



Cognitive Vitality Reports[®] are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-indevelopment, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Breathing Techniques

Evidence Summary

Breathing techniques regulate the autonomic nervous system to mitigate the negative health effects of stress and improve respiratory efficiency.

Neuroprotective Benefit: Slow breathing techniques, particularly alternate nostril breathing, can improve measures of attention and reduce anxiety.

Aging and related health concerns: Breathing training may improve lung function, lower blood pressure, and reduce the risk of cardiovascular disease. Resonant breathing can improve heart rate variability.

Safety: Slow breathing techniques are safe but proper training is required.

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What is it?

There are a variety of breathing techniques which have been shown to improve cardiopulmonary function, mood, focus, and may increase healthspan. The primary mechanism by which they exert their effects is via the regulation of the autonomic nervous system. Although training is generally necessary to learn the techniques properly, once mastered, they can be readily incorporated into the course of daily life, and do not necessarily require a separate time commitment.

Clinical trials have been conducted using these techniques for a variety of conditions including, but not limited to, cognition, anxiety, depression, stress-disorders, asthma, chronic obstructive pulmonary disease, reflux, sleep apnea, cardiovascular disease, hypertension, and cancer.

<u>Buteyko</u>: This breathing practice was developed by the Ukrainian doctor Konstantin Buteyko and is designed to prevent over-breathing, such that one breathes more in line with his or her metabolic needs [1]. This method is a form of breathing retraining designed to move away from taking deep full breaths through the mouth, toward light diaphragmatic breathing through the nose. Most of the techniques involve some form of breathholding, including controlled pauses and mini breathholds which train the body to recognize the feeling of mild air hunger in a relaxed, controlled manner that eventually allows for an increase in respiratory efficiency. Mouth taping at night to promote nasal breathing is also a recommended part of the practice. The techniques are hypothesized to work by increasing tolerance to elevated CO_2 levels, but clinical studies do not necessarily support this mechanism.

<u>Diaphragmatic deep breathing</u>: This technique involves slow deep breathing, inhaling through the nose using the diaphragm to fill the belly, with minimal chest movement, then exhaling, usually through the mouth [2]. This method is designed to fill the lungs more efficiently, strengthen the diaphragm, and promote oxygen exchange.

<u>Resonant breathing</u>: Coherent breathing is a form of slow diaphragmatic breathing of approximately five breaths per minute that is meant to drive coordination between the heart rate and respiratory rate [3]. It increases respiratory efficiency. Resonant breathing involves breathing at the particular frequency that will maximize heart rate variability, and is typically close to five breaths per minute, or in the range of three to seven breaths per minute. The resonant frequency can be measured by a medical provider by determining the breathing rate that maximizes the peak spectral frequency on an electrocardiogram (i.e., maximizes the change in heart rate between inhale and exhale). Biofeedback training can be used to promote breathing at one's resonant frequency.

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<u>Pranayama</u>: This is the yogic practice of breath control. There are a variety of different kinds of pranayamas, which are designed to have different physiological effects [4]. Prana refers to breath or life force, while ayama refers to expansion or regulation, thus pranayama is the practice of conscious control of one's lifeforce through breathwork. Pranayama can be practiced on its own, or in combination with yogic postures, called asanas.

<u>Alternate nostril breathing</u>: This is a form of pranayama which is meant to balance the two brain hemispheres and improve mental focus [5]. It is traditionally performed by placing the forefinger and middle finger of the right hand between the eyebrows, then using the thumb to control the opening and closing of the right nostril and the ring finger to control the left nostril. To start, close the right nostril and exhale through the left nostril, then inhale through the left nostril, close the left, open the right nostril and exhale through the right nostril. Then perform the cycle starting with the right side, and continue cycling between left and right.

Neuroprotective Benefit: Slow breathing techniques, particularly alternate nostril breathing, can improve measures of attention and reduce anxiety.

Types of evidence:

- 1 systematic review on slow breathing for cognition and psychology
- 1 meta-analysis of yoga/pranayama on mental disorders
- 1 review on pranayama for brain activation
- 1 review on yoga for brain activation
- 1 clinical trial for diaphragmatic breathing and cognition
- 1 clinical trial for diaphragmatic breathing and anxiety
- 6 clinical trials for pranayama and cognition
- 12 clinical trials for alternate nostril breathing and cognition
- 1 clinical trial on Iyengar yoga and coherent breathing for major depression

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

There is ample anecdotal evidence to indicate that regular practice of various breathing techniques, particularly those that involve slow, deep breathing, can induce a state of relaxation and enhance focus. Practices in which the regulation of breath are a critical component, such as yoga and meditation, are associated with decreased risk for dementia [6; 7], however, the exact contribution of the breath

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regulation to these effects has not been established. For example, yoga exercises can involve both asanas (postures) and pranayamas (breath regulation), and most analyses combine studies involving multiple forms of yoga.

Many clinical studies have been conducted to determine the effect of a particular breathing technique on cognitive function and/or stress states, however, these studies are typically small and of low methodological quality. Furthermore, the studies use a combination of different breathing techniques, populations, timeframes, and outcome measures, which makes it difficult to make meaningful comparisons as to the best breathing techniques for cognitive health. The studies suggest that the population can influence the outcome in that effects may be more apparent in long-term practitioners than in those who are new to the technique. Thus, for acute studies, the inclusion of long-term practitioners may provide more meaningful information, but to understand the changes that take place as a consequence of repeated practice, baseline naïve participants are more informative. Despite these methodological shortcomings, some trends do emerge which support the anecdotal evidence regarding a promotion of relaxation and focus.

Diaphragmatic breathing: In a study of healthy adults (n=40), eight weeks of diaphragmatic breathing was associated with improvement on the Number Cancellation Test, a measure of sustained attention, as well as reductions in negative affect, as measured by the Positive and Negative Affect Schedule (PANAS), and a reduction in levels of the stress hormone cortisol [8].

Pranayama: In healthy volunteers, 12 weeks of either fast or slow pranayama practice led to improvements on the Perceived Stress Scale (PSS), as well as improvements on performance on a variety of cognitive measures of executive function and reaction time [9]. Similarly, a study in healthy adolescents (n=520) found that Bhramari pranayama, often referred to as humming bee breathing, three times a week for six months shortened both auditory (from 237.42 ± 48.12 to 227.91 ± 34.60 ms) and visual (from 267.13 ± 52.65 to 249.87 ± 39.41 ms) reaction times [10]. This is indicative of an improvement in information processing. The P300 is an event-related potential measured by electroencephalogram (EEG) that is generated when individuals attend and discriminate between stimuli [5]. Increases in the P300 peak amplitudes are indicative of increased attention. In participants with hypertension (n=100), four weeks of pranayama practice (Sheetali pranayama 30 min/day) led to an increase in the peak amplitude (7.88 \pm 3.99 to 11.83 ± 4.56 uV, Cohen's d=0.92) of auditory-evoked P300 potentials and a decrease in peak latencies (367.80 ± 29.82 to 331.53 ± 34.39 ms, Cohen's d= 1.13) [11]. Yoga breathing with intermittent breath holding for three days improved response inhibition, as measured by a decrease in stop signal reaction time (231.98 ± 29.54 to 218.33 ± 38.38 ms) in healthy young adults (n=36) [12]. In middle-aged adults (n=45), yoga consisting of pranayamas and mudras

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(hand gestures) in combination with working memory training improved performance on short term memory tasks, particularly with respect to verbal fluency, relative to working memory training alone [13].

Alternate nostril breathing: In terms of cognitive assessments, alternate or unilateral nostril breathing practices have been the most well characterized pranayamas. Breathing through one nostril may be associated with activation in the contralateral brain hemisphere, though the data has been inconsistent [14]. Recall memory, associate learning and spatial memory scores were improved in female participants following the practice of alternate or unilateral nostril breathing (n=51) for 45 minutes/day for one week [15]. There were trends toward better performance on verbal learning with left nostril breathing and with spatial memory with right nostril breathing. Similarly, both right nostril breathing and alternative nostril breathing improved performance on the Digit Span Forward (DSF) and Digit Span Backward (DSB) tests in healthy adults (n=30) [16], while both right nostril breathing and alternate nostril breathing improved performance on the letter cancellation task in male volunteers (n=20) [17]. Alternate nostril breathing (18 minutes) decreased the time to perform a digit vigilance test (6.54 ±1.09 to 5.98 ±1.15 min) (n=15) [18], and reduced the error scores in a size and shape discrimination task by 33% (Cohen's d=0.67) (n=50), a task that requires focused attention, in healthy male volunteers [19]. Alternate nostril breathing, in those who had practiced the technique for over three months, significantly increased P300 auditory-evoked potential peak amplitudes and decreased peak latencies at frontal and parietal sites, further supporting the promotion of attention [20]. The acute effects on cognitive performance following a bout of alternate nostril breathing are likely only achieved after a period of training and continued practice, as the ability to detect changes in cognitive performance in beginners has been less consistent [21].

Deep alternate nostril breathing (30 minutes) was associated with improved retention of motor skill learning in healthy adults (n=40), for at least 24 hours [22]. The effect on motor training may have benefit for rehabilitation following stroke. A small study in 16 stroke patients found that alternate nostril breathing (3 sets of 10 rounds) improved performance on the Timed Up and Go Test, a measure of functional mobility, from 33.43 ± 19.56 to 26.06 ± 20.69 seconds [23]. Unilateral right nostril breathing in stroke patients (n=11) with left hemisphere brain damage for ten weeks reduced measures of anxiety and improved measures of language capacity in those with aphasia [24].

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Human research to suggest benefits to patients with dementia:

There are case studies to support that the inclusion of diaphragmatic breathing exercises into cognitive behavioral therapy can reduce anxiety in patients with dementia [25]. More rigorous studies are needed to determine the optimal method of breathing training for this population.

A small study in patients with mild cognitive impairment (MCI) (n=72), found that eight weeks of an integrated yoga intervention, which included a pranayama component, improved performance on measures of executive function, attention, verbal fluency, and memory [26]. However, due to the multimodal nature of this intervention, the contribution of the pranayama component to these effects is unclear.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Autonomic nervous system regulation: SLOW BREATHING DRIVES PARASYMPATHETIC NERVOUS SYSTEM

The central mechanism whereby breathing techniques influence brain function is via the autonomic nervous system. Slow breathing is associated with activation of the parasympathetic nervous system, which promotes a state of relaxation. Meanwhile fast pranayamas lead to activation of the sympathetic nervous system, which can promote a state of vigilance. These changes are also associated with alterations in cerebral blood flow. EEG studies have found changes in alpha, beta, and theta brain waves in response to various breathing techniques [4]. Right nostril breathing is associated with activation of the sympathetic nervous system, while left nostril breathing is associated with activation of the parasympathetic nervous system [5]. The sympathetic/parasympathetic dominance for alternate nostril breathing appears to be determined by the nostril used for inspiration. Most protocols used in clinical studies involve starting with the left nostril. The mixed data seen in studies using unilateral or alternate nostril breathing could be a byproduct of disparities in the ultradian nasal cycle across participants. The nasal cycle involves rhythmic changes in blood flow to the nasal mucosa, such that one nostril is more congested than the other, and thus more air flows in and out of a certain nostril at a given time. This cycle varies across people, and studies do not stratify their participants according to the phase of their nasal cycle at the time of the analysis [5]. Thus, it has been hypothesized, but not validated, that the effects of unilateral nostril breathing may be amplified in those breathing through their more open nostril, and mitigated for those breathing through the congested nostril. Similarly, in the context of alternate nostril breathing, the effects may be influenced by the nasal cycle of a given participant.

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Receptors in the superior nasal meatus may drive the effects on the autonomic nervous system and brain activity downstream of nasal breathing [27].

Brain imaging functional magnetic resonance imaging (fMRI) studies indicate that slow breathing increases activity in brain areas involved in the regulation of internal body states including the prefrontal, motor, and parietal cortices, as well as the pons, thalamus, sub-parabrachial nucleus, periaqueductal gray, and hypothalamus [27]. In healthy young adults (n=30), Bhastrika pranayama practice for four weeks decreased measures of anxiety and negative affect, based on the PANAS scores [28]. These changes in emotional state were associated with changes in connectivity between the right anterior insula and the ventrolateral prefrontal cortex, based on resting-state fMRI. On emotional processing tasks, the greatest changes occurred in the right amygdala and the bilateral insula. Gray matter volume of the insular cortex has been found to be higher in regular yoga practitioners, and this is associated with higher pain thresholds [4]. These studies suggest that the regulation of breathing can, in turn, modulate the activity of brain regions involved in emotional processing and cognitive control.

The locus coeruleus has been proposed as the brain region driving the connection between respiration and attention [29]. The maintenance of attention requires locus coeruleus activity that is matched to the task. Task reaction time variability is correlated with attentional performance, and also covaries with the tonic firing rate of the locus coeruleus. Synchronization between task locus coeruleus activation and the respiratory phase has been observed. Breath training techniques could impact this relationship by reducing the influence of noise in locus coeruleus activity, which reduces the level of effort needed to maintain an attentional state.

Anxiety and Depression: SLOW BREATHING CAN REDUCE NEGATIVE MOOD STATES

Slow breathing techniques can reduce the physiological aspects of sympathetic nervous system overactivation that often accompany anxiety by driving the parasympathetic nervous system. This can lead to a reduction in hyperventilation and hyper arousal, to promote a state of relaxation rather than vigilance [30]. Various studies have shown that the balancing of the autonomic nervous system promotes emotional regulation, and can alleviate negative mood states. Although these techniques alone may not be sufficient to eliminate anxiety or depression, they can modulate physiological components, which may, in turn, mitigate some of the deleterious psychological components.

In a meta-analysis of 25 studies (n=1,339 participants), yoga practice consisting of asanas and pranayama was associated with a significant reduction in mental disorder-specific symptom severity (Hedges' g: 0.91, 95% confidence interval [CI] 0.55 to 1.28) [31]. A systematic review of three studies

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(n=1,046 participants) found that diaphragmatic breathing was associated with a reduction in both physiological and psychological measures of stress [32]. A randomized controlled dosing study testing lyengar yoga with coherent breathing at five breaths per minute for 12 weeks in the context of major depressive disorder (n=32) found that this intervention improved scores on all eight psychological domains tested, along with a decrease in Patient Health Questionnaire-9 (PHQ) scores from 11.23 ±4.80 to 4.13 ±3.10 [33]. Beck Depression Inventory-II (BDI-II) scores significantly decreased from 24.6±1.7 to 6.0±3.8 [34]. There was a resolution of suicidal ideations in eight out of nine cases [35]. The decrease in depression scores was correlated with an increase in brain GABA levels based on magnetic resonance spectroscopy (MRS) imaging (Pearson correlation: -0.562, p = 0.045) [36]. The increase in GABA levels was time limited, only detectable within eight days of the yoga/breathing intervention, suggesting that weekly practice would be needed for sustained benefit.

APOE4 interactions: Not established

Aging and related health concerns: Breathing training may improve lung function, lower blood pressure, and reduce the risk of cardiovascular disease. Resonant breathing can improve heart rate variability.

Types of evidence:

- 3 meta-analyses on breathing techniques for COPD
- 1 meta-analysis of slow breathing techniques for hypertension
- 1 meta-analysis of pranayama for hypertension
- 1 systematic review of pranayama for hypertension
- 1 systematic review of diaphragmatic breathing for hypertension
- 1 systematic review on breathing techniques for COPD
- 1 review of diaphragmatic breathing for lung function/COPD
- 1 systematic review on breathing techniques for asthma
- 1 systematic review for breathing techniques for sleep apnea
- 4 clinical trials on Buteyko for asthma/lung function
- 2 clinical trials on breathing retraining for dysfunctional breathing
- 3 clinical trials on alternate nostril breathing for lung function in healthy adults
- 3 clinical trials for resonant breathing with biofeedback
- 2 clinical trials for diaphragmatic breathing and reflux
- 5 clinical trials for alternate nostril breathing on blood pressure

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- 1 observational study on breathing exercises for lung function and lifespan in cancer
- 3 longitudinal cohort studies on lung function and mortality

Lifespan: REDUCED LUNG FUNCTION ASSOCIATED WITH MORTALITY RISK

There is ample anecdotal evidence that lifetime practice and mastery of some breathing techniques, such as achieved by certain groups of monks and yogis, is associated with longevity. However, these individuals tend to engage in a variety of longevity-promoting behaviors, so the effects cannot be conclusively tied to the breathing practices. Several longitudinal studies provide evidence that decreased lung function is a significant risk factor for mortality. The Framingham Heart Study (n=5,209) found that forced vital capacity, a measure of lung function, was a predictor of cardiovascular mortality [37]. Similarly, a study of participants from the Third National Health and Nutrition Examination Survey (n=5,485) found that those with low forced vital capacity had a greater risk for mortality (Hazard Ratio [HR]: 2.64) [38]. Pulmonary function, as measured by forced expiratory volume (FEV1), was also a predictor of all-cause mortality in the Buffalo Health Study cohort (n=1,195) (HR: 2.24, 95% CI 1.60 to 3.13 for men and HR: 1.81, 95% CI 1.24 to 2.63 for women) [39]. An observational study found that respiratory cancer survivors (n=122) that practiced morning breathing exercises had higher average survival rates (9.8 \pm 9.5 vs 3.3 \pm 2.8 years), with a significantly longer 5-year survival rate (Relative risk [RR]: 5.371, 95% CI 2.271 to 12.636, P < 0.001), and a 17.9-fold increase in the 10-year survival rate [40]. The practitioners also showed lower levels of metastasis (40.9% vs 74.1%) and better lung function. These studies suggest that improving lung function may prevent premature mortality.

Respiratory function: BENEFIT

Breathing techniques have primarily been evaluated for their ability to improve respiratory function. It is hypothesized that these techniques can correct abnormal breathing patterns. It is estimated that 9.5% of the adult population has some form of dysfunctional breathing, which involves breathing too deeply, rapidly, or erratically that is interspersed with breath holding [41]. A study examining measures of dysfunctional breathing (n=83) found that those with shorter breath holding time were more likely to have abnormal spirometry readings [42]. This group showed a thoracic-dominant breathing pattern. This suggests that the implementation of breathing training may alter the biomechanics of breathing in a manner that improves efficiency, and reduces the symptoms of dysfunctional breathing. A small RCT (n=45) reported a significant reduction in the frequency and severity of hyperventilation attacks in response to breathing exercise therapy in patients with hyperventilation syndrome [41].

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Breathing practices, especially nasal breathing, are associated with increased respiratory efficiency and improved athletic performance. In young competitive swimmers (n=27), yogic breathing practices (Vibhagiya pranayama, Bhastrika pranayama and alternate nostril breathing with voluntary internal breath holding) performed half an hour a day for one month, significantly improved maximal voluntary ventilation, forced vital capacity, and the number of strokes performed per breath [43]. In healthy young adults (n=100), alternate nostril breathing for ten minutes per day for four weeks improved the respiratory parameters forced vital capacity, forced expiratory volume in 1st second (FEV1), and peak expiratory flow rate [44]. Alternate nostril breathing has also been shown to decrease the respiration rate and increase the expiration: inspiration ratio in healthy male volunteers [45]. The benefits are attributed to promoting the production of lung surfactants, which promotes gas exchange, and improving the oxygen carrying capacity of red blood cells [43]. Breathing allows for the inspiration of warm, moist, filtered air, so the value for some respiratory conditions may depend on climate, such that it may offer more pronounced benefits in colder, drier environments.

Asthma: LONG-TERM BREATHING TRAINING MAY REDUCE SYMPTOMS

A systematic review of 22 RCTs (n=2,880 participants) involving the use of breathing techniques for asthma primarily involved yoga as an intervention (n=14) [<u>30</u>]. The evidence was of moderate to low quality, with primarily inconclusive results, though there are trends for favorable outcomes with longer term practice. Meta-analyses of the studies found that effects on asthma symptoms, measured by the Asthma Control Questionnaire, hyperventilation symptoms, measured by the Nijmegen Questionnaire, and forced expiratory volume in 1 second (FEV1) were inconclusive at three months. But, quality of life and hyperventilation measures favored the breathing exercises in longer duration studies. The FEV1% predicted, a measure of expiration efficiency and vital capacity, was also associated with an improvement favoring breathing training (Mean Difference 6.88%, 95% CI 5.03 to 8.73; based on five studies, 618 participants).

One of the studies, which compared Buteyko breathing with pranayama (n=120), found that the trends for improvement on quality of life and asthma symptoms were greater for Buteyko, but neither significantly impacted pulmonary function measures during the three-month study [46]. Two separate six-month RCTs testing Buteyko (n=90, n=129), found that Buteyko breathing practice led to a decrease in inhaled corticosteroid use, although significant changes in FEV1 were not detected [47; 48]. Because Buteyko advocates for decreasing reliance on corticosteroids, it is unclear whether the reductions in use reflect an improvement in breathing, or simply an effort to adhere to broader guidelines advocated by Buteyko. The effects seen in clinical trials are not as robust as those reported anecdotally. It is claimed

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that over 90% of those who completed the Buteyko course in Russia were able to discontinue asthma medication following training, with a comparable success rate reported for 8,000 course participants in Australia [47]. The discrepancy may be due to differences in the teaching and adherence to the method, as those enrolling in a certified course may be more committed. A separate study found that perceived benefit of a simplified Buteyko technique was correlated with level of adherence and effort to put into the practice, suggesting that there is a strong motivational component [49]. The mechanism by which Buteyko improves asthma has been suggested to be due to an increase in CO_2 , however, the data do not support this mechanism. Although CO_2 has a relaxant effect on the airway, breathing CO_2 -enriched (3%) air did not prevent exercise-induced asthma in a small clinical study [50]. Another study found that end-tidal CO_2 levels did not significantly differ between those with normal and abnormal spirometry [42].

COPD: BREATHING TRAINING MAY ENHANCE EXERCISE CAPACITY

A Cochrane systematic review of 16 studies (n=1,233 participants) found evidence for improved functional exercise capacity in individuals with chronic obstructive pulmonary disease (COPD) following breathing exercises performed for at least four weeks [51]. This was assessed by the six-minute walking test, and improvements were found with pranayama, pursed lip breathing, and diaphragmatic breathing techniques, with mean differences ranging from 35 to 50 meters. Measures on quality of life and dyspnea, or shortness of breath, were inconclusive. A meta-analysis of six RCTs (n=280 participants) found that pranayama practice increases the strength of respiratory muscles, while diaphragmatic breathing training can improve ventilation in the context of COPD [52]. Similarly, a review of systematic reviews concluded that diaphragmatic breathing can improve exercise capacity and respiratory function [2]. A meta-analysis of 15 RCTs (n=1,098 participants) examining pursed lip breathing and diaphragmatic breathing for COPD found that these practices were associated with improvements in forced expiratory volume in 1 second (FEV1) (Standardized Mean Difference: 0.47, 95% CI 0.27 to 0.67, P < 0.001), forced vital capacity (SMD: 0.87, 95% CI 0.59 to 1.15, P <0 .001), FEV1 as a proportion of forced vital capacity (MD: 8.30, 95% CI 1.17 to 15.43, P =0 .02), and the six-minute walk test (MD: 29.09, 95% CI 19.35 to 38.83, P < 0.001) [53]. A meta-analysis of 19 studies (n=745 participants) of breathing exercises for COPD found that respiratory rate was significantly improved by pursed-lip breathing, ventilatory feedback plus exercise, or diaphragmatic breathing, though the quality of evidence was low to moderate [54]. The use of multiple breathing exercises was associated with the greatest level of improvement (MD: -5.53, 95% CI -6.98 to -4.09). There was, however, no significant effect on dyspnea.

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Cardiovascular function: BENEFIT

Breathing techniques can impact cardiovascular function via regulation of the autonomic nervous system. Chronic stress is associated with sustained activation of the sympathetic nervous system and a corresponding elevation of blood pressure and heart rate [55]. Long-term practice of slow breathing techniques can establish a parasympathetic dominance. Breathing can modulate cardiac activity through a variety of mechanisms, including a direct effect of the medullary respiratory neurons on cardiomotor neurons [56]. In this way, breathing can serve as an oscillator to drive the rhythm of the heart [3]. A key mechanism involves the alteration of baroreflex efficiency. The baroreflex controls cardiac function to maintain a constant blood pressure.

Heart rate variability: RESONANT BREATHING INCREASES HRV

Heart rate variability is the beat-to-beat change in the interbeat interval, and is influenced by the autonomic nervous system. Having low heart rate variability is associated with increased vulnerability to stress and chronic disease [3]. There is heterogeneity across studies, but the overall body of evidence suggests a role for breathing techniques in improving heart rate variability. Some yogic breathing and diaphragmatic breathing practices have been shown to have a beneficial effect on heart rate variability, however, the effects are not always consistent. The breathing practices that affect heart rate variability involve coherent breathing, which is generally on the order of five breaths per minute. The resonant breathing frequency is the frequency that will maximize the amplitude of the respiratory sinus arrhythmia, which involves an increase in heart rate during inspiration and a decrease during expiration [57]. Under this condition, the heart rate variability is synchronized with the respiratory cycle. Every person has his or her own resonant breathing frequency, which can be determined by a medical professional. Heart rate variability involves low frequency and high frequency components, which involve contributions of the sympathetic and parasympathetic nervous systems. The high frequency component primarily reflects the activity of the vagus nerve, while the low frequency component is associated with the baroreflex [3]. The resonant frequency can be calculated as the number of breaths that maximize the low frequency spectrum peak. Resonant frequency breathing stimulates and reinforces the baroreflex. Although the frequency varies from person to person, it is typically in the range of five to seven breaths per minute, so the use of a tempo in this range is likely to increase heart rate variability in most people, though not necessarily to an optimal degree. Once established, biofeedback programs can be utilized to teach someone to breathe at his or her established resonant frequency.

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A variety of small clinical studies have established the proof-of-concept that resonant breathing with biofeedback training can be used to impact physiological and psychological measures of stress. Elevated sympathetic activity during sleep is associated with low heart rate variability and poor sleep quality. Studies support the concept that breathing practices, such as resonant breathing, which increase parasympathetic tone and heart rate variability also improve sleep quality. A study including cancer patients (n=50) and their caregivers (n=54) involved the use of a portable device (iPad) containing a breath pacer application (ProComp Infiniti/BioGraph Infiniti, Thought Technology) programmed to the participant's resonant frequency [58; 59]. In cancer patients, the intervention significantly improved sleep efficiency, sleep duration and the low-frequency component of heart rate variability within two weeks [59]. The low-frequency component of heart rate variability also improved in the caregiver group [58].

Resonant breathing can also temper emotional state-related disruptions to the heart rhythm and alleviate psychological elements of stress. The signal between the heart and the brain can be filtered by limbic brain regions. Emotional states, especially negative ones, reduce heart rate variability, as measured by the standard deviation of the normal-to-normal inter-beat intervals (SDNN), through EEG and ECG monitoring, while diaphragmatic breathing at six breaths per minute was found to increase heart rate variability, especially the low frequency component [57]. The vagus nerve can impact the brain's effect on cardiac activity, thus slow breathing techniques that increase vagal tone can counteract some of the disruptive effects of negative emotions. This mechanism may contribute to the decrease in depression, anxiety, and stress scale (DASS) scores in female manufacturing operators (n=36) following five weeks of resonant breathing with biofeedback training [3]. There were also improvements in sleep quality and PSQI scores in patients with major depressive disorder (n=32) following an intervention of yoga and coherent breathing at five breaths per minute for 12 weeks [33].

Hypertension: SLOW BREATHING REDUCES BLOOD PRESSURE

Slow breathing techniques can reduce blood pressure through regulation of the autonomic nervous system, via activation of the parasympathetic nervous system and promotion of baroreflex efficiency. A meta-analysis of six RCTs (n=269 participants) involving the use of slow breathing techniques in patients with cardiovascular disease found that these techniques were associated with reductions in systolic blood pressure (SBP) (MD: -6.36 mmHg, 95% CI -10.32 to -2.39) and diastolic blood pressure (DBP) (MD: -6.39 mmHg, 95% CI -7.30 to -5.49) [60]. A systematic review of 13 studies involving diaphragmatic deep breathing in hypertensive or prehypertensive adults concluded that this technique can decrease systolic and diastolic blood pressures, reduce heart rate, and reduce anxiety in this population [55]. With device-guided slow breathing for 15 to 30 minutes, SBP was reduced an average of

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6 to 8 mmHg, and DBP was reduced an average of 4 to 6 mmHg. A meta-analysis of 17 RCTs of pranayama slow breathing found that across trials this technique reduced SBP by -5.62 mmHg (95% CI -7.86 to -3.38) and DBP by -2.97 mmHg (95% CI -4.28 to -1.66) [61]. The effect size was dependent on the duration of the intervention, as those who performed the technique for over 200 minutes per week showed the greatest effects (SBP MD: -14.00 mmHg, 95% CI -18.85 to -9.15). A systematic review of 13 trials involving pranayama (n=239 participants) found that blood pressure reductions were evident in both acute (SBP change of 2 to 10 mmHg) and chronic studies (4 to 21 mmHg), but greater reductions were seen in the chronic studies [62]. Alternate nostril breathing has been shown to reduce blood pressure in a variety of small clinical studies [5; 18; 63; 64; 65]. In an RCT (n=170), alternate nostril breathing reduced SBP following five days of practice for ten minute per day. At baseline SBP was similar before and immediately after the breathing practice $(134.64 \pm 6.735 \text{ vs} 134.47 \pm 6.645 \text{ mmHg})$, and by the fifth day of practice, SBP was significantly reduced immediately after the alternate nostril breathing session from 126.64 ±6.548 mmHg prior to the breathing exercise to 80.42 ±2.897 mmHg after completion of the breathing exercise [63]. Many of these studies include patients already taking antihypertensives, indicating that these techniques can be used to supplement medical interventions. These studies suggest that slow breathing techniques are an effective way to modestly reduce blood pressures, especially when practiced regularly.

Sleep apnea: BREATHING RETRAINING MAY IMPROVE SLEEP

A systematic review of 14 studies assessing various methods of breathing retraining for sleep apnea, including the Buteyko method, inspiratory resistance training, diaphragmatic breathing, and singing/wind instruments, found evidence to support the use of these techniques in improving sleepdisordered breathing [66]. Musicians who play a double reed wind instrument have a lower risk of obstructive sleep apnea. Didgeridoo playing was found to have a beneficial effect on sleep outcomes with a moderate effect size, while singing reduced daytime sleepiness and snoring. Diaphragmatic breathing was associated with improvements in sleep apnea and sleep quality, and inspiratory resistance training improved sleep and oxygenation levels. The efficacy of the Buteyko method appears high, but the supportive evidence is largely anecdotal based on survey reporting. Following a training course, 95% of Buteyko method practitioners reported an increase in sleep quality, and 80% reported a decrease in use of continuous positive airway pressure therapy (CPAP) therapy. There are a few cases where remission of sleep apnea following Buteyko method training was achieved based on polysomnography data. Three practitioners showed evidence of remission based on the apnea-hypopnea index (AHI) with changes from 40 to 6, 22 to 2, and 28 to 4, respectively. The case study of a 44-year-old man also indicated the absence of sleep apnea and improvement of oxygen saturation from

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87% to 97% after five months of Buteyko practice. In general, reported success rates for Buteyko are much higher in surveys of those who participated in Buteyko clinics relative to the effects seen in clinical studies.

The proposed mechanisms by which these breathing techniques alleviate sleep apnea include improving the strength of respiratory muscles, enhancing respiratory plasticity, improved autonomic nervous system regulation, improved oxygenation, reduced hyperventilation, reduced mouth breathing, as well as generalized metabolic and anti-inflammatory effects [66]. Different techniques will preferentially utilize different mechanisms. For example, instrument and vocal training primarily involves muscle strengthening, while Buteyko focuses on reducing hyperventilation and mouth breathing. Consequently, different populations may preferentially benefit from different breathing interventions depending on the etiology of their dysfunctional breathing.

Gastroesophageal Reflux: DIAPHRAGMATIC BREATHING REDUCES REFLUX

Reflux is associated with increased postprandial gastric pressure. Small RCTs provide a proof-of-concept that diaphragmatic breathing can be used to reduce postprandial reflux events in patients with gastroesophageal reflux disease (GERD) (0.36 vs 2.60, P < 0.001), as well as in healthy volunteers (0.00 vs 1.75, P < 0.001) [67]. The reduction in reflux events was also associated with decreased levels of esophageal acid exposure. Diaphragmatic breathing is also beneficial for a form of regurgitative reflux called Rumination syndrome, also caused by excessive postprandial gastric pressure [68].

Safety: Slow breathing techniques are safe but proper training is required.

Types of evidence:

- 12 meta-analyses or systematic reviews
- Numerous clinical trials

Slow breathing techniques have been safely used as part of cultural practices for hundreds of years. Clinical trials also provide evidence for a strong safety profile. Adverse events have typically only been seen in the context of yoga interventions, and are usually related to the asana component, such as mild muscle soreness [35]. In contrast, fast breathing interventions which activate the sympathetic nervous system may acutely exacerbate conditions such as anxiety, and are best performed in a supervised manner [69]. Hyperventilation can lead to poor oxygenation and light-headedness. Breathing techniques require proper training from a medical professional or experienced practitioner. Performing these

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breathing techniques improperly could potentially exacerbate dysfunctional breathing. Although most studies show a benefit for respiratory disorders, the effects may depend on disease severity, as there is some evidence to suggest that some of these techniques could be harmful in cases of severe COPD or limited lung function [2].

Since these breathing techniques modulate the autonomic nervous system, caution is warranted in populations with autonomic nervous system disorders.

Sources and dosing:

Buteyko breathing: There are <u>clinics</u> that are designed to teach the Buteyko method.

Diaphragmatic deep breathing: Medical providers can offer proper training for this technique. This technique has not been standardized and can be performed from difference positions or postures (sitting, laying down, etc.), with a range of inspiration and expiration times, generally between four to eight seconds [2]. The optimal session duration may depend on the condition, but often range from 10 to 30 minutes in clinical studies [55].

Pranayama: These techniques are generally taught as part of yoga instruction. Clinical studies suggest that benefits may require long-term practice, such that the more regularly one practices these techniques, the greater the potential for health benefits [4]. Practice at least once per week may be necessary for sustained effects [36], though the duration of the practice may vary depending on the type of pranayama.

Resonant breathing: The resonant frequency is calculated by a medical provider, and this information can then be used in combination with biofeedback training, such as App-based breathing pacers to entrain breathing at this frequency [59]. There are a variety of breathing pacer Apps, which assist with coherent breathing at a given frequency. No optimal level of resonant breathing has been established, but since it maximizes respiratory efficiency, regular breathing at this frequency is associated with health benefits.

Alternate nostril breathing: Based on several clinical studies, one group concluded that 18 minutes was the optimal time to perform alternate nostril breathing in order to achieve cognitive benefits [18]. Proper technique can be taught through yogic instruction.

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Research underway:

There are currently 202 active clinical trials that involve diaphragmatic breathing as part of the therapeutic intervention on Clinicaltrials.gov. They cover a variety of conditions, including respiratory disorders, anxiety, pain management, reflux, cardiovascular disorders, cognitive disorders, sleep apnea, cancer, and various other indications.

There are currently 10 yoga-pranayama-based intervention trials on Clinicaltrials.gov. There are 3 clinical trials that involve Buteyko, for asthma and/or dysfunctional breathing. There are 3 clinical trials involving resonant breathing in conjunction with biofeedback monitoring to regulate heart rate variability. There is one yoga invention that involves alternate nostril breathing for irritable bowel syndrome.

Most of the clinical research involving breathing techniques takes places outside of the United States, thus it is likely that only a small fraction of the research currently being conducted in this area is captured on this U.S. based clinical trial registry.

Search terms:

Pubmed, Google: Buteyko, Diaphragmatic breathing, Pranayama, Resonant breathing, Coherent breathing, Alternate nostril breathing +

• Alzheimer's disease, cognition, anxiety, lifespan, cardiovascular, asthma, clinical trial, metaanalysis, systematic review

Websites visited for Breathing techniques:

- Clinicaltrials.gov (<u>Diaphragmatic breathing</u>, <u>pranayama</u>, <u>resonant breathing</u>, <u>alternate nostril</u> <u>breathing</u>)
- Drugs.com (breathing techniques)
- WebMD.com (pranayama, breathing exercises)
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