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Comparison of two isometric handgrip protocols on sympathetic arousal in women

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HIGHLIGHTS

- Isometric handgrip is used in stress research because it increases arousal.
- We tested if two different handgrip tasks elicited similar arousal changes.
- Pupil dilation increased significantly to handgrip only in the 18-s protocol.
- The 18-s paradigm should induce arousal, regardless of experiment parameters.

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ABSTRACT

Isometric handgrip is commonly used in stress research because the task reliably increases sympathetic arousal. Various handgrip protocols have been used; they vary in handgrip strength, duration of grip, and the number of cycles of handgrip and rest. However, most protocols require the calibration of a maximum voluntary contraction (MVC) prior to the handgrip task, which is not always convenient (i.e., in a functional magnetic resonance imaging study). Here, we wanted to test whether two handgrip protocols with different strength, duration and cycle protocols would reliably elicit sympathetic arousal in the absence of calibrating an MVC. Sixty-two healthy naturally cycling women and women on hormonal contraception participated in one of the two isometric handgrip protocols using a hand therapy ball of medium resistance. Women completed one of the following handgrip protocols: 1) 30% of a perceived maximum voluntary contraction for 3 min or 2) 3 cycles of maximum voluntary contraction for 18 s with a one minute rest in between. All handgrip blocks were counterbalanced with a control condition. Sympathetic arousal was measured throughout the session via pupil diameter changes and salivary alpha-amylase. Results indicate that in the absence of calibrating an MVC, the handgrip tasks elicited different changes in sympathetic arousal. Pupil dilation responses increased significantly in the handgrip versus control blocks only in participants in the 18-s protocol. Additionally, more participants exhibited a salivary alpha-amylase response to the handgrip block in the 18-s condition compared to the 3-min condition. Thus, these results suggest that neuroimaging and behavioral studies with isometric handgrip should be able to successfully induce sympathetic nervous activity with the 18-s paradigm, regardless of the handgrip device and the ability to calibrate an MVC.

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1. Introduction

For decades, researchers have used isometric handgrip, a form of static exercise, to investigate the cardiovascular response to stress [1]. Isometric handgrip acts as pressor stimulus to the cardiovascular system through efferent sympathetic pathways [2], and it tends to increase arterial blood pressure and heart rate [3]. Researchers typically employ isometric handgrip to test cardiovascular responses to stress; however, it can also be used to investigate the underlying mechanisms of sympathetic nervous activity [3].

In studies of sympathetic nervous activity, the most common handgrip paradigm is a 3-min task [4] that implements the use of a dynamometer, a special device that quantitatively assesses hand muscle strength. In the 3-min paradigm, participants are first asked to maximally squeeze a hand-held dynamometer several times to determine their average maximum voluntary contraction (MVC). After the MVC is calibrated, participants maintain handgrip pressure on the dynamometer at 30–40% of their MVC for 3 min [4] or until they are too fatigued to continue [5]. Throughout the task, they receive constant feedback about the strength of their sustained handgrip. Although the duration of the

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task is short, studies have shown task-related increases in sympathetic nervous activity [5–10].

More recent studies with handgrip, namely those with neuroimaging, have modified the widely used 3-min 30% of MVC task. Instead, participants are asked to squeeze maximally for short periods of time [11–13]; squeeze periods are followed by rest periods. Topolovec and colleagues (2004) showed that not only was the 18 s maximum squeeze/60 s rest paradigm successful at inducing sympathetic nervous activity, but neuroimaging data from the study suggests that the underlying neural mechanism involves the nucleus of the solitary tract, which innervates the locus coeruleus, a major noradrenergic nucleus [14]. Thus, even though these maximal squeeze paradigms are relatively new, they seem to induce sympathetic arousal as well. Additionally, maximal squeeze paradigms can be run without the use of a dynamometer. For example, studies have used a cylinder [11–13] or a pressure transducer [13] for their hand grip task. In any case, it would seem that maximal squeezes can be done without the feedback component of the dynamometer.

Although both the 18-s and 3-min paradigms have been used in previous research studies, no studies have assessed how sympathetic responses might differ between them or whether all isometric handgrip tasks effectively increase sympathetic nervous activity, even in the absence of calibrating an MVC. Given that the effort involved in maximal intermittent static exercise is greater than the effort involved in sustained static exercise at 30% of maximal exertion, one might expect that the 18-s task induces greater sympathetic arousal.

Isometric handgrip reliably increases plasma norepinephrine [8, 15–19], but no studies with the 18-s or 3-min paradigms have examined pupil dilation responses or salivary alpha-amylase as indices of arousal, despite the fact that these are widely used non-invasive measures of noradrenergic activity [20,21]. The only study to use pupil dilation as an index of arousal used a paradigm with 2-min of isometric handgrip at 30% of maximal exertion; results showed increased pupil dilation to the handgrip task [9].

Thus, the present study was designed to address several unexplored aspects of isometric handgrip. First, we wanted to assess whether different isometric hand grip paradigms would successfully increase sympathetic nervous activity in the absence of calibrating an MVC. In theory, any of the isometric hand grip tasks should be able to increase sympathetic nervous activity even without calibrating a maximum voluntary contraction; sympathetic arousal during either the 3-min perceived 30% of MVC (3-min) or the shorter 18-s MVC (18-s) should still be possible.

Therefore, we hypothesized that the 3-min and the 18-s paradigms would both induce increases on different measures of sympathetic arousal; however, we also predicted that the 18-s paradigm would induce greater arousal than the 3-min paradigm. For the current study, we assessed changes on a previously used measure (pupil dilation) and a new measure, salivary alpha-amylase. Salivary alpha-amylase (sAA) is a known biomarker for norepinephrine, as changes in sAA correlate with changes in plasma norepinephrine [21]. It has been used in previous studies of sympathetic arousal [22–26], and seemed well-suited to measure sympathetic arousal during isometric handgrip.

Secondly, we wanted to assess the relationship between pupil dilation and sAA responses to isometric handgrip. Since previous work with isometric handgrip has shown that changes on different sympathetic measures are of similar magnitude and are in the same direction, we predicted that an increase in the pupil dilation response during handgrip would predict an increase in sAA. We also predicted that sAA responders (see Section 2) would exhibit greater pupil dilation responses to handgrip.

Lastly, we wanted to assess whether hormonal contraception use altered sympathetic responses to isometric handgrip. To date, no studies of isometric handgrip have explored the potential effects of hormonal contraception use on sympathetic nervous activity. Previous studies of sympathetic arousal have shown that women on hormonal contraception exhibit blunted noradrenergic responses to exercise [27] and arousing images [25] compared with naturally cycling women. Thus, insofar as the two groups of women in our study exhibited significantly different sex steroid hormone profiles, we predicted that women on hormonal contraception would show blunted noradrenergic responses to both hand grip tasks compared to naturally cycling women.

2. Materials and methods

2.1. Participants

Sixty-two female undergraduates from the University of Southern California between the ages of 18–34 participated in this study, which was approved by the university's Institutional Review Board. The participants received course credit or payment for their participation. Participants were asked to refrain from alcohol, caffeine, and cardiovascular exercise for twenty-four hours prior to each experimental session to control for outside influences that could affect baseline salivary alpha-amylase levels. To avoid contamination of salivary samples, participants were asked to fast 1 h prior to each experimental session as well as refrain from brushing teeth and chewing gum within the hour before their appointment. Their compliance with these criteria was confirmed with them upon their arrival.

Of the participants included in the final analyses, 42 were naturally cycling (NC women) and 20 were currently taking hormonal contraception (HC women). The NC women were recruited in the "follicular" phase (1–15 days from the start of menstruation) and the "luteal" phase of the menstrual cycle (15–30 days from the start of menstruation [28–31]). We used a forward day count from the first day of menstruation to determine menstrual cycle position. Of the HC women, all participants were on combined contraceptive formulations that had both ethinyl estradiol and a synthetic progestin; 3 HC women reported using triphasic formulations, 16 used monophasic formulations, and one participant's contraceptive phasicity was not reported.

2.2. Procedures

All experimental sessions were conducted between the hours of 12:00 and 18:00 to control for the effects of circadian rhythm on stress hormone levels. Upon arrival, participants rinsed their mouth by drinking an 8 oz. bottle of water; they also completed a demographic information packet. Approximately 10 min after their arrival, participants provided a 1-mL saliva sample using the "passive drool" collection method. Following the baseline saliva sample, participants completed a 5-pt. calibration on the iView X RED eye-tracking system (SensoMotoric Instruments). After successful calibration, participants were randomly assigned to one of five conditions for their first experiment block: 1) 3-min handgrip, 2) 18-s handgrip, 3) 3-min water bottle fingertip rest (control), 4) 18-s control, or 5) 3-min control. The five conditions were created to counterbalance the order of handgrip and control tasks across participants. Isometric handgrip tasks were completed with a hand therapy exercise ball of medium resistance (Gaiam), and the water bottle fingertip rest task was performed using an 8 oz. empty water bottle. All participants we asked to use their right hand for the isometric handgrip and control tasks. This was done to maintain consistency across the participants and to generate a paradigm that would easily translate into a neuroimaging study; fMRI studies with isometric handgrip have followed this hand protocol to aid in interpretation of neuroimaging data [12,32].

In each condition, participants were presented with a grayscale screen, and in the center of the screen was either a yellow or a blue circle (normed for luminance). During the yellow circle "rest" periods, participants were asked to rest and relax while maintaining their gaze on the screen. During the blue circle "squeeze" periods, participants were asked to either squeeze the hand therapy exercise ball at 30–40% of their perceived maximum grip for 3-min, maximally for three 18 s squeeze/60 s rest cycles, or they were asked to gently rest their fingertips on an empty water bottle. All conditions started with a 10-s yellow