Sports Medicine (2021) 51:1335–1351
https://doi.org/10.1007/s40279-021-01455-4

CURRENT OPINION

Strengthening the Case for Cluster Set Resistance Training in Aged and Clinical Settings: Emerging Evidence, Proposed Benefits and Suggestions

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Accepted: 16 March 2021 / Published online: 13 May 2021
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Abstract

Resistance training (RT) is a fundamental component of exercise prescription aimed at improving overall health and function. RT techniques such as cluster set (CS) configurations, characterized by additional short intra-set or inter-repetition rest intervals, have been shown to maintain acute muscular force, velocity, and 'power' outputs across a RT session, and facilitate positive longer-term neuromuscular adaptations. However, to date CS have mainly been explored from a human performance perspective despite potential for application in health and clinical exercise settings. Therefore, this current opinion piece aims to highlight emerging evidence and provide a rationale for why CS may be an advantageous RT technique for older adults, and across several neurological, neuromuscular, cardiovascular and pulmonary settings. Specifically, CS may minimize acute fatigue and adverse physiologic responses, improve patient tolerance of RT and promote functional adaptations (i.e., force, velocity, and power). Moreover, we propose that CS may be a particularly useful exercise rehabilitation technique where injury or illness, persistent fatigue, weakness and dysfunction exist. We further suggest that CS offer an alternative RT strategy that can be easily implemented alongside existing exercise/rehabilitation programs requiring no extra cost, minimal upskilling and/or time commitment for the patient and professional. In light of the emerging evidence and likely efficacy in clinical exercise practice, future research should move toward further direct investigation of CS-based RT in a variety of adverse health conditions and across the lifespan given the already demonstrated benefits in healthy populations.

Key Points

Cluster set (CS) resistance training (RT) paradigms are commonly used in human performance settings, but emerging evidence shows potential for application in older adult populations and a number of clinical exercise domains.

CS may minimize fatigue, reduce perceptions of effort and thus, may improve resistance exercise tolerance and adherence compared to traditional set (TS) training.

CS may be an efficacious RT strategy that appears to demonstrate similar effectiveness compared to TS to facilitate chronic muscular and neuromuscular adaptations including hypertrophy, strength, and power requiring little, or no extra time or equipment.

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1 Introduction

1.1 Background

The loss of muscle mass, strength, and ‘power’ (i.e., impulsivity)[1] is a critical area of concern in older adults and disease. Specifically, a loss of muscular strength and power in older adults contributes to reduced physical function, an inability to perform activities of daily living, and greater risk of falls and fractures [1, 2]. In neurological injury or neuromuscular disease, muscle fatigue and weakness can severely impact overall physical function. Such factors can result in reduced quality of life and increased incidence of secondary adverse health outcomes [2, 3]. Exercise capacity and tolerance are also compromised in cardiovascular and pulmonary conditions where factors such as dyspnea, fatigue, and pain are highly prevalent [4]. Collectively, many of these symptoms are associated with psychological distress and activity avoidance, which further exacerbates the loss of muscular strength and power [5–7]. Indeed, reduced strength has been linked to increased mortality risk [8]. Thus, strategies to prevent, or reverse the loss of muscle size, strength and power, and maintain physical activity are of critical importance across an array of demographics.

Resistance training (RT) is an integral component of targeted exercise programs that aim to improve muscle structure and function (e.g., strength, power, endurance, and hypertrophy) across multidisciplinary settings. Generally, clinical RT prescription has been based largely on ‘traditional set’ (TS) approaches (e.g., high-load low-volume and/or high-volume low-to-moderate-load continuous repetitions) (for examples see [9, 10]). However, it is unclear whether TS RT paradigms are ‘optimal’ in clinical settings. Firstly, TS requiring continuous application of effort across a set performed to, or close to momentary task failure, with moderate-to-heavy loads can cause greater motor unit recruitment and both higher metabolic and mechanical stress, but also results in large amounts of immediate and prolonged neuromuscular fatigue [12–15]. Secondly, greater perceptions of effort (see [16] for further discussion) and more negative affective responses have been shown to adversely impact future physical activity adherence and progress [17–19]. Thirdly, it is unclear if TS are the most efficacious method to stimulate functional, morphological, and neuromuscular adaptations. Considering that many of these points also apply to healthy populations, there has been emerging interest regarding RT programs that utilize alternative set and repetition configurations to facilitate positive and optimal adaptations whilst minimizing adverse exercise effects.

1.2 Cluster Set Rationale

Cluster sets (CS) have been popularized in human performance settings, with growing evidence demonstrating their efficacy to minimize fatigue-related reductions in force, movement velocity and power during a RT bout [20–23]. Similar effects are commonly reported across a majority of CS sub-structures, between exercises and across levels of training experience [24]. This is in contrast to TS paradigms that, as mentioned, can cause comparatively greater fatigue, and prolong the recovery period when performed at, or close to momentary failure [12–15]; though when not performed to failure neuromuscular fatigue is less pronounced [12, 15]. Additionally, some evidence also demonstrates less pronounced autonomic responses (e.g., cardiovascular) with CS [25]. CS may also allow for a greater overall training volume (load and/or repetitions) to be achieved given fatigue is minimized [26, 27], and/or improve exercise tolerance via reduced effort perception [28], though evidence is equivocal[2] [28–31] (see [32] for further discussion of effort). Furthermore, it is unclear whether a given magnitude of fatigue, or metabolite accumulation is required for muscle and neuromuscular adaptations [33–35]. Indeed this is evidenced by similar hypertrophic adaptations to higher- and lower-load RT when performed to failure [36], despite greater fatigue known to occur with lower loads [37–39]. Thus, efforts to maximise the RT stimulus but minimize fatigue appear warranted. Growing evidence also demonstrates that CS may result in equivalent [40] or better [41] muscular and/or neuromuscular adaptations over several weeks or months of training (for review see [42]). Importantly, these adaptations appear to occur with less ‘physiological’ stress compared to TS.

1.3 Cluster Set Structures

In TS paradigms, repetitions are performed continuously [43, 44] with rest intervals occurring at the completion of each set. Alternatively, CS implement short intra-set rest [27, 45, 46] between small groups of (e.g., 15–45 s), or between single repetitions (e.g., 6–20 s) (i.e., inter-repetition rest) and both have been applied and discussed in a number of articles

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[1] The term ‘power’ is commonly referred to in sport, exercise, and physical activity settings. Despite this, there are some suggestions that this term is often used incorrectly and rather ‘impulse’ would be more appropriate in such contexts (refer to Winter et al. [11] for in depth discussion). However, given its wide colloquial use to refer to such applications, we continue to use the term ‘power’ here for ease of communication given the primary intention of this article is not to debate terminology.

[2] Possibly due to the typical lack of standardization in the application self report perceptual scales such as for perception of effort or affect within our field (see [32]).

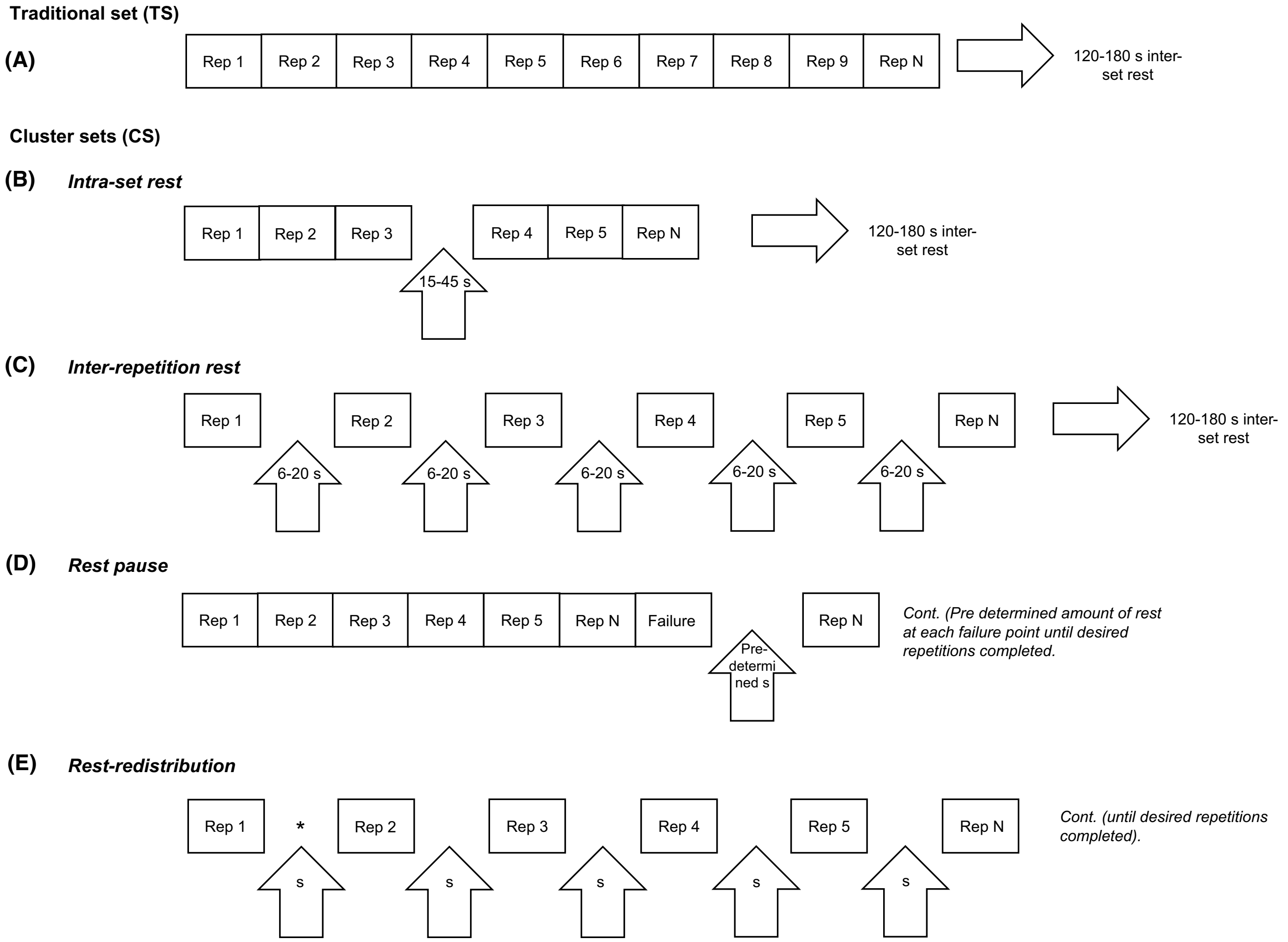

Fig. 1 Example set configurations adapted from Latella et al. [25] comparing a traditional set (TS) structure (**a**) and commonly used cluster set (CS) structures: intra-set rest (**b**), inter-repetition rest (**c**), rest-pause (**d**) and rest-redistribution (**e**) methods. *s = Inter-repetition rest is calculated by dividing the total rest usually allowed across all sets in a TS paradigm. E.g. 3 × 10 with 120 s rest between sets = 360 s) and dividing this by 30 (e.g., 12 s). One set of 30 repetitions with 12 s inter-repetition rest is then used. Rep N = Repetitions would continue until prescribed number is completed

[e.g., 21, 30, 45, 47–50]. There is also the rest re-distribution method, whereby the total rest time of a TS configuration is calculated and interspersed evenly between repetitions. Alternatively, the rest-pause method entails a continuous set performed until momentary failure (although not always the case [50]), followed by additional sets to failure with short rest periods until the desired repetitions are completed [21, 24, 49] (see Fig. 1).

2 Purpose

This article seeks to highlight emerging evidence, and discuss the rationale and potential application of CS RT in older adults and several other clinical exercise settings. We present evidence from the current body of research in healthy individuals, as well as data in several aged and clinical cohorts. We also briefly describe common symptoms in selected conditions (e.g., aging, neurological injury and neuromuscular disease, cardiovascular and pulmonary disorders) which may be more severely exacerbated when performing TS paradigms. Subsequently, an overview of how CS may benefit such populations is outlined alongside suggestions for their implementation. It is intended that the information presented also helps to provide a framework for future research and facilitate the further development of optimal preventative and rehabilitative RT approaches.

3 Aged Populations

3.1 Brief Overview of Age-Related Neuromuscular Decline

Aging is accompanied by numerous physical changes including declines in functional mobility, muscle mass, strength, and power [1, 2]. Reductions in muscle mass and strength begin in the third decade and decline at a rate of ~ 1 to 3% per year [51], with further suggestion that power is lost at twice the rate of strength [51–55]. Muscular strength and power, particularly in the lower extremity, is a critical variable to understand the relationships between functional decline, falls and disability among older adults. Indeed, power has been identified as an independent predictor of physical function, with low muscular power associated with a 2–3-fold greater risk of impaired mobility compared to low muscular strength [55, 56]. The physiological mechanisms underlying the decline in power extend beyond age-related muscle atrophy [1, 52]. Demyelination of motor neurons and subsequent reductions in axonal conduction velocity, selective denervation and atrophy of type-II fibers, alterations in muscle composition and function, and disuse are all thought to contribute [2, 52].

3.2 Brief Overview of Resistance Training Evidence in Aged Populations

RT is a well-established method to combat declines in muscle strength and power in older adults [57, 58]. Current guidelines suggest that RT prescription should include additional high-speed exercises, further highlighting the importance of targeting muscular power [53, 59]. Specifically, high-speed resistance training (HSRT) refers to executing the concentric phase of each repetition as fast as possible, while controlling the eccentric phase. Randomized-controlled trials have demonstrated the efficacy of HSRT (e.g., 3 sets, 6–14 repetitions, 40–80% one-repetition maximum [1RM], 2–3 s eccentric phase, concentric phase as fast as possible) for improving power compared to TS (e.g. 3 sets, 6–10 repetitions, 50–80% 1RM, with 2–3 s concentric and eccentric phases) [60–64] and non-training controls [60–63, 65]. Although the magnitude of the estimated differences between HSRT and non-HSRT are seldom reported, a previous investigation demonstrated that a 9–10% increase in leg extensor power was associated with clinically meaningful endpoints in older adults with impaired mobility [66]. Moreover, HSRT at high (70–80% 1RM), moderate (50% 1RM) and low (< 40% 1RM) loads [67–69] have all been shown to improve power and further evidence suggests that there is no clear relationship between load and the magnitude of improvement [58]. Collectively, the results of trials and meta-analyses indicate that HSRT may yield superior benefits in muscular power than traditional non-HSRT programs and can be performed using a variety of loads [57, 58, 67–70].

3.3 Cluster Set Evidence and Proposed Rationale in Aged Populations

CS may be an efficacious form of HSRT to stimulate muscular, neuromuscular and functional adaptations in older adults, as movement velocity and power are maintained across sets performed in this manner. In eldery men, CS consisting of single- or double-repetitions results in greater power output, lower perceived effort, and fatigue, compared to TS of six repetitions or CS with greater repetitions in each cluster (i.e., 4) using loads optimized for power in the back squat exercise [71]. However, we acknowledge that the squat may not be the most optimal exercise to either express or develop power, given that deceleration is required during the latter phases of the movement when light-moderate loads are used, and movement velocity is intended to be maximal. Despite this, Miller et al. [72] suggests that a supervised inter-repetition paradigm is both feasible and enjoyable for older adults. However, to our knowledge, longer CS training interventions in older adults is limited to three studies [73–75]. Ramirez-Campillo et al. [73] compared the effects of 12 weeks of HSRT using CS or TS configurations versus non-training controls in 52 older women. Both groups completed a total of 3 × 8 repetitions at 45%, 60% and 75% of baseline 1RM. The CS group received 30 s of rest after two consecutive repetitions, while the TS group rested for 120 s following the completion of each set only. The CS group improved physical function (i.e., 8-foot up-and-go, sit-to-stand, 10 m walking speed) and quality of life when compared to the TS group [73]. Although measures of peak power and strength were not directly examined, it seems probable that these factors mediated improvements in physical function. Indeed, Caneiro et al. [75] showed that heavy load (e.g., 3 × 4 repetitions at 90%1RM) unilateral CS leg strength training for 8 weeks increased peak power at 40% 1RM in post-menopausal women. The results of Caneiro et al. [75] provide some support that neuromuscular adaptations likely underpin functional improvements observed by Ramirez-Campillo et al. [73]. That being said, in the same study by Caneiro et al. [75], both CS and TS elicited similar adaptations in thigh muscle mass, strength and maximum power. However, despite similar adaptations in these outcomes the authors reported distinct changes in the force–velocity curve. In particular, CS tended to favour an improvement in velocity, while TS tended to favour an increase in force. Thus, it is plausable that both CS and TS improve physical function albeit through somewhat distinct characteristics. Despite somewhat positive results in the

Table 1 Overview of conditions and subsequent physiological and functional consequences with proposed potential benefit of cluster sets (CS)

	Common physiological consequences	Common functional consequences	Proposed benefits of CS	
			Acute	Chronic
Aging	↓ Myelination of motor neurons and selective denervation ↓ Type II muscle fibers (i.e. atrophy) ↑ Fat infiltration of muscle ↓ Myosin content ↓ Muscle contractility ↓ Muscle mass	↓ Muscle strength and power ↓ Functional mobility ↑ Falls risk ↑ Risk of mortality ↓ Quality of life ↓ Independence	↓ Exertional dyspnea and symptom exacerbation during exercise ↓ Neuromuscular fatigue during exercise, possible quicker recovery? ↑ Muscle force, power and movement velocity across an exercise session ↑ Volume of work performed ↓ Perception of effort during exercise ↓ Reduced parasympathetic withdrawal ↓ Cardiovascular response/load ↑ Exercise tolerance ↓ Anxiety during exercise ↑ Affective response to exercise	↑ Long-term behaviour maintenance and exercise adoption ↑ Neuromuscular capacity (e.g. strength and power) ↑ Functional mobility and capacity ↑ Physiological function ↑ Physical quality of life ↑ Improved psychological wellbeing as a secondary effect resulting from increased function and physical activity ↔ No extra cost or likely time requirement of intervention
Neuromuscular diseases and neurological injury	↑ Muscle fibre atrophy ↓ Muscle fibre innervaion ↑ Incidence of secondary disease ↑ Adverse autonomic response to exercise (e.g. circulatory dysregulation, insuffiency and chronotropic response)	↑ Muscle spasticity and rigidity ↓ Movement (partial or complete) ↓ Locomotor ability (e.g. gait) ↑ Muscle fatigue ↓ Reduced muscle force and power capacity ↓ Quality of life ↓ Independence ↑ Risk of mortality		
Chronic heart and cardiovascular disease(s)	↑ Blood pressure (systolic, diastolic and mean) during exercise ↑ Peripheral vascular resistance ↑ Likelihood of light headedness, dizziness ↑ Likelihood of muscle and myocardial ischemia ↓ Muscle mass	↓ Exercise capacity ↑ Sedentarism ↓ Muscle function ↑ Secondary health consequences ↑ Activity avoidance ↑ Risk of mortality		
Pulmonary diseases	↑ Muscle fibre atrophy and shift in muscle fiber-type to slow twitch ↓ Capillarization ↓ Oxidative capacity ↑ Mitochondrial dysfunction ↓ Muscle mass	↓ Muscle strength and power ↑ Deconditioning ↓ Functional mobility ↓ Exercise tolerance ↑ Exertional dyspnea ↑ Anxiety ↑ Activity avoidance ↑ Risk of mortality ↓ Quality of life ↓ Independence		

aforementioned studies, not all evidence suggests an additional benefit of CS over TS in aged populations. For example, most recently, Dias et al. [74] used the same TS and CS structures as Ramirez-Campillo et al. [73] and found no between-group differences after 12 weeks of RT in a sample of 66 postmenopausal elderly women.

Although direct evidence is limited, at the very least, additional rest periods implemented during CS appear feasible for older adults despite similar reported muscular adaptations and improvements in maximum strength compared to TS. Prospectively, the application of CS into RT programs may also allow older adults to perform HSRT at higher-loads and velocities to support functional improvements (Table 1); though evidence is equivocal. In light of the limited evidence that is available we suggest that additional randomized controlled trials are required to examine the application of CS in older adults in comparison to TS approaches, with consideration for potential moderators (e.g., load, rest length, volume). Additionally, we suggest that the psychological responses and long-term adherence to CS compared to TS programs should be evaluated to further establish their efficacy and sustainability.

4 Neurological and Neuromuscular Conditions

4.1 Brief Overview of Symptoms in Neurological Injury and Neuromuscular Disease

Neurological injury can have debilitating effects on physical function resulting from trauma or sudden adverse event (e.g., stroke, spinal cord injury [SCI]). Neuromuscular diseases encompass a range of conditions that affect central-, motor-nerves and/or associated neuromuscular junctions. Neurodegenerative disorders (e.g., motor neuron disease [MND]/amyotrophic lateral sclerosis [ALS]) result in the progressive loss of neuronal structure and function while others may be considered age-related (e.g., Parkinson's disease [PD]). Each neurological and neuromuscular conditon has unique pathological characteristics often causing dysfuncton via spasticity, rigidity, paralysis, impaired gait, cognitive deficits, and autonomic dysregulation amongst others (SCI example; [76]). Given the breadth of parameters that can be affected, in this article we focus on voluntary physical effects. For example, progressive muscle atrophy often occurs as a result of disuse or deinnervation [77] causing increasing muscle fatigue and weakness; the latter generally associated with increased mortality risk [9]. Moreover, acquired motor impairment can be confined or widespread, and can demonstrate laterality, that is, one side of the body is affected (e.g., stroke and SCI) to a greater extent, with impacts ranging from minor to complete impairment. Although the mechanisms of neurodegeneration are multifactorial and complex, exercise is thought to play an important role in maintaining and improving function [78]. Below we provide brief overview of symptoms in several common conditions, highlight evidence of the general efficacy of RT in each, and discuss the potential benefit of CS application in exercise rehabilitation programs.

4.2 Brief Symptom Overview and Resistance Training Evidence in Several Neuromuscular and Neurological Conditions

4.2.1 Incomplete Spinal Cord Injury

Incomplete SCI causes acute and lasting loss of neuromuscular function due to damage or lesion. The cause of SCI is varied resulting from, but not limited to, traumatic road accidents, sporting and water activities, and falls in both children and adults (see [79, 80]). Further to a reduction of contractile capability, ongoing impairment also leads to muscle fiber atrophy [81]. Consequently, individuals with SCI suffer paralysis, muscle weakness, loss of function and independence, reduced quality of life, increased financial burden and secondary adverse health outcomes [82–84]. Secondary health consequences can include cardiovascular disease due to increased prevalence of hypertension, type-II diabetes, or impaired glucose tolerance resulting from physical inactivity [76]. Despite ongoing research and current rehabilitation strategies, functional recovery varies greatly based on injury etiology and severity [83].

Many neurorehabilitatory exercise programs aim to improve neuromuscular function by increasing muscle size and strength to perform everyday tasks (e.g., locomotion). For example, interventions focusing on lower-body combined resistance- and plyometric-training in SCI have demonstrated reduced neuromuscular impairment and improved gait speed [85]. Further preliminary evidence suggests strength may be increased in muscles with partial paralysis without increasing spasticity [86], which is an important consideration for proper function. However, although traditional RT interventions can improve strength in SCI injured patients [85–87], it is unclear whether this translates to clinically meaningful changes [87]. Indeed, strength gains from eccentric RT are smaller in incomplete SCI patients compared to healthy controls [87]. Other benefits such as reduced pain, stress and depression, improved satisfaction with physical function, perceived health and quality of life have been reported after 9 months of multimodal (i.e., aerobic- and strength-based) exercise [88]. However, despite exercise attendance being similar to that seen in studies of healthy persons (~ 80% of sessions attended) during the intervention, there was a considerable reduction in attendance over the following 3-month follow-up [88]. Specifically, only 7 of 11 patients continued supervised exercise and attendance dropped to 42.7% which was strongly correlated with pain ($r = -0.91$ [95% CIs − 0.99 to − 0.50]). Thus, at least for longer term adherence, optimising RT paradigms that not only improve functional outcomes but also perceptions during exercise are desirable. Further consideration must be given to increased fatiguability during physical activity [89], likely reduced exercise capacity [90], and potential for unfavourable autonomic responses caused by circulatory dysregulation, insufficiency and the chronotropic response to muscular work [91]. Therefore, although RT is recommended [84], the effectiveness of current paradigms are mixed.

4.2.2 Stroke

Both ischemic and hemorrhagic stroke are common subtypes [92]. Functional impairments such as muscle weakness and/or spasticity often result [93–96] with up to 50% of patients suffering chonic disability [97, 98]. Thus, effort has been made toward toward practical diagnosis, clinical detection and management [92] and as such, research into physical and assited therapies to improve stroke outcomes is ongoing but success varies [99–101].

Specifically, RT has been trialled across early [102–104], late [105], and chronic [106, 107] phases of stroke rehabilitation. Although it is generally agreed that RT improves muscle strength in stroke patients, there remains conjecture as to whether increases in strength improve functional task performance (e.g., walking, stair climbing) [108–111]. Evidence also suggests high-volumes of practice of repetitive motor task-orientated- and specific-training is effective in stroke rehabilitation [101]. However, as noted in studies in healthy populations comparing CS and TS RT [21–24], the power output and movement velocity required to optimally perform such actions becomes compromised with continuous efforts compared to intermittent efforts. Alternatively, unilateral high-load training of the unaffected limb has been shown to induce 'cross-education' (e.g., improved strength, function or increased range of motion of contralateral muscle group) in stroke survivors [112–115]. Specifically, some evidence suggests that the contralateral improvement in strength may also translate to functional task improvements (e.g., gait) [114]. Other evidence also suggests that interlimb neural plasticity is increased in stroke patients [116], presenting an opportunity for further exploration of different RT paradigms (e.g., paradigms facilitating the delivery of greater training loads), such as CS, to promote cross-education.

4.2.3 Parkinson's Disease

Parkinson's disease affects ~ 2% of the population over 60 years of age [117]. Slowness of movement (i.e., bradykinesia), is a primary symptom associated with tremor, impaired balance, muscle weakness, and reductions in muscular power and velocity during movement repetition [118, 119]. The extent to which muscle weakness and bradykinesia can be attenuated or reversed in PD is yet to be fully elucidated. Typical medications including dopamine agonists and levodopa are associated with a number of side effects, including nausea, confusion, postural hypotension and potentiation of bradykinesia amongst others [120]. Whilst pharmacological strategies can be effective, the functional consequences of motor symptoms and reduced mobility often remain.

Consequently, exercise interventions have been implemented in PD [121] with evidence suggesting that exercise can stimulate positive neurotrophic, inflammatory, and microglial responses [122]. Functionally speaking, RT has been employed to mitigate bradykinesia and muscle weakness with a three-fold rationale: (1) RT may target strength deficits typically associated with bradykinesia; (2) exercise may delay the progression of self-reported PD symptoms (Unified Parkinson's Disease Rating Scale); and (3) RT increases force- and power-generating capacity of the muscle, which may contribute to improvements in functional capacity. PD symptom progression contributes to a decline in motor functionality, thus, interventions promoting aspects of physical function such as strength and power are of critical importance [123]. In support, a systematic review [119] and several studies [124–127] have shown improvements in strength, physical performance, balance, gait, PD specific scales and/or quality of life following RT interventions. More specifically, some evidence also demonstrates that power-based RT can improve upper- and lower-limb bradykinesia scores, peak power, and can modify both load-velocity and load-power profiles [128, 129]. Consequently, Ramazzina et al. [119] also highlight the need to investigate different RT paradigms in PD to understand the specific benefit and efficacy of each.

4.2.4 Motor Neuron Disease, Amyotrophic Lateral Sclerosis and Sub-Types

Motor neuron disease/ALS and various sub-types can result in progressive muscle weakness, fatigue, spasticity, and respiratory insufficiency [130, 131]. Negative psychological effects are also prevalent, such as depression and anxiety [131]. Expected survival typically ranges from 20 to 48 months although ~ 10% of patients may survive longer than 10 years [132]. Thus, encouraging exercise in light of progressive paralysis and severely reduced life expectancy may seem difficult. Consequently, the benefits of RT in MND/ALS are poorly understood and the number of exercise trials are limited (for review see [133]). However, it appears worthwhile to understand whether strategic RT can serve to reduce the loss of motor units, and partially preserve neuromuscular function in MND/ALS. That being said physical activity in MND/ALS in somewhat controversial and whether pre-disease chronic vigorous exercise [134], or that prescribed as treatment [135], is beneficial or detrimental has been debated. For example, intense exercise can cause high oxidative stress and glutamate excitotoxicity which is thought to facilitate disease progression [134] as higher than normal glutamate concentrations can lead to neuronal cell damage and death [136]. Therefore, physical exercise that serves to improve or maintain function and psychological well-being, but does not contribute to more rapid disease progression is favorable; but further trials are required.

4.3 Proposed Cluster Set Rationale in Neurological and Neuromuscular Conditions

From a physical perspective, partial or complete impairment of motor function (immediate or progressive) resulting in muscle atrophy, weakness, fatigue, and reduced functionality are common across neurological and neuromuscular conditions. Although RT is often used as a rehabilitative tool, it is unclear if current approaches are optimal. Alternatively, we propose that CS RT may contribute to functional adaptations, or at the very least improve patient perceptions of RT. Given the heterogeneity of disability and functional capacities of such patients we also emphasise that CS can be easily adapted to suit exercises specific to each condition, individual and stage of the rehabilitation program at the discretion of the exercise professional; which may not always be as simple with techniques that require additional equipment or expertise (i.e., stimulated muscle contractions). CS may also be programmed to minimize acute neuromuscular fatigue which is of benefit to such patients, avoid large declines in movement or session quality, and minimize the recovery period required. Additionally, it can be theroized that CS may help attenuate adverse autonomic responses caused by circulatory dysregulation, insufficiency and chronotropic responses to muscular work, but specific research is required. RT is also known to elicit cross-education of strength between limbs in both upper- and lower-body muscles [137] and has been used in neurorehabilitatory settings with unilateral impairment [115]. To our knowledge, only two studies have assessed the cross-education effects of CS [138, 139]. Specifically, Farinas et al. [138] compared 5 weeks of TS (5 × 6 repetitions at a 10RM load) and CS (30 × 1 repetitions with 18.5 s rest between repetitions) bicep curl training versus control in 35 active young adults ($n = 11$–12 per group) [138]. TS produced greater improvements in maximum dynamic and isometric strength of untrained elbow flexors, with greater fatigue purported as the reason for this observation. Alternatively, Iglesias-Soler et al. [139] conducted a complimentary study whereby leg extension was performed with TS (4 × 8 repetitions at a 10RM load) or the rest-redistribution CS method (1 × 32 repetitions with 17.4 s rest between repetitions) twice per week for 5 weeks in healthy adults ($n = 6$ per group). Similar changes in maximum dynamic and isometric force were reported for TS and CS with results from their main experiment suggesting both protocols result in a similar total volume load. Thus, although direct evidence in neurological and neuromuscular conditions is lacking, the potential benefits and use of CS warrants at least some discussion. For example, CS may be configured to enable a greater unilateral training load to be performed [140] rather than purposefully equating the volume to TS and minimizing fatigue. In particular, mechanisms underpinning cross-education are thought to be largely neural [141–143] and RT adaptations are generally greater when higher relative training loads (i.e., as a percentage of maximum) are used [144]. Thus, unilateral CS interventions that minimize fatigue and allow relatively higher loads to be performed may be a plausible strategy in conditions with unilateral impairment (e.g., stroke and SCI) and specific investigation is warranted. However, it should also be noted that the greater fatigue induced by TS may also be an important stimulus for adaptation in untrained limbs [138], and therefore, these factors should also be considered when deciding on the most appropriate approach. Alternatively, CS can be programmed to reduce physiological stress or higher levels of muscular activation compared to fatiguing TS which may be applicable in other conditions (e.g., MND/ALS), although this is speculative. We further speculate that CS may also be more tolerable and improve long-term adherence, whilst promoting muscle strength, speed, and power, and improve functional independence and psychological wellbeing (Table 1).

5 Chronic Heart and Cardiovascular Disease(s)

5.1 Symptom Burden and Implications in Chronic Heart and Cardiovascular Diseases

Globally, cardiovascular diseases are considered the leading cause of mortality [145, 146]. Many risk factors for cardiovascular disease exist (see [147]), however, several are modifiable via positive lifestyle changes (e.g., increased physical activity). In individuals already suffering from cardiac disease and chronic heart failure, the benefit of rehabilitative exercise programs is well recognized but underutilized [148, 149]. Previously, RT has been suggested as less suitable in cardiac rehabilitation due to early evidence reporting adverse blood pressure responses [150, 151]. Both systolic and diastolic blood pressure can increase resulting in greater mean pressure [152], and both blood pressure and heart rate changes are more apparent during forceful muscular contractions [153]. Furthermore, greater relative contraction forces increase intramuscular pressure and muscle ischemia. In turn, this causes vasoconstriction and combined with increased cardiovascular output during muscular work results in unfavourable changes in systolic, diastolic and mean blood pressure, and peripheral vascular resistance [153, 154]. Additionally, performing a Valsalva manoeuvre during strong muscle effort can also increase intrathoracic pressure, decrease venous return and the possibility of lower cardiac output [155]. However, increased systolic blood pressure may occur secondary to increased intrathoracic pressure during a Valsalva manoeuvre, where the increased pressure can exert a direct effect on arterial vessels [156, 157]. Light-headedness or dizziness may also result [151, 158] and other physiological responses during RT include increased oxygen uptake, heart rate and an early increase then plateau in stroke volume [152].

5.2 Cluster Set Evidence and Proposed Rationale in Cardiac Rehabilitation

Exercise strategies that implement short bouts of work interspersed with rest intervals may allow cardiac patients to exercise safely and effectively at higher intensities of effort [159–161]. Despite emphasis on aerobic training, the benefits of RT are well-known and include improved muscle strength, function, exercise capacity, independence and quality of life [162–164], all of which support its application in cardiac patients. When applied in addition to aerobic training, both strength and aerobic fitness are improved [165], and cardiovascular and all-cause mortality is reduced [166]. However, many cardiac RT programs tend to employ TS paradigms (e.g., 3 sets of 6–15 repetitions with light to moderate loads which are not often performed to momentary muscle failure). In general, continuous high repetitions increase cardiovascular load [167] and result in unfavourable hemodynamic [168] and subsequent blood pressure [169] responses. Combined with greater fatigue and perception of effort, this may become problematic due to already compromised cardiovascular function, poor exercise capacity, and tolerance of patients [170]. However, shorter continuous efforts (i.e., 6 repetitions) minimize adverse cardiovascular autonomic responses (e.g., blood pressure, heart-rate and cardiac output) compared to higher repetition (i.e., 15 repetition) protocols despite greater relative loads [171]. When the contraction period is shortened further and rest between each repetition (e.g., 1–2 s) is allowed in the same fashion as CS, pressure load on the cardiovascular system appears to be reduced [163]. Evidence in healthy individuals shows that rest re-distribution CS result in less metabolic acidosis and parasympathetic withdrawal [167]. In addition, less pronounced parasympathetic withdrawal has also been noted with the inter-repetition CS method compared to TS and the rest-pause CS configuration [26], and is suggested to also reduce post-exercise impacts on cardiac vagal control and baroreflex sensitivity [172]. However, mixed blood pressure responses are reported with either higher [173, 174] or lower [175] values recorded when repetitions are performed intermittently (i.e., CS) compared to TS in healthy individuals. To our knowledge, only one study has directly investigated CS in cardiac patients [176] where such benefits may have the most relevance. Specifically, the authors utilized the inter-repetition rest method and compared this to TS in elderly (~ 75 years) male coronary patients. The use of CS delayed the increase in the rate pressure product compared to TS configurations. Thus, higher levels of cardiovascular stress are experienced for a shorter period and may allow for a safer delivery of RT. However, upon further investigation a modified version of the rest-pause technique has also been trialled in elderly heart failure patients (73 years, 80% males) [177]. Modified rest-pause RT or combined aerobic and traditional RT was implemented for 4 weeks, prior to a further 4-week period of combined aerobic and traditional RT for both groups [177]. Specifically, patients were permitted self-determined breaks (minimum of 30 s) until the whole duration of the exercise (5 min) was completed with initial loads corresponding to 40% 1RM. After 8 weeks, patients in the modified rest-pause group showed greater improvements in aerobic capacity, and muscular strength (effect size for muscular strength only). Based on emerging evidence we suggest that further acute and chronic investigations are required to comprehensively examine the efficacy of CS across various cohorts of cardiac patients.

6 Pulmonary Diseases

6.1 Symptom Burden and Implications in Pulmonary Diseases

Lung cancer and chronic respiratory conditions, including chronic obstructive pulmonary disease (COPD), cystic fibrosis and interstitial lung disease involve abnormalities of the airways or other structures and tissues of the lung [178]. Muscle dysfunction and physical dysfunction are common in chronic lung disease [7] and cancer [179–181]. Physiological mechanisms underpinning muscular dysfunction in COPD include muscle atrophy, fiber-type shift (i.e., type-I to type-IIx), reduced capillary number and density, poor oxidative capacity, and reduced mitochondrial density and function (see [7]). However, a common distressing symptom experienced by individuals is the feeling of shortness of breath (i.e., dyspnea) defined as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity" [182–184] and is recognized as a contributor to reduced exercise capacity in pulmonary conditions [185, 186]. Individuals with COPD experience greater perceptions of effort, discomfort, and "unsatisfied inspiration" during exercise compared to healthy individuals [187]. It is also suggested that the heightened perception of effort and exertional dyspnea can generate strong emotional reactions including fear, anxiety, and distress, and contribute to activity avoidance [8, 188]. Activity avoidance begins a subsequent vicious cycle of physiological deconditioning that further exacerbates symptoms of dyspnea and fatigue. In turn, this results in reduced tolerance of even lower effort activity (i.e., reduced capacity to perform daily activities), and further avoidance [5, 8, 189]. This cycle can continue to progress, reducing physical function and quality of life, ultimately accelerating the trajectory towards mortality [8, 190, 191] (Fig. 2). Consequently, relevant strategies to reduce exertional dyspnea with exercise are important to avoid activity deterance and foster ongoing participation [192].

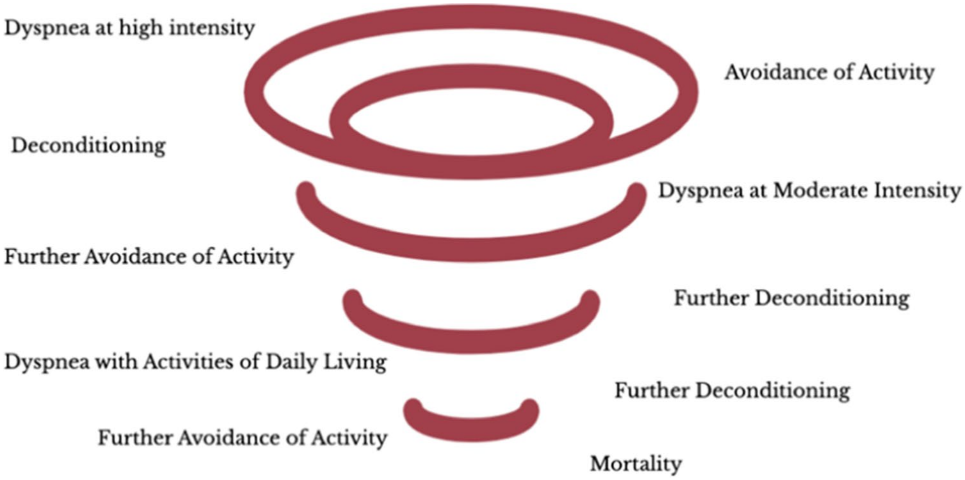

Fig. 2 Theoretical influence of dyspnea on exercise avoidance and physiological decline, adapted from [193, 194]

6.2 Physiological and Psychosocial Rationale for Cluster Sets in the Management of Dyspnea

Although it is increasingly recognized that exercise participation may improve symptoms of dyspnea, there is no consensus on the optimal training strategy [195]. Further, the therapeutic efficacy to manage symptoms is often limited by the amount of exercise that individuals experiencing dyspnea can achieve [182, 192, 196]. The concept of modifying the exercise stimulus around dyspnea in clinical populations is not novel and evidence from pulmonary rehabilitation suggests that the exercise prescription needs to be targeted to symptom burden [197, 198]. Results from aerobic exercise literature indicate that individuals partaking in interval training experience reduced dyspnea and leg discomfort, fewer unintended breaks compared to continuous training [196], and achieve intensities of effort during exercise that are otherwise intolerable [178, 192, 196]. Moreover, interval training can increase the overall duration/work performed compared to continuous training in individuals with COPD [196, 199].

With preliminary evidence indicating that aerobic exercise can be configured in a way to impact symptoms of dyspnea, it is not unreasonable to suggest that these principles also apply to CS as a form of "interval-like" RT [200]. Thus, we speculate that CS could result in similar reductions in dyspnea as with other modes of exercise. Essentially, by incorporating additional rest periods within each RT set (Fig. 1), the effects of accumulated fatigue and exertional dyspnea on exercise performance may be minimized, and serve to improve the volume of work performed [196]. As highlighted, prior research shows CS result in fatigue minimization, but may also result in lower perceptions of effort in comparison to traditional configurations; though this is somewhat equivocal [29–32, 203]. Furthermore, the consensus from the field of pulmonary rehabilitation is that the future of exercise prescription should address the key contributors limiting exercise, including but not limited to, dyspnea, fatigue, anxiety, and self-efficacy. Specific consideration should also be given to session tolerability and promotion of independent adoption and maintenance of exercise [178, 184, 186, 196, 198, 201, 202, 204]. Given the demonstrated benefits of CS in healthy populations and potential benefit in pulmonary settings [200] future research should directly examine their effect on measures of dyspnea and psychosocial responses. Positive evidence will assist efforts to promote exercise participation and work towards optimization in this area.

7 Practical Considerations and Suggestions

Given the potential efficacy and benefit of CS proposed, here we provide several practical strategies and suggestions for their tentative and future implementation in aged and clinical settings. However, we caveat that, though there is growing evidence in healthy populations, less is available across clinical populations and so their plausibility and benefit still requires further condition-specific investigation. First, exercise professionals should familiarize themselves with CS. This should include obtaining an understanding of documented benefits in both acute and chronic settings, different CS structures and their applicability for use at the individual and condition level. These benefits should also be discussed and explained to the patient/individual prior to implementation to ensure understanding of the reasons for modification of resistance- or rehabilitative-exercise programming. This may help to create further interest in the exercise and perceived benefits, possibly contributing to the likelihood of adoption and/or adherence. Initially, it may be better to modify the set-structure of current exercises performed by patients/individuals, and it is plausible that CS can be adopted across a range of resistive exercises to suit individual needs (see [25]). Importantly, CS can be adapted to

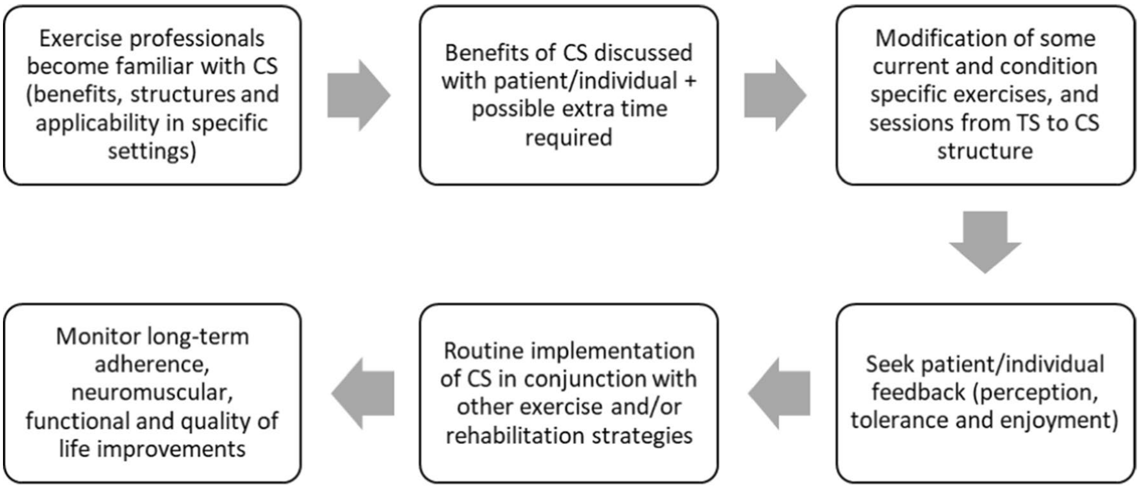

Fig. 3 Flowchart of practical suggestions for the adoption and implementation of CS into health-related and clinical exercise practice. CS: cluster sets

suit resistance-type exercises specific to the condition, individual, stage of rehabilitation and exercise program, as more typical exercises performed in healthy individual exercise programs are not always possible or advantageous. We suggest that this occurs before the implementation of new exercises to avoid difficulty in learning a new movement skill/task and set configuration simultaneously, or conversely, this may serve to help learn a movement more effectively if the CS is configured so that fatigue is minimized. Patient feedback on fatigue perception, tolerance, and enjoyment should also be sought early as this is also likley to provide insight into the likelihood of independent adherence and behaviour modification. It should also be highlighted that depending on the CS structure implemented (bar the rest-redistribution method), extra time, albeit it minimal, is required compared to TS RT. We also suggest that CS, as with all forms of RT, should compliment other rehabilitation or exercise strategies rather than used in an exclusive fashion. Lastly, we acknowledge that other RT strategies (e.g., stimulated or eccentric exercise for example), also demonstrate potential benefits in the aforementioned settings. Thus, it should be clarified that the information presented here does not aim to discredit or suggest the avoidance of such approaches. Rather, CS provide a promising new avenue to build upon existing evidence and advance research and practice in clinical settings. Their potential benefits may be either somewhat unique, or likely achieve equivalent positive outcomes compared to other strategies (Fig. 3).

8 Conclusion

Emerging evidence suggests that, even when fatigue during RT is minimized, positive adaptations still occur and may improve subjective experiences. CS are one such paradigm that is used in human performance settings but have only begun to be utilized in aged and clinical settings. Overall, CS show potential for application where older age, injury, and/or disease cause weakness and fatigue, and limit exercise capacity or tolerance. In an acute sense, CS may improve exercise tolerance and reduce perception of effort and discomfort, maintain acute neuromuscular performance (or where necessary, allow greater training loads/volumes to be achieved) and mitigate adverse physiological responses. Subsequently, this may help facilitate long-term adherence and thus, continued positive adaptations in muscle and physical function. In light of this, further research should also seek to closely monitor autonomic responses (e.g., blood pressure and heart rate responses) to gain a greater understanding of the acute physiologic stimulus across conditions, and further exploration of specific kinetic and kinematic variables and outcomes in relevant clinical populations of interest. Specifically, the rest re-distribution CS method may have the added benefit of not requiring any additional training time. Collectively, we have highlighted emerging evidence, and sought to give insight into several settings where CS may be advantageous. The information presented is intended to be useful for exercise professionals working in clinical settings who may wish to consider the application of CS for their patients. However, we acknowledge that there are numerous health-related settings that are beyond the scope of this article. We also emphasise the need for further high-quality CS-specific research (acute and chronic examing both efficacy and effectiveness) in these areas.

Declarations

Funding No financial support was received for the conduct of this article or for the preparation of this manuscript.

Conflict of interest The authors declare that they had no conflicts of interest.

Ethical approval Due to the nature of the study, ethical approval was not required.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material: Not applicable.

Code availability Not applicable.

Author contributions CL, CF and KK conceptualised the article. CL, CF, LM, JS drafted the article and KK and CP-M provided critical review.

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