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HEMODYNAMIC FUNCTION DURING FINGER FORCE PRODUCTION TASKS IN HEALTHY ADULTS

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Abstract

Introduction: Near-infrared spectroscopy (NIRS) is a non-invasive technique utilized to measure muscle hemodynamics. The focus of this study was to evaluate changes in muscle oxygenation during sustained maximal force production in young, healthy control individuals to establish baseline function in an ideal population.

Methods: NIRS was used to monitor reduced hemoglobin (HbR) and oxygenated hemoglobin (HbO) in forearm muscles. Hemodynamic responses during force production tasks were monitored in real time.

Results: During handgrip exercises, maximal force production declined significantly. Increased HbR was found while HbO remained constant. The correlation between force production and HbO was positive ($r=0.18$), while the correlation between force and HbR was negative ($r=-0.48$).

Discussion: The application of NIRS to monitor the correlation between force production and hemodynamic measures in the forearm was successful. These data set the foundation for future use of NIRS as a diagnostic tool for individuals with peripheral vascular disease.

Keywords

hemodynamic function; near infrared spectroscopy; muscle; forearm; hand; finger

Introduction

Muscle oximetry is a method utilized to measure hemodynamic function of muscles without the need for a blood sample. Near-infrared spectroscopy (NIRS) is a relatively inexpensive and noninvasive oximetry technique that can be used to monitor muscle and neural metabolism. The NIRS technique allows for monitoring of tissue oxygenation in real time and has been utilized to monitor oxygenation levels of various muscles and cerebral tissue^{1,2}. NIRS has been shown to be a reliable and valid technique for continuous

monitoring of hemodynamic function during muscle contraction. It has been established as a credible tool for measuring muscle metabolism in extrinsic hand muscles during handgrip exercises^{3,4}. This approach has also been validated via test-retest reliability when testing forearm muscles³. Further, MasoudiMotlagh et al.⁵ observed no significant differences between dominant and non-dominant muscles in healthy individuals. Thus, any differences observed in muscle NIRS in patient populations is most likely attributed to pathological conditions such as hemiparesis or neuropathy rather than hand dominance.

A long-term interest in our lab is investigation of future application of this technology to study muscle changes in patients with Type II diabetes due to the microvascular complications associated with the disease. The NIRS apparatus may provide an affordable way to detect and monitor muscle changes in patients with diabetes as well as individuals at risk for Type II diabetes or other cardiovascular disease (CVD). Measuring muscle function during hand motor tasks in adults with diabetes will be a major step in linking motor changes and muscle metabolism in CVD, however several aspects of our experimental approach need to be tested on young healthy control individuals to establish baseline function in an ideal population.

Thus, the focus of this study was to evaluate changes in muscle oxygenation and features of kinetic performance during sustained maximal grip and pinch force production. We expected to see changes in muscle oxygenation indices such as oxygenated hemoglobin (HbO) and deoxygenated or reduced hemoglobin (HbR) in hand/finger extrinsic muscles during a sustained maximal force production task (Hypothesis #1). Given the sustained contraction, we expected to see declines in force produced between the onset and end of each trial (Hypothesis #2); however, we did not expect to see task-specific changes in the structure of force variability nor hemodynamic variability in this healthy population (Hypothesis #3). *A priori*, we suspected that changes in muscle oxygenation indices may correlate with force production changes during the task, however the direction of these correlations was not initially predicted.

Materials and Methods

Participants

Eleven young healthy individuals (20 ± 2 years; 5 men and 6 women) volunteered to participate in the study. The average height and weight were 1.66 ± 0.09 m and 62.1 ± 10.4 kg. Average blood pressure was 108 ± 13 / 70 ± 11 mm Hg, measured via a commercially available device (Omron BP785Intellisense Automatic Blood Pressure Monitor, Omron, Bannockburn, IL, USA). Handedness was assessed by the Edinburgh Inventory⁶, ranging from a laterality quotient (LQ) of -100 (strong left-handedness) to $+100$ (strong right-handedness). All subjects were strongly right-handed (LQ average = $+76$) and had no previous history of trauma to the upper limbs. Study participants were excluded if they reported a history of neurological and/or musculoskeletal disorders (Parkinson disease, Huntington's disease, polio, multiple sclerosis, stroke, traumatic brain injury, carpal tunnel syndrome, rheumatoid arthritis, Monoclonal Gammopathy of Undetermined Significance (MGUS), Paraproteinaemic Demyelinating Neuropathy (PDN), Myasthenia Gravis, Raynaud's Syndrome, Lyme disease, Scleroderma, a history of chemotherapy treatments,

limb amputation, cardiovascular and/or peripheral vascular disease, or hereditary or compression neuropathies. In accordance with the Declaration of Helsinki, participants provided informed consent according to the regulations established by the Committee for the Protection of Human Subjects at the University of Houston.

Sensory Evaluations

The Semmes-Weinstein monofilament test was used to evaluate tactile sensation of the dominant hand⁷. Monofilament testing sites included: tip of the thumb/digit 1 (median nerve) and the tip of digit 5 (ulnar nerve). During the test, participants kept their eyes closed and verbally indicated if and where they perceived monofilament touch. The monofilament size was increased until the subject was able to detect its touch a minimum of 2 times at the same location. These data collected on healthy controls serve as a reference for future studies involving patient populations.

NIRS Placement & Measurement

To measure hemodynamic function, we used an NIRS sensor measuring changes in concentrations of HbO and HbR of the flexor digitorum superficialis (FDS) muscle. NIRS is an optical technique in which light in the near-infrared wavelength range (650–1000 nm) is shone into tissues using low-power emitters [laser emitting diodes (LEDs)], and, after being partially absorbed by HbO and HbR and partially back-scattered to the skin surface by the tissue structure, is detected at a certain distance using a photodetector. Since HbO and HbR are the primary light absorbers in the NIR bandwidth, the photodetected intensity is strictly related to tissue oxygenation and, over time to the hemodynamic activity occurring in the volume of tissue through which the light travels. Different absorption spectra of HbO and HbR as a function of wavelength allow one to discriminate the contribution to overall light absorption of each chromophore, which in turn depend on their individual concentrations according to the modified Beer-Lambert Law⁸.

The custom-designed NIRS apparatus we used was previously described⁹. Briefly, the NIRS probe consisted of 3 laser diodes emitting at 685nm, 830nm, and 980nm and a photodetector located 30mm away from the diodes. The light emitters were activated sequentially (i.e., time-multiplexed) to avoid any crosstalk between different wavelengths. Such an optical layout is estimated to probe tissues at an average of 13–15mm¹⁰, thus sufficient to investigate the FDS muscle during exertion of force production tasks. Previous publications have indicated similar devices (e.g. 30mm separation distances) as appropriate for hemodynamic analysis of the FDS^{11,12}. The 3-wavelength scheme including the peak optical absorption of water in the near-infrared spectrum (i.e., 980nm) enabled estimation of stoichiometric concentration of HbO and HbR⁹. Muscle oxygenation measurements were acquired at 50Hz before, during, and after the force production tasks. Muscle oxygenation measurements are reported in micromolar (μ M).

The optical probe was placed on the dominant forearm of each subject, directly over the radial aspect of the FDS muscle. The probe emitter and detector were aligned with the estimated line of action of the FDS, as determined by palpation of the muscle during repeated flexion of the fingers (Fig. 1A–B). Palpation of wrist flexors near the elbow was

also performed. Placement of the probe distal to superficial wrist flexors was performed to avoid signal contamination. The probe was lightly, yet securely, attached to the forearm of the subject using a self-adherent wrap (Coban, 3M, St. Paul, MN, USA) (Fig. 1C). The measurement site was covered with a black cloth to prevent light contamination from the testing environment. Prior to the application of the probe, the depth of the subcutaneous fat layer was measured over the radial aspect of the FDS belly using a commercial skinfold caliper (Slim Guide, Creative Health Products, Ann Arbor, MI, USA). The average forearm fat layer in study participants was 2.8 ± 0.5 mm. This particular oximeter device used a software algorithm to adjust the HbO and HbR readings to account for the thickness of the fat layer¹³. In order to prevent compression of the NIRS probe into the forearm, participants sat with their dominant forearms completely supported in the supine position by a custom padded support rig. All force production tasks were completed with the arm extended and supinated. Given this configuration, subjects were not asked to bear the weight of the object, instead all kinetic testing devices were suspended so that participants could easily touch and exert force on the devices without movement of the hand/fingers/forearm (SnakeClamp, Riner, VA, USA).

Force Production Tasks & Evaluation

We asked subjects to perform a series of force tasks consisting of hand gripping at maximal strength and pinching at maximal strength using the dominant hand. All force production trials were preceded by a 5s baseline NIRS evaluation of forearm hemodynamic function followed by a 30s NIRS evaluation of hemodynamic recovery. Maximal hand grip strength was evaluated using a Biometrics Hand Dynamometer and wireless DataLOG system (Dynamometer Model G200, DataLOG model MWX8, Biometrics Ltd., Newport, UK). Once the word “begin” was announced, participants were to exert maximal grip using a 5-fingered grasp for 30s before relaxing. Force production during the 30s interval was monitored visually by study personnel to ensure the participants exerted force for the entire duration. Verbal encouragement was provided throughout each trial. After each trial, a break was permitted for at least 2 full minutes. Three maximum grip force production trials were collected. Maximal pinch evaluation was conducted using a Biometrics Pinch Dynamometer and wireless DataLOG system (Precision Pinchmeter model P200, DataLOG model MWX8, Biometrics Ltd., Newport, UK). At the instruction of the examiner, the participant was to pinch the device using digits 1 and 2 only for approximately 30s before relaxing. We collected 3 maximum pinch force production trials, allowing for a minimum of a 2-minute resting period between trials.

The structure of force output variability and hemodynamic function variability was quantified via Approximate Entropy (ApEn) and Detrended Fluctuation Analysis (DFA). The range of ApEn is 0 to 2, where lower values reflect signal predictability, while higher values reflect less predictable (more complex) signals. The amount of time-dependent variability in the signal is also reflected by DFA, such that long-range predictability in the signal is reflected by DFA values. DFA values of approximately 1.0 indicate a 1/frequency spectrum (pink) noise, whereas values of 1.5 indicate a 1/frequency² spectrum (Brownian noise). A shift towards Brownian noise indicates an increased incidence of lower frequency components in the signal, reflecting greater signal predictability. Additional details regarding

these analyses can be found in our previous publications^{14,15}. Further analysis of the correlation among force production and hemodynamic responses during the 30s force production interval were evaluated via simple correlation and cross-correlations (taking time lags between the 2 data types into account).

Statistical Analysis

The data are presented as means $\pm$ standard errors. Basic assessment of changes in hemodynamic function (HbO and HbR) was performed using 1-sample *t*-tests with a test mean of zero to indicate any directional changes. Repeated measures analyses of variance (RM-ANOVAs) were performed with the factors of *Task* (2 levels: Grip or Pinch) and *Measure* (2 levels: HbO or HbR, measured during the 30s interval of maximal force production) for primary analysis. Evaluation of sensory function was assessed in a separate RM-ANOVA with *Site* (2 levels: digit 1 and digit 5) as a factor. Both bivariate- and cross-correlation values were then subjected to RM-ANOVA to evaluate differences among correlation pairs with the factors of: *Task* (2 levels: Grip or Pinch) and *Pairs* (3 levels: HbO & Force, HbR & Force, HbO & HbR). Bonferroni corrections were used to assess pairwise *post-hoc* comparisons. All correlation data were log transformed prior to analysis due to floor/ceiling effects. Sensory data were log transformed prior to analysis due to non-linearity and heteroskedasticity. Non-transformed data are reported and shown in the Figures to avoid confusion.

Results

Sensory Evaluations

Evaluation of sensory function did not differ among different locations (*Sites*) with sensory innervation by the median and ulnar nerves, respectively, within the hand. Average tactile detection thresholds were 0.11 ± 0.01 g across portions of the hand innervated by the median and ulnar nerves (digits 1 and 5, respectively).

Maximal Force Production

The average force produced at the onset of the 30 second interval for grip and pinch testing was 189.3 ± 25.6 N and 43.1 ± 6.1 N, respectively (Fig. 2A). During maximal force production tasks lasting 30s, forces produced in both task dropped $54.7 \pm 4.7\%$ in grip trials and $59.2 \pm 3.7\%$ in pinch trials between the maximal force produced and the end of the force production period, Fig. 2A. Exemplar data for maximal grip and maximal pinch force production in the 30s interval can be found in Figs. 2B and 2D. Non-linear analysis (ApEn, DFA) of maximal strength profiles did not yield any significant differences between the force profiles across all subjects.

Hemodynamic Responses

At baseline, average HbO and HbR values were $62.2 \pm 4.2\mu\text{M}$ and $12.7 \pm 3.5\mu\text{M}$, respectively across all tasks. In grip force production tasks, average HbO and HbR values were $61.9 \pm 4.3\mu\text{M}$ and $13.4 \pm 3.6\mu\text{M}$. Average HbO and HbR values were $61.9 \pm 4.3\mu\text{M}$ and $12.9 \pm 3.3\mu\text{M}$ during maximal pinch force production. Exemplar data for HbO and HbR during maximal grip and maximal pinch force production in the 30s interval can be found in

Figs. 2C and 2E. During maximal force production tasks lasting 30 seconds, HbO stayed the same (no overall change), while HbR increased overall, confirmed via 1-sample *t*-test, shown in Fig. 3A. HbR increased by $15 \pm 6\%$ and $5 \pm 3\%$ in grip and pinch tasks, respectively. Non-linear analysis (ApEn, DFA) of hemodynamic data did not yield any significant differences between the hemodynamic responses across all subjects.

Correlations

Assessment of bivariate and maximal correlation (via cross-correlation) values did not differ in any of the hemodynamics or force data assessed. Analysis of cross-correlation lag values did not return significant differences across measures of interest. The average cross-correlation lag was 153 ± 359 ms. Differences in correlations between hemodynamic measures and forces produced were found between HbO & Force and HbR & Force (*Comparison*: $F_{2,21} = 3.53$, $P < 0.05$), confirmed via Bonferroni *post-hoc* analysis (Fig. 3B). The correlation between HbO & Force was positive ($r = 0.18$), while the correlation between HbR & Force was negative ($r = -0.48$).

Discussion

The purpose of this study was to evaluate changes in muscle oxygenation and features of kinetic performance during sustained maximal force production. In terms of our hypotheses, the data support (at least in part) each hypothesis. With respect to hypothesis #1, HbR values increased during force production tasks, while HbO values remained mostly constant. In support of hypothesis #2, declines in maximal force production output were observed in both tasks across all subjects. Regarding hypothesis #3, no task-specific changes were found in the structure of force variability nor hemodynamic data, as the data were from a young healthy population. With respect to our exploratory hypothesis, a weak positive correlation between HbO and force production was found, while a moderate negative correlation was found between HbR and force production.

Two previous studies have focused on the reliability of NIRS for measurement of oxygenation in forearm muscles^{4,12}. In both, test-retest reliability of the NIRS method was established; however, differing muscle oxygenation outcomes were reported, likely due to task differences (submaximal force production versus incremental cyclic contractions)^{4,12}. In the study we report here, we also used a different task as compared to previous studies, as our long-term interests are in how muscle oxygenation may be used as a non-invasive tool to measure muscle oxygenation/function in patient populations. Specifically, we are interested in how muscle function, both hemodynamic function and force production function, deteriorates during sustained contractions and muscle fatigue. This data set provides baseline knowledge on the hemodynamic behaviors of a young healthy population, thus providing a benchmark to compare behavior of other populations in future studies.

Specifically, we utilized an isometric contraction method in order to create a naturally occurring sustained occlusion of the muscle to induce significant hemodynamic changes within the muscle of interest. We chose this method over another technique in which external pressure is applied to a limb to cause occlusion distal to the site of pressure (blood pressure cuff method). The naturally occurring muscle contraction occlusion technique is

safer for our primary populations of interest (CVD patients) as compared to the commonly used blood pressure cuff ischemia technique. With the blood pressure cuff method, it is possible that the large external and prolonged pressure via pressure cuff on the limb may dislodge arterial plaque within the limb undergoing ischemia. This may result in a stroke in patients with known cardiovascular problems. Given the high risk of stroke in our target population (Type II diabetes), we avoided the external ischemia method and employed the isometric contraction approach as a safety precaution in this initial study as well as subsequent ongoing work in our lab. With this technique, it is possible that fatigue may occur during the 30s contractions, however the natural occlusion that occurs with isometric contraction can be reversed by rest periods between contractions. The rest periods given to our subjects were a minimum of 2 minutes in order to restore nutrients via blood flow to the muscle and acetylcholine to the neuromuscular junctions¹⁶.

Additionally, we assessed hemodynamic functions of the FDS, one of the major extrinsic finger flexors. We acknowledge that some of the task-based differences in hemodynamic function are likely due to the multicompartiment structure of this particular muscle. While only the digit 2 compartment of the FDS should ideally be activated during pinch tasks (in contrast to all compartments of the FDS during grip tasks), neuromuscular and passive mechanical enslaving both occur within the FDS and nearby compartments (such as the digit 3 compartment) and contribute to both force production and hemodynamic changes during pinch tasks^{17,18}.

Hemodynamic and sensorimotor functions of muscles of the forearm are directly related to successful performance of activities of daily living (ADLs). Reduction of hemodynamic function via vascular disease and/or aging may significantly impair both sensory and motor function of the arms, hands, and fingers and result in reduced capability to perform ADLs. Data from our previous studies^{15,19} suggest that vascular dysfunction may contribute to significantly altered hand and finger sensory and motor functions in patient populations (such as patients with Type II diabetes). However, few studies of hemodynamic function of the forearm exist in the literature. A recent study by MasoudiMotlagh and colleagues⁵ reported differences in HbO values in forearm extensors of stroke patients during isometric contractions. Significantly reduced HbO values appeared in the paretic limb of stroke patients compared to the non-paretic limb. Further, HbO values were found to be overall lower in stroke patients as compared to controls. Of note, a 30+ year age gap existed between the stroke and healthy control population in that study, thereby potentially confounding the conclusions that can be safely drawn. Despite this drawback, the work by MasoudiMotlagh and colleagues is an important first step in using NIRS oximetry in evaluation of muscle in patient populations, as their study reinforces the possible applications of NIRS as a diagnostic tool.

One interesting application of muscle oximetry evaluation may be to evaluate limb-specific differences in muscle hemodynamic and motor function due to peripheral vascular disease, mononeuropathy (e.g. carpal tunnel syndrome), or even long-term musculoskeletal degeneration.⁵ Any hemodynamic changes coupled with force production changes may be particularly insightful for clinicians in developing rehabilitation plans for patients showing: (1) bilateral functional differences or (2) chronic neuromuscular degeneration. Our data,

particularly the correlation findings between hemodynamic function and force production, may be used as a benchmark for comparison in this sense. If a patient presents with no correlation between hemodynamic function and force production, then it is likely that functional impairment of the limb either currently exists or will develop in time. Tracking of the correlation between hemodynamic function and force production may also assist clinicians in monitoring functional limb recovery in the physical therapy period after: (1) a vascular incident, or (2) treatment of persistent vascular disease (such as Type II diabetes). Currently, we are collecting data on a cohort of patients with Type II diabetes (compared to age- and gender-matched healthy controls) in order to evaluate the usefulness of muscle oximetry for detecting and tracking long-term functional muscular hemodynamic deterioration along with known motor deficits in this particular population.

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Abbreviations:

ADLs	activities of daily living
ApEn	approximate entropy
CVD	cardiovascular disease
DFA	detrended fluctuation analysis
FDS	flexor digitorum superficialis
HbO	oxygenated hemoglobin
HbR	reduced or deoxygenated hemoglobin
LED	laser emitting diode
LQ	laterality quotient
MGUS	Monoclonal Gammopathy of Undetermined Significance
MVC	maximal voluntary contraction; nm, nanometers
NIR	near-infrared light
NIRS	near-infrared spectroscopy
PDN	Paraproteinaemic Demyelinating Neuropathy
RM-ANOVA	repeated-measures analysis of variance
SE	standard error
μM	micromolar

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Figure 1.

Picture of the NIRS device placement. The light-blocking fabric overlay for the device was removed in all photos in this series to illustrate the location of the NIRS device on the forearm. **A:** Palpation of the FDS. **B:** Orientation of the NIRS probe directly on top of the palpated FDS. **C:** The NIRS device secured to the forearm using a self-adherent wrap (Coban, 3M, St. Paul, MN, USA).

Figure 2.

Force production data. **A:** Mean and standard error (SE) of forces produced in maximal grip and pinch trials. Changes in force production level are noted between the onset and end of each trial. **B:** Exemplar data illustrating the decline of force production in a grip force production trial from Subject 7. **C:** Exemplar HbO (left axis) and HbR (right axis) during grip force production from Subject 7. **D:** Exemplar data illustrating the decline of force production in a pinch force production trial from Subject 11. **E:** Exemplar HbO (left axis) and HbR (right axis) during pinch force production from Subject 11.

Figure 3. Hemodynamic change and bivariate correlations data. **A:** Mean and standard error (SE) of average changes in HbO and HbR in both grip and pinch force production trials. **B:** Bivariate correlation values.