mystical consciousness: a thesis. Harvard University].
Papp, L.A., Martinez, J.M., Klein, D.F., Coplan, J.D., Norman, R.G., Cole, R., de Jesus, M. J., Ross, D., Goetz, R., Gorman, J.M., 1997. Respiratory psychophysiology of panic disorder: three respiratory challenges in 98 subjects. Am. J. Psychiatry 154 (11), 1557–1565.
Pinna, A., Colasanti, A., 2021. The neurometabolic basis of mood instability: the parvalbumin interneuron link—a systematic review and meta-analysis. Front. Pharmacol. 12, 689473 https://doi.org/10.3389/fphar.2021.689473.
Posse, S., Olthoff, U., Weckesser, M., Jäncke, L., Müller-Gärtner, H.-W., Dager, S.R., 1997. Regional dynamic signal changes during controlled hyperventilation assessed with blood oxygen level-dependent functional MR imaging. Am. J. Neuroradiol. 18 (9), 1763–1770.
Poulin, M.J., Liang, P.-J., Robbins, P.A., 1998. Fast and slow components of cerebral blood flow response to step decreases in end-tidal P co 2 in humans. J. Appl. Physiol. 85 (2), 388–397. https://doi.org/10.1152/jappl.1998.85.2.388.
Pramanik, T., Sharma, H.O., Mishra, S., Mishra, A., Prajapati, R., Singh, S., 2009. Immediate effect of slow pace bhastrika pranayama on blood pressure and heart rate. J. Altern. Complement. Med. 15 (3), 293–295. https://doi.org/10.1089/acm.2008.0440.
Puente, I., 2013. A Quasi-Experimental Study of Holorenic Breathwork in a psychotherapeutical context: preliminary results. J. Transpers. Res. 5 (2), 7–18.
Puente, I., 2014a. Effects of holotropic breathwork in personal orientation, levels of distress, meaning of life and death anxiety in the context of a weeklong workshop: A pilot study. J. Transpers. Res. 6 (1), 49–63.
Puente, I., 2014b. Holotropic breathwork can occasion mystical experiences in the context of a daylong workshop. J. Transpers. Res. 6 (2), 40–50.
Raghuraj, P., Ramakrishnan, A., Nagendra, H., Telles, S., 1998. Effect of two selected yogic breathing techniques on heart rate variability. Indian J. Physiol. Pharmacol. 42, 467–472.
Raichle, M.E., Plum, F., 1972. Hyperventilation and cerebral blood flow. Stroke 3 (5), 566–575. https://doi.org/10.1161/01.str.3.5.566.
Raichle, M.E., Posner, J.B., Plum, F., 1970. Cerebral blood flow during. Arch. Neurol. 23 (5), 394–403. https://doi.org/10.1001/archneur.1970.00480290014002.
Ravindran, A.V., McKay, M.S., Silva, T.D., Tindall, C., Garfinkel, T., Paric, A., Ravindran, L., 2021. Breathing-focused Yoga as Augmentation for Unipolar and Bipolar Depression: A Randomized Controlled Trial: Le yoga axé sur la respiration comme traitement d'appoint pour la dépression unipolaire et bipolaire: Un essai randomisé contrôlé. Can. J. Psychiatry 66 (2), 159–169. https://doi.org/10.1177/07067437209405.
Reivich, M., Dickson, J., Clark, J., Hedden, M., Lambertsen, C., 1968. Role of hypoxia in cerebral circulatory and metabolic changes during hypocarbia in man: studies in hyperbaric milieu. Scand. J. Clin. Lab. Investig. 21 (sup102), IV-B-IV-B. https://doi.org/10.3109/00365516809168978.
Rhinewine, J.P., Williams, O.J., 2007. Holotropic breathwork: The potential role of a prolonged, voluntary hyperventilation procedure as an adjunct to psychotherapy. J. Altern. Complement. Med. 13 (7), 771–776. https://doi.org/10.1089/acm.2006.6203.
Salvati, K.A., Beenhakker, M.P., 2019. Out of thin air: Hyperventilation-triggered seizures. Brain Res. 1703, 41–52. https://doi.org/10.1016/j.brainres.2017.12.037.
Saraswati, S.N., 1994. Prana, pranayama, prana vidya. Bihar School of Yoga.
Schulz, E., Tiemann, L., Witkovsky, V., Schmidt, P., Ploner, M., 2012. Gamma oscillations are involved in the sensorimotor transformation of pain. J. Neurophysiol. 108 (4), 1025–1031. https://doi.org/10.1152/jn.00186.2012.
Schüttler, D., Von Stülpnagel, L., Rizas, K.D., Bauer, A., Brunner, S., Hamm, W., 2020. Effect of hyperventilation on periodic repolarization dynamics. Front. Physiol. 11, 542183 https://doi.org/10.3389/fphys.2020.542183.
Scudder, S.L., Baimel, C., Macdonald, E.E., Carter, A.G., 2018. Hippocampal-evoked feedforward inhibition in the nucleus accumbens. J. Neurosci. 38 (42), 9091–9104. https://doi.org/10.1523/JNEUROSCI.1971-18.2018.
Sederberg, P.B., Schulze-Bonhage, A., Madsen, J.R., Bromfield, E.B., McCarthy, D.C., Brandt, A., Tully, M.S., Kahana, M.J., 2007. Hippocampal and neocortical gamma oscillations predict memory formation in humans. Cereb. Cortex 17 (5), 1190–1196. https://doi.org/10.1093/cercor/bhl030.
Seppälä, E.M., Nitschke, J.B., Tudorascu, D.L., Hayes, A., Goldstein, M.R., Nguyen, D.T., Perlman, D., Davidson, R.J., 2014. Breathing-based meditation decreases posttraumatic stress disorder symptoms in US Military veterans: a randomized controlled longitudinal study. J. Trauma. Stress 27 (4), 397–405. https://doi.org/10.1002/jts.21936.
Seppälä, E.M., Bradley, C., Moeller, J., Harouni, L., Nandamudi, D., Brackett, M.A., 2020. Promoting mental health and psychological thriving in university students: a randomized controlled trial of three well-being interventions. Front. Psychiatry 590. https://doi.org/10.3389/fpsyt.2020.00590.
Severinghaus, J.W., Lassen, N., 1967. Step hypocapnia to separate arterial from tissue PCO2 in the regulation of cerebral blood flow. Circ. Res. 20 (2), 272–278. https://doi.org/10.1161/01.RES.20.2.272.
Sharma, A., Barrett, M.S., Cucchiara, A.J., Gooneratne, N.S., Thase, M.E., 2017. A breathing-based meditation intervention for patients with major depressive disorder following inadequate response to antidepressants: a randomized pilot study. J. Clin. Psychiatry 78 (1), 493. https://doi.org/10.4088/JCP.16m10819.
Sivananda, S.S., 1962. The science of pranayama. Divine Life Society.
Sohal, V.S., Zhang, F., Yizhar, O., Deisseroth, K., 2009. Parvalbumin neurons and gamma rhythms enhance cortical circuit performance. Nature 459 (7247), 698–702. https://doi.org/10.1038/nature07991.
Stäubli, M., Bigger, K., Kammer, P., Rohner, F., Straub, P., 1988. Mechanisms of the haematological changes induced by hyperventilation. Eur. J. Appl. Physiol. Occup. Physiol. 58, 233–238. https://doi.org/10.1007/BF00417255.
Steenkamp, M.M., Litz, B.T., Hoge, C.W., Marmar, C.R., 2015. Psychotherapy for military-related PTSD: a review of randomized clinical trials. JAMA 314 (5), 489–500. https://doi.org/10.1001/jama.2015.8370.
Stenkamp, K., Palva, J.M., Uusisaari, M., Schuchmann, S., Schmitz, D., Heinemann, U., Kaila, K., 2001. Enhanced temporal stability of cholinergic hippocampal gamma oscillations following respiratory alkalosis in vitro. J. Neurophysiol. 85 (5), 2063–2069. https://doi.org/10.1152/jn.2001.85.5.2063.
Stephan, K.E., Manjaly, Z.M., Mathys, C.D., Weber, L.A., Paliwal, S., Gard, T., Tittgemeyer, M., Fleming, S.M., Haker, H., Seth, A.K., 2016. Allostatic self-efficacy: a metacognitive theory of dyshomeostasis-induced fatigue and depression. Front. Hum. Neurosci. 10, 550. https://doi.org/10.3389/fnhum.2016.00550.
Stocchetti, N., Maas, A.I., Chieregato, A., van der Plas, A.A., 2005. Hyperventilation in head injury. Chest 127 (5), 1812–1827. https://doi.org/10.1378/chest.127.5.1812.
Subramanian, S., Elango, T., Malligarjunan, H., Kochupillai, V., Dayalan, H., 2012. Role of sudarshan kriya and pranayam on lipid profile and blood cell parameters during exam stress: a randomized controlled trial. Int. J. Yoga 5 (1), 21.
Sun, Y.-G., Wu, C.-S., Renger, J.J., Uebele, V.N., Lu, H.-C., Beierlein, M., 2012. GABAergic synaptic transmission triggers action potentials in thalamic reticular nucleus neurons. J. Neurosci. 32 (23), 7782–7790. https://doi.org/10.1523/JNEUROSCI.0839-12.2012.
Sureka, P., Govil, S., Dash, D., Dash, C., Kumar, M., Singhal, V., 2014. Effect of Sudarshan Kriya on male prisoners with non psychotic psychiatric disorders: a randomized control trial. Asian J. Psychiatry 12, 43–49. https://doi.org/10.1016/j.ajp.2014.06.010.
Taborsky Jr, G.J., Mundinger, T.O., 2012. Minireview: the role of the autonomic nervous system in mediating the glucagon response to hypoglycemia. Endocrinology 153 (3), 1055–1062. https://doi.org/10.1210/en.2011-2040.
Taha, B.H., Simon, P., Dempsey, J., Skatrud, J., Iber, C., 1995. Respiratory sinus arrhythmia in humans: an obligatory role for vagal feedback from the lungs. J. Appl. Physiol. 78 (2), 638–645. https://doi.org/10.1152/jappl.1995.78.2.638.
Tang, Y.-Y., Lu, Q., Fan, M., Yang, Y., Posner, M.I., 2012. Mechanisms of white matter changes induced by meditation. Proc. Natl. Acad. Sci. 109 (26), 10570–10574. https://doi.org/10.1073/pnas.1207817109.
Touskova, T., Bob, P., Bares, Z., Vanickova, Z., Nyvlt, D., Raboch, J., 2022. A novel Wim Hof psychophysiological training program to reduce stress responses during an Antarctic expedition, 03000605221089883 J. Int. Med. Res. 50 (4). https://doi.org/10.1177/03000605221089883.
Tukker, J.J., Lasztóczi, B., Katona, L., Roberts, J.D.B., Pissadaki, E.K., Dalezios, Y., Márton, L., Zhang, L., Klausberger, T., Somogyi, P., 2013. Distinct dendritic arborization and in vivo firing patterns of parvalbumin-expressing basket cells in the hippocampal area CA3. J. Neurosci. 33 (16), 6809–6825. https://doi.org/10.1523/JNEUROSCI.5052-12.2013.
Ueda, Y., Aizawa, M., Takahashi, A., Fujii, M., Isaka, Y., 2009. Exaggerated compensatory response to acute respiratory alkalosis in panic disorder is induced by increased lactic acid production. Nephrol. Dial. Transplant. 24 (3), 825–828. https://doi.org/10.1093/ndt/gfn585.
Ultsch, G.R., Brainerd, E.L., Jackson, D.C., 2004. Lung collapse among aquatic reptiles and amphibians during long-term diving. Comp. Biochem. Physiol. Part A: Mol. Integr. Physiol. 139 (1), 111–115. https://doi.org/10.1016/j.cbpb.2004.07.002.
Uthaug, M., Lancelotta, R., Van Oorsouw, K., Kuypers, K., Mason, N., Rak, J., Šuláková, A., Jurok, R., Maryška, M., Kuchař, M., 2019. A single inhalation of vapor from dried toad secretion containing 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) in a naturalistic setting is related to sustained enhancement of satisfaction with life, mindfulness-related capacities, and a decrement of psychopathological symptoms. Psychopharmacology 236, 2653–2666. https://doi.org/10.1007/s00213-019-05236-w.
Uthaug, M., Mason, N., Toennes, S., Reckweg, J., de Sousa Fernandes Perna, E., Kuypers, K., van Oorsouw, K., Riba, J., Ramaekers, J., 2021. A placebo-controlled study of the effects of ayahuasca, set and setting on mental health of participants in ayahuasca group retreats. Psychopharmacology 238, 1899–1910. https://doi.org/10.1007/s00213-021-05817-8.
Uthaug, M.V., Lancelotta, R., Szabo, A., Davis, A.K., Riba, J., Ramaekers, J.G., 2020. Prospective examination of synthetic 5-methoxy-N, N-dimethyltryptamine inhalation: effects on salivary IL-6, cortisol levels, affect, and non-judgment. Psychopharmacology 237, 773–785. https://doi.org/10.1007/s00213-019-05414-w.
Uthaug, M.V., Mason, N.L., Havenith, M.N., Vancura, M., Ramaekers, J.G., 2022. An experience with Holotropic Breathwork is associated with improvement in non-

judgement and satisfaction with life while reducing symptoms of stress in a Czech-speaking population. J. Psychedelic Stud. 5 (3), 176–189. https://doi.org/10.1556/2054.2021.00193.

Van Vugt, M.K., Schulze-Bonhage, A., Litt, B., Brandt, A., Kahana, M.J., 2010. Hippocampal gamma oscillations increase with memory load. J. Neurosci. 30 (7), 2694–2699. https://doi.org/10.1523/JNEUROSCI.0567-09.2010.

Vedamurthachar, A., Janakiramaiah, N., Hegde, J.M., Shetty, T.K., Subbakrishna, D., Sureshbabu, S., Gangadhar, B., 2006. Antidepressant efficacy and hormonal effects of Sudarshana Kriya Yoga (SKY) in alcohol dependent individuals. J. Affect. Disord. 94 (1–3), 249–253. https://doi.org/10.1016/j.jad.2006.04.025.

Veit, J., Hakim, R., Jadi, M.P., Sejnowski, T.J., Adesnik, H., 2017. Cortical gamma band synchronization through somatostatin interneurons. Nat. Neurosci. 20 (7), 951–959. https://doi.org/10.1038/nn.4562.

Victoria, H.K., Caldwell, C., 2013. Breathwork in body psychotherapy: clinical applications. Body, Mov. Dance Psychother. 8 (4), 216–228. https://doi.org/10.1080/17432979.2013.828657.

Wang, S., Benamer, N., Zanella, S., Kumar, N.N., Shi, Y., Bévengut, M., Penton, D., Guyenet, P.G., Lesage, F., Gestreau, C., 2013. TASK-2 channels contribute to pH sensitivity of retrotrapezoid nucleus chemoreceptor neurons. J. Neurosci. 33 (41), 16033–16044. https://doi.org/10.1523/JNEUROSCI.2451-13.2013.

Watemberg, N., Farkash, M., Har-Gil, M., Sezer, T., Goldberg-Stern, H., Alehan, F., 2015. Hyperventilation during routine electroencephalography: are three minutes really necessary? Pediatr. Neurol. 52 (4), 410–413. https://doi.org/10.1016/j.pediatrneurol.2014.12.003.

Watts, M.E., Pocock, R., Claudianos, C., 2018. Brain energy and oxygen metabolism: emerging role in normal function and disease. Front. Mol. Neurosci. 11, 216. https://doi.org/10.3389/fnmol.2018.00216.

Wei, E.P., Kontos, H.A., 1999. Blockade of ATP-sensitive potassium channels in cerebral arterioles inhibits vasoconstriction from hypocapnic alkalosis in cats. Stroke 30 (4), 851–854. https://doi.org/10.1161/01.STR.30.4.851.

Wilhelm, F.H., Gerlach, A.L., Roth, W.T., 2001. Slow recovery from voluntary hyperventilation in panic disorder. Psychosom. Med. 63 (4), 638–649.

de Wit, P., Cruz, R.M., 2021. Treating PTSD with connected breathing: a clinical case study and theoretical implications. Eur. J. Trauma Dissociation 5 (3), 100152. https://doi.org/10.1016/j.ejtd.2020.100152.

de Wit, P., Menezes, C., Oliveira, C., Costa, R., Cruz, R., 2018. Rebirthing-Breathwork, activation of the autonomic nervous system, and psychophysiological defenses. Rev. Bras. De. Psicoter. 20 (2), 2318-0404.20180017.

Yang, X.-F., Shi, X.-Y., Ju, J., Zhang, W.-N., Liu, Y.-J., Li, X.-Y., Zou, L.-P., 2014. 5% CO_2 inhalation suppresses hyperventilation-induced absence seizures in children. Epilepsy Res. 108 (2), 345–348. https://doi.org/10.1016/j.eplepsyres.2013.11.012.

Yehuda, R., 2001. Biology of posttraumatic stress disorder. J. Clin. Psychiatry 62, 41–46.

Zaccaro, A., Piarulli, A., Laurino, M., Garbella, E., Menicucci, D., Neri, B., Gemignani, A., 2018. How breath-control can change your life: a systematic review on psycho-physiological correlates of slow breathing. Front Hum. Neurosci. 12, 353. https://doi.org/10.3389/fnhum.2018.00353.

Zandbergen, J., Pols, H., Fernandez, I., Griez, E., 1991. An analysis of panic symptoms during hypercarbia compared to hypocarbia in patients with panic attacks. J. Affect. Disord. 23 (3), 131–136. https://doi.org/10.1016/0165-0327(91)90025-N.

Zope, S.A., Zope, R.A., 2013. Sudarshan kriya yoga: breathing for health. Int. J. Yoga 6 (1), 4. https://doi.org/10.4103/0973-6131.105935.

Zwaag, J., Ter Horst, R., Blaženović, I., Stoessel, D., Ratter, J., Worseck, J.M., Schauer, N., Stienstra, R., Netea, M.G., Jahn, D., 2020. Involvement of lactate and pyruvate in the anti-inflammatory effects exerted by voluntary activation of the sympathetic nervous system. Metabolites 10 (4), 148. https://doi.org/10.3390/metabo10040148.

Zwaag, J., Naaktgeboren, R., van Herwaarden, A.E., Pickkers, P., Kox, M., 2022. The effects of cold exposure training and a breathing exercise on the inflammatory response in humans: a pilot study. Psychosom. Med. 84 (4), 457. https://doi.org/10.1097/PSY.0000000000001065.