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REVIEW

The assessment of inspiratory muscle fatigue in healthy individuals: A systematic review

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Summary
Inspiratory muscle fatigue (IMF) may contribute to the development of exercise limitation and respiratory failure. Identifying fatigue of the inspiratory muscles requires a rigorous and integrative methodological approach. However, there is no consensus about an optimal protocol to induce and assess the fatigability of the inspiratory muscles.

A systematic review was performed to identify, evaluate, and summarize the literature related to the assessment of induced IMF in healthy individuals. The aim was to identify factors that are related consistently to IMF, as well as to suggest possible assessment methods. MEDLINE and EMBASE were searched for relevant articles until February 2012. Only studies with a quantitative description of assessment and outcome were included.

The search yielded 460 citations and a total of 77 studies were included. Inspiratory muscle fatigue was produced acutely by inspiratory resistive loading (IRL), whole body exercise (WBE), hyperpnea, or WBE combined with IRL, and under normocapnic, hypoxic or hypercapnic conditions. To detect IMF, most studies (64%) used phrenic nerve stimulation, 44% used a maximal

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voluntary inspiratory maneuver and the remainder used electromyography. The heterogeneity of the published reports precluded a quantitative analysis.

Inspiratory resistive loadings at intensities of 60–80% of maximum, and cycling at 85% of maximum were found to produce IMF most consistently. Hypoxic or hypercapnic conditions, and WBE combined with IRL, exacerbated IMF. The specific outcome measures employed to detect IMF, the magnitude of their change, as well as their functional significance, are ultimately dependent upon the research question being addressed.

Contents

Introduction

The primary function of the respiratory control system is to drive alveolar ventilation in proportion to the metabolic requirements. The human diaphragm is the primary muscle involved in active inspiration.[1] Increased inspiratory muscle work may induce fatigue of the respiratory muscles, as well as of the non-respiratory muscles by central changes at spinal and supraspinal level.[2] Fatigue is defined as a loss in the capacity for developing force and/or velocity of a muscle, resulting from muscle activity under load and which is reversible by rest.[3] However, this definition is rather vague since the amount of loss, the intensity of muscle activity and applied load is not further defined. Furthermore, inspiratory muscle fatigue (IMF) is defined regardless of whether it is caused by peripheral contractile fatigue,[4,5] or failure of the neural drive, which is called central fatigue.[2,6–9]

In the last 30 years, the function of the respiratory muscles has received considerable attention. Roussos and Macklem were the first to suggest that respiratory muscle fatigue may contribute to the development of respiratory failure.[10] Respiratory muscle fatigue may develop in pathological states, such as chronic obstructive pulmonary disease,[11] or amyotrophic lateral sclerosis,[12] but also in healthy individuals during temporary increases in respiratory work, such as strenuous physical exercise.[13]

Despite the complex process of IMF, diagnostic measures are essential to provide optimal treatment in e.g. pulmonary rehabilitation, intensive care, sports medicine and neurology.[14] Although a variety of methods have been employed, there is no consensus about an optimal protocol to induce and interpret IMF, either in research, or clinical settings. The purpose of this systematic review is to outline the potential diagnostic strategies to assess the fatigability of the inspiratory muscles in healthy humans. More specifically the objective is to identify factors in the loading protocols contributing to the extent of IMF, as well as to define the possible measurement tools to identify IMF.

Methods

Search strategy

Papers were selected from electronic databases as follows: MEDLINE and EMBASE (from their earliest date until February 2012). We used a broad search strategy using the terms "diaphragm", "respiratory muscles", "respiration", "muscle fatigue" and "muscle weakness" with a limit on articles in English, French, German or Dutch. A detailed search strategy is available in Appendix 1. The reference lists of all included studies were screened for potential additional eligible studies.

Study selection

Inclusion criteria were: (1) Types of studies: prospective cohort, retrospective cohort, cross-sectional, case-control and randomized controlled studies (only full text). (2) Types of interventions: any intervention causing acute loading of the inspiratory muscles (3) Types of assessment tools: quantitative description of diagnostic tool to assess IMF; (4) Types of outcome measures: quantitative result in terms of an absolute or relative value; (5) Types of participants: homogeneous samples of healthy adult humans; Exclusion criteria were: (1) Types of studies: case reports, case series, editorials, letters, replies, reviews and guidelines. These types of studies were only used for cross-references; (2) Types of interventions: any intervention causing unloading of the inspiratory muscles (e.g. by training) or loading of the expiratory muscles; (3) Types of assessment tools: no quantitative description of diagnostic tool to assess IMF; (4) Types of outcome measures: no quantitative result; (5) Types of participants: animals, children or adult humans with a pathological condition. Three reviewers independently screened all titles and abstracts returned by the search strategy. Studies not clearly eligible after reading the title and/or abstract were evaluated for selection after retrieving the full text. In case of disagreement, the full article was read and consensus was reached after discussion.

Data extraction

Three reviewers independently extracted all relevant data-items from the included studies using a data extraction form. The quality of the studies was assessed using a quality checklist based on the STROBE statement.[15]

Methods of analysis and synthesis

The results were summarized qualitatively. It was judged that the data were not suitable for statistical pooling due to the heterogeneity of the study designs. For each eligible study we described how IMF was assessed. If the data allowed we described the mode, intensity and duration of the loading protocol. For each study, the change in outcome measure as the difference between pre and post the loading protocol, was described in percentage. Common article results were compared when statistically significant results were reported.

Results

The search strategy yielded a total of 460 citations. A total of 84 were deemed potentially relevant based on title and/or abstract screening. After excluding articles not meeting the prespecified inclusion criteria and after including supplementary articles by cross-references, a total of 77 studies were considered for the final analysis. Fig. 1 displays the flowchart of the search strategy. Tables 1–5 summarize how IMF was assessed in detail and show the mean decline in measured outcome in percentage.

Loading protocol

Of the selected studies, 32 used inspiratory resistive loading (IRL) (Table 1), 30 studies used whole body exercise (WBE) (Table 2), 11 used hyperpnea (HYP) (Table 3), 6 used IRL, WBE or HYP under changed oxygen or carbon dioxide fractions (Table 4) and 4 used a combination of WBE and IRL (WBE + IRL) (Table 5) to induce possible IMF.

Most studies used IRL by breathing against an inspiratory threshold load (Table 1). In most of these studies ($n = 27$) subjects were instructed to breathe against a predefined percentage of their maximal inspiratory mouth pressure (Pi_{max}) or maximal inspiratory transdiaphragmatic pressure (Pdi_{max}). However, this percentage ranged from 50 to 100% of Pi_{max} or Pdi_{max}, with a mean of 67% (interquartile range (IQR) 60–80). Only four studies used an incremental IRL to induce IMF,[15–19] and one study used a preset resistance from 40 to 50 cmH_2O of the maximal inspiratory oesophageal pressure ($Poes_{max}$).[20] Duty cycle (0.5 ± 0.1) and breathing frequency (15.3 ± 3 breaths/min) were quite consistent between the IRL protocols. However, the length of the IRL protocols ranged from 3 to 50 min (18.3 ± 13.3 min), with some tests performed to task failure and others to a defined time limit.

The remainder of studies used WBE to overload the inspiratory muscles. The WBE was undertaken using cycling (19 studies), running (10 studies), or swimming (5 studies) (Table 2). The mean exercise intensity was 85% of maximal oxygen uptake (VO_{2max}) (IQR 80–90). In a small number of studies normocapnic hyperpnea (HYP) at high percentage of maximal voluntary ventilation (MVV) was used to induce IMF (Table 3). Four studies combined a reduced inspiratory oxygen fraction (hypoxia) or hypoventilation (hypercapnea) with WBE,[21–24] and two studies used HYP under hypoxic[25] and hypercapnic[26] conditions to induce IMF (Table 4). Four studies combined WBE and IRL to induce IMF, both at the same time,[27] or with WBE immediately following IRL.[28–30]

Pre-post measurement techniques

Of the selected studies, 64% ($n = 49$) used phrenic nerve stimulation to detect possible diaphragmatic fatigue (Tables 1–5). This technique involves bilateral anterolateral or cervical stimulation of the phrenic nerves via electrical or magnetic stimulation while measuring gastric pressure (Pga), oesophageal pressure (Poes), transdiaphragmatic pressure (Pdi = Pga − Poes) or mouth pressure (Pmouth), both before and after the overloading protocol. Two studies used transcranial stimulation of the phrenic nerves via a magnetic[31] and electrical[32] stimulus. Most studies measured the twitch response during rest (unpotentiated twitch), but a few studies measured a potentiated twitch response to rule out a possible potentiation effect.[4,19,33–36]

Forty-four percent of the studies ($n = 34$) used a pre-post maximal voluntary inspiratory maneuver (Mueller) while measuring maximal Pmouth (Pi_{max}), Pga, Poes, Pdi. In five studies subjects performed a powerful sniff maneuver.[18,22,37–39] Besides the pressure measurements, some older studies used surface or catheter electromyography (EMG) to assess IMF.[7,18,40–48]

Presence of inspiratory muscle fatigue

Tables 1–5 (right column) show the mean decline (%) of measured outcome of each study. All studies showed

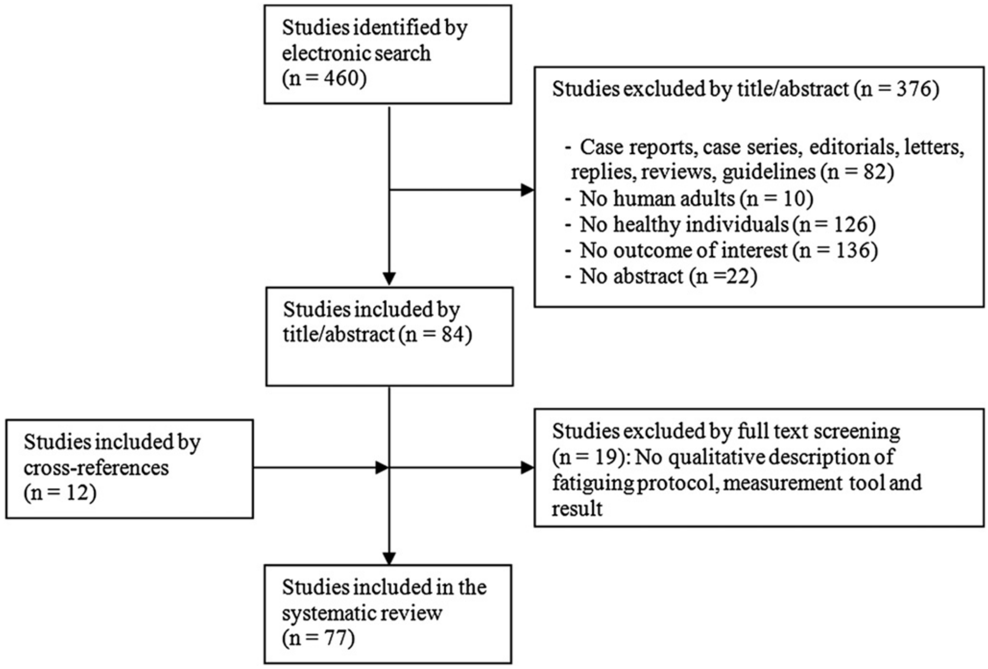

Figure 1 Flowchart search strategy.

a significant decline in mean Pdi, Poes, Pga and Pmouth twitch response following IRL (Table 1). After only 2 min of IRL Laghi et al.[4] showed no decline in unpotentiated Pdi,tw, although a significant fall of 9.7% was reached after 4 min IRL. The potentiated Pdi,tw, however, showed a significant fall after just 2 min of IRL.[4] Sheel et al.[49] showed a significant fall in Pdi,tw following IRL at 60% Pi_{max}, however, this was not observed after breathing against 50% Pi_{max},[50] or 95% Pi_{max}.[49] Rohrbach et al.[51] showed no decrease in Pga,tw after IRL, although Pdi,tw and Poes,tw showed a significant decline. Decreases in Pdi,tw ranged from significant mean changes of 8.5% (20 min post IRL)[52] to 50% (immediately after IRL).[8,53] Maximal inspiratory pressure (Pi_{max}) declined after IRL, except for two studies that showed no decline immediately after loading at 80% Pi_{max},[54] and at 25 h post IRL at 80% Pi_{max}.[8] Decreases in Pi_{max} ranged from significant mean changes of 9.3% (20 min post IRL)[4] to 50% (immediately after IRL).[7] Fig. 2 displays the changes in outcome measures in relation to the IRL intensity for all included studies.

Following WBE most studies showed a significant decline in Pdi, Poes, Pga and Pmouth twitch response (Table 2). Two studies showed no decrease in Pga,tw immediately after cycling at 85% and 95% VO_{2max}, respectively,[5,52] and two studies showed no decrease in Pdi,tw 20 min after incremental treadmill exercise, and 40–60 min after cycling at 85% VO_{2max}, respectively.[31,55] Significant mean decreases in Pdi,tw ranged from 9%[55] to 30.6%.[56] Most WBE studies showed a decline in Pdi, Poes, Pga and Pmouth pressure using a maximal voluntary inspiratory effort, although some did not.[5,28,57,58] After a marathon Chevrolet et al.[59] found a decreased Pi_{max} up to 2 h after exercise whereas this decrease could not be confirmed after four hours, one day and 3 days.[60,61] Significant mean decreases in Pi_{max} following WBE ranged from 8.2%[62] to 28.6%[63]; the latter study added a specific inspiratory warm-up procedure prior to pre-WBE measurements.

Most studies showed the same decline in Pdi twitch response following HYP (Table 3). However, the decline in Pdi,tw after HYP may depend on the intensity of MVV,[41] mode of phrenic nerve stimulation,[32] or time point post HYP.[26] Significant mean decreases in Pdi,tw ranged from 8.1% (immediately after HYP)[26] to 28.1% (20 min post HYP).[64]

Under hypoxic or hypercapnic conditions, all studies showed a greater fall in Pdi_{max}, Pdi,sniff or Pdi,tw post WBE or HYP compared to control conditions (Table 4).[21–26,65] Significant mean decreases in Pdi,tw ranged from 10% (20 min post hypercapnic HYP)[26] to 34% (immediately after hypoxic HYP)[25] compared to pre-loading.

When IRL was added to the WBE protocol (WBE + IRL), all studies showed a greater fall in Pi_{max} and Pdi,tw compared to WBE only (Table 5).[27–30] Significant mean decreases in Pdi,tw after WBE + IRL ranged from 13.5%[30] to 35%.[27] However, only four studies using WBE + IRL were included.

Discussion

This systematic review identified 77 studies in which IMF was induced by IRL, WBE, HYP or WBE combined with IRL and both under normocapnic, hypoxic or hypercapnic conditions. Most studies defined IMF by a decrease in Pdi, Poes, Pga or Pmouth in response of phrenic nerve stimulation. The remainder of studies used the same pressure measurements in response of a maximal voluntary inspiratory maneuver to detect IMF. However, the variability in the overloading protocols, pre-post assessment tools, timing of measurements, and interpretation of results requires further discussion.

Table 1 Assessment of inspiratory muscle fatigue following inspiratory resistive loading (IRL).

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% outcome change pre versus post fatiguing protocol
Aubier et al. 1981[40]	80% Pi_{max}	Pdi	Twitch (BAENS)	Max	**41.7%**↓ (20 Hz, 2 & 60 min post), **12.3%**↓ (100 Hz, 2 min post), 1%↓ (100 Hz, 15 min post)
		EMGdi (surface)	Inspiration	H/L	EMGdi: >**40%**↓
Aubier et al. 1985[74]	80% Pi_{max} – 27 min	Pdi	Twitch (BAENS)	Max	**45%**↓ (5 min post), **45%**↓ (15 min post), **45%**↓ (30 min post)
				T	**40%**↑ (5 min post), **47.3%**↑ (15 min post), **60%**↑ (30 min post)
Bellemare and Grassino 1982[43]	50 & 75% Pdi_{max} – 30–45 min	EMGdi	Inspiration	H/L	↓
Bellemare and Bigland-Ritchie 1987[7]	50 & 75% Pdi_{max} – 0.6 duty cycle – 12 br/min – 45 min	Pdi	Twitch (BAENS)	Max	**25%**↓
		EMGdi	Inspiration	RMS	**25%**↓
		Pdi	Inspiration	Max	**50%**↓
Bezzi et al. 2003[85]	60% Pdi_{max}, 0.5 duty cycle – 12–34 min	Pdi, Poes, Pga	Twitch (CMS)	Max	**28%**↓ (Pdi), **14%**↓ (Poes), **51%**↓ (Pga) (all 15 min post)
		EEG			0%↓
Delpech et al. 2003[52]	62% Pi_{max} – 0.5 duty cycle – 12–15 br/min	Pdi, Poes, Pga, Pmouth	Twitch (CMS)	Max	**8.5%**↓, **18.2%**↓, 0%↓, **8.8%**↓ (all 20 min post)
Eastwood et al. 1994[16]	Start at 40% Pi_{max}, increase every 2 min by 10% – 10–20 min	Pdi	Twitch (BAENS)	Max	**15%**↓ (0 min post), **25%**↓ (25 min post)
Esau et al. 1983[17]	High alinear inspiratory resistance – 12 br/min	Pdi	Sniff	MRR	**18%**↓ (0 min post)
				T	**41%**↑ (0 min post)
Esau et al. 1983[18]	High alinear inspiratory resistance – 12 br/min	Pdi	Inspiration	MRR	**50%**↓
		Pdi		T	**60%**↑
		EMGdi (oes)		H/L	**50%**↓
Gallagher et al. 1985[44]	70% Pi_{max} – 0.6 duty cycle – 12 br/min – 250 s	EMGdi (surface)	Inspiration	H/L	**42%**↓ (70% Pi_{max})
	56% Pi_{max} – 0.6 duty cycle – 12 br/min – 685 s				**30%**↓ (56% Pi_{max})
Gonzales and Williams 2006[78]	70% Pi_{max}	Pmouth	Inspiration	Max	**15%**↓
Gorman et al. 1999[54]	80% Pi_{max} (244 cmH_2O l/s) – free duty cycle & freq – 3 min	Pmouth	Inspiration	Max	0%↓
Gross et al. 1979[45]	25, 50 & 75% Pdi_{max} – 0.6 duty cycle – 12 br/min – 15 min	EMGdi (surface)		H/L	0%↓ (25% Pdi_{max}), **40%**↓ (50% Pdi_{max}), **58%**↓ (75% Pdi_{max})
		EMGdi (oes)			0%↓ (25% Pdi_{max}), **60%**↓ (50% Pdi_{max}), **67%**↓ (75% Pdi_{max})

(*continued on next page*)

Table 1 (*continued*)

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% outcome change pre versus post fatiguing protocol
Guleria et al. 2002[19]	Incremental: start at 30% Pi_{max}, increase every 3 min by 10% — 16.7 min	Pdi (unpot)	Twitch (BAMPS)	Max	6%↓ (20 min post), **9%**↓ (40 min post), 5%↓ (60 min post)
		Pdi (pot)			**28%**↓ (0 min post), **25%**↓ (20 min post), **23%**↓ (40 min post), **20%**↓ (60 min post)
Hershenson et al. 1989[20]	40—50 cmH_2O Poes — 0.5 duty cycle — 3—5 min	Poes (Ppl)	Inspiration	Max	**20%**↓
		Pabd			0%↓
		Pdi			**16%**↓
		Pdi (open glottis)			0%↓
Laghi et al. 1996[67]	60% Pdi_{max} — 0.5 duty cycle — 15 br/min — 28 min	Pdi, Pga, Poes	Twitch (CMPS) Twitch (BAEPS)	Max	Pdi: CMPS: **37.3%**↓ (10 min post), **37.3%**↓ (30 min post), **32.5%**↓ (60 min post) Pdi: BAEMPS: **41.2%**↓ (10 min post), **38.8%**↓ (30 min post), **35.7%**↓ (60 min post) Pga: CMPS: **33.1%**↓ (10 min post), **38%**↓ (30 min post), **31.5%**↓ (60 min post) Pga: BAEMPS: **33.8%**↓ (10 min post), **32.6%**↓ (30 min post), **29.5%**↓ (60 min post) Poes: CMPS: **39.2%**↓ (10 min post), **36.8%**↓ (30 min post), **32.5%**↓ (60 min post) Poes: BAEMPS: **45%**↓ (10 min post), **45.5%**↓ (30 min post), **39.1%**↓ (60 min post)
Laghi et al. 1998[4]	60% Pdi_{max} — 0.5 duty cycle — 15 br/min — 2 min, 4 min & till task failure	Pdi Pdi (unpot) Pdi (pot)	Inspiration Twitch (CMPS) Twitch (CMPS)	Max	Pdi_{max} — 2 min IRL: **17%**↓ (0 min post), **9.3%**↓ (20 min post) Pdi_{max} — 4 min IRL: **19.6%**↓ (0 min post), **9.3%**↓ (20 min post) Pdi_{max} — till task failure IRL: **21.2%**↓, **11.9%**↓ (20 min post), **11.4%**↓ (20 h post) Pdi,tw (unpot) — 2 min IRL: 0%↓ Pdi,tw (unpot) — 4 min IRL: **9.7%**↓ (0 min post) Pdi,tw (unpot) — till task failure IRL: **15.3%**↓ (0 min post), 15%↓ (20hours post) Pdi,tw (pot) — 2 min IRL: **11%**↓ (0 min post), **17.4%**↓ (20 min post) Pdi,tw (pot) — 4 min IRL: **20.4%**↓ (0 min post), **23.2%**↓ (20 min post) Pdi,tw (pot) — till task failure IRL: **26.1%**↓ (0 min post), **29.8%**↓ (20 min post), **11%**↓ (20 h post)
Luo et al. 2001[79]	Pdi_{max} — 0.66 duty cycle — 3 × 5 min (in between 10 min rest)	Pdi	Twitch (BAMPS)	Max	**20%**↓ (0 min post)
Mador and Kufel 1992[37]	80% $Poes_{max}$	Poes	$Sniff_{mouth}$	MRR	**14%**↓
			$Sniff_{nostrils}$	MRR	**15%**↓
			$Sniff_{mouth}$	T	**17%**↓
			$Sniff_{nostrils}$	T	**17%**↓

McKenzie et al. 1992[6]	50% Pi_{max} – 0.6 duty cycle – 40–45 min	Pdi	Twitch (BAEPS)	Max	**33%↓**
Moxham et al. 1981[90]	70% Pi_{max} – 10–20 min	Pdi	Twitch (CEPS)	Max	**30%↓**
Moxham et al. 1982[46]	80% Pdi_{max} – 3 × 10–20 min	Pdi	Twitch (CEPS)	Max	**36%↓** (10 min post), **30%↓** (20 min post), **30%↓** (30 min post)
		EMG	MVC	H/L	**14%↑** (10 min post), **16%↑** (20 min post), **10%↑** (30 min post)
Petitjean et al. 1996[53]	60% Pdi_{max} – 0.6 duty cycle – max 50 min	Pdi PMG	Twitch (CEPS)	Max	**50%↓** **48%↓**
Rohrbach et al. 2003[51]	67% Pi_{max} – 9.1 min – 18 br/min 67% Pi_{max} – 8.4 min – 18 br/min 67% Pi_{max} – 9.1 min + 8.4 min – 18 br/min	Pdi, Pga, Poes	Twitch (CMPS)	Max	**21.8%↓** (Pdi), 10%↓ (Pab), **21.8%** (Poes) **15.3%↓** (Pdi), 10%↓ (Pab), **13%↓** (Poes) **29.3%↓** (Pdi), 10%↓ (Pab), **28%↓** (Poes)
Sheel et al. 2001[49]	60% Pi_{max} – 0.7 duty cycle – 6.5 min – 15 br/min 60% Pi_{max} – 0.4 duty cycle – 8 min – 20 br/min 95% Pi_{max} – 0.35 duty cycle – 3 min – 12 br/min	Pmouth	Twitch (BAEPS)	Max	**43.5%↓** **30.2%↓** 0%↓
Sheel et al. 2002[50]	(30, 40,) 50 & 60% Pi_{max} – 0.4 duty cycle – 8 min – 20 br/min	Pmouth	Twitch (BAEPS)	Max	3%↓ & **30%↓**
Similowski et al. 1998[71]	60% Pdi_{max} – 18–43 min	Pdi	Twitch (CEPS) Twitch (CMPS)	Max	**39%↓** (CEPS) **26%↓** (CMPS)
Supinski et al. 1987[93]	60 & 90% Pi_{max} – 0.4 duty cycle – 15 br/min		Inspiration	Max	**11%↓** (60% Pi_{max}), **11.5%↓** (90% Pi_{max})
Suzuki et al. 1996[94]	60% Pi_{max} – 0.5 duty cycle	Pdi Pmouth	Inspiration	Max	**12%↓** **12%↓**
Travaline et al. 1997[8]	80% Pdi_{max} – 25 min	Pdi	Twitch (CEPS) Inspiration	Max	**50%↓**, **28%↓** (3 h post), 0%↓ (25 h post) **25%↓**, **13%↓** (3 h post), 0%↓ (25 h post)
Ward et al. 1988[48]	65% Pdi_{max}, 60% $Poes_{max}$ – 0.4 duty cycle – 18 br/min 50% Pdi_{max}, 60% $Poes_{max}$ – 0.4 duty cycle – 18 br/min 50% Pdi_{max}, 20% $Poes_{max}$ – 0.4 duty cycle – 18 br/min	EMGdi		Max	**54.2%↓** (0 min post) **40.8%↓** (0 min post) **36.9%↓** (0 min post)
Yan et al. 1993[9]	80% Pi_{max} – 0.6 duty cycle – 10–20 min	Pdi Pmouth	Twitch (BAEPS) Inspiration	Max Max	**33.9%↓** **25.8%↓**

Significant changes pre versus post fatiguing protocol are marked in bold ($p < 0.05$).

Table 2 Assessment of inspiratory muscle fatigue following whole body exercise (WBE).

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% change pre versus post fatiguing protocol
Babcock et al. 1995[65]	Treadmill/Bicycle − 86–93% VO_{2max} − 13.2 min	Pdi	Twitch (BAEPS)	Max	**26%↓** (0 min post)
Babcock et al. 1996[83]	Treadmill/Bicycle − 88–92% VO_{2max} − 15.2 min	Pdi	Twitch (BAEPS)	Max	**23.1%↓** (0 min post)
Babcock et al. 1998[84]	Treadmill/Bicycle − 93.3% VO_{2max} − 9.9 min	Pdi	Twitch (BAEPS)	Max	**23.4%↓** (0 min post)
Brown and Kilding 2011[62]	100 m, 200m & 400m front-crawl swim	Pmouth	Inspiration	Max	**8.2%↓** (100m), 5%↓ (200m), 4.9%↓ (400m)
Bye et al. 1984[42]	Bicycle − 80% VO_{2max}	Pdi	Inspiration	Max	**13%↓** (0 min post)
		EMGdi	Inspiration	H/L	**20%↓** (0 min post)
Chevrolet et al. 1993[59]	Marathon − 190 min	Pmouth	Inspiration	Max	**27%↓** (18 min post), **21%↓** (84 min post), **16%↓** (118 min post)
Delpech et al. 2003[52]	Bicycle − 85% VO_{2max}	Pdi, Poes, Pga, Pmouth	Twitch (CMS)	Max	**13.1%↓**, **8.7%↓**, 0%↓, **9.2%↓** (all 20 min post)
Gonzales and Williams 2010[78]	Bicycle − 80% VO_{2max}	Pmouth	Inspiration	Max	**12%↓**
Guenette et al. 2010[56]	Bicycle − 90% VO_{2max}	Pdi	Twitch (CMS)	Max	Male: **30.6%↓** (10 min post), **20.7%↓** (30 min post), **13.3%↓** (60 min post) Female: **21%↓** (10 min post), **11.6%↓** (30 min post), **9.7%↓** (60 min post)
Hill et al. 1991[87]	Triathlon	Pmouth	Inspiration	Max	0%↓ (post swim), **26%↓** (post cycle), **25%↓** (post run)
Jakovljevic and McConnell 2009[80]	2 × 200 m front-crawl swim (90% of race pace) − breath every 2nd & 4th stroke	Pmouth	Inspiration	Max	**11%↓** & **21%↓**
Johnson et al. 1993[5]	Bicycle − 85 VO_{2max} − 14 min	Pdi, Poes, Pga	Twitch (BAEPS)	Max	**17.8%↓** (Pdi), **17.6%↓** (Poes), **14.8%↓** (Pga) (all 0 min post)
		Pdi, Poes, Pga	Inspiration		0%↓ (Pdi), 0%↓ (Poes), 0%↓ (Pga) (all 0 min post)
	Bicycle − 95% VO_{2max} − 14 min	Pdi, Poes, Pga	Twitch (BAEPS)		**13.7%↓** (Pdi), **17%↓** (Poes), 7%↓ (Pga) (all 0 min post)
		Pdi, Poes, Pga	Inspiration		10.5%↓ (Pdi), 0%↓ (Poes), 0%↓ (Pga) (all 0 min post)
Kabitz et al. 2008[33]	Bicycle − 85% VO_{2max}	Pdi	Twitch (BAMPS)	Max	**15%↓** (6 min post)
Kabitz et al. 2008[34]	Bicycle − 85% VO_{2max}	Pdi (pot)	Twitch (BAMPS)	Max	**21.9%↑** (1.5 min post), **8.9%↓** (3 min post), **8.4%↓** (4.5 min post), **8%↓** (6 min post)
Kabitz et al. 2008[35]	Bicycle − 85% VO_{2max}	Pdi (pot)	Twitch (BAMPS)	Max	**14.2%↓** (6 min post)
Kabitz et al. 2010[75]	Bicycle − 85% VO_{2max} − 45 min + endspurt	Pdi (pot)	Twitch (BAMPS)	Max	**28%↓**
Ker and Schultz 1996[60]	Ultra-marathon (87 km)	Pmouth	Inspiration	Max	0%↓ (3 days post)
Loke et al. 1982[88]	Marathon Bicycle − 85% VO_{2max}	Pmouth, Pdi	Inspiration	Max	**16%↓** (Pmouth), **19.7%↓** (Pdi)

Lomax and McConnell 2003[63]	200 m front-crawl swim (90–95% of race pace)	Pmouth	Inspiration	Max	**28.6%↓**
Lomax and Castle 2011[28]	200 m front-crawl swim (85% of race pace)	Pmouth	Inspiration	Max	0%↓
Mador and Dahuja 1996[73]	Bicycle – 70–75% VO_{2max}	Pdi	Twitch (BAEPS)	Max	**19%↓** (10 min post)
McConnell et al. 1997[81]	Run – incremental multistage shuttle run	Pmouth	Inspiration	Max	**10.5%↓**
Nava et al. 1992[57]	Run – 17 km	Pmouth	Inspiration	Max	0%↓ (0 min post), 0%↓ (30 min post)
Ozkaplan et al. 2005[91]	Bicycle – incremental	Pmouth	Inspiration	Max	**17%↓** (male), **22%↓** (female)
Perlovitch et al. 2007[47]	Treadmill – 2 km, 8 km/u	EMGmm.intercost. ext. (surface)	Inspiration	Slope RMS	**34%↑**
Perret et al. 1999[58]	Bicycle – 85% VO_{2max}	Pmouth	Inspiration	Max	0%↓
Romer et al. 2004[92]	Bicycle – 65% VO_{2max} 40 min + 30 min time trial (pedaling-rate-dependent mode)	Pmouth	Inspiration	Max	**20%↓** (< 2 min post), **12.5%↓** (30 min post, cool), **11.9%↓** (30 min post, heat), **7.5%↓** (60 min post, cool), **10%↓** (60 min post, heat)
Ross et al. 2008[61]	Marathon	Pmouth	Inspiration	Max	**15%↓** (0 min post), 6%↓ (4 h post), 5%↑ (24 hours post)
Tomczak et al. 2011[36]	Bicycle – 45% VO_{2max} + chest wall restriction	Pdi (unpot) Pdi (pot)	Twitch (CMPS)	Max	**20.2%↓** (Pdi unpot) **23.3%↓** (Pdi pot)
Verin et al. 2004[31]	Treadmill – incremental – 18 min	Pdi MEP-CMAP	Twitch (BAMPS) Twitch (TMS)	Max	0%↓ (20 min post) **40%↓** (5 min post), **55%↓** (20 min post)
Vogiatzis et al. 2006[55]	Bicycle – 85% VO_{2max} – 5 min	Pdi	Twitch (CMS)	Max	**9%↓** (10 min post), **5%↓** (20 min post), 3%↓ (40 min post), 0%↓ (60 min post)

Significant changes pre versus post fatiguing protocol are marked in bold ($p < 0.05$).

Table 3 Assessment of inspiratory muscle fatigue following hyperpnea (HYP).

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% change pre versus post fatiguing protocol
Bai et al. 1984[41]	76, 79, 86, 100% MVV (isocapnic)	Pmouth	Inspiration	Max	**22%↓** (0 min post, 76% MVV); **21%↓** (0 min post, 79% MVV); 11%↓ (0 min post, 86% MVV)
		Pdi	Twitch (BAENS)	Max	In accordance to Pdimax
		Pdi	Inspiration	Max	10%↓ (0 min post, 76% MVV); **27%↓** (0 min post, 79% MVV); 11%↓ (0 min post, 86% MVV)
		EMGdi		H/L	**60%↓** (within 2 min, 76, 79, 86, 100% MVV)
Coast et al. 1999[86]	MVV (isocapnic)	Pmouth	Inspiration	Max	**15%↓** (0 min post)
Kabitz et al. 2008[34]	MVV (isocapnic)	Pdi (pot)	Twitch (BPNS)	Max	**28%↑** (1.5 min post), **10%↓** (3 min post), **8%↓** (4.5 min post), **10%↓** (6 min post)
Kyroussis et al. 1994[38]	MVV (isocapnic)	Pnasal	Sniff	MRR	**28.5%↓** (Pnasal)
		Poes			**27.4%↓** (Poes)
Luo et al. 2001[79]	MVV (isocapnic) – 2 min	Pdi	Twitch (BAMPS)	Max	**22%↓** (0 min post)
			Sniff		**8.6%↓** (0 min post)
Mador et al. 2002[32]	60% MVV (isocapnic)	Pdi	Twitch (TES)	Max	**25%↓** (10 min post), **12%↓** (30 min post), **12%↓** (60 min post)
			Twitch (CMPS)		**15%↓** (10 min post), **14%↓** (30 min post), 6%↓ (60 min post)
			Twitch (BAMPS)		**23%↓** (10 min post), **22%↓** (30 min post), 6%↓ (60 min post)
Mulvey et al. 1991[39]	MVV (isocapnic) – 2 min	Poes	Sniff	Max	↓
Polkey et al. 1997[64]	MVV (isocapnic) – 20 min	Pdi	Twitch (single CMPS)	Max	**17.9%↓** (20 min post), **14.6%↓** (60 min post)
			Twitch (paired CMPS)		**28.1%↓** (20 min post), **22.9%↓** (60 min post)
Rafferty et al. 1999[26]	MVV (isocapnic) – 2 min	Pdi	Twitch (CMPS)	Max	**8.1%↓** (0 min post), **11.2%↓** (20 min post), **10%↓** (40 min post), **12%↓** (60 min post), 5%↓ (90 min post)
Renggli et al. 2008[95]	70% MVV (isocapnic) – 25.3 min – alternately 8 min task & 6 min rest	Pdi	Twitch (CMPS)	Max	**25%↓** (0 min post), **15%↓** (30 min post), **10%↓** (60 min post)
Verges et al. 2010[25]	85% MVV (isocapnic)	Pdi	Twitch (CMPS)	Max	**22%↓** (0 min post), **10%↓** (30 min post)

Significant changes pre versus post fatiguing protocol are marked in bold ($p < 0.05$).

Table 4 Assessment of inspiratory muscle fatigue following whole body exercise (WBE) or hyperpnea (HYP) under changed O_2 or CO_2 fractions (+hypoxia, +hypercapnea).

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% change pre versus post fatiguing protocol
Babcock et al. 1995[21]	WBE (85% VO_{2max}) + hypoxia (15% O_2) − 15.8 min	Pdi	Twitch (BAEPS) Inspiration	Max	**22%**↓ (0 min post), **10.5%**↓ (90 min post) **9.6%**↓ (0 min post)
Gudjonsdottir et al. 2001[22]	WBE (100% VO_{2max}) + hypoxia (high altitude) − 10 min	Pdi	Sniff Twitch (CMPS)	Max	**27%**↓ (10 min post), 6%↓ (60 min post) **27%**↓ (10 min post), 8%↓ (60 min post)
Jonville et al. 2002[23]	WBE (60% VO_{2max}) + hypercapnea (voluntary hypoventilation) − 16 min	Pmouth	Twitch (CMPS)	Max	**7.6%**↓ (10 & 30 min post)
Rafferty et al. 1999[26]	HYP (MVV) + hypercapnea (8% CO_2) − 2–14 min	Pdi	Twitch (CMPS)	Max	**15%**↓ (0 min post), **10%**↓ (20 min post), **11%**↓ (40 min post), **11%**↓ (60 min post), 5%↓ (90 min post)
Verges et al. 2010[25]	HYP (85% MVV) + hypoxia (15% O_2)	Pdi Pga	Twitch (CMPS) Twitch (TMPS)	Max	**34%**↓ (0 min post), **16%**↓ (30 min post) **26%**↓ (0 min post), **21%**↓ (30 min post)
Vogiatzis et al. 2007[24]	WBE (85% VO_{2max}) + hypoxia (13% & 17% O_2) − 5 min	Pdi	Twitch (BAMPS)	Max	**26.9%**↓ (13% O_2), **27.4%**↓ (17% O_2)

Significant changes pre versus post fatiguing protocol are marked in bold ($p < 0.05$).

Loading protocol

Sheel et al.[49] identified a >30% decline in Pmouth,tw after IRL at 60% Pi_{max}, but no evidence of IMF was found after breathing at 95% Pi_{max}[49] or at 80% Pi_{max}[54] after 3 min of IRL. McConnell & Griffiths[66] have recently shown that the amount of inspiratory muscle work undertaken during pressure threshold IRL is reduced at loading intensities above 60% Pi_{max}. This paradoxical finding is explained by the interplay of the threshold load with the pressure–volume relationship of the inspiratory muscles. Both total inspiratory muscle work and the amount of work per breath, were maximized at 60% Pi_{max}, declining at lower and higher loads.[66] Our analysis also confirmed a lower threshold of intensity for provoking IMF, such that IRL at 25% Pi_{max}[45] and 50% Pi_{max}[50] failed to elicit significant IMF. This pattern, that both very low, and very high intensity IRL, do not produce IMF at the point of task failure, seems consistent with our observation summarizing all studies using IRL (Fig. 2). Besides the intensity, the length of the IRL protocol also appears to influence the ability to detect IMF. Laghi et al. showed a decline in Pdi,tw after 2 min of IRL, at the intensity of 60% $Pi_{max.}$, which became larger when the length of IRL increased to 4 min, 28 min and up to task failure.[4,67,68] Based on our findings, we suggest IMF can be induced by IRL to task failure at an intensity of 60–80% of Pi_{max} or Pdi_{max}.

Cycling exercise at 85% VO_{2max} has been utilized most often to examine possible effects of WBE upon IMF. The mean exercise intensity of all studies was 85% ± 7% VO_{2max}, which shows a low range of different intensities over all WBE protocols. This is most likely because studies have based their methods on the early study of Johnson et al.[5] who reported that 85% of VO_{2max} was the threshold for inducing IMF during cycling. Their data suggested that cycling at a higher intensity (95% VO_{2max}) does not produce greater fatigue, which may be explained by the shorter test duration resulting in a lower total inspiratory muscle work.[5] This suggests that for both during IRL and WBE there is a specific range of intensities that are associated with induction of IMF.[5,66] One study failed to detect IMF after swimming time trails over 200 m and 400 m.[62] Brown and Kilding[62] attribute this to the lack of a specific inspiratory warm-up procedure, which may lead to under-estimation of pre-exercise Pi_{max}.[69] The warm-up typically increases Pi_{max}, thereby preventing the masking of fatigue by a submaximal baseline Pi_{max}.[62] Based on these findings, we suggest IMF can be induced by WBE by cycling at 85% of $VO_{2max,}$ and that preceding baseline measurements with a specific inspiratory warm-up will maximize the magnitude of IMF; thereby enhancing the sensitivity of the measurement.

Hypoxia[21,22,24,25] and hypercapnia[23,26] during WBE or HYP appear to exacerbate diaphragmatic fatigue, compared to normocapnic conditions. At similar intensities of WBE, hypoxia or hypercapnia may increase diaphragm fatigue because of increased minute ventilation and therefore work of breathing. One study found that hypercapnia does not intensify long lasting fatigue, but may reduce inspiratory muscle function immediately after a MVV.[26] Based on these findings, we suggest IRL, WBE and HYP be undertaken under

Table 5 Assessment of inspiratory muscle fatigue following a combination of whole body exercise and inspiratory resistive loading (WBE + IRL).

Author + year	Fatiguing protocol	Measurement	Maneuver	Outcome	% change pre versus post fatiguing protocol
Levine and Henson 1988[27]	WBE (incremental treadmill) + IRL (38 $cmH_2O\ l^{-1}\ s^{-1}$)	Pdi	Twitch (BAEPS)	Max MRR T	**35%↓** **34%↓** 22%↓
Lomax and Castle 2011[28]	WBE (swim) + IRL (70% Pi_{max}, 0.6 duty cycle − 12 br/min)	Pmouth	Inspiration	Max	**17%↓**
Sliwiński et al. 1996[29]	WBE (30, 60, 90% VO_{2max}) + IRL (80% Pi_{max}) − 4 min	Pdi Pmouth	Twitch Inspiration	Max	**16%↓** **24%↓**
Verges et al. 2006[30]	WBE (85% VO_{2max}) + IRL (80% Pi_{max}) − 11.5 min + 20 min	Pdi, Pga, Poes	Twitch (CMPS)	Max	**13.5%↓** (Pdi), **16.4%↓** (Pga), **17.3%↓** (Poes)

Significant changes pre versus post fatiguing protocol are marked in bold ($p < 0.05$).

hypoxic or hypercapnic conditions to exacerbate IMF, provided this is appropriate to the research question, or clinical situation under investigation.

Pre-post measurement techniques

The majority of studies measured twitch transdiaphragmatic pressure in response to supramaximal phrenic nerve stimulation (Pdi,tw) for assessing diaphragmatic fatigue. In contrast to maximum voluntary contractions (Pi_{max} or Psniff), this technique reveals specific contractile fatigue of the diaphragm. The technique eliminates the contribution of the accessory muscles, and of the central nervous system, and thus motivation, in the assessment of IMF.[14] However, the technique also excludes 1) the contribution of accessory muscles to global IMF, and 2) the physiological effects of supraspinal and spinal

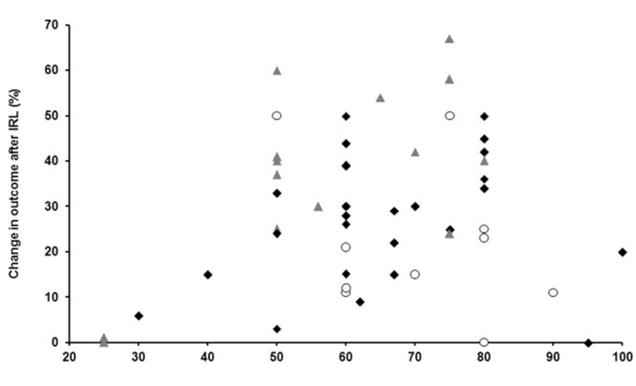

Figure 2 Changes in outcome (%) after inspiratory resistive loading (IRL) compared to pre IRL for all included studies in relation to IRL intensity (% Pi_{max}). Black squares show the mean changes in (transdiaphragmatic, oesophageal, gastric and mouth) pressure following twitch stimulation; Gray triangles show the changes in (transdiaphragmatic, oesophageal, gastric and mouth) pressure following maximal voluntary inspiratory maneuver; White circles show the changes in (surface or deep) diaphragmatic electromyographic response.

components of fatigue upon muscle force production. Furthermore, the gastro-oesphageal catheter and the electrical stimulation are uncomfortable. Accordingly, some researchers have proposed to use mouth pressure following phrenic nerve stimulation as an index for inspiratory muscle contractility, which reduces the discomfort of the catheters, but still overlooks central fatigue.[23,49,50,52] Whilst some authors have proposed Pmouth,tw as a promising tool to assess IMF,[70] others discourage its use because it may result in less reliable prediction of Pdi,tw and Poes,tw.[68] Because of the limited number of studies using Pmouth,tw in the assessment of IMF, further investigation is warranted to evaluate this method fully. Over the past decade, electrical stimulation of the phrenic nerves was replaced by magnetic stimulation since this also reduces discomfort. Some differences have been found between the two stimulation modes.[32,67,71] For example, the absolute Pdi,tw obtained at baseline is larger during magnetic compared with electrical stimulation.[32,67,71–73] Following IRL Similowski et al.[71] found that Pdi,tw fell more using electrical stimulation, compared to magnetic, although Laghi et al.[67] found a similar sized decrease. In addition, bilateral anterior magnetic stimulation elicited larger Pdi,tw declines compared to cervical magnetic stimulation.[32] Although Pdi,tw is regarded as the most objective method for assessing contractile fatigue of the diaphragm, small sample sizes are typical, due to the invasive nature of the experimental protocol.[36,54,74,75] Based on these findings, contractile fatigue of the diaphragm can be assessed objectively using transdiaphragmatic pressure measurement following bilateral anterior magnetic phrenic nerve stimulation.

Some studies measured a potentiated instead of unpotentiated twitch response, since twitch amplitude is sensitive to the preceding contraction history.[4,19,33–36] During a fatiguing protocol, the consecutive maximal voluntary contractions result in a marked increase in twitch amplitude, which is called twitch potentiation.[37,76,89] This is similar to the effect observed with successive measurements of Pi_{max}.[69] Therefore, some researchers maximally potentiate the twitch by a preceding maximal voluntary inspiration and use changes in the amplitude of the potentiated twitch as their index of IMF.[77] After a fatiguing protocol the fall in potentiated twitch was larger than the unpotentiated twitch response, which suggests that the potentiated twitch might be a more sensitive method to evaluate IMF.[4,19,36] This is consistent with observations in other skeletal muscles, e.g., quadriceps, in which fatigue was more pronounced when examined using potentiated twitches compared to unpotentiated twitches.[77] Based on these findings, we recommend the use of potentiated twitch responses in the assessment of IMF, due to the greater sensitivity of this method.

Besides phrenic nerve stimulation, Pdi, Poes, Pga and Pmouth pressure measured during maximal voluntary inspiratory efforts can also provide a meaningful measure to identify IMF. Whilst this less invasive method is vulnerable to the effects of subject's motivation and muscular coordination,[14] it has the advantage of revealing the neural contribution to IMF. While Bai et al.[41] showed similar falls in voluntary Pdi (Pdi_{max}) and stimulated twitch Pdi (Pdi,tw), other studies showed a larger fall in Pdi_{max} than Pdi,tw, which suggests a contribution of central fatigue to Pdi_{max}.[7–9] However, other studies have shown the reverse.[4,5] The response of a maximal voluntary inspiratory effort is a widely used assessment tool for IMF since it is a non-invasive and easy applicable method that provides an index of IMF. However, the potential for overestimation of IMF magnitude owing to the subject's motivation cannot be excluded.

Some older studies utilized frequency domain analysis of the EMG signal from the inspiratory muscles to detect the presence of IMF. Most often a ratio of the EMG power contained between the high-frequency band and the low-frequency one (H/L) is used to quantify IMF. The ratio decreases with IMF since the EMG power spectrum shifts to a lower frequency during fatigue. However, the etiology of power spectral shifts following fatigue is still controversial.[37] Therefore, the assessment of IMF using EMG is not considered to be a reliable method to identify IMF.

Presence of inspiratory muscle fatigue

Nearly all studies showed significant changes in indices of inspiratory muscle function, after WBE, IRL, HYP, WBR + IRL, as well as when these overloading stimuli are delivered under hypoxic and hypercapnic conditions. When different forms of inspiratory muscle work are compared, no differences in the magnitude of the fall in Pdi,tw were found after IRL compared to WBE,[52–78] or after IRL compared to HYP.[79] Thus, IMF appears to be independent of the activity mode used to increase inspiratory muscle work.

Most studies conclude that IMF was present using a decline in the pressure generating capacity in the inspiratory muscles. However, the decrement in inspiratory muscle function varied widely between studies, ranging from 5% to 67%. Some studies used a critical threshold of 15% for the decline in function to be classified as fatigue,[32] but some have used 10%,[72,79] whilst others have defined fatigue as a statistically significant mean fall from baseline, rather than using a minimum threshold.[28,63,80,81] It is reasonable to suggest that any significant fall from baseline is indicative of a decline in inspiratory muscle function. However, the functional significance of such a decline, and its magnitude, is dependent upon the research question under examination.

Conclusion

The qualitative analysis of this systematic review suggests that IMF is present after IRL, WBE and HYP. Specific IRL at intensities of 60–80% of Pi_{max} or Pdi_{max} appear to maximize the change in outcome measures of inspiratory muscle function, and thus IMF. Similarly, cycling at 85% of VO_{2max} to the limit of tolerance was found to produce IMF, whereas the overloading characteristics for running and swimming require further exploration. Furthermore, hypoxic or hypercapnic conditions, and WBE combined with IRL appear to exacerbate IMF. In addition, a specific bout of inspiratory "warm-up" is indicated,[69] since this creates narrower limits of agreement for the outcome measure,[82] as well as maximizes the magnitude of IMF. Similarly, the use of potentiated twitch pressures is recommended.[77]

Following overloading of the inspiratory muscles, the measurement of transdiaphragmatic pressure in response to phrenic nerve stimulation (Pdi,tw) provides the most objective method of evaluating contractile fatigue of the diaphragm. This measurement eliminates the influence of motivation,[14] but overlooks the contribution of neural fatigue mechanisms. Subsequent to the overloading, a statistically significant fall in an outcome measure compared to baseline, is indicative of a decline in inspiratory muscle function. However, it is arguable whether a minimum percentage change is required in order for this to be considered indicative of IMF. The use of a minimum threshold based on the inherent reliability of the outcome measure (e.g. minimum change of 10% or 15%) may be appropriate, but this is ultimately dependent upon the research question being addressed. The functional significance of changes in inspiratory muscle function remains an area for further research. Functional repercussions of IMF include changes in breathing effort, breathing pattern, limb blood flow and exercise tolerance.[13]

Conflict of interest

Alison McConnell acknowledges a beneficial interest in an inspiratory muscle training product in the form of a share of license income to the University of Birmingham and Brunel University, and acts as a consultant to POWERbreathe International Ltd.

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Appendix 1

Search strategy: ((("Diaphragm"[Mesh] AND "muscle fatigue"[Mesh]) OR ("Diaphragm"[Mesh] AND "Muscle

Weakness"[Mesh]) OR ("Diaphragm"[Mesh] AND "fatigue"[Mesh])) OR (("respiratory muscles"[Mesh] AND "muscle fatigue"[Mesh]) OR ("respiratory muscles"[Mesh] AND "Muscle Weakness"[Mesh]) OR ("respiratory muscles"[Mesh] AND "fatigue"[Mesh])) OR (("respiration"[Mesh] AND "muscle fatigue"[Mesh]) OR ("respiration"[Mesh] AND "Muscle Weakness"[Mesh]) OR ("respiration"[Mesh] AND "fatigue"[Mesh]))) AND ("diaphragmatic"[All Fields] OR "diaphragm"[All Fields] OR "diaphragms"[All Fields] OR "respiratory"[All Fields]) AND fatigue[All Fields]

Limits:

Species: humans

Language: English, French, German, Dutch

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List of abbreviations

BAEPS: bilateral anterior electrical phrenic nerve stimulation;
BAMPS: bilateral anterior magnetic phrenic nerve stimulation;
Duty cycle: ratio of contraction time over duration cycle;
CEPS: cervical magnetic electrical stimulation;
CMPS: cervical magnetic phrenic nerve stimulation;
EEG: electroencephalography;
EMG: electromyogram;
H/L: ratio of the EMG power contained between the high-frequency component and the low-frequency component; method to quantify the power spectrum of EMG; ratio decreased with fatigue;
MRR: maximal relaxation rate;
MVV: maximal voluntary ventilation;
Pdi: average transdiaphragmatic pressure during one inspiration (cmH_2O);
Pdi (pot): potentiated Pdi (cmH_2O);
Pdi (unpot): unpotentiated Pdi (cmH_2O);
Pdi_{max}: maximal Pdi that can be achieved (cmH_2O);
Pga: gastric pressure (cmH_2O);
Pi_{max}: maximal Pmouth that can be achieved (cmH_2O);
Poes: oesophageal pressure (cmH_2O);
PMG: phonomyogram;
T: time constant of relaxation;
TMPS: thoracic magnetic phrenic nerve stimulation;
UAMNS: unilateral anterior magnetic phrenic nerve stimulation;
VO_{2max}: maximal oxygen uptake