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Effect of Respiratory Muscle Training on Exercise Performance in Healthy Individuals

A Systematic Review and Meta-Analysis

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Abstract

Objectives: Two distinct types of specific respiratory muscle training (RMT), i.e. respiratory muscle strength (resistive/threshold) and endurance (hyperpnoea) training, have been established to improve the endurance performance of healthy individuals. We performed a systematic review and meta-analysis in order to determine the factors that affect the change in endurance performance after RMT in healthy subjects.
Data sources: A computerized search was performed without language restriction in MEDLINE, EMBASE and CINAHL and references of original studies and reviews were searched for further relevant studies.
Review methods: RMT studies with healthy individuals assessing changes in endurance exercise performance by maximal tests (constant load, time trial, intermittent incremental, conventional [non-intermittent] incremental) were screened and abstracted by two independent investigators. A multiple linear regression model was used to identify effects of subjects' fitness, type of RMT (inspiratory or combined inspiratory/expiratory muscle strength training, respiratory muscle endurance training), type of exercise test, test duration and type of sport (rowing, running, swimming, cycling) on changes in performance after RMT. In addition, a meta-analysis was performed to determine the effect of RMT on endurance performance in those studies providing the necessary data.
Results: The multiple linear regression analysis including 46 original studies revealed that less fit subjects benefit more from RMT than highly trained athletes (6.0% per $10\,mL \bullet kg^{-1} \bullet min^{-1}$ decrease in maximal oxygen uptake, 95% confidence interval [CI] 1.8, 10.2%; $p = 0.005$) and that improvements do not differ significantly between inspiratory muscle strength and respiratory

muscle endurance training ($p = 0.208$), while combined inspiratory and expiratory muscle strength training seems to be superior in improving performance, although based on only 6 studies (+12.8% compared with inspiratory muscle strength training, 95% CI 3.6, 22.0%; $p = 0.006$). Furthermore, constant load tests (+16%, 95% CI 10.2, 22.9%) and intermittent incremental tests (+18.5%, 95% CI 10.8, 26.3%) detect changes in endurance performance better than conventional incremental tests (both $p < 0.001$) with no difference between time trials and conventional incremental tests ($p = 0.286$). With increasing test duration, improvements in performance are greater (+0.4% per minute test duration, 95% CI 0.1, 0.6%; $p = 0.011$) and the type of sport does not influence the magnitude of improvements (all $p > 0.05$). The meta-analysis, performed on eight controlled trials revealed a significant improvement in performance after RMT, which was detected by constant load tests, time trials and intermittent incremental tests, but not by conventional incremental tests.

Conclusion: RMT improves endurance exercise performance in healthy individuals with greater improvements in less fit individuals and in sports of longer durations. The two most common types of RMT (inspiratory muscle strength and respiratory muscle endurance training) do not differ significantly in their effect, while combined inspiratory/expiratory strength training might be superior. Improvements are similar between different types of sports. Changes in performance can be detected by constant load tests, time trials and intermittent incremental tests only. Thus, all types of RMT can be used to improve exercise performance in healthy subjects but care must be taken regarding the test used to investigate the improvements.

1. Introduction

Respiratory muscle fatigue is known to compromise exercise performance in healthy subjects.[1,2] Evidence is emerging that fatiguing respiratory muscles may affect exercise performance via the so-called metaboreflex,[3] i.e. accumulation of metabolites, such as lactic acid, in the respiratory muscles activates group III and especially group IV nerve afferents[4-6] that then trigger an increase in sympathetic outflow from the brain causing vasoconstriction in the (exercising) limbs.[7-11] This consequently increases limb muscle fatigue during exercise[12,13] and results in earlier exercise termination compared with conditions where respiratory muscle fatigue is prevented.[14,15]

Respiratory muscle training (RMT) has been shown to reduce the development of respiratory muscle fatigue,[16-18] blood lactate concentration during exercise[18-21] and sympathetic activation.[12,22] Therefore, a reduction or delay of the metaboreflex[3] described earlier might be an important mechanism for improving exercise performance by RMT. Interestingly, however, of those studies addressing the effects of specific RMT on exercise performance in healthy subjects, only about two-thirds report significant improvements. Therefore, a detailed analysis of potential factors that may contribute to the success or failure of RMT is urgently needed. A brief overview of these factors is given below.

First, study outcome may be related to study design, considering that only about half of the RMT studies included a sham-training group to account for a possible placebo effect of RMT. Second, subject selection might influence study outcome, since the extent to which respiratory muscles fatigue may differ, for example, with subjects' fitness level. Indeed, several studies showed increased respiratory muscle endurance in physically trained compared with sedentary subjects.[23-25] However, when comparing subjects' physical performance relative to their maximal performance, trained subjects worked at a higher percentage of their maximum and performed more respiratory muscle work,[26] which may theoretically neutralize the effect of increased respiratory muscle endurance on fatigue development. Only two studies[27,28] investigated the difference in development of respiratory muscle fatigue depending on subjects' fitness. These suggested that respiratory muscles indeed fatigue less in endurance trained subjects compared with sedentary subjects during exhaustive physical exercise.[27,28] This indicates that less fit subjects would generally benefit more from RMT than highly trained athletes. Third, it is unclear whether the type of RMT might influence the degree of improvement in exercise performance. Currently, two distinct forms of RMT are used in healthy subjects: respiratory muscle strength training (RMST; also known as inspiratory muscle [strength] training [IM(S)T], inspiratory [flow] resistive loading [I(F)RL], resistive/resistance respiratory muscle training [RRMT], concurrent inspiratory and expiratory muscle training [CRMT], or expiratory muscle training [EMT]) and respiratory muscle endurance training (RMET; also referred to as ventilatory muscle training [VMT], voluntary isocapnic hyperpnoea [VIH] or endurance respiratory muscle training [ERMT]). RMST is performed by breathing against an external inspiratory and/or expiratory load. This load consists either of a flow-dependent resistance or of a pressure threshold that needs to be overcome and sustained to generate flow. RMST includes high-force, low-velocity contractions and was shown to specifically increase respiratory muscle strength, i.e. maximal pressure generation capacity of the inspiratory and/or expiratory muscles against a closed airway.[29] In contrast, RMET is performed using normocapnic hyperpnoea. This training consists of low-force, high-velocity contractions of inspiratory and expiratory muscles, and results in improved respiratory endurance.[29] Whether strength or endurance training of the respiratory muscles is more effective in terms of improving exercise performance, remains unclear. From a physiological point of view, it seems that training both inspiratory and expiratory muscles would be most effective, since with elevated breathing, inspiratory as well as expiratory muscles are increasingly recruited. In fact, it has been shown by objectively assessing changes in transdiaphragmatic and abdominal muscle contractility after exercise that not only inspiratory[30-33] but also expiratory muscles[16,34-36] fatigue during exhaustive high-intensity endurance exercise. Therefore, a closer look at the effects of different training regimens is needed. Fourth, different studies use different types of exercise testing, e.g. incremental tests (IT), constant load tests (CLT) or time trials (TT) of different intensities, to assess the effect of RMT on exercise performance. Whether RMT is more likely to result in positive effects during some types of performance compared with others remains to be verified. Considering the degree to which respiratory muscles fatigue after these different types of tests, it could be argued that the effects of RMT are less likely to be detected in ITs than in the other types of tests. This assumption is based on the results of Romer et al.,[37] who demonstrated that the diaphragm of moderately fit subjects did not fatigue during an incremental cycling test, despite subjects reaching maximal exercise intensity. This is surprising, since Johnson et al.[30] showed that higher exercise intensities (oxygen consumption [$\dot{V}O_2$] at >85% maximal $\dot{V}O_2$ [$\dot{V}O_{2max}$]) increase the likelihood for diaphragmatic fatigue to develop. It seems, therefore, that the duration for which a given intensity is sustained is as important as the intensity itself, with respect to both development of respiratory muscle fatigue and a possible benefit from RMT. Finally, the effect of RMT on performance might differ depending on the exercise modality used, e.g. rowing, running, swimming or cycling, since respiratory muscles are well known to realize more than just respiratory tasks, and these tasks differ between exercise modalities. In rowing, for instance, respiratory muscles need to combine the motion of the thorax expanding and contracting with the – sometimes opposing – rowing stroke movement.[38-40] In running, intra-abdominal pressure is increased, which has been attributed to a protecting function of the spine by the abdominal muscles.[41] Furthermore, the diaphragm has been shown to be activated to increase intra-abdominal pressure during movements of upper limbs, such as when running.[42,43] Thus, when running, respiratory muscles of the trunk also serve postural tasks. During swimming and diving, the work of breathing is increased due to the hydrostatic pressure against which the thorax expands causing an increase in end-expiratory lung volume, which in turn leads to suboptimal length for tension development of respiratory muscles.[44] In addition, respiratory muscles are involved in propulsion. Thus, subjects performing exercise modalities that require additional work from respiratory muscles might be more susceptible to respiratory muscle fatigue.[45] Consequently, subjects performing these exercise modalities might benefit the most from RMT.

The aim of the present work was, therefore, to assess the importance of the above factors on the effect of RMT to improve exercise performance. For this purpose, a systematic review was performed in MEDLINE, EMBASE and CINAHL (up to October 2011), without language restriction, on all studies including an RMT intervention and assessment of endurance performance as an outcome variable, independent of the presence or absence of a sham-training and/or no-training control group. To specifically analyse the evidence of a positive effect of RMT on exercise performance, a meta-analysis including only controlled studies was performed.

2. Methods

A systematic review and meta-analysis were performed on original studies that assessed the effect of RMT (RMST or RMET) on endurance performance in healthy humans by use of at least one of the following exercise tests: a CLT with fixed exercise intensity and subjects performing to exhaustion; a TT with either a fixed distance or a fixed duration and with subjects being required to row, run, swim, cycle, etc. as fast as possible or to cover the largest possible distance; an intermittent incremental test (IIT) with a stepwise increase in exercise intensity including active recovery between steps and subjects performing to exhaustion; or a conventional (non-intermittent) IT with a stepwise increase in exercise intensity and subjects performing to exhaustion, a test that is frequently used to determine $\dot{V}O_{2max}$ and/or the anaerobic threshold.

2.1 Search

A computerized search without language restriction was performed in MEDLINE, EMBASE and CINAHL (up to 31 October 2011). The search strategy included the following keywords: 'respiratory muscle training', 'inspiratory muscle training', 'expiratory muscle training', 'inspiratory training', 'expiratory training', 'hyperpnoea training', 'hyperpnea training', 'respiratory muscle endurance training', 'threshold training', 'resistive training', 'inspiratory loading', 'expiratory loading' and 'resistive loading' combined with 'human', 'healthy' and 'not patient'. Only published studies were included in the analysis.

2.2 Selection

All studies performing RMT in healthy subjects and assessing endurance performance as a main outcome were selected. RMT had to consist of either RMST or RMET. One study[46] combined RMST and RMET and was excluded due to the interaction of combined strength and endurance training in skeletal muscles yielding different specific adaptations compared with training in one modality alone.[47] Studies performing unloaded breathing exercises, breathing therapy, or similar, were not considered. First, all titles of the primary search were screened for potentially relevant articles. Of those, abstracts, reviews, short reports, case reports, editorials and letters were excluded. Original studies were excluded when RMT was not performed, endurance performance was not assessed, physical training was included as an additional intervention and when exercise tests were non-exhaustive. References of the included studies and of the excluded reviews were searched for further relevant studies.

2.3 Quality Assessment

The quality of the selected RMT studies was assessed using the following criteria.[48,49] (i) *Randomization:* random allocation of the subjects to intervention and sham-training or no-training control group. If a trial was called 'randomized controlled' but randomization was not described, it was considered to be a randomized trial (0 points if not reported or not randomized, 1 point if reported, 2 points if randomization procedure specified); (ii) *Blinding:* observer blinding to group allocation of the subjects (0 points if not reported, 1 point if the observer was blinded); (iii) *Allocation of concealment:* person in charge of subject recruitment was (at that time) unaware of potential group allocation (0 points if not reported, 1 point if specified); (iv) *Dropouts:* information about missing data (0 points if not reported, 1 point if reported); (v) *Intention-to-treat analysis:* all subjects initially considered for the study were included and data was assessed (0 points if not performed, 1 point if performed); (vi) *Power calculation:* statistical power of the study (0 points if not reported, 1 point if reported). Thus, a maximum of 7 points corresponding to 100% could be reached.

2.4 Data Abstraction

Two investigators (IF, SKI) independently abstracted the data. Inconsistencies were cross checked, discussed with the third investigator (CMS) and resolved by consensus.

2.5 Quantitative Data Synthesis

The main variable of interest was the change in endurance performance reported or calculated as the relative difference in test duration or – in case of a TT with fixed duration – the relative change in maximal distance covered. Additional variables of interest were (i) fitness level of the subjects (categorized as follows: level 1 if $\dot{V}O_{2max}$ <40 mL • kg^{-1} • min^{-1}, level 2 if $\dot{V}O_{2max}$ 40–49 mL • kg^{-1} • min^{-1}, level 3 if $\dot{V}O_{2max}$ 50–59 mL • kg^{-1} • min^{-1}, level 4 if $\dot{V}O_{2max}$ ≥60 mL • kg^{-1} • min^{-1}; if $\dot{V}O_{2max}$ was not provided,[50-59] fitness level was estimated from [a] endurance performance of subjects and [b] description of daily activities compared with subjects in the other studies using the same exercise modality); (ii) respiratory muscles that were trained, i.e. inspiratory and/or expiratory muscles and type of training, i.e. RMST or RMET (since specific expiratory muscle training was investigated in one single subgroup only,[60] it was excluded from the analysis and three categories were generated for the remaining types of training: RMST.IN [inspiratory muscle strength training], RMST.INEX [combined inspiratory and expiratory muscle strength training] and RMET); (iii) type of test, i.e. CLT, TT, IIT or IT; (iv) test duration before RMT; and (v) exercise modality, i.e. rowing, running, swimming (including diving) or cycling. Further potentially relevant variables, such as training modalities (e.g. number of training sessions, duration of a single training session, training intensity, etc.), intensity of the physical endurance test or subjective ratings of breathlessness and respiratory effort, were not included in the multiple linear regression model in order to prevent collinearity and/or as a consequence of missing information in too many of the studies. Collinearity means that two or more variables are interchangeable, e.g. test duration and test intensity are interchangeable because test duration becomes shorter with a higher test intensity. If both variables were included in the model at the same time, this would mean a high degree of multicollinearity and would give invalid estimates for individual predictors.

Generalized estimating equations (GEE; with exchangeable correlation structure) were fitted to the dependent variable 'change in endurance performance' in order to account for clustered data. Independent variables in the multiple linear regression model were fitness, type of training (RMST.IN, RMST.INEX and RMET), type of test (CLT, TT, IIT and IT), test duration and type of sport (rowing, running, swimming and cycling), including all RMT studies independent of the presence or absence of a sham-training or no-training control group. The multiple linear regression model thus accounts for the influence of the above confounders on changes in exercise performance after RMT. The analyses were performed with R 2.13.1 (statistical computing software).[61] Data from two studies were reported in more than one publication.[17,62-64] In this case, the study that provided more details of the relevant data[63,64] was included in the analysis. Data from two tests were reported in two studies.[65,66] This data appears only once in the present analysis.[66] In three studies,[55,67,68] test duration at baseline was not indicated nor could it be calculated by use of the test protocol. Therefore, these studies were excluded from the regression model.

Furthermore, a meta-analysis was performed on the main outcome of those studies that included a sham-training or no-training control group, and that reported the relative change and standard deviation in exercise performance, such that the overall difference in exercise performance including 95% confidence intervals (CIs) between RMT and sham/no-training control group could be calculated. Additionally, subgroup analysis for the different exercise tests was performed. Heterogeneity of the studies was assessed by calculating the I^2-statistics, which are known to be independent of the number of studies included in the meta-analysis, and thus preferable compared with the Cochrane's chi-squared or Q test.[69] A value of I^2 >50% was considered as evidence for heterogeneity.[70] A random effects model was chosen for all tests, since substantial heterogeneity was expected due to differences between fitness level, type of RMT, type and duration of test and exercise modality. As relative improvements in TTs are generally much smaller compared with those in CLTs, mean relative differences in exercise performance were standardized based on their standard deviations. A potential publication bias was assessed by use of a funnel plot. These analyses were performed with Review Manager (RevMan, Version 5.1, The Nordic Cochrane Centre, The Cochrane Collaboration, 2011, Copenhagen, Denmark). In both the multiple linear regression model and the meta-analysis, a p-value of 0.05 was considered significant.

In those studies that did not report the standard deviations of relative changes in endurance performance, the relative differences between the RMT and sham/no-training control group are presented without 95% CIs. If this difference was not given, it was calculated from the difference in mean absolute values before and after RMT.

3. Results

3.1 Trial Flow and Study Characteristics

7385 citations were identified of which 236 potentially relevant articles remained for further evaluation (figure 1). Finally, 49 studies were selected.[16,20,21,38,39,50-60,63-68,71-97] Of these, 28 (57%) were randomized controlled trials, 6 (12%) were controlled trials, and 15 (31%) were non-controlled trials. Further characteristics of the studies are given in supplemental table I of the online Supplemental Digital Content (SDC) [http://links.adisonline.com/SMZ/A9]. Note that three[55,67,68] of the 49 studies were excluded from the multiple regression analysis due to missing test durations. Of these, the study by Lomax et al.[55] was included in the meta-analysis and the study by Chatham et al.[67] was included in the fourth figure (see section 3.4) only. Methodological quality scored between 14% and 86% (median 29%, i.e. 2 of maximum 7 points; see supplemental table II of the SDC). Study quality did not correlate with the main outcome, i.e. with the relative change in performance.

3.2 Study Design: Presence/Absence and Type of Control Group

Thirteen studies (27%) included a no-training control group while 21 studies (43%) had a sham-training group. Seventy-five percent of the non-controlled studies showed an improvement in exercise performance after RMT. In studies with sham-training or no-training control groups, improvements for the RMT group were seen in 71% and 54%, respectively. In those studies that compared improvements of RMT and no-training control groups, improvements in the RMT group were significantly greater in 75% of studies with no-training control and in 69% of studies with sham-training control.

3.3 Linear Regression Model

Table I depicts the linear regression model. The model revealed that (i) less fit subjects benefit more from RMT than fitter subjects; (ii) effects of RMET

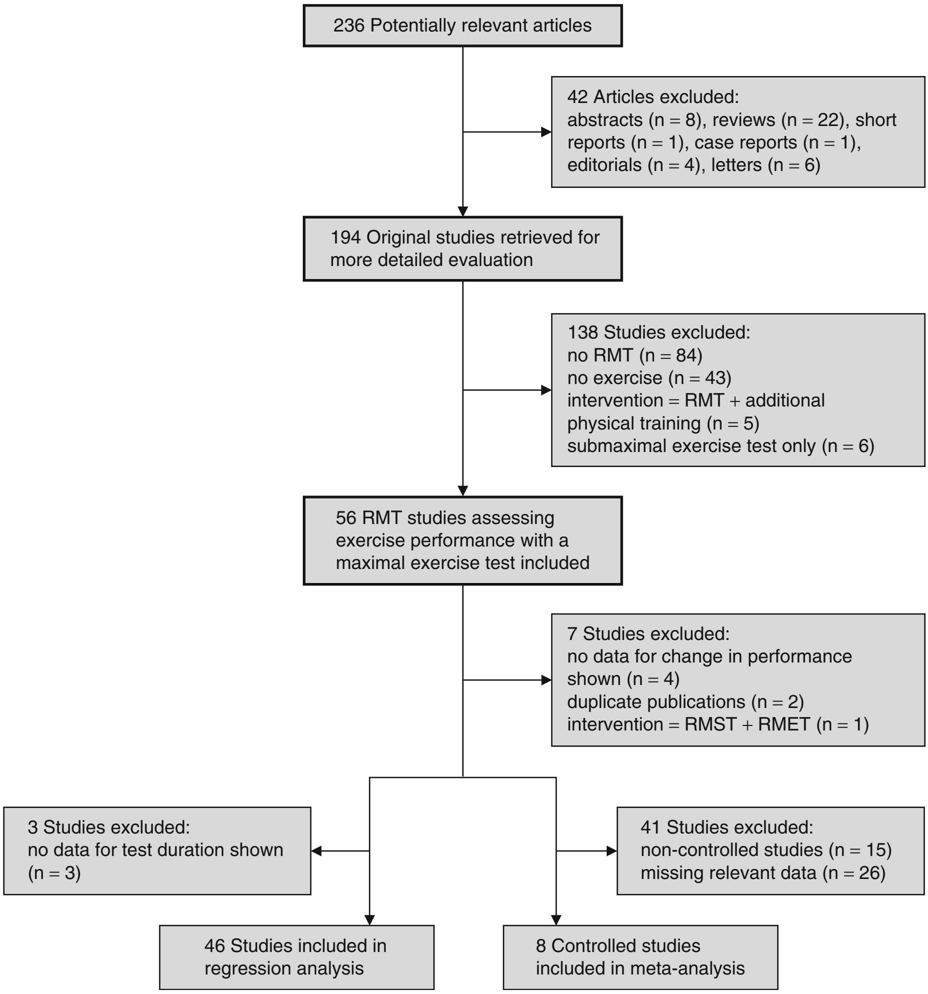

Fig. 1. Flow diagram of the studies excluded from and included in the linear regression model and/or the meta-analysis. **RMET** = respiratory muscle endurance training; **RMST** = respiratory muscle strength training; **RMT** = respiratory muscle training.

and RMST.IN are similar, while RMST.INEX seems to be superior to RMST.IN and RMET; (iii) improvements in performance are greater in CLTs and IITs than in ITs, with no significant difference between TTs and ITs; (iv) greater improvements are seen with increasing test duration; and (v) improvements are independent of exercise modality.

3.4 Meta-Analysis

RMT results in a significant increase in exercise performance (figure 2, standardized mean difference [SMD] 1.11, 95% CI 0.61, 1.61; $p<0.001$), although with moderate heterogeneity ($I^2=71\%$). Subgroup analysis of different tests revealed significant improvements in exercise performance when assessed by a CLT (SMD 0.66, 95% CI 0.20, 1.12; $p=0.005$), a TT (SMD 1.85, 95% CI 0.88, 2.82; $p<0.001$) or by an IIT (SMD 2.96, 95% CI 1.12, 4.80; $p=0.002$), whereas no significant improvement in exercise performance was detected when assessed by an IT (SMD 0.30, 95% CI –0.20, 0.79; $p=0.30$). Furthermore, a significant difference between groups was found ($p=0.003$) favouring TT

Table I. Multiple linear regression model

	Estimate	SE	95% CI	p-Value
Intercept	17.8	8.8	0.6, 35.1	0.043
Fitness	–6.0	2.1	–10.2, –1.8	0.005
RMST.INEX vs RMST.IN[a]	12.8	4.7	3.6, 22.0	0.006
RMET vs RMST.IN[a]	–4.7	3.7	–12.0, 2.6	0.208
CLT vs IT	16.5	3.2	10.2, 22.8	0.000
TT vs IT	–3.7	3.4	–10.4, 3.1	0.286
IIT vs IT	18.5	3.9	10.8, 26.3	0.000
Test duration	0.4	0.1	0.1, 0.6	0.011
Rowing vs cycling	1.9	4.9	–7.7, 11.4	0.701
Running vs cycling	–4.6	5.3	–14.9, 5.8	0.390
Swimming vs cycling	5.2	5.5	–5.6, 16.1	0.347

a When RMET was chosen as the reference group, the estimate for the comparison between RMST.INEX and RMET (17.5, SE 4.8, 95% CI 8.2, 26.9) was also significant (p = 0.000).

CI = confidence interval; **CLT** = constant load test; **IIT** = intermittent incremental test; **IT** = conventional (non-intermittent) incremental test; **RMET** = respiratory muscle endurance training; **RMST.IN** = inspiratory muscle strength training; **RMST.INEX** = inspiratory and expiratory muscle strength training; **SE** = standard error; **TT** = time trial.

and IIT over CLT and IT (individual p-values not shown), although with substantial heterogeneity ($I^2 = 78.3\%$). Subgroup analysis showed evidence for low heterogeneity in CLT and IT ($I^2 = 0\%$ and 18%, respectively) but high heterogeneity in TT ($I^2 = 77\%$). Heterogeneity for IIT could not be calculated as only one study was included in the meta-analysis. Figure 3 shows a funnel plot of those studies that were included in the meta-analysis.

Figure 4 shows the overall mean difference of the relative change in exercise performance for all controlled studies. The overall improvement for the RMT group over the sham-training or no-training control group was 11%, while subgroup differences were 21% for CLT, 2% for TT, 13% for IIT and 7% for IT (2% without the studies by Enright et al.[50,51]). These results are in agreement with those of the controlled studies included in the meta-analysis, i.e. RMT effects are seen in CLTs, IITs and TTs.

4. Discussion

The key finding of this analysis is that RMT improves performance in healthy subjects, independent of the type of RMT and exercise modality. Less fit individuals seem to benefit more from RMT than highly trained athletes, and improvements are greater with longer exercise durations. Improvements are significant when the effect of RMT is tested in CLTs, TTs and IITs, while none are seen in ITs, commonly used to assess $\dot{V}O_{2max}$ or anaerobic threshold.

4.1 Study Design: Presence/Absence and Type of Control Group

It could be assumed that study outcome may be related to study design, since only 43% of RMT studies included a sham-training group to account for a possible placebo effect of RMT. However, a closer look reveals that the presence and type of control group do not influence outcome. When considering differences between RMT and control groups, 75% of studies including a no-training control group and 69% of placebo-controlled studies showed a positive outcome for RMT (i.e. performance improvements for the RMT groups significantly exceeded those for the control groups), similar to the 75% positive outcome in studies without any controls. Thus, the presence or absence and type of control group did not affect the outcome regarding performance improvements for RMT studies in healthy subjects.

Likely reasons for the lack of improvement in exercise performance after RMT in some studies include the use of only an IT to evaluate the effects of RMT on endurance performance,[73,82,86,94] low power of the studies,[78,89] lack of recovery time for respiratory muscles prior to the endurance exercise test,[38,46,76,78,96,97] very high-intensity exercise,[20,38,58,78,89] a highly trained group of subjects[58,78,96,97] or an increased respiratory drive with concomitantly increased work of breathing in some subjects after RMET.[16,96]

4.2 Effect of Subjects' Fitness on Improvements in Exercise Performance

The multiple linear regression analysis showed that less fit subjects benefit more from RMT than highly trained athletes. This finding is in accordance with the initial hypothesis suggesting that untrained subjects might benefit more from

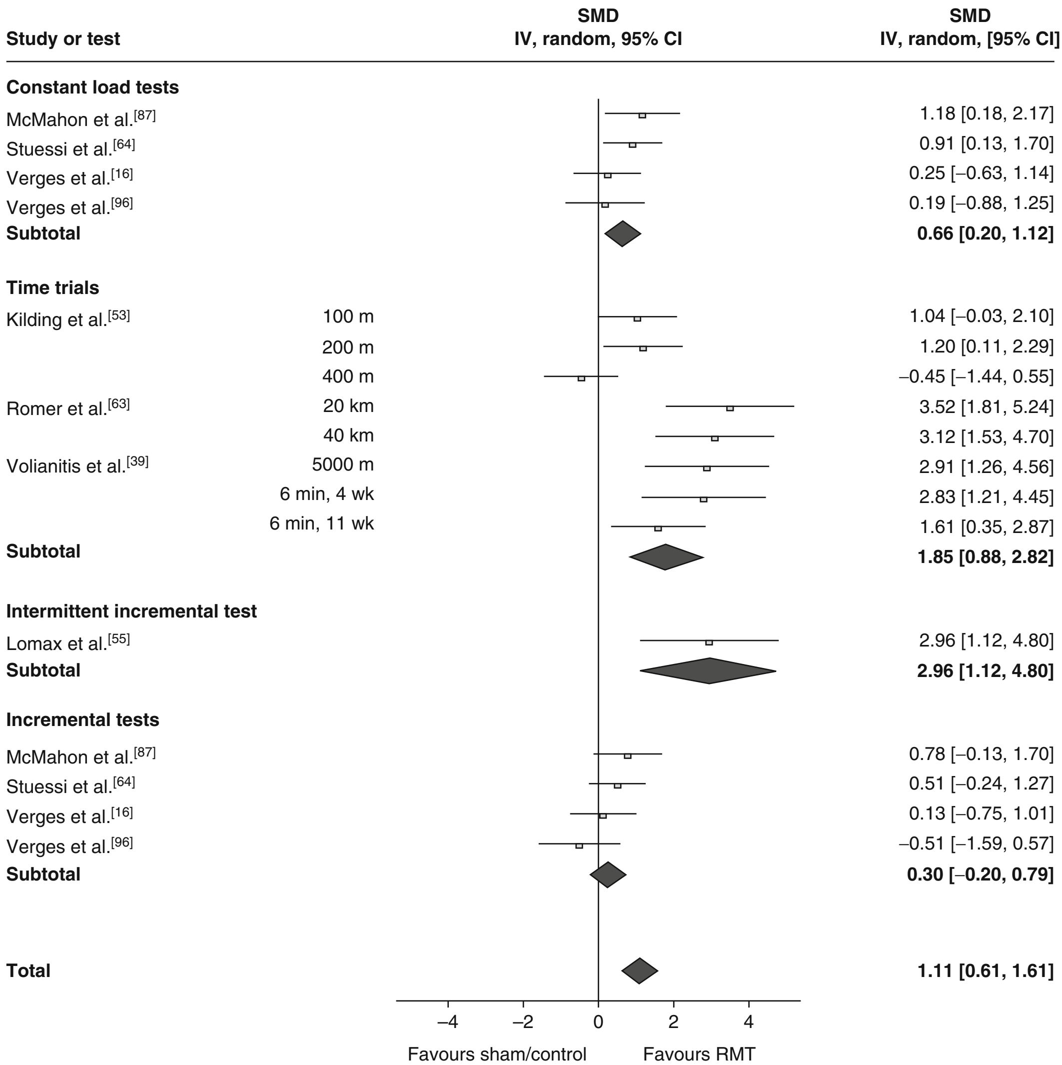

Fig. 2. Effect of respiratory muscle training on exercise performance in constant load tests, time trials, intermittent incremental test, and conventional (non-intermittent) incremental tests. Only those studies providing the necessary information are included in this forest plot. **CI** = confidence interval; **IV** = inverse variance; **random** = random effects model; **RMT** = respiratory muscle training; **sham/control** = sham-training/no-training control; **SMD** = standardized mean difference.

RMT, since respiratory muscles of less fit subjects were shown to fatigue more during exhaustive endurance performance.[27,28] However, although less fit subjects have a higher potential to increase their physical endurance performance compared with highly trained athletes,[98-101] respiratory muscle performance seems to improve to a similar extent with all levels of fitness. Also, when analysing improvements in maximal inspiratory mouth pressure (MIP), maximal expiratory mouth pressure (MEP) or respiratory muscle endurance separately for the different types of training, no effect of fitness could be observed (data not shown).

On the other hand, it might be argued that greater improvements in performance are associated with older age rather than lower fitness,

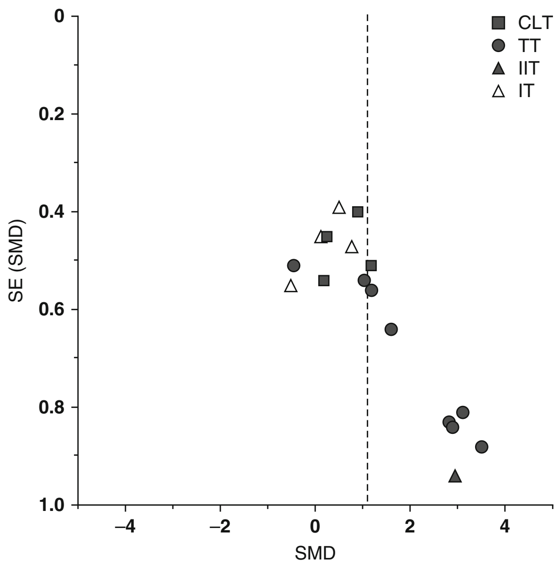

Fig. 3. Funnel plot of the studies included in the meta-analysis. **CLT** = constant load test; **IIT** = intermittent incremental test; **IT** = conventional (non-intermittent) incremental test; **SE** = standard error; **SMD** = standardized mean difference; **TT** = time trial.

since $\dot{V}O_{2max}$ is known to decrease with age.[102] However, separate analyses showed that the relative improvement in exercise performance was negatively correlated with the level of fitness ($r = –0.440$; $p < 0.001$), while it was not correlated with age ($r = –0.018$; $p = 0.882$). Thus, it seems that the level of fitness is more important than age in affecting the amount of improvement in performance after RMT.

4.3 Influence of the Type of RMT on Improvements in Exercise Performance

The multiple regression analysis revealed that RMST.IN and RMET did not differ in their effect on improving exercise performance. This result seems astonishing, since the degree of fatigue developing during exhaustive exercise was shown to be similar in inspiratory and expiratory muscles[16,30-36] and both of these muscle groups[7,10] were shown to elicit the metaboreflex that is known to impair exercise performance.[14] Thus, one would assume that training both muscle groups, as with RMET, would yield a greater effect than training inspiratory muscles alone, such as during RMST.IN.

Thus, the question arises: why would increased inspiratory muscle strength be advantageous for exercise hyperpnoea? Despite exercise hyperpnoea being characterized by high flows, it is known that inspiratory rib-cage muscles produce the pressures needed to expand the rib cage and thereby let the diaphragm act as the main flow generator.[103] Consequently, rib-cage muscles fatigue during high-flow tasks,[104] although to a lesser extent than with high resistances.[105] Thus, it seems likely that RMST.IN provides a larger training stimulus to inspiratory muscles than RMET and that more effectively trained inspiratory muscles, as with RMST.IN, may be superior in preventing or delaying the development of inspiratory rib-cage muscle fatigue, compared with RMET. This *per se* would translate into a greater improvement in exercise performance with RMST.IN than with RMET of inspiratory muscles only. It has, however, been shown that RMET also trains expiratory rib-cage and abdominal muscles, in addition to the inspiratory muscles, which is substantiated in a smaller degree of expiratory muscle fatigue during exercise after this type of training.[16] Therefore, an explanation for the similar improvements in performance with RMST.IN and RMET might be that, on the one hand, inspiratory muscles were trained more effectively with RMST.IN than with RMET, and on the other hand, the combination of 'less effective' inspiratory muscle training with expiratory muscle training during RMET results in the same net effect with respect to improvements in exercise performance.

The need for training the expiratory in addition to the inspiratory muscles on the one hand and the potential superiority of respiratory muscle strength over endurance training to improve exercise performance, on the other hand, would also be supported by the model showing that the combination of both inspiratory as well as expiratory muscle strength training, i.e. RMST.INEX, improved exercise performance more than RMST.IN or RMET. It should, however, be pointed out that so far only three research groups (six studies) used RMST.INEX and – although

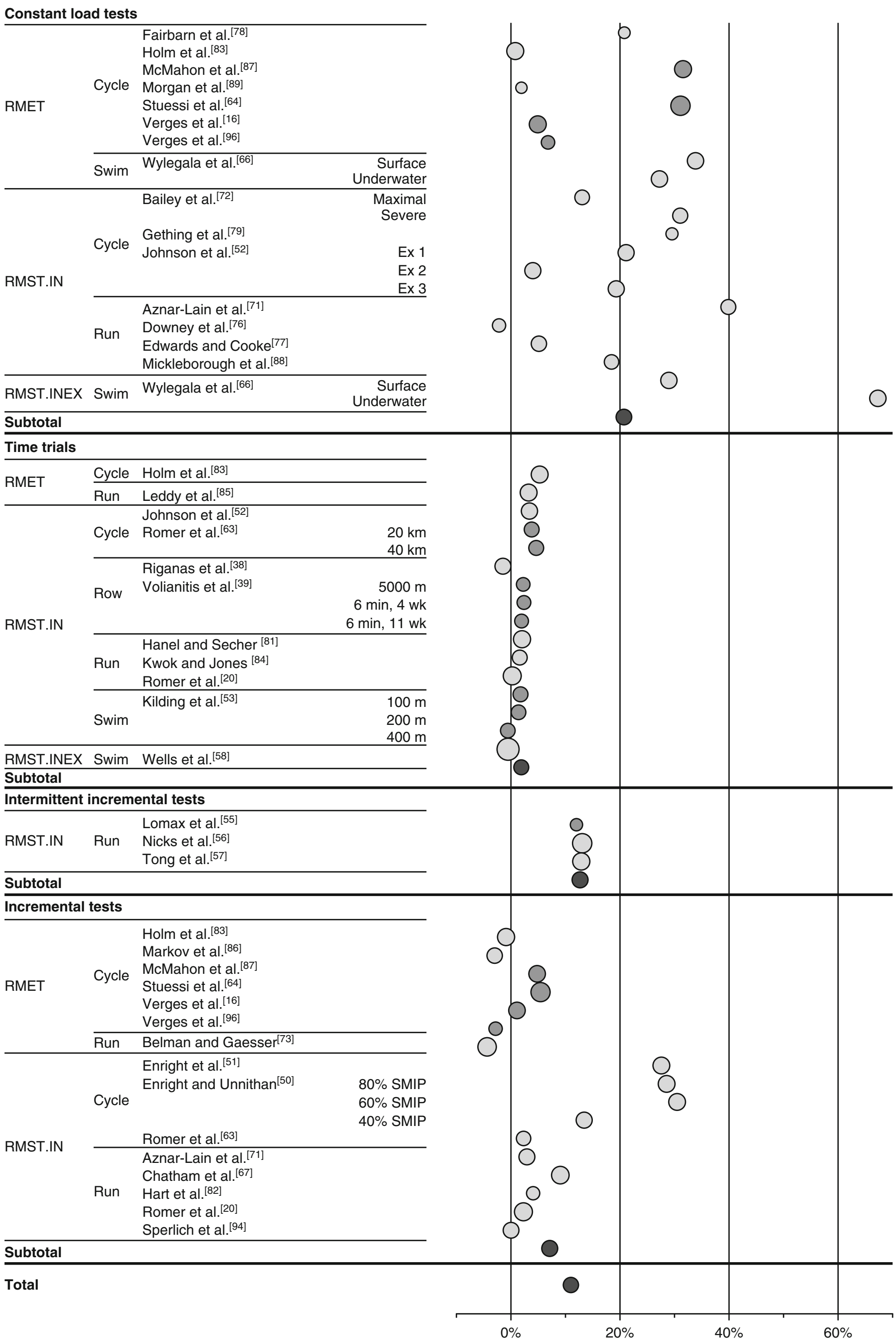

Fig. 4. Mean difference in the effect of respiratory muscle training on exercise performance between intervention and sham-training/no-training control groups. Dark grey circles: average mean difference of each type of exercise test. Medium grey circles: tests also included in the forest plot of figure 2. Light grey circles: tests not included in the meta-analysis because data to calculate the confidence interval was not provided. The size of the circles represents the number of subjects included in the study. **RMET** = respiratory muscle endurance training; **RMST.IN** = inspiratory muscle strength training; **RMST.INEX** = inspiratory and expiratory muscle strength training; **SMIP** = sustained maximal inspiratory pressure (i.e. maximal pressure generation capacity from residual volume to total lung capacity).

the model accounted for differences in fitness, type of testing and sports – one might need to consider that subjects in these studies were slightly less fit than those performing RMST.IN and RMET, and evidence for physical improvements came from one single research group (four studies) testing with CLTs only (known to yield greater improvements). Final proof of a potential difference between RMST.INEX versus RMST.IN and RMET can therefore only be provided when all three types of training are tested in the same study having similar groups of subjects and similar performance tests. For example, a direct comparison of RMST.IN and RMET in one single study showed that the effects of RMET were larger than those of RMST.IN, with respect to the reduction in blood lactate concentration and perception of respiratory sensations.[18] Thus, it also remains to be tested whether alternating RMST and RMET yield even greater improvements in performance than one type of RMT alone.

4.4 Effect of the Type of Exercise Test and Test Duration on the Improvement in Exercise Performance

The multiple regression analysis showed that improvements in exercise performance after RMT were significantly greater when tested with CLTs or IITs compared with ITs, with no difference between TTs and ITs. The meta-analysis of controlled studies revealed no significant effect of RMT when tested with ITs, while improvements in CLTs, TTs and in the IIT were all significant. The fact that RMT does not seem to affect IT performance is consistent with the notion that the duration a subject spends exercising above the threshold of 85% $\dot{V}O_{2max}$, the exercise intensity where respiratory muscles are most likely to fatigue,[30] is too short to elicit respiratory muscle fatigue.[37] This is also supported by the finding that improvements in performance after RMT are greater with longer test duration (+0.4% per minute test duration, table I). Furthermore, of 22 studies assessing $\dot{V}O_{2max}$ before and after RMT, all but two studies found no change in $\dot{V}O_{2max}$. Leddy et al.[85] observed a significant increase, while Verges et al.[96] observed a significant decrease in $\dot{V}O_{2max}$.

Interestingly, half of those tests that reported exercise intensity (n = 40) were performed below the threshold of 85% $\dot{V}O_{2max}$, maximal workload (W_{max}) or maximal velocity (v_{max}) – the average of the forty tests being 80% $\dot{V}O_{2max}$, 81% W_{max} or 98% v_{max}. All but two of the 20 tests that were performed below 85% showed an improvement in exercise performance after RMT. In contrast, only nine of the 20 tests that were performed above 85% showed increased performance. However, subjects performing above 85% $\dot{V}O_{2max}$, W_{max} or v_{max} were fitter than those performing below this threshold (fitness level of 3.1 and 2.1, respectively), which could partly explain this finding and illustrates the importance of using a model that accounts for confounders. Nevertheless, if respiratory muscles do not fatigue below the suggested threshold of 85% $\dot{V}O_{2max}$, this would mean that a reduction in respiratory muscle fatigue could not be the only mechanism to increase endurance performance after RMT.

It is known, for example, that in CLTs, psychological factors such as motivation or boredom may play an important role in determining the point of exhaustion.[106] Accordingly, after an extended period of RMT, motivation to withstand task failure in a CLT might be higher. However, in studies using CLTs at intensities below the threshold and including a sham-training group, improvements in the RMT groups exceeded those of the sham-training groups[66,71,79,85,88] with only one exception.[83] Thus, again, motivation cannot be the only reason for improvements in CLT performance after RMT. Another possible explanation for improved endurance performance after RMT is a reduced perception of respiratory exertion and/or breathlessness. Of the 15 studies testing with a CLT below the 85% threshold, only three specified changes in respiratory sensations, two[79,88] of them reported a significant decrease while one[83] did not.

While the regression model, which accounted for confounders such as test duration, subjects' fitness, type of training and type of sports did not find TTs to be more sensitive than ITs in showing improvements after RMT, the meta-analysis showed greater standardized mean differences in TTs and in the IIT compared with CLTs and ITs meaning that TTs would detect changes better than CLTs and ITs. This seems confusing at first; however, it should be considered that the model is based on all RMT studies, while the meta-analysis is based only on those studies that provided the necessary data. A comparison of average changes of the studies included in the regression model and in the meta-analysis shows that the average change in test duration in studies included in the regression model was significantly larger (+15%) than that of the studies included in the meta-analysis (+5%; $p = 0.002$). However, the average fitness of subjects included in the regression model tended to be lower (2.6) than fitness of subjects included in the meta-analysis (3.1; $p = 0.065$), which might possibly explain the greater average improvement in performance of subjects included in the regression model. Thus, it seems that the studies included in the meta-analysis – despite a similar number of positive outcomes – are not fully representative of all of the RMT studies included in the regression model. Also, the studies by Enright et al.[50,51] might contribute to the discrepancy between model and meta-analysis. These authors used a protocol resulting in much shorter test durations (4.4–4.5 minutes) than the suggested 8–12 minutes required for $\dot{V}O_{2max}$ determination.[107] Improvements after RMT[50,51] were even greater (approximately 25%) than those reported for physical endurance training (approximately 10%[108]), which raises questions regarding the validity of this protocol. Without the two studies by Enright et al.,[50,51] the overall difference between improvements in IT performance after the RMT and sham/no-training period is 2% – equal to that for TTs. Thus, the relatively small improvements generally seen in TTs, although consistent, might be too small to exceed the changes found in ITs. However, it must be noted that these small improvements in TT performance are highly relevant. For example, mean improvements in the 40 TTs would result in 40 m or five skiff lengths in a 2 km rowing regatta, 100 m in a 2 km running race, 1.2 m in a 200 m swimming competition and 1 km in a 30 km cycling race.

The fact that improvements in exercise performance after RMT were significantly greater (19%) also in IITs compared with ITs, suggests that amateur and professional athletes performing intermittent sports, such as football, soccer, basketball, team handball, etc. might benefit from RMT similar to subjects performing endurance-type sports. This is further supported by one study that showed a reduction in recovery duration between sprints, which was in part attributed to a decreased perception of respiratory effort.[20]

4.5 Effects of RMT in Different Types of Sports

Although physiological evidence would suggest that RMT might be more effective in sports where respiratory muscles are subjected to increased respiratory work[44] (swimming) and/or increased non-respiratory work, i.e. postural[41-43] (running) or moving[38-40] (rowing) tasks, the model did not reveal any significant difference between improvements in the different types of sports. Thus, one could assume that respiratory muscles involved in additional tasks resulting in higher respiratory muscle work are sufficiently trained, such that the likelihood to fatigue is similar to that during, for example, cycling. Supporting this assumption is the following interesting observation: for the studies included in the present review that give respiratory muscle strength data and include subjects with a fitness level of 3 or 4, baseline values of MIP and especially MEP expressed as a percentage of predicted values[109] are lowest in cycling and increase with rowing, running and swimming (data not shown).

4.6 Limitations

Several variables of interest were not included in the analysis. For example, duration of the training period or training intensity might also influence changes in endurance performance although these variables were quite similar within RMST and within RMET studies. Therefore, only the type of training was included in the multiple linear regression model, while factors describing training regimens were omitted to prevent collinearity. Furthermore, exercise intensity is believed to play a crucial role with respect to the development of respiratory muscle fatigue and, therefore, with respect to a possible benefit from RMT. Intensity of the exercise tests was not, however, included in the model. Since too many studies did not provide detailed information on exercise intensity (n = 24), the inclusion of this variable would have led to the exclusion of too many studies from the regression model. Furthermore, since only exhaustive tests were included in the model, test duration and intensity would have led to collinearity, with the consequence of excluding one or the other variable from the model. The same holds true for ratings of perceived breathlessness or respiratory effort, which have been shown to be lower after RMT in some studies[16,20,39,53,55,59,60,63,67,72,73,76,79,88,96,110] but not in others.[38,56,58,60,83,97,111] As only 21 studies provided this information, the inclusion of these variables in the linear regression model would have led to the exclusion of too many studies. Therefore, the variables ‘intensity’ and ‘respiratory sensations’ were omitted, despite their potential to explain possible changes after RMT. These variables might, however, be included in the intercept. The significance of the intercept indicates that additional factors not included in the model play a role in determining improvements in exercise performance.

A further consideration is that the funnel plot shows a potential publication bias. In general, without publication bias, studies would be evenly distributed around the mean, in the form of a triangle. Studies with small standard errors (often those with many subjects included) are found at the top of the triangle close to the mean. Studies with large standard errors (frequently smaller studies) are found at the bottom of the triangle, with some of them having a greater distance to the mean. In the present meta-analysis, studies at the bottom left of the triangle are missing. This could mean that smaller studies with negative outcome were not published in addition to the possibility that no such studies were ever conducted. If those small studies with a negative outcome were present in the funnel plot, this would mean that the effect of RMT would be smaller than shown in the present analysis.

5. Conclusions

This is the first study to systematically assess the effect of different types of RMT used to improve exercise performance in healthy subjects. It clearly shows that RMT significantly improves endurance performance, independent of the type of RMT or the type of sport. No difference was found between the effects of the two most commonly used respiratory muscle training modalities, RMST.IN and RMET, while RMST.INEX seemed to be superior. Less fit individuals benefit more from RMT than highly trained athletes, and improvements are greater with longer exercise durations even at intensities lower than the postulated threshold for development of respiratory muscle fatigue (85% $\dot{V}O_{2max}$). This emphasizes the importance to report changes in respiratory sensations after RMT so that this variable can be included in future regression models as well. Furthermore, when assessing the effect of RMT, care must be taken regarding the choice of the test, since effects are not seen in ITs that are commonly used to assess $\dot{V}O_{2max}$ or anaerobic threshold. Also, more well controlled studies are needed to prove a superiority of RMST.INEX over the commonly used types of RMT to confirm the positive results observed in the few studies using IITs, and to investigate a possible additional benefit from alternating RMET and RMST.

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