A COMPARISON OF THE HAEMODYNAMIC AND CARDIAC AUTONOMIC RESPONSES FOLLOWING AN ACUTE BOUT OF ISOMETRIC WALL SQUAT AND ISOMETRIC HANDGRIP EXERCISE

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Abstract

Purpose. Isometric exercise (IE) training has been shown to be effective at reducing resting blood pressure (BP). However, there is a lack of clarity as to which IE modality is more effective at reducing resting BP. Acute responses following a single session of IE have been shown to predict long-term training adaptions. It was hypothesised that when using a comparative workload, exercises that recruit more muscle mass have a greater proclivity to induce transient reductions in BP than those that use smaller amounts of muscle mass. To test this hypothesis, the current study set out to compare the acute haemodynamic and autonomic responses following a single session of isometric wall squat (IWS) and isometric handgrip (IHG). **Method.** Twenty-six sedentary participants performed a single IWS and IHG session comprised of 4 x 2-min contractions, with 2-min rest, at 95 HR^{peak} and 30% MVC, respectively. Total power spectral density of HR variability and associated low-frequency and high-frequency power spectral components were recorded in absolute and normalized units before, during, and 10-min and 1-hour after each IE session. Heart rate (HR) was recorded via electrocardiography and baroreceptor reflex sensitivity via the sequence method. Continuous BP was recorded via the vascular unloading technique and stroke volume and cardiac output ($\dot{Q}$) via impedance cardiography. Total peripheral resistance (TPR) was calculated according to Ohm's law. The change from baseline for each variable was used for comparative analysis. **Results.** During IE, there was a significantly greater increase in systolic BP, diastolic BP, mean BP, HR and $\dot{Q}$ in the IWS condition (all P= <0.001). There was also significantly less TPR during IWS exercise (P= 0.006). During the 10-min recovery window, there was a significantly greater reduction in systolic BP, diastolic BP, mean BP (all P= 0.005) and TPR (P= <0.001). There were no differences in any autonomic variables during recovery, and no differences in any variables 1-hour post exercise. **Conclusion.** Isometric wall squat exercise produces a greater cardiovascular response during exercise, with a greater reduction in BP and TPR during a 10-min recovery period. These acute responses may be mechanistically linked to the chronic reductions in resting BP reported after IE training interventions.

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ABBREVIATIONS

BP - Blood pressure

CV - Cardiovascular

dBP - Diastolic blood pressure

HR - Heart rate

HR_{peak} - Peak heart rate

IE - Isometric exercise

mBP - Mean arterial blood pressure

MVC - Maximal voluntary contraction

$\dot{Q}$ - Cardiac output

sBP - Systolic blood pressure

TPR - Total peripheral resistance

SYMBOLS

Δ Delta (change)

1.0 Introduction

Hypertension is a major risk factor in the development of a variety of cardiovascular diseases, such as coronary artery disease, atrial fibrillation, stroke, and peripheral vascular, and is estimated to affect ~30% of the global population, resulting in an estimated 9.4 million deaths a year (Chan, 2013). The substantial public health burden that this presents emphasises the need for effective antihypertensive treatments. However, although pharmacological treatments have shown to be considerably effective in the battle against hypertension, many medications frequently fail to reach clinical targets. Additionally, as few as 50% of patients adhere to such treatment, for numerous reasons, including harmful side effects (Burnier and Egan, 2019). These, together with the economic burden that antihypertensive medications inflict on health services, places great emphasis on the need for a more patient friendly and sustainable approach to dealing with hypertension (Wang *et al*., 2017).

A pragmatic solution that has been put forward to solve this health epidemic is the use of alternative lifestyle modification treatments, which are a widely recommended approach to reduce resting blood pressure (BP) (Brook *et al*., 2013). Such treatments include weight loss, following a healthy diet, and exercise/physical activity, all of which have no harmful side effects and are relatively low in cost (Ndanuko *et al*., 2016). Indeed, physical activity has been proposed as the cornerstone lifestyle modification for the treatment of hypertension with guidelines suggesting aerobic exercise training with dynamic resistance training as the most effective intervention (Baddeley-White *et al*., 2019).

However, research has now shown that there are other exercise modalities possibly more effective at reducing resting BP than the traditional aerobic guidelines, such as isometric handgrip (IHG) training (a form of isometric exercise (IE) training). Meta-analysis has shown significant reductions in both systolic BP (sBP) and diastolic BP (dBP) following IHG training, by 13.4 mmHg and 7.8 mmHg respectively (Kelley and Kelley, 2010). This effect has been shown in both normotensive and hypertensive populations, with a magnitude larger than previously evidenced with dynamic aerobic or resistance training (Carlson *et al*., 2014). Given its cited effectiveness, the American Heart Association has endorsed IHG training as a potential alternative strategy to lower resting BP (Class IIB, Level of Evidence C) (Brook *et al*., 2015; Brook *et al*., 2013).

Recently, alternative IE protocols have been proposed in an attempt to progress the clinical applicability of this exercise modality. The proclivity of sedentary individuals to abstain from physical activity underlines the importance to enhance not only the physiological effectiveness of current exercise prescription, but also circumvent the factors that may inhibit participation, such as economic costs and accessibility (Morgan *et al*., 2016). Indeed, it could be argued that the expensive and/or laboratory-based

equipment, as typically associated with IHG exercise, hinders the effectiveness of IE as a therapy for reducing resting BP (Goldring *et al*., 2014).

Isometric wall squat (IWS) exercise is one such protocol that has been proposed as an effective alternative to IHG exercise (Goldring *et al*., 2014; Wiles *et al*., 2017). Isometric wall squat exercise involves maintaining a constant position wall squat at a participant specific knee angle, relative to a target heart rate (HR) determined in a familiarisation session (Wiles *et al*., 2017). Minimal equipment is required to execute the IWS, making it economical, accessible and time efficient (Goldring *et al*., 2014). Total costing for the protocol comes in at <£30 (Wiles *et al.,* 2017), which is a fraction of the price compared to the latest Zona plus series 3 handgrip device, priced at £549.00 (Baddeley-White *et al*., 2019). Following a 4-week programme consisting over 4 x 2-min bouts of IWS, 3 times per week, IWS training has produced clinically relevant reductions in resting sBP and dBP by 4 mmHg and 3 mmHg, respectively (Wiles *et al*., 2017). However, more recently amongst a cohort of stage 1 hypertensive/prehypertensive participants, Taylor *et al*., (2019) found that 4 weeks of IWS training significantly reduced resting sBP and dBP by 12.4 mmHg and 11.8 mmHg respectively.

Despite the aforementioned benefits of IWS training, the literature remains inconclusive as to which IE modality has more physiological capacity to reduce resting BP. A selection of literature has suggested that exercises involving a larger amount of muscle mass induce a greater CV response than those with a small amount of muscle mass (Mitchell *et al*., 1980; Kilbom and Persson, 1981; Seals *et al*., 1983; Misner *et al*., 1990; Iellamo *et al*., 1999; Gálvez *et al*., 2000). As IHG exercise only uses a small isolated muscle group in the arm, it does not recruit as much muscle mass in comparison to IWS exercise, which utilises larger muscle groups. Typically, the IHG only recruits the forearm-ulna and forearm-radius (Abe and Loenneke, 2015) whereas the IWS uses a larger group of muscles, in particular the hamstrings, quadriceps and gluteal muscles, as well as a variety of other supporting muscles (Blanpied, 1999). It has been suggested that IE contractions of a greater muscle mass require an increased autonomic response (Mitchell *et al*., 1980; Gálvez *et al*., 2000). There are two potential mechanisms that have been proposed that may help to explain this; central command and the peripherally modulated exercise pressor reflex (Gálvez *et al*., 2000).

The central command theory involves activation of higher brain centres, through a feedforward mechanism involving parallel activation of motor and cardiovascular centres (Williamson, 2010). It is suggested that at the onset of a muscular contraction, signals are irradiated from the motor cortex to the CV control centre in the medullar oblongata (Seals *et al*., 1983). Muscular contractions that utilise a greater number of motor units require stronger nervous stimulation which in turn reciprocally enhances the signal that is irradiated to the CV control centre. Therefore, exercises that involve a greater amount

of muscle mass will stimulate a greater central command input to the brain stem CV centres, which subsequently enhances the CV response (Gálvez *et al*., 2000).

The peripheral mechanism consists of a reflex pathway originating in the nerve endings of the contracting muscle (Gálvez *et al*., 2000). This theory suggests that a reflex stimulus in the contracted musculature is stimulated by chemical substances released during the contraction and/or by the physical deformation that occurs in the muscle and surrounding structures. The former may involve the release of metabolites and/or an increase in the osmolarity of the interstitial fluid which could activate nerve endings that feedback centrally to the CV centre (Seals *et al*., 1983). Nonetheless, it should be acknowledged that there are some circumstances in which muscle mass is a secondary influence, and thus is only of primary influence when programme variables, such as intensity, duration, and rest periods are closely matched (Seals and Enoka, 1989; Williams *et al.*, 1991).

One the other hand, in a meta-analysis by Inder *et al*., (2016), it was suggested that IE contractions of the arm have a greater potential to reduce BP than IE contractions using the leg. Inder *et al*., (2016) argued that this is due to the muscles in the arm are smaller, and thus the threshold at which the arteries become occluded is lower, resulting in repeated bouts of hypoxia in the forearm which is a potential stimulus for changes in arterial stiffness. Baross *et al*., (2012) has also suggested that local conduit arterial remodelling may be an important mechanism for BP reductions following IE (Baross *et al.*, 2012). Therefore, given the inherent vasculature heterogeneity in the human body, the relative effects on local arterial remodelling in the trained muscle may differ between the IHG and IWS, independent of the muscle mass recruited. Walther *et al.*, (2008) has argued that there is little evidence to support shear stress (SS) induced adaptation in the common femoral artery (CFA) and suggests this may be due to a reduced ability in the CFA to dilate in response to a SS stimulus (Walther *et al.*, 2008). In comparison, other arteries such as the brachial artery appear to be more sensitive to a SS stimulus and induce a greater dilatory response (Walther *et al.*, 2008). As such, it could be argued that the IHG may have more potential to reduce resting BP due to greater sensitivity to SS.

The latter potentially conflicting arguments reinforce that the underlying mechanisms responsible for these BP reductions remain largely inconclusive. Despite the mounting evidence regarding the beneficial effects of IE on BP management, few studies have assessed the acute effects of IHG and IWS on BP control, with no study directly comparing the acute responses between the two forms of IE. Interpreting the acute responses following IE is important as there are strong associations between the acute and chronic responses. Liu *et al*., (2012) remarked that the magnitude of post exercise hypotension (PEH) following an acute bout of exercise may predict the extent of BP reductions following a chronic intervention. Moreover, Somani *et al*., (2017) found that acute sBP changes to 2-min IHG and isometric

leg exercise (ILE) tests were associated with IHG and ILE training-induced reductions in sBP after 10 weeks of training, respectively (r = 0.58 and r = 0.77; for IHG and ILE; *P*= < 0.05). Farah *et al*., (2017) also suggested that chronic adaptations may result from temporal summation of acute responses. As such, further research in this area of study may help to confirm mechanistic pathways related to IWS and IHG training, and also ascertain which modality is more effective at reducing resting BP.

1.1 Acute studies

During an acute bout of IWS exercise consisting of 4 x 2-min bouts at 95% HR_{peak}, Taylor *et al*., (2017) found an increase in sBP of 33.3 mmHg from baseline (132.6 ± 5.6 mmHg) to the final stage of IE (165.9 ± 21 mmHg). This increase in sBP was accompanied by a significant stepwise increase in HR during the 4 x 2-min IWS contractions. There was also a significant stepwise reduction in power spectral density R-R interval (PSD-RRI) from baseline to IE2, IE3 and IE4, represented by a decrease in high frequency (HF) oscillations with an increase in the low frequency (LF) oscillations of HR. This alteration in the RR interval is generally associated with a decrease in parasympathetic outflow to sinus node occurring during exercise and an increase in sympathetic modulation to the sinoatrial node (Iellamo *et al*., 1999).

The contraction intensity and duration, the number of contractions and total workload, in addition to the muscle mass involved have all been shown to influence the CV response during IET (Olher *et al*., 2013). It is thought that these responses are induced through both central command and the muscle ergoreflex (Park *et al*., 2012). The magnitude of these responses are a probable stimulus for changes in resting BP (Gálvez *et al*., 2000).

The latter point is demonstrated by Stewart *et al*., (2007), who used a single 2-min unilateral IHG contraction at 35% MVC, and found sBP increased by 29 mmHg, less than the IWS used by Taylor *et al*., (2017). Likewise, Garg *et al*., (2013) only managed increases of 11mmHg sBP during a single 2-min unilateral IHG contraction at 30% MVC. Nonetheless, when using a comparative volume of exercise, the outcome changes somewhat. For example, during the first single 2-min contraction, BP only increased by 8.9 mmHg during IWS exercise (Taylor *et al*., 2017), entailing a reduced pressor response after a single bout compared to both the IHG protocols (Stewart *et al*., 2007; Garg *et al*., 2013). It could be argued that this finding is somewhat unexpected as more muscle mass is recruited during the IWS than the IHG. The result is further perplexed by results from the Iellamo *et al*., (1999) study that found during a short 60 sec acute bout of ILE, sBP increased by 26.5 mmHg from baseline (118.2 ± 2.9 mmHg) to exercise (144.7 ± 5.7 mmHg), similar to those found following IHG exercise (Stewart *et al*., 2007; Garg *et al*., 2013).

In addition, Stewart *et al*., (2007) found no increase in sympathetic modulation during a single 2 min IHG contraction, instead finding a decrease during the first minute, represented by a decrease in LF

oscillations, which may be a result of the reduced central and peripheral drive associated with the smaller muscle mass recruitment (Mitchell *et al*., 1980; Gálvez *et al*., 2000). However, after 4 x 2-min bouts of bilateral IHG at 30% MVC Millar *et al*., (2010) found a significant increase in sympathetic nervous activity represented by a decrease in sample entropy, which suggests that like the BP response, the autonomic response is also dependant on variables such as the duration of exercise and total workload.

The influence of muscle mass on the CV response during has been reported in the study by Iellamo *et al*., (1999), who compared ILE to IHG exercise. The study found greater increases in both HR and BP during ILE exercise compared to IHG exercise when performed at the same intensity, and suggested these responses to IE appear to be dependent on the size of contracting muscles. Iellamo *et al*., (1999) also hypothesised that during IE contractions with larger muscle mass recruitment, metabolite production is greater, with a consequent greater activation of the muscle metaboreflex. Another potential mechanism cited for this greater increase in HR during IE was a greater reduction in baroreceptor reflex sensitivity (BRS). Taylor *et al*., (2017) also found a significant decrease in BRS following IWS exercise, which is associated with the resetting of baroreceptors to higher operating point by the action of central command on the central neuron pool receiving baroreceptor afferents. This allows for a sympathetically controlled increase in HR and BP, resulting in the pressor response associated with IE (Ichinose *et al*., 2009).

Other physiological mechanisms that are altered during IE include total peripheral resistance (TPR). Bakke *et al*., (2007) found that during a single 2-min IHG contraction at 40% MVC, TPR was significantly increased, and explain that this was the main contributing factor to the increase in mBP found (25.3 ± 8.9 mmHg). Bond *et al*., (2016) also found that during a 3-min IHG contraction at 30% amongst a prehypertensive group, TPR was significantly increased from 1713 ± 91 to 2807 ± 370 dyne.s.cm^{-5} (64%). Conversely, Taylor *et al*., (2017) found that during 4 x 2 min of IWS exercise amongst a group of prehypertensives, TPR was significantly reduced, amid a significantly greater increase in BP. Although Bakke *et al*., (2007) only used a single 2-min contraction and Bond *et al*., (2016) only used 3-min compared to the 4 x 2 min in the Taylor *et al*., (2017) study, these contrasting findings potentially highlight the different mechanistic actions at work during these contraction types.

At the cessation of an IE contraction, there is a rapid perfusion of the previously occluded muscle. This is accompanied by a transient pressure undershoot, generally resulting in a hypotensive response (Clifford and Hellsten, 2004). Millar *et al*., (2009) found a significant drop of 3 mmHg in sBP 5 min following 4 x 2-min bouts of bilateral IHG exercise at 30% MVC. Likewise, Millar *et al*., (2011) found sBP reductions (approx. 2/3 mmHg) 5-min following a mixture of IHG protocols (4 × 2-min, 8 × 1-min, and 16 × 30-s).

These PEH effects were also found by Stewart *et al*., (2007), who reported a significant reduction of 4 mmHg in sBP 1-min following a single 2-min unilateral IHG contraction.

Following 4 x 2 min of IWS, Taylor *et al*., (2017) found significant reductions of 23.2 ± 18.1 mmHg, 18.7 ± 16.9 mmHg and 15.8 ± 15.5 mmHg below baseline values for sBP, dBP, and mBP, respectively (Taylor *et al*., 2017). O'Driscoll *et al*., (2017) also found a significant reduction in sBP (132.6 ± 5.6 vs. 109.4 ± 19.6 mmHg), dBP (77.6 ± 9.4 vs. 58.8 ± 17.2 mmHg), and mBP (94.7 ±10.1 vs. 78.8 ± 18 mmHg) in recovery. However, it must be acknowledged that the baseline BP values may have influenced the resulting PEH found by the latter studies (Moraes *et al*., 2012). Indeed, O'Driscoll *et al*., (2017) and Taylor *et al*., (2017) used sedentary pre-hypertensive participants, whereas the IHG studies used normotensive participants (Stewart *et al*., 2007; Millar *et al*., 2009, 2011). Nevertheless, numerous studies have found that an acute bout of IHG exercise produces no significant reductions in BP amongst hypertensive cohorts. For example, McGowan *et al*., (2006a) and Olher *et al*., (2013) found no effect on BP following an IHG protocol in medicated hypertensive patients. Likewise, Goessler *et al*., (2016) found that bilateral IHG at 30% MVC evoked no transient reductions in BP amongst a cohort of hypertensives 5-min post, 1-hour post, or 24-post exercise. More recently, Silva *et al*., (2018) used 12 hypertensive participants and compared the effects from three acute IHG protocols. The study found no reduction in BP following IHG exercise, even after a 4 x 2-min protocol that used 50% MVC.

Taylor *et al*., (2017) found that cessation of IWS exercise resulted in an overall increase in HRV above baseline, with a greater proportion in the HF domain, which signifies parasympathetic activation and sympathetic withdrawal. Similar autonomic responses have also been shown following IHG exercise. Millar *et al*., (2009) found an increase in parasympathetic modulation during recovery following a 4 x 2-min of bilateral IHG exercise. Millar *et al*., (2011) also found cardiac vagal modulation, demonstrated by HR sample entropy, was increased 5-min after a 4 x 2-min of IHG. Furthermore, following IWS exercise, Taylor *et al*., (2017) found a significant threefold increase in BRS (19.9 ± 10.3 ms·mmHg^{-1} to 60.04 ± 53.1 ms·mmHg^{-1}). On the other hand, Stewart *et al*., (2007) found that the HF oscillations were similar to baseline following a single 2-min bout of unilateral IHG exercise. Moreover, Iellamo *et al*., (1994) found BRS was not increased following a single 2-min bout of IHG exercise, potentially highlighting the influence of total workload.

Comparisons of cardiac impedance following IWS and IHG exercise have shown some contrasting findings. O'Driscoll *et al*., (2017) found a significant increase in cardiac output ($\dot{Q}$) (4.3 ± 0.7 vs. 6.1 ± 1 Lmin-1, $P < 0.001$), predominantly mediated via a significant increase in SV (74.6 ± 11 vs. 96.3 ± 13.5 mL, $P < 0.001$) as HR was unchanged (62 ± 9.4 vs. 63 ±7.5 bmin-1 , $P = 0.63$) post exercise. Taylor *et al*., (2017) also found SV was significantly increased during recovery but found that $\dot{Q}$ was decreased. On the other

hand, Weiner *et al*., (2012) found a significant decrease in SV (63.9 ± 12.0 vs. 49.4 ± 7.8; P < 0.001; Fig. 2) following 3 min of unilateral IHG exercise at 40% MVC. The decrease in SV was paralleled with a simultaneous increase in HR, resulting in no significant change in Q̇ (3.9 ± 0.5 vs. 4.2 ± 0.7 l min−1; *P*= 0.27).

Decreases in BP following IE have been shown to be related to reductions in TPR. For example, Taylor *et al*., (2017) found that TPR was significantly lower during the recovery period compared with baseline (*P*= <0.05). On the other hand, following 2 x 3-min bouts of bilateral IHG at 30% MVC, Krzemiński *et al*., (2012) found that there were no significant differences in TPR during a 5 min recovery period compared to baseline. Taylor *et al*., (2017) suggested that this reduction in TPR may be related to an increase in vasodilation caused by an increase in nitric oxide (NO) synthesis. The synthesis of NO is increased in response to the SS induced by hyperaemic blood flow, which may be increased during IWS due to the elevated HR. Reductions in TPR post exercise have also been related to the sympathovagal balance.

From the available literature, it is apparent that IWS exercise, which recruits a larger amount of muscle mass than the IHG, produces a greater increase in CV parameters during exercise, which results in a greater episode of PEH. The mechanisms responsible for these acute BP reductions may be related to alterations in HRV, and/or from reductions in TPR. However, although there is a selection of acute studies conducted to make a consensus on the haemodynamic and autonomic responses following IWS and IHG exercise, it is clear from searching the literature that more research is needed in order to make reliable and robust comparisons between the two isometric modalities.

One of the main problems with the current selection of literature is a lack of consistency between the methods used in each study, with differing populations, exercise durations, and intensities. Therefore, the aim of this study was to investigate the transient cardiac autonomic, central and peripheral haemodynamic responses, measured continuously pre, during, 10-min post, and 1-hour post an acute bout of IWS and IHG exercise (4 x 2-min) using a repeated measures crossover design. The study aimed to utilise the most widely adopted protocols used within IWS and IHG training programmes, but also match the acute programme variables as closely as possible in order to specifically ascertain the relevant acute responses induced from each form of IE. From the available data, it was hypothesised that due to the larger muscle recruitment, the IWS would induce a greater increase in sympathetic modulation, and thus a followed by a greater parasympathetic over sympathetic activity in recovery, mediated by an increase in baroreceptor reflex control of HR. This would correspond with a greater increase in BP during IWS exercise, followed by a significantly greater reduction in BP at the cessation of exercise.

2.0 Method

2.1 Participants

26 male and female participants (50:50) who were not meeting the current guidelines for physical activity (<150 minutes p/week) were recruited for the study (mean ± SD: age 27 ± 4.3 years; mass 79.8 ± 22.2 kg; height 173.5 ± 6.9 cm). The sample size (26) in the current study was based on previous studies analysing the acute responses following an IWS session (Taylor *et al*., 2017). All participants were non-smokers and were not be taking any pharmaceuticals known to influence the output measures. All exercise was carried out at the same time of day (within 2 hours), in a quiet, temperature-controlled room. All female participants reported using oral contraception. Exercise took place 4 hours following a light meal, with a 24-hour abstinence from alcohol, caffeine, and vigorous physical activity (Taylor *et al*., 2017). Participants were required to void their bladder prior to the testing session to avoid a possible rise in BP arising from bladder distention (Fagius & Karhuvaara, 1989). Prior to testing, and after receiving a written explanation of the testing protocol along with any potential risks, each participant completed a written informed consent form along with a health questionnaire. The study had ethical approval by Canterbury Christ Church University Sport and Exercise Science Ethics Committee and all procedures were conducted according to the Declaration of Helsinki.

2.2 Study design

There were total of four visits to the laboratory. During the first visit, a seated resting BP was performed using an automated BP monitor (Dinamap, PRO 200, GE Medical Systems Information Technologies GmbH, Munzinger Strasse 3, 79111, Freiburg, Germany) to confirm participants were not hypertensive (>130/70 mmHg) (Whelton *et al*., 2018). The Dinamap ProCare 200 utilises an oscillometric technique and a pneumatic cuff positioned around the upper left arm of the participant. The inflation and deflation of the cuff is controlled by a microprocessor, and each inflation cycle took approximately 30-45 s. The device has been calibrated against the Baumanometer Mercury Gravity Sphygmomanometer (W.A. Baum Co., Copiague, NY, USA) for oscillometric BP measurements (Lee *et al*., 2011). Although the Dinamap ProCare 200 was found to overestimate dBP, the results are similar in accuracy to other semi-automated devices (Lewis *et al*., 2002).

Upon arrival to the laboratory, BP was measured three times at 5-min intervals after a 15-min period of quiet seated rest. Participant stature in centimetres (cm) using a stadiometer (Seca 213, Seca GmbH & Co. Kg., Hamburg, Germany) and body mass in kilograms (kg) using mechanical column scales (Seca 710, Seca GmbH & Co. Kg, Hamburg, Germany) were also measured during this first visit. Prior to the commencement of BP measurements, participants were also familiarised with all the equipment and BP

measurement procedures. Eligible participants were then invited to a second preliminary session to complete an IWS incremental test and an IHG maximum voluntary contraction (MVC) test. These tests were used to establish the appropriate exercise intensity to use in the forthcoming sessions.

Data collection was conducted during the second and third visits. The study used a crossover design in which each participant performed both an acute bout of IHG and IWS in a separate session; the order of which was dictated by blind randomisation using the Microsoft Excel random number generator. Each session was carried out at least 48 h after the previous visit.

Each testing session began with 15-min of rest. Baseline autonomic and haemodynamic functions were then recorded continuously for 5-min in the supine position. Previous work by Taylor *et al*., (2017) has acknowledged that a change in posture and subsequent gravitational stress will influence cardiovascular haemodynamics. Pickering *et al*., (2005) and Vischer and Burkard (2016) have also discussed how BP changes based upon body position. Therefore, in order to minimise the influence of gravity, the currently study utilised a 5-min period of seated rest following the 5-min supine rest. All measures were then recorded continuously throughout each 2-min interval of IE (IWS1/IHG1, IWS2/IHG2, IWS3/IHG3, and IWS4/IHG4). Autonomic and haemodynamic parameters were then recorded during a 10-min recovery period (5-min seated followed by 5-min supine) immediately following the cessation of IET. After 1-hour from the termination of the last bout of IE, resting measures were again taken during a 5-min seated and 5-min supine window. During the hour period from the last IE bout participants were required to stay rested in the laboratory. Intervention marks enable the separation of the cumulative data into independent stages of the IE session. The current study used intervention marks at baseline, at each 2-minute exercise period, and at 10-min recovery. Data for the 1-hour recovery window was taken during a separate measurement.

2.3 Experimental procedures

Isometric wall squat

During the IWS session, participants were required to exercise at a prescribed knee joint angle based on HR responses to the incremental IWS test performed during the first laboratory visit. It has been shown that the intensity of the IWS can be attuned by manipulating the angle of the knee (Goldring *et al*., 2014). This is due to the inverse relationship found between knee joint angle and HR that is reproducible ($r = -0.9940$; $P<0.05$) using an incremental test (Wiles *et al*., 2008).

During the incremental wall squat test (IWST), participants were required to perform continuous wall squat exercise. During the test, the intensity was incrementally increased via alterations in knee joint angle. The knee angle was dictated using a clinical goniometer (MIE Clinical Goniometer, MIE Medical

Research Ltd., Leeds, U.K.). The goniometer was strapped to the participants leg using four 25 mm elastic Velcro straps, ensuring that the muscle was not compressed in any way. The fulcrum of the goniometer was aligned with the lateral epicondyle of the femur, with the moving arm placed on the lateral midline of the femur using the greater trochanter for reference. The stationary arm was positioned on the lateral midline of the fibula using the lateral malleolus and fibular head for reference. A spirit level was attached to the stationary arm to ensure that the lower leg was kept vertical during the IWST.

The first stage of the IWST began at 135˚ of knee flexion. Every 2-min, the exercise intensity was increased by decreasing the knee joint angle by 10˚. There are five stages in the test, with the final stage finishing at 95 ˚. The test ended when either the participant reached the end of the 95˚ stage, or if the participant was no longer able to continue the required knee joint angle within 5˚ of the target value (volitional fatigue). Upon cessation, all participants verbally confirmed that the test had been completed to maximum.

The data obtained during the incremental test was then used to prescribe a working intensity. In order to obtain the participant specific training angle, the knee joint angles during the IWST were plotted against the mean HR for the last 30 seconds of each stage. This relationship was then used to calculate the required knee joint angle to elicit a target HR of 95% heart rate peak - HR_{peak} (CV =2.8%, 95% CI =2.1-4.1%) as utilised by Devereux *et al*., (2010), with HR_{peak} defined as the mean HR of the last 30 seconds achieved during the IWST. Each participant's foot and coccyx placement were also recorded at each stage of the test. This enabled the target knee joint angle to be correlated against the foot and coccyx placements, allowing the participant to position themselves into their specific knee angle without the use of a laboratory-based equipment (e.g. a goniometer). This is based on the principal that lower wall squat exercise positions required participants to move their feet forward and back down the wall - preliminary testing demonstrated that knee joint angle produced linear relationships with both the feet ($r = -1.00$; $P < 0.05$) and back ($r = 0.99$; $P < 0.05$) positions.

The IWS testing session utilised the most widely used IWS protocol, comprised of 4 x 2-min bouts of IWS exercise at 95 $HR_{peak,}$ separated with 2-min of rest (Wiles *et al*., 2017). Participants positioned themselves into their participant specific knee angle by manoeuvring their back and feet into the correct placement. A makeshift blue tac rounded lip was used to ensure correct placement of the coccyx on the wall, and a fixed ruler on the floor allowed the participant to align their heel to the correct measurement. Both HR and BP were monitored throughout to ensure participants remained within the safe exercising limits defined by the American College of Sports Medicine. Verbal encouragement was given and participants were regularly informed of the elapsed time. Participants were reminded to breathe normally throughout

the exercise to avoid performing a Valsalva manoeuvre. At the end of each stage, the participants gave an RPD score based on the Borg CR-10 (Borg, 1982).

Isometric hand grip

During the IHG session, participants were required to exercise at 30% MVC. The MVC was carried out during the first visit to the laboratory using a programmed dynamometer (DHD-3 Digital Hand Dynamometer, Saehan Corp, South Korea). Participants completed three maximum isometric voluntary contractions using their non-dominant arm, each separated by >1 min of rest. The highest of three maximal efforts was designated the MVC.

The IHG session comprised of 4 x 2-min bouts of unilateral IHG exercise at 30% MVC. The use of a unilateral protocol was founded upon several factors. Firstly, it appears that unilateral IHG training provides the ideal stimulus for BP reductions. A recent meta-analysis by Inder *et al*., (2016) found that bilateral IHG interventions appear to be suboptimal for isometric training-induced BP reduction. Interestingly, Pagonas *et al*., (2017) found no reduction in BP variables following 12 weeks of bilateral IHG training. Smart *et al*., (2017) suggested that IE lowers BP through local rather than systemic effects, and thus the study design by Pagonas *et al*., (2017), which alternates the hand used, may have hindered the localised effects of IE.

Secondly, it is evident that unilateral IHG protocols (n=16) are more commonly prescribed than bilateral (n=11) (see appendix 1). Amongst these unilateral studies, the non-dominant arm is more widely utilised (McGowan *et al*., 2006b; Peters *et al*., 2006; McGowan *et al*., 2007a,b; Millar *et al*., 2007; Badrov *et al*., 2013a; Millar *et al*., 2013; Garg *et al*., 2013; Badrov *et al*., 2016; Carlson *et al*., 2016; Hess *et al*., 2016; Bentley *et al*., 2018) than the dominant arm (Wiley *et al.,* 1992; Ray and Carrasco, 2000). Compared to the 16 studies that have used a unilateral intervention, only 11 have opted for a bilateral protocol (Wiley *et al.,* 1992; Taylor *et al*., 2003; McGowan *et al*.,2006a; Millar *et al*., 2007; Millar *et al*., 2008; Stiller-Moldovan *et al*., 2012; Badrov *et al*., 2013b,c; Somani *et al*., 2017; Pagonas *et al*., 2017; Goessler *et al*., 2018).

The current study also opted for 30% MVC as this the most commonly used intensity adopted in unilateral handgrip protocols (Kelley and Kelley, 2010). Typically, unilateral IHG protocols at 30% MVC utilise a 3-min rest period. However, the current study used a 2-min rest period to match the acute programme variables and data collection protocols as closely as possible for both the IWS and IHG conditions. As the aim of the study was to analyse the comparative acute responses, using identical rest periods helped to eliminate any influence that the contrasting rest periods may have had on the outcome variables, without affecting the fundamental programme variables of the IHG protocol.

During the IHG testing session, participants were seated in an erect position so that the shoulder was adducted in a neutral position. The elbow was flexed at a 90°, with the forearm and wrist also in a neutral position. The handgrip was arranged in the participants' hand in a comfortable position. Participants were instructed to apply grip force gently and smoothly. A direct-reading light box was attached directly to the dynamometer to provide visual feedback to aid participants in maintaining the required contraction force. The display was monitored closely by a researcher to ensure the participant did not significantly fluctuate from the required intensity. Participants were reminded to breathe normally throughout the exercise to avoid performing a Valsalva manoeuvre. At the end of each stage, the participants gave an RPE score based on the Borg CR-10 (Borg, 1982).

2.4 Measurement variables

All experimental procedures carried out in a controlled laboratory environment. Autonomic and haemodynamic assessment was performed using the Physio Flow (Manatec Biomedical, Paris, France) and Task Force Monitor (TFM).

Continuous blood pressure

Continuous measurement of sBP, dBP, and mBP were recorded using the vascular unloading technique at the proximal limb of the index or middle finger (Fortin *et al*., 1998; Gratze *et al*., 1998). The continuous data is automatically corrected to oscillometric BP values obtained at the brachial artery of the contralateral arm.

Cardiac autonomics

A 6-channel ECG was used for HR measurement, and also R-R interval determination via PSD analysis (Valipour *et al*., 2005; Fortin *et al*., 2001). Before commencing testing, the ECG traces were manually screened to check for traces of any erroneous data. The beat-to-beat values obtained were then used for the real-time calculation of HRV by an autoregressive model (Fortin *et al*., 2001; Bianchi *et al*., 1997). High and low frequency parameters of HRV were automatically calculated by the TFM and expressed in absolute (ms^2) and normalized units (nu). The general consensus is that LF oscillations represent sympathetic outflow, while HF oscillations represent parasympathetic outflow and that the LF:HF ratio provides a measure of cardiac sympathovagal balance (Pomeranz *et al*., 1985). Baroreceptor reflex sensitivity was automatically evaluated via the sequence method and displayed on-line.

Impedance cardiography

Impedance cardiography (ICG) is a non-invasive method to measure the total conductivity of the thorax and analyse how it changes over time in relation to the cardiac cycle (Fortin *et al*., 2001). The PhysioFlow

uses a low amplitude/high frequency current that is transmitted through the chest which detects changes in impedance. Calculation of SV is founded on the notion that changes in aorta blood volume evoke contrasting changes in electrical impedance (Moshkovitz *et al*., 2004). Six electrodes were attached to the subject's upper body to calculate SV and Q̇ continuously, with values averaged over 15-sec.

Other haemodynamic variables

Rate pressure product (RPP) was calculated as the product of HR and sBP, and TPR was calculated according to Ohm's law. A selection of haemodynamic parameters measured were indexed to the participants body surface area.

2.5 Data Analysis

All data were analysed using the statistical package for social sciences (SPSS 22 release version for Windows; SPSS Inc., Chicago IL, USA). Unless otherwise stated, continuous variables are expressed as mean ± SD. All data were checked for parametric assumptions. For analysis, the changes from baseline were used in order to factor in any differences that may have occurred between conditions at baseline. A two-way repeated measure analysis of variance (RMANOVA) was used to compare the change from baseline between conditions followed by LSD *post hoc* tests for pairwise comparisons; the Wilcoxon signed-rank test was used for pairwise comparisons of non-parametric data. Data were log-transformed if needed to satisfy the underlying assumption of normality. If there was a violation of the sphericity assumption, then the degrees of freedom (DoF) were corrected using either the Greenhouse-Geisser or the Huynh-Feldt. If the Greenhouse-Geisser estimate of sphericity (ε) was > 0.75 then the Huynh-Feldt correction was used, and if ε was < 0.75 then the Greenhouse-Geisser was used (Field, 2013). Corrected DoF are reported throughout. A *P* value of 0.05 was regarded as statistically significant.

3.0 Results

All participants completed all four bouts of IWS at their prescribed knee joint angle. However, four participants consistently failed to maintain the unilateral handgrip contraction within 10% of the 30% MVC threshold through all bouts of IHG. Baseline characteristics are displayed in table 3.0.1.

Table 3.0.1 Baseline characteristics of population.

Age (yr)	27 ± 4.3
Height (cm)	173.5 ± 6.9
Mass (kg)	79.8 ± 22.2
HR (bpm)	67.2 ± 8.5
sBP (mmHg)	129.4 ± 10
dBP (mmHg)	74.7 ± 7.5

3.1 Haemodynamic response

Baseline data and the change from baseline delta scores (Δ) for each haemodynamic variable during each bout of IE, and in the 10-min and 1-hour recovery are displayed in Table 3.1.1 and Figure 3.1.2. There was a significant condition by time interaction for each BP parameter: sBP [$F(2.727, 68.164) = 19.058$, $P = <0.001$] (Figure 3.1.2.A), mBP [$F(2.610, 65.252) = 17.754$, $P = <0.001$] (Figure 3.1.2.B), and dBP [$F(2.697, 67.429) = 17.142$, $P = <0.001$] (Figure 3.1.2.C). The Δ sBP from baseline to IE1, IE2, IE3, and IE4 was significantly higher during the IWS, with the biggest difference occurring at IE1 ($P = <0.001$). The mean increase in sBP at IE1 was 38 ± 21.7 mmHg from baseline for the IWS condition, compared to 11.9 ± 15.6 mmHg during the first bout of IHG. Both dBP and mBP paralleled this haemodynamic response, with a significantly greater increase from baseline during all 4 exercise bouts compared to the IHG condition, and the biggest difference occurring at IE1 ($Z = -3.721$, $P = <0.001$ and $P = <0.001$, respectively).

There was also a significantly greater drop in sBP (20 ± 14.6 mmHg) during the 10-min following the cessation of IWS exercise ($Z = -2.832$, $P = 0.005$) compared to the IHG condition (6.8 ± 12 mmHg). This response during the 10-min recovery window was again paralleled by dBP and mBP, which both demonstrated significantly greater reductions of 20 ± 14.3 mmHg and 20 ± 14.5 mmHg, respectively. There were no significant differences between the conditions for any BP variable when measured 1-hour post exercise.

There was a significant condition by time interaction for HR [$F(2.884, 72.093) = 66.390$, $P = <0.001$] (Figure 3.1.2.E). Pairwise comparisons demonstrated that the increase in HR from baseline in the IWS condition was significantly greater during IE1, IE2, IE3 and IE4, with the biggest difference occurring at IE4 (Z=-

4.432, *P*= <0.001). During the 10-min recovery window, HR remained significantly higher in the IWS condition (*P*= <0.001). During this period, the HR in the IHG condition was reduced compared to baseline (-2.1 ± 4.6 bpm) whereas the HR in the IWS condition remained elevated (5.8 ± 7.3 bpm). There were no significant differences between conditions at 1-hour post.

As a consequence of the BP and HR responses, there was also a significant condition by time interaction for RPP [F(2.559, 63.978)= 55.079, *P*= <0.001] (Figure 3.1.2.D). However, the increase in RPP was significantly higher during all four bouts of IWS, with the greatest difference at IE4, in which RPP increased by 9765.1 ± 4142.9 (bpm·mmHg) from baseline, compared to 3102.9 ± 2031.4 (bpm·mmHg) in the IHG condition (*P*= <0.001). There were no significant differences between conditions at any recovery time points.

The TPR response demonstrated a significant condition by time interaction [F(3.329, 83.227)= 4.221, *P*= 0.006] (Figure 3.1.2.H). Total peripheral resistance was significantly higher in the IHG condition during IE2, IE3, with the biggest difference occurring at IE4 (*P*= <0.001); there was no significant difference at IE1. The reduction in TPR during the 10-min recovery window was significantly greater in the IWS condition (*P*= <0.001). There were no significant differences 1-hour post exercise.

There was a significant condition by time interaction for $\dot{Q}$ [F(2.545, 63.620)= 20.077, *P*= <0.001] (Figure 3.1.2.G), but not for SV [F(6,150)= 0.923, p= 0.434, ηp2= 0.036] (Figure 3.1.2.F). During all four exercise bouts, $\dot{Q}$ was significantly higher in the IWS condition, with the greatest difference at IE4 (Z= -4.203, *P*= <0.001). Like the HR response, $\dot{Q}$ remained significantly higher during the 10-min recovery period in the IWS condition (*P*= <0.001) although $\dot{Q}$ remained above baseline for both conditions. There were no significant differences 1-hour post exercise.

Table 3.1.1 Haemodynamic parameters at baseline, and Δ scores during IE, and in recovery.

Parameter		Baseline	IE1Δ	IE2Δ	IE3Δ	IE4Δ	10-minΔ	1-HourΔ
sBP	IWS	126.9 ± 9.4	38 ± 21.7	39.2 ± 30	35.9 ± 27.6	35.6 ± 28.5	-20 ± 14.6	-14 ± 10.4
	IHG	124.5 ± 7.5	11.9 ± 15.6	16 ± 16.5	12.3 ± 16.4	15.6 ± 19.5	-6.8 ± 12	-10 ± 8.5
			*	*	*	*	*	
mBP	IWS	98.1 ± 8.5	37.4 ± 19.1	36 ± 25.5	32.5 ± 24.1	30.9 ± 24.7	-20 ± 14.5	-12.2 ± 7.8
	IHG	97.1 ± 8.4	14 ± 16.4	17.8 ± 15.9	12.8 ± 15.3	17.4 ± 18.1	-7.5 ± 10.4	-10 ± 8.9
			*	*	*	*	*	
dBP	IWS	79.8 ± 8.1	36.1 ± 17.7	33 ± 22.6	29.9 ± 22.7	28.8 ± 23	-20.4 ± 14.3	-11.8 ± 6.8
	IHG	79.6 ± 8.7	12.5 ± 17.9	16.2 ± 16.2	10.2 ± 16.1	15.8 ± 18.3	-9.3 ± 11.3	-9.9 ± 10
			*	*	*	*	*	
RPP	IWS	8422.9 ± 1309.4	7617.7 ± 3047.9	8428.4 ± 3089.3	8944.6 ± 3448.3	9765.1 ± 4142.9	-646.8 ± 1527.5	-1548.7 ± 1105.2
	IHG	8167.6 ± 1288.6	2039.3 ± 1343.5	2633.2 ± 1481.8	2388.4 ± 1427.9	3102.9 ± 2031.4	-714.3 ± 1005.1	-1417.4 ± 763.1
			*	*	*	*		
HR	IWS	66.2 ± 9.9	30.6 ± 11.1	35.8 ± 12.7	40.8 ± 14	45.8 ± 16.3	5.8 ± 7.3	-5.3 ± 6.6
	IHG	65.5 ± 9.6	9.7 ± 4.4	11.7 ± 5.1	12.2 ± 5.6	15.5 ± 10	-2.1 ± 4.6	-6.6 ± 4.8
			*	*	*	*		
SI	IWS	55.6 ± 15.7	-2.6 ± 6.7	-0.2 ± 6.8	-1.4 ± 6.1	-1.9 ± 7.5	4.6 ± 5.2	1.5 ± 15.6
	IHG	57.9 ± 16.9	-5.5 ± 8.9	-5.3 ± 8.4	-4.9 ± 7.9	-5.4 ± 8.7	2.0 ± 4.6	0.4 ± 12.4
CI	IWS	3.6 ± 0.9	1.4 ± 1.2	1.9 ± 1.4	2 ± 1.3	2.2 ± 1.5	0.7 ± 0.6	-0.2 ± 0.8
	IHG	3.7 ± 1.2	0.2 ± 0.7	0.2 ± 0.6	0.4 ± 0.7	0.4 ± 0.8	0 ± 0.4	-0.3 ± 0.9
			*	*	*	*		
TPRI	IWS	2251.1 ± 547	97.2 ± 497.1	-72.5 ± 595	-237.4 ± 573.2	-307 ± 610	-739.2 ± 453.2	-213.9 ± 482.3
	IHG	2229.2 ± 677.9	291.7 ± 509.3	338 ± 515.9	159.6 ± 528.1	279 ± 609.2	-170.7 ± 272.2	-122.1 ± 466.9
			*	*	*	*	*	

Data are presented as the mean change from baseline ± SD. sBP = systolic blood pressure (mmHg); dBP = diastolic blood pressure (mmHg); mBP = mean blood pressure (mmHg); RPP = rate pressure product; HR = heart rate (bpm); SI = stroke index ($mL \cdot m^{-2}$); CI = cardiac index ($L \cdot min^{-1}\ m^{-2}$; TPRI = total peripheral resistance index ($dyn \cdot s^{-1} \cdot m^{-2} \cdot cm^{-5}$). *=sig.

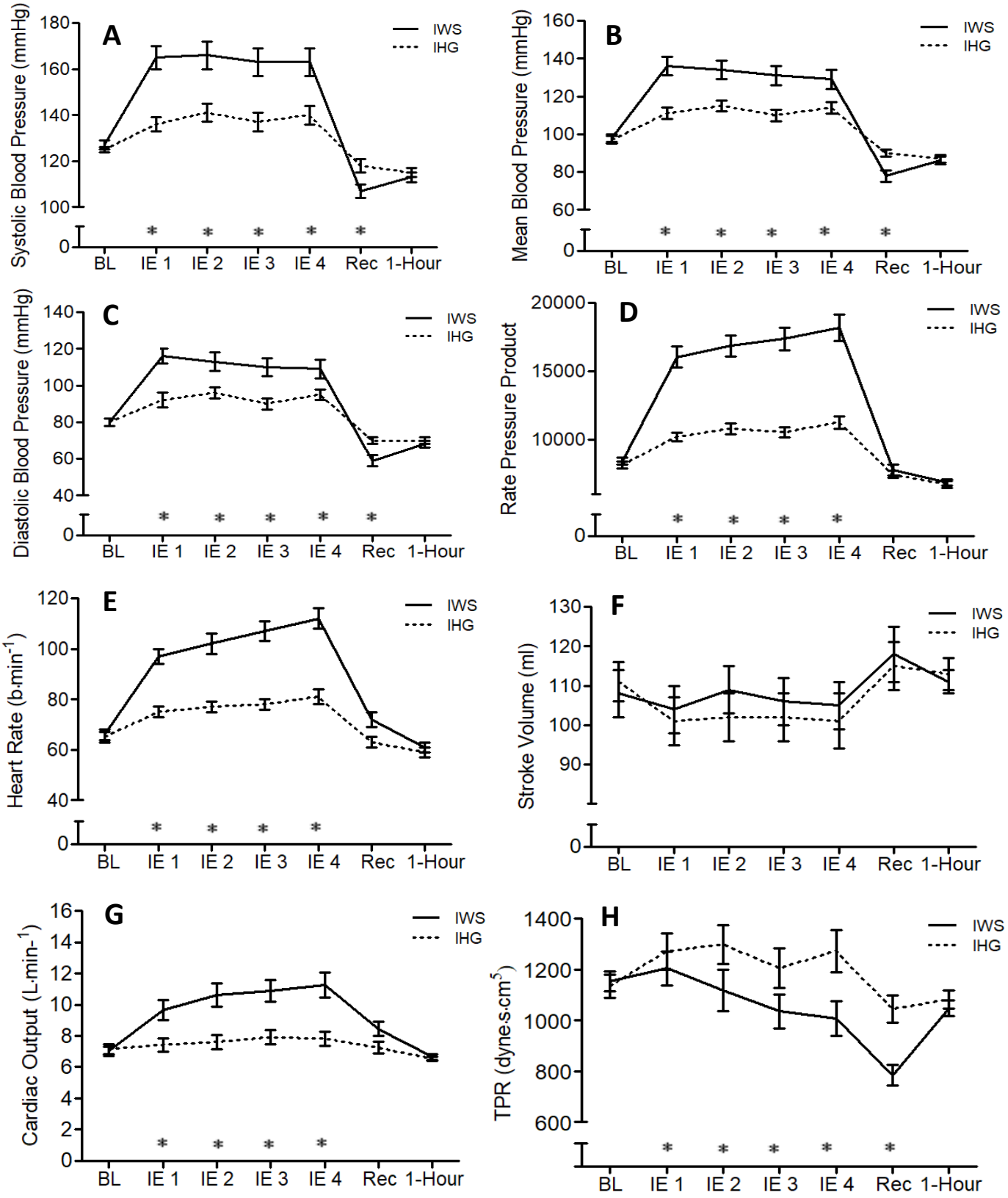

Figure 3.1.2 Hemodynamic responses to IWS and IHG. Values are presented as mean ± SEM. A, sBP. B, mBP. C, dBP. D, RPP. E, HR. F, SV. G, CO. H, TPR. *=sig.

3.2 Cardiac autonomic response

Baseline data and Δ scores during each bout of IE, and in recovery for each autonomic variable are displayed in Table 3.2.1 and Figure 3.2.2. There was a significant condition by time effect for PSD-RRI (log10) [F(3.251, 81.267)= 7.768, *P*= <0.001] (Figure 3.2.2.A). Pairwise comparisons show PSD-RRI was significantly lower in the IWS condition throughout all exercise bouts (all *P*= <0.001), and remained significantly lower during the 10-min recovery period (*P*= <0.001). There were no significant differences 1-hour post exercise.

Both Lfnu [F(4.352, 108.804)= 2.741, *P*= 0.028] (Figure 3.2.2.C) and HFnu [F(4.352, 108.804)= 2.741, *P*= 0.028] (Figure 3.2.2.D) data showed significant condition by time interactions. Pairwise comparisons revealed a significant difference between conditions at IE4 for both LFnu (*P*= 0.018) and HFnu (*P*= 0.018), with the IHG producing a greater increase in LFnu (8.461) and a greater decrease in HFnu (-8.461) compared to the IWS (1.037 and -1.037, respectively). There were no significant differences during the 10-min recovery or 1-hour post exercise. There was no condition by time interaction for either absolute LF (ms^2) [F(2.486, 62.138)= 2.254, *P*= 0.102] or HF (ms^2) [F(3.102, 77.555)= 0.058, *P*= 0.983] HRV data.

There was a significant interaction between condition and time for the LF/HF ratio [F(3.298, 82.438)= 5.729, *P*= 0.001] (Figure 3.2.2.E). Pairwise comparisons show the LF/HF ratio was significantly higher in the IWS condition at IE1 (*P*= 0.002). At IE4, the difference remained significant (Z= -2.426, *P*= 0.015), but the ratio was higher in the IHG condition. There were no significant differences during the 10-min recovery or 1-hour post exercise.

The BRS data showed a significant interaction between condition and time [F(3.571, 89.274)= 4.752, *P*= 0.002] (Figure 3.2.2.B). The reduction of BRS was significantly greater during all 4 bouts of IWS. The greatest reduction in was at IE4 (-13.041), which was significantly lower than the IHG condition (Z=-2.400, *P*= 0.016). There were no significant differences during the 10-min recovery or 1-hour post exercise.

3.3 Rate of perceived exertion

The rate of perceived exertion (RPE) data showed a significant interaction between condition and time [F(3.187,84.126)= 3.232, *P*= 0.001]. Pairwise comparisons show RPE was higher during IHG exercise at both IE3 (*P*= <0.001) and IE4 (*P*= <0.001).

Table 3.2.1 Autonomic parameters at baseline, and Δ during IE, and in recovery.

Parameter		Baseline	ΔIE1	IE2Δ	IE3Δ	IE4Δ	10-minΔ	1-HourΔ
PSD-RRI	IWS	3.3 ± 0.3	-0.2 ± 0.3	-0.4 ± 0.3	-0.4 ± 0.3	-0.5 ± 0.4	-0.2 ± 0.3	0 ± 0.3
	IHG	3.4 ± 0.4	0 ± 0.3	0 ± 0.3	-0.1 ± 0.3	-0.1 ± 0.3	0.1 ± 0.2	0 ± 0.2
			*	*	*	*	*	
LF - RRI	IWS	1188.2 ± 799.4	-384.2 ± 834.8	-623.5 ± 690	-704.7 ± 603.2	-783.2 ± 682.1	-407.8 ± 394.9	31 ± 644.4
	IHG	1510.6 ± 1178.1	-89.4 ± 885.7	-50.8 ± 903.3	-144.5 ± 956.6	-90.3 ± 977.9	177.8 ± 598.3	23.4 ± 826.9
HF - RRI	IWS	826.2 ± 831.9	-427.1 ± 907.6	-444.7 ± 888.2	-506.6 ± 848.9	-522.6 ± 934.7	-70 ± 610.9	373.2 ± 847.5
	IHG	1128.7 ± 1100.5	-327.5 ± 889	-315 ± 1005.4	-458.4 ± 753.2	-423.3 ± 933.5	29.5 ± 537.5	554.5 ± 1506.4
LF/HF	IWS	2.2 ± 1.1	1.9 ± 2.1	0.7 ± 2.6	0.7 ± 1.6	0.2 ± 1.5	-0.3 ± 0.9	-0.8 ± 0.8
	IHG	2.1 ± 1	0.4 ± 1.4	0.6 ± 1.9	1.3 ± 1.8	1.2 ± 2.2	0.1 ± 1.2	-0.5 ± 0.9
			*			*		
BRS	IWS	18.7 ± 9.1	-11.3 ± 9.8	-12 ± 9	-13 ± 9.2	-13.6 ± 9	-1.4 ± 7.2	4.5 ± 6.7
	IHG	20.2 ± 9.7	-5.3 ± 7.3	-6.3 ± 9.6	-8.6 ± 8.2	-9.4 ± 8.8	0.3 ± 5.1	2.9 ± 9.2
			*	*	*	*		

Data are presented as the mean change from baseline ± SD. PSD–RRI = power spectral density (ms^2); LF-RRI = low frequency (ms^2); HF-RRI = high frequency (ms^2); LF/HF-RRI = LF/HF ratio; BRS = baroreceptor reflex sensitivity ($ms \cdot mmHg^{-1}$). *=sig.

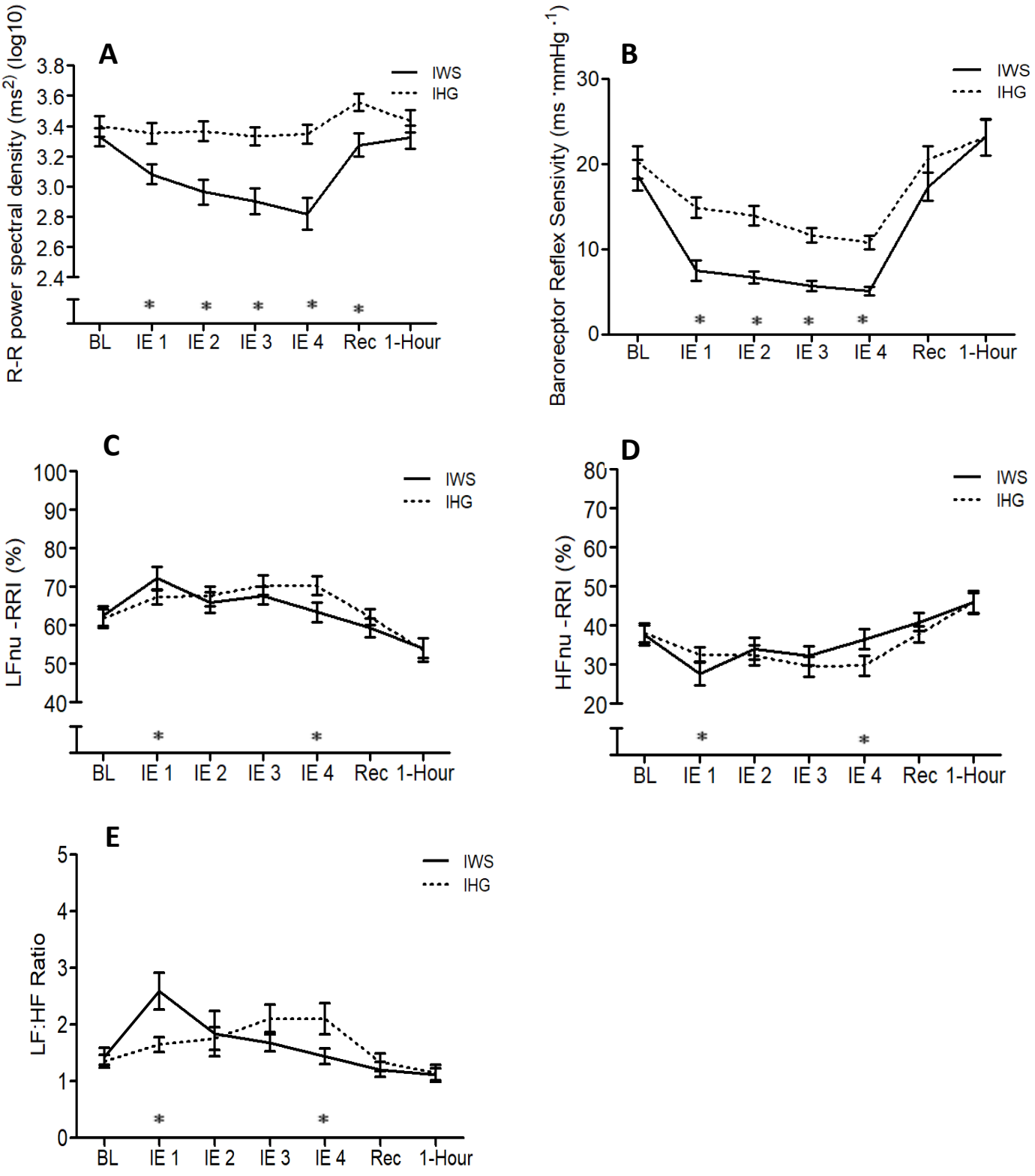

Figure 3.2.2 Autonomic responses to IWS and IHG. Values are presented as mean ± SEM. A, PSD-RRI. B, BRS. C, LFnu. D, HFnu. E, LF:HF ratio. *=sig.

4.0 Discussion

4.1 Executive summary of findings

This study is the first of its type to compare the continuous cardiac autonomic and haemodynamic regulatory responses during and following a single isometric wall squat (IWS) and isometric hand grip (IHG) exercise session. The study employed the two most commonly used protocols for IWS and IHG training. However, as this was a study focused upon the acute cardiovascular responses, programme variables and data collection protocols were matched wherever possible. A repeated measures design was used, in which a cohort of 26 male and female (50:50) sedentary participants undertook both an IWS and an IHG exercise session in a randomised order. Cardiac autonomic and haemodynamic variables were measured continuously during and following each exercise session, and results were analysed for comparisons using the change from baseline as the independent variable.

The current study hypothesised that the IWS, which uses a larger amount of muscle mass than the IHG, would result in a significantly greater CV response. This hypothesis was founded on previous research which has demonstrated that when performed at the same relative intensity and duration (Seals and Enoka, 1989; Williams *et al.,* 1991), exercises involving a larger amount of muscle mass induce a greater CV response than those with a small amount of muscle mass (Mitchell *et al*., 1980; Kilbom and Persson, 1981; Seals *et al*., 1983; Misner *et al*., 1990; Iellamo *et al*., 1999; Gálvez *et al*., 2000), which has been argued as a likely stimulus for reductions in BP (Gálvez *et al*., 2000). Data from the current study has demonstrated a significantly greater elevation in CV parameters throughout all IWS exercise bouts, followed by a significantly greater corresponding drop in BP and TPR during the 10-min post exercise window.

4.2 During IE

During IWS exercise, there was a significantly greater increase in BP. The increased BP coincided with a significantly greater increase in HR and $\dot{Q}$ compared to the IHG condition. Since there were no significant differences in SV between conditions, the difference in $\dot{Q}$ would be attributable to the change in HR. This finding further supports the theoretical argument that an increased CV drive is related to a larger amount of muscle mass recruitment.

During all four bouts of IWS exercise there was a significantly greater drop of PSD-RRI and BRS than during IHG exercise, which correlated inversely with the greater CV alterations. Studies have shown that decreases in HRV and BRS occur during exercise and that the magnitude of the decrease in variation is strongly correlated with muscle mass recruitment and exercise intensity (Iellamo *et al*., 1999; Saboul *et al*., 2016). This finding is consistent with the study conducted by Taylor *et al*., (2017) who also found a

significant decrease in PSD-RRI and BRS and reciprocal increases in HR and BP. Taylor *et al*., (2017) argued that the greater muscle mass activation and the relatively high contraction intensity used during IWS exercise results in a greater engagement of the muscle metaboreflex, which produces a reflex inhibition of cardiac vagal tone and increase in sympathetic nerve activity (Taylor *et al*., 2017). However, frequency parameters of heart rate variability (HRV) data in the current study were inconclusive and do support this notion.

As there was a significantly reduced BRS during all four IWS bouts, the lack of sympathetic activation may partly be explained by the DeBoer hypothesis (DeBoer *et al*., 1987). The DeBoer hypothesis is based on a mathematical model of the circulation which examines the interactions of the fast vagal response to baroreceptor stimulation and the slower response of the sympathetic efferents controlling the arterial smooth muscle. The model explains why conditions that are associated with a reduction in gain of the arterial baroreflex control (such as exercise) are also associated with diminution of the LF peak, despite other good evidence of increased sympathetic tone (Sleight *et al*., 1995).

The LF/HF ratio shift in the current study was significantly greater during the first bout of IWS exercise compared to the IHG condition. This suggests that the greater muscle mass utilised during IWS exercise induced a greater increase in sympathetic activity, compared to the smaller muscle mass utilised during IHG exercise. The significant difference in the BP response at IE1 between IWS and IHG exercise supports this concept. However, although the shift in the LF/HF ratio remained above baseline throughout all IWS exercise bouts, the ratio was not significantly different at IE2 and IE3 to coincide with the significantly greater increase in HR during all IWS exercise bouts. In fact, during IE4, IHG exercise produced a significantly greater increase in LF oscillations and a higher LF/HF ratio than IWS exercise, signifying a greater sympathetic response in the IHG condition. However, HR remained significantly higher in the IWS condition throughout all exercise bouts compared to IHG. Therefore, it is difficult to accept that a gradual increase in parasympathetic modulation and/or a decrease in sympathetic activation could be responsible for this shift in the LF/HF ratio at a time when HR was increasing in response to the IWS.

It has been suggested that HR alterations are not simply the result of simple algebraic summation of sympathetic and parasympathetic nerve activity, and that physiological interventions can produce either parallel or complex non-linear reciprocal changes in both domains of the autonomic nervous system (Billman, 2013). Interventions that, in line with the theorised linear model of autonomics, would be expected to induce sympathetic activation, such as acute exercise and even acute myocardial ischaemia, have not only failed to evoke an increase in LF oscillations, but have produced reductions in this parameter. Houle and Billman, (1999) showed that despite large increases in HR, the LF/HF ratio was unaffected by either acute myocardial ischaemia or exercise. Stewart *et al*., (2007) also found that

sympathetic activation decreased during a single 2-min bout of unilateral IHG exercise, but still found sBP increased by 29 mmHg.

However, although the IWS data in the current study may not have followed the expected autonomic trends, data from the IHG condition performed a lot more predictably, with a coherent response between HR, and LF and HF data. As such, a more likely explanation is that the complexity of neural control precedes the arguably simplistic presumptions for a linear, fixed, model of autonomics. This gives scope to the likelihood of a dichotomy between HR and autonomics, one that may be related to, differences in the muscle mass recruitment and relative intensity during IWS exercise.

In line with the significantly greater Δ RPP during IWS exercise, it is possible that a protective mechanism modulated the neural drive to prevent myocardial damage. Indeed, a high RPP is indicative of a greater myocardial load. During an IWS contraction, this greater myocardial load will also be coincided with an increased pressor response, which collectively, at a certain threshold, may stimulate a myocardial protective mechanism.

One myocardial protective mechanism that may be at work is the cardiac natriuretic system (Hamasaki, 2016). It has also been reported that circulating atrial natriuretic peptides (ANP) increases during mild exercise, with the dominant stimulus for its release being elevations in atrial wall tension. During an IHG contraction, Barletta *et al*., (1998) found increases in HR were accompanied by comparable increases in plasma ANP (+77%). The release of ANP was induced by an increase in mean left atrial pressure evoked through an increase in BP and HR (Barletta *et al*., 1998). Therefore, as the IWS in the current study produced significantly greater increases in HR and BP, there may have been a greater increase in these peptides. Butler *et al*., (1994) used spectral analysis of HRV to investigate the effects of exogenous ANP on the sympathetic and parasympathetic nervous system in healthy individuals. It was concluded that ANP lowered parameters of sympathetic nervous activity but had no significant effects on indicators of parasympathetic nervous activity (Butler *et al*., 1994). It should also be noted that the response derived from the stimulation of these peptides has been shown to regulate endothelial function through vasodilatory properties (Luchner and Schunkert, 2004). As such, the significantly greater reduction of TPR in the IWS condition may be related to the secretion of these peptides. However, more research is needed to determine whether these peptides have any influence on cardiac autonomics during IE.

The effects of exercise on circulating catecholamine (adrenaline and noradrenaline) release should also not be overlooked when comparing the acute responses following IWS and IHG exercise. Exercise induces a rise in catecholamines that is observed across a wide range of exercise modalities (Christensen & Brandsborg 1973, Galbo *et al*., 1975, Vecht *et al*., 1978, Hickson *et al*., 1979). For example, Watson *et al*., (1980) showed an increase in plasma catecholamine during a lower limb unilateral IE contraction of the

quadricep. Studies have shown that both adrenaline and noradrenaline are involved in cardiovascular modulation, and the secretion of these hormones are positively related to increases in HR (Zouhal *et al*., 2008). Therefore, it is conceivable that catecholamine secretion was greater during IWS exercise in the current study, which may have been influential on the significantly greater CV response observed.

Isolated muscle contractions during IE typically result in an increased sympathetically modulation vasoconstriction and hyperaemia to the working muscle (Lawrence *et al.,* 2015). In the current study there was also significantly less TPR during IWS exercise. The decreased TPR during successive bouts of IWS suggests that there was increased arterial dilation. Taylor *et al*., (2017) also found TPR was significantly decreased during IWS exercise and argued that there may have been a more dominant vascular response that could have overridden any sympathetically modulation venous compliance. It may be that there were a number of peripheral and vascular mechanisms that influenced TPR, such as increased concentrations of adenosine triphosphate (ATP) and nitric oxide (NO) and other potential vasodilators that downregulated the release of noradrenaline produced by sympathetic activation (Taylor et al., 2017). It could be argued that this potential downregulation may have influenced efferent pathways and subsequent LF oscillations during IWS. However, this is only speculative and requires further research.

4.3 Additional findings

Aside from a greater recruitment of muscle mass and the subsequently greater pressor response, one theory that has not yet been explored to explain the greater CV response during IWS exercise is the location of the occluded musculature. It has been shown that using blood flow restriction during exercise expedites fatigue in the areas distal to the occluded muscles (Jessee *et al*., 2018). This works by reducing arterial flow and occluding venous flow, resulting in a pooling of blood and metabolites distal to the cuff position when exercising (Yasuda *et al*., 2010). As such, although the occlusion may be greater during the IHG, there are no major muscles affected in the areas distal to the forearm and hand. Conversely, the IWS, which predominately uses the quadriceps, has the lower leg muscles, such as the gastrocnemius and the soleus, in its distal periphery, which are arguably more indispensable. Therefore, during IWS exercise, in an attempt to alleviate any distal fatigue in areas distal to the occluded muscles, the body will try to ensure that adequate blood flow is maintained, either through an increased $\dot{Q}$ or a decrease in occlusion at the quadricep (reduced TPR). Conversely, it could be that the areas distal to the occluded quadricep during IWS exercise do have a restricted blood flow, which stimulates afferent fibres in these areas, inducing an increased CV response. Further research is needed to investigate the influence that the location of occlusion has on the CV response during IE.

Another interesting finding in the current study is in relation to the rate of BP elevations during IWS. Previous research has shown a single 2-min bout of unilateral IHG exercise produced a greater increase in sBP (Stewart *et al*., 2007; Garg *et al*., 2013) than IWS exercise in the study by Taylor *et al*., (2017). Conversely, the current study found that in the IWS condition, sBP was significantly higher during the first 2-min bout than the IHG condition - and also remained higher throughout all successive bouts. The study by Taylor *et al*., (2017) only observed an increase in sBP of 8.9 mmHg during the first bout of IWS, compared to the much larger increase of 38 mmHg in the current study. One potential explanation for the blunted BP increase during the first bout of IWS in the study by Taylor *et al*., (2017) compared to the current study may be related to the different baseline resting protocols used. The current study measured baseline resting measures using 5 min of supine rest followed by 5 min of seated rest, whereas Taylor *et al*., (2017) only utilised 5 min of supine rest. Taylor *et al*., (2017) acknowledged that a change in posture and subsequent gravitational stress may influence cardiovascular haemodynamics and remarked that the pattern of the haemodynamic response may differ if using a seated or upright position (Taylor *et al*., 2017). It has been suggested that there may be a transient decrease in BP seen when humans stand up (Secher, 2007). Indeed, Sprangers *et al*., (1991) found that moving from a supine to standing position elicited a transient 25% fall in mBP as a result of a 36% fall in TPR, and therefore utilising a seated resting position prior to standing up for the IWS may eliminate any hypotensive responses when going straight from supine to standing.

This finding suggests that the resting protocol in the Taylor *et al*., (2017) study with no additional 5 min of seated rest may have influenced the reactivity of the cardiovascular system prior to exercise which translates to an attenuated BP response in bout 1 resulting in a more gradual increase over the 4 bouts. Another reason the different patterns in BP responses between Taylor *et al*., (2017) and the current study may be related to orthostatic stress which occurs during periods of seated rest (de Brito *et al*., 2019). Orthostatic stress results in a shift of blood away from the chest towards the distensible venous capacitance system below the diaphragm; commonly referred to as venous pooling (Wieling and Groothuis, 2012). This pooling reduces the volume of blood available to the cardiac ventricles which reduces arterial BP unless compensatory adjustments are made, such as an increase in muscle sympathetic nerve activity. It is thought that this increase in sympathetic activity is a result of the inhibition of the cardiopulmonary reflex due to the venous pooling (Gibbons and Freeman, 2012). As such, it could be argued that this increase in sympathetic outflow at the onset of IE may help prime the body, resulting in a sharper rise in CV parameters. Nonetheless, the current study used a normotensive population with both male and females compared to the all-male pre-hypertensive population used by Taylor *et al*., (2017), which may have altered the patterns of BP elevations. For example, Wong *et al*., (2007) found that women had smaller increases in HR and BP than men at the onset of IHG exercise, and

suggested it could be a result of differential neural activation in several forebrain sites associated with autonomic regulation.

4.4 Post IE

As hypothesised, this exaggerated response led to a significantly greater transient drop in sBP, dBP, and mBP during the 10-min recovery period post exercise than in the IHG condition. This finding also supports previous work by Taylor *et al*., (2017) and O'Driscoll *et al*., (2017) who, amongst pre-hypertensive participants, also found similar results in a 5-min recovery window following an acute bout of IWS exercise. Likewise, the relatively small reductions induced in the IHG condition in the current study are similar to those found by Millar *et al*., (2009) who only found a significant drop of 3 mmHg in sBP amongst a normotensive cohort following 4x2-min bouts of IHG exercise at 30% MVC; albeit bilateral IHG.

Short-term responses after acute IE have been shown to play an important role in chronic BP adaptations following an IE training programme (Liu *et al*., 2012; Farah *et al*., 2017; Somani *et al*., 2017). Inder *et al*., (2016) argued that upper body IHG exercise leads to repeated bouts of hypoxia in the forearm, ultimately causing alterations in arterial stiffness, resulting in greater chronic BP reductions when compared to lower limb IE. However, the significantly greater PEH response in the IWS condition may represent a greater potentiality for chronic BP reductions following lower limb IWS training, which may be related to the larger muscle mass recruitment and pressor response.

Although the mechanisms responsible for the BP adaptations seen with IE training remain unclear, according to Ohms law it can be said that BP reductions are a result of either altered modulation of $\dot{Q}$, TPR, or both (Millar *et al*., 2014). As the current study did not find any significant differences between conditions for $\dot{Q}$ during the 10-min recovery, it is likely that any reductions were mainly influenced through alterations in peripheral resistance.

During recovery, TPR was significantly lower in the IWS condition. This response corresponds with the findings from Taylor *et al*., (2017) who found TPR was significantly reduced following IWS exercise. Taylor *et al*., (2017) remarked that changes in post exercise TPR may be associated with a significant increase in parasympathetic activity. However, during recovery in the current study, there were no differences in HF oscillations parameters between conditions; although it must be noted that HFnu was above baseline in both conditions.

There was also a significantly greater PSD-RRI during the 10-min recovery following IHG, which represents a better recovery from exercise. In fact, PSD-RRI did not return to baseline during the 10-min recovery window in the IWS condition, which may be related to a higher intensity during IWS exercise

compared to IHG. This finding supports previous research that has suggested high intensity exercise can impair immediate post-exercise HRV recovery (Buchheit *et al*., 2007; Kaikkonen *et al*., 2008; Kaikkonen *et al*., 2010). The current study also found no differences between conditions for BRS. In fact, BRS stayed below baseline during the 10-min recovery window. It is thought that the PEH following IE may be related the baroreceptors resetting to a lower operating range with an increased sensitivity (Taylor *et al*., 2017). However, the current study found no differences between conditions for BRS, or any autonomic variables, which may suggest that reductions in TPR following IWS exercise were not primarily substantiated through autonomic modulation and may have been facilitated through more peripherally originated mechanisms.

The evidenced reductions in TPR may be related to SS. Hyperaemia and BP can induce vessels to stretch under different biological or physical mechanisms. An increase in blood flow results in vasodilation, while an increase in BP causes mechanical distension (Lu and Kassab, 2011). The primary mediator in a flow-mediated dilatory SS response is NO, which is generated from endothelial NO synthase (Ignarro *et al*., 1987; Huang *et al*., 1995). One of the main mechanisms for the increases in circumferential stretch is alterations in vascular tone (Birukova *et al*., 2006). As there were no differences in parasympathetic activation post exercise, this may signify that the flow-mediated response was the more dominant mechanistic pathway associated with the evidenced differences between IWS and IHG exercise.

Nonetheless, previous research has argued that the brachial artery is more sensitive to SS associated dilatory adaptations than the CFA. Walther *et al.*, (2008) has argued that there is little evidence to support SS induced adaptation in the CFA and suggests this may be due to a reduced ability in the CFA to dilate in response to a SS stimulus (Walther *et al.*, 2008). The base of this argument was founded on the assumption that the threshold for the femoral artery to become occluded during IWS is much greater than the occlusive capacity of the brachial artery due to the latter's smaller diameter (Inder *et al*., 2016). Indeed, vessels with the same diameter will be exposed to equivalent increases in flow and SS. However, occluded vessels with a smaller diameter will be affected substantially more by levels of SS. This leads to not only morphological changes of endothelium and blood vessel wall, but can also result in biochemical and biological events (Lu and Kassab, 2011).

The latter argument has some prevalence in the current study, in that TPR was significantly higher during IHG2, IHG3, and IHG4, potentially signifying a greater level of occlusion. Indeed, higher levels of SS caused by an increased level of occlusion during IHG exercise may lead to higher levels of local circumferential wall stress (Lu and Kassab, 2011). However, the increased blood flow during IWS exercise, evidenced by the greater $\dot{Q}$ response, along with an increased pressor response arising from the increase BP, may have stimulated a greater relative post-exercise vascular response. Indeed, as previously

discussed, during IWS exercise, Taylor *et al*., (2017) argued that arterial dilatation occurs and that the release of sympathetic neurotransmitters may be superseded by a more dominant vascular reaction. Taylor *et al*., (2017) also remarked that only the working muscles receive hyperaemic blood flow during IE and the extent of the hyperaemic response is muscle mass dependent (Taylor *et al*., 2017). Therefore, it could be argued that due to the greater muscular recruitment in the IWS exercise, there is a larger surface area of vasculature exposed to hyperaemic blood flow, thus increasing the overall exposure to SS.

Studies have also shown that exercise can enhance vascular function beyond the active regions (Linke *et al*., 2001; Green, 2005). For example, Thijssen *et al*., (2013) showed that dynamic leg cycling caused systemic arterial wall adaptations due to increase blood flow, resulting in enhanced arterial vessel compliance and a decrease in TPR. Moreover, Birk *et al*., (2012) found that amongst health participants, lower limb cycle exercise evoked a transient increase in upper limb vascular function, and suggested that this response was mediated, at least partly, via SS. Indeed, the increased blood flow and BP during IWS exercise may have subsequently increased systemic levels of frictional and circumferential SS (Lu and Kassab, 2011).

This study was the first of its type to compare the haemodynamic and autonomic responses 1-hour following an acute bout of IWS and IHG exercise. The duration of PEH is important to reveal whether the acute responses can have a clinical impact reducing the subject's CV load and risk for a long period of time (de Brito *et al*., 2019). Data from the current study showed no significant differences between conditions in any parameters 1-hour post exercise. Thus, although some evidence exists to support a relation between the length of the PEH response and the intensity and duration of the exercise stimulus (Seals and Kenney, 1993), this has not been demonstrated in the current study. Nevertheless, all BP parameters for both conditions did remain below baseline 1-hour post exercise. One interesting finding that is worth mentioning is the trend for a greater reduction 1-hour post than during the 10-min recovery for the IHG condition. All BP measurements in the IHG condition continued to decline, whereas the IWS reductions were returning to baseline; although the magnitude of reductions was still greater in the IWS condition 1-hour post. Although comparisons are difficult to make, this contrasts the findings by Goessler *et al*., (2016) who found that bilateral IHG at 30% MVC evoked no transient reductions in BP amongst a cohort of hypertensives 5-min or 1-hour post exercise. More research is needed to understand the differences in the duration and magnitude of PEH following an acute bout of IWS and IHG exercise.

4.5 Practical application

The practical application of these findings may provide health care professionals and practitioners with guidance on the more effective protocol to reduce resting BP. Indeed, it has been suggested that chronic adaptations may result from temporal summation of acute responses (Farah *et al*., 2017) and that the

magnitude of PEH following an acute bout of exercise may predict the extent of BP reductions following a chronic intervention (Liu *et al*., 2012). As such, it could be argued that due to the greater PEH experienced following an acute bout of IWS exercise, chronic reductions following an IWS training programme would be greater than following an IHG training programme. However, amongst normotensive populations, reductions following IWS and IHG training programmes have been similar (Kelley and Kelley, 2010; Wiles *et al*., 2017; Taylor *et al*., 2019). A follow up intervention would be ideal to investigate any links between acute responses and long-term adaptions following IWS and IHG training.

Another practical finding from the current study is in relation to the significant differences found in RPE data between the IWS and IHG conditions. As the intensities were methodically different in their setup, 95% HR_{peak} vs. 30% MVC, and due to the contrasting contraction types, constant position vs. constant tension, it could be argued that the relative intensity in the IWS had a greater capacity to influence changes in CV parameters. Interestingly, Wiles *et al*., (2010) found that IWS exercise prescribed at 95% HR_{peak} was relative to approx. 22% MVC during ILE. This may suggest that even though the intensity was lower during IWS exercise when adjusting to MVC, the stimulus was still greater, potentially due to the larger muscle mass recruitment. However, MVC during ILE does not directly relate to MVC during IHG exercise, and thus comparisons are difficult to make. However, as previously discussed, RPE was higher during IHG3 and IHG4. Therefore, in many ways the intensity/stimulus was greater during IWS, yet the perceived exertion was lower. Furthermore, four participants failed to maintain the unilateral IHG contraction within approx. 10% of the 30% MVC threshold. This is important and may have health/clinical implications surrounding future IE prescription. The primary aim for the collection of RPE data was to ascertain any correlations between exertion and changes in CV parameters. However, from a prescriptive perspective, the RPE data suggests that participants may prefer IWS exercise due to less perceived exertion. This finding warrants future research from a qualitative perspective.

Notwithstanding the above, it must be acknowledged that although the IHG condition evoked significantly less PEH than the IWS condition, there was also significantly less myocardial load. Data from the current study shows that RPP was significantly lower in the IHG condition, suggesting that IHG exercise does not elicit the same level of CV stress as IWS exercise. However, Inder *et al*., (2016) suggests that IE per se does not elicit the same level of CV stress as aerobic activity. Indeed, when comparing the RPP data during IWS in the current study (18,188 ± 4829 beats min^{-1} mmHg) to an aerobic intervention (32,837 ± 2251 beats min^{-1} mmHg), it is arguably much less (Maiorana, *et al*., 2002).

A study by Wiles *et al*., (2018) investigating the safety of IWS exercise also evoked similar RPP values (18074 ± 3209 beats min^{-1} mmHg) using a hypertensive population during an acute bout of IWS. The study showed that IWS exercise was safe amongst a hypertensive cohort by comparing BP values induced

during IWS exercise to the current ACSM guidelines for aerobic exercise termination. Some participants (12/26) exceeded the 115 mm Hg threshold for dBP, whereas no participants had sBP values outside of the 250 mmHg guidelines. The same findings were prevalent in the current study, in which 14 out of 26 participants exceeded the dBP threshold, but none exceeded the sBP limit. Wiles *et al*., (2018) suggested the need to individualise IE training prescription with participants that have suboptimal BP control. For participants with suboptimal BP control, IHG may be a more appropriate first step in the treatment process, with IWS treatment being a prospective modality based on reasonable improvement in cardiovascular reactivity. Indeed, all good training programmes will have an element of progressive overload, with a variety of exercises (Hass, Feigenbaum and Franklin, 2001). Moreover, when factoring in the sustainability of IE prescription, and the fact that drop-out rates during resistance exercise programmes have been reported to be around 22–38% (Zech *et al*., 2012; Ericsson *et al*., 2016), it is important to acknowledge that an increased variety of exercises available will enhance the overall application of IE to the wider population (Geirsdottir *et al*., 2017). Therefore, a more holistic outlook of the findings from the current study is that data collected from both conditions can enhance our understanding of the comparative acute responses from a variety of isometric modalities, enhancing the overall applicability of IE prescription.

The application of these findings can also be representative of a more heterogenous population. The finding that IWS can produce greater transient reductions in BP amongst both men and women expands on previous research who have used a male cohort (O'Driscoll *et al*., 2017; Taylor *et al*., 2017). Although exploring sex differences was not a primary aim of this study, previous research has demonstrated that there are differences between males and females in the acute recovery from IHG. For example, an increased BRS during exercise, and a reduced HR in recovery for females, which may be related to female sex hormones (Teixeira *et al*., 2017). However, future studies are needed to ascertain the difference haemodynamic and autonomic responses between males and females following IWS and IHG exercise.

It should also be recognised that using an additional 5-min seated rest in the current study enhances the generalisability of the results. Although the supine position favours haemodynamic measurements without the orthostatic stress inferring (Gotshall *et al*., 1994), it may decrease the real-world application of the findings as outside of research studies, as individuals are less likely to start exercise and recover from exercise in the supine position. On the other hand, an additional seated position may be more appropriate as a person may be more likely to sit and talk before or after exercise (de Brito *et al*., 2019).

4.6 Limitations

This study is not without limitations, most notably the robustness of cardiac autonomic data. It has been suggested that changes in HRV can be influenced by respiratory rates. A selection of studies that have investigated HRV during dynamic exercise have found similar results to the current study, in that at peak exercise intensity (indicative of an elevated HR), HF components become more dominant over the LF, technically signifying a greater parasympathetic response (Bernardi *et al*., 1990; Casadei *et al*., 1995; Casadei *et al*., 1996; Pichon *et al*., 2004). One potential argument put forward is that the predominance of HFnu relates to the respiratory sinus arrhythmia that occurs in response to an increase in the oscillations of venous input to the heart, due to increasing tidal pressure and volumes (Bernardi *et al*., 1990; De Meersman, 1992; Casadei *et al*., 1996; Keselbrener and Akselrod, 1996). Another potential mechanism put forward suggests that the increased stretch of the atrial wall, due to the increased changes in intrathoracic pressure, may influence the HF component during strenuous exercise (Bernardi *et al*., 1990).

The theory that respiratory parameters can alter HR and R–R interval variability independent of changes in cardiac autonomic regulation is commonly cited throughout the literature (Angelone and Coulter, 1964; Davies and Neilson, 1967; Hainsworth, 1974; Melcher, 1976; Hirsch and Bishop, 1981; Brown *et al*., 1993; Van De Borne *et al*., 2001). Although no study has compared the respiratory rates between the two modalities, isometric and dynamic exercises are considered with different physiological characteristics, and it would be assumed that continuous dynamic exercise respiratory rates would be significantly higher. Nevertheless, the current study did not investigate respiratory rates, and therefore any associations are difficult to justify. However, it must be noted that Iellamo *et al*., (1999) found increases in respiratory rates were minimal during ILE, amounting to approx. 2 breaths/min, which would arguably have very little influence on HF alterations.

Another potential limitation concerns the use of single pre–post measurements of resting BP. It is conceivable that BP readings could be exaggerated at the onset of a study due as undertaking a novel laboratory or training setting may lead to nervousness or excitement. As such, resting BP may have experienced a normal reduction (e.g. regression to the mean) and the observed pre–post effects may be misleadingly pronounced. Consequently, potential errors in the pre-study and post-study BP measurements make it hard to determine any training effects and may contribute to false negative and positive results (Millar *et al*., 2007). However, the methodology used to record resting measures has been shown to be reliable at rest, giving confidence that any changes measured from baseline can be attributed to IE (Taylor *et al*., 2017). Furthermore, it has been suggested that where PEH is a primary outcome, at least two familiarisation sessions should be used in accordance with reliability and

familiarisation studies (Rosner and Polk, 1981; Stolt *et al*., 1990). The current study used two familiarisation sessions, one for baseline BP to gauge suitability for the study, and one for the incremental IWS test and IHG MVC test, which strengthens the opposition to this potential pre-post limitation.

4.7 Conclusion

The results of the current study are the first to demonstrate that IWS exercise results in greater PEH than IHG exercise using a repeated measures crossover design. The study found a greater Δ increase in HR and BP during IWS exercise, resulting in a greater Δ reduction in TPR post exercise, potentially stimulated through peripheral vasodilatory mechanisms. This may be explained by more muscle mass being recruited during IWS exercise. However, there are a number of practical benefits for both IWS and IHG exercise potentiated in this study, such as a greater potential for BP reductions following IWS exercise, but less myocardial load during IHG exercise. Future research is needed to ascertain any associations between these acute responses and long-term training adaptions.

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