An experimental knee joint effusion does not affect plasma catecholamine concentration in humans

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Abstract
Knee joint effusion causes quadriceps inhibition and is accompanied by increased soleus muscle excitability. In order to reverse the neurological alterations that occur to the musculature following effusion, we need to understand the extent of neural involvement. Ten healthy adults were tested on two occasions; during one session, subjects had their knees injected with saline and in the other admission, they did not. Soleus Hmax, Mmax, plasma epinephrine, and norepinephrine concentrations were obtained at five intervals. Results showed that Hmax increased following the effusion, while norepinephrine and epinephrine levels were not altered. We suggest that the soleus facilitation seen following knee effusion results from stimulation of joint mechanoreceptors and removal of descending spinal and supraspinal inhibition and is not the result of a sympathetic response.

Keywords: Arthrogenic muscle inhibition; Knee; Injury; H-reflex

Increased soleus neuromuscular excitability accompanies quadriceps inhibition in the presence of knee joint effusion [9,11]. An inverse relationship exists between the soleus and quadriceps Hoffmann reflex (H-reflex): as the soleus H-reflex amplitude increases, the quadriceps H-reflex decreases. The increased soleus motor output has been attributed to a compensatory reaction to the quadriceps inhibition [9,11], which may promote the maintenance of upright posture and locomotion [16,20]. The central mechanism(s) responsible for this facilitation remain unknown. It is of clinical interest to determine the processes responsible for the soleus facilitation so we can better understand the neuromuscular consequences of joint injury. Maintaining homeostasis is essential to human survival. It is widely accepted that homeostatic processes are the result of autonomic, endocrine, metabolic, and behavioral components that are regarded as unique regulatory events. Catecholamines help to maintain homeostasis by regulating fuel metabolism, heart rate, blood vessel tone, and thermogenesis [6]. When homeostasis is disturbed by a stress, the sympathetic nervous system and hypothalamic–pituitary adrenal axis are activated resulting in increased peripheral levels of catecholamines acting to regain a state of equilibrium [4]. Injury is perceived as a stressor to the body and may result in altered catecholamine levels [2].

The knee effusion model is used to simulate the presence of fluid in the joint capsule following damage and is perceived as an injury by the central nervous system (CNS) potentially resulting in increased release of catecholamines. An excess of epinephrine and norepinephrine may contribute to the facilitation seen in the soleus musculature accompanying the quadriceps inhibition when a knee joint effusion is present [9,11]. Establishing the presence of these substances is critical in understanding the systemic response.

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to joint effusion and how each substance contributes to the soleus muscle facilitation. Therefore, the purpose of this investigation was to determine if an experimental knee joint effusion results in an increase in plasma epinephrine and norepinephrine levels.

Ten healthy subjects (two females and eight males: age, 24 ± 4 years; height, 177.3 ± 5.1 cm; mass, 76.2 ± 13.6 kg) with no previous lower extremity injury volunteered to participate. Subjects were not currently taking any medication that could affect CNS function; additionally, females were not taking oral contraceptives and reported for testing during the early follicular phase of their menstrual cycle. Human subject approval was obtained prior to beginning the study and informed consent was acquired from each subject.

H-reflex and M-response measurements were collected using surface electromyography (MP150, BIOPAC Systems Inc., Santa Barbara, CA).

Signals were amplified (EMG100B, BIOPAC Systems Inc.; Gain 1000), band-pass filtered from 10 to 500 Hz and sampled at 1024 Hz with a common-mode rejection ratio of 110 dB. Reflex measurements were elicited using a stimulator (STM100A, BIOPAC Systems Inc.) with a 200 V (maximum) isolation adapter (STMIISO, BIOPAC Systems Inc.), 2 mm shielded electrode (EL254S, BIOPAC Systems Inc.), and a 7 cm dispersive pad.

For the effusion condition, volunteers were admitted into the General Clinical Research Center (GCRC), the evening before testing and had a venous catheter placed in their ante-cubital fossa at 22:00. Subjects were fed a snack at 23:00, then fasted until the completion of the protocol. At 05:50, subjects were awoken, asked to void, and then returned to bed and remained lying down until the completion of testing. Beginning at 06:30, baseline Hmax and Mmax amplitudes were elicited. Immediately following these measurements, a blood sample was taken. A 25 G 1.5 in. needle was now inserted and removed to mimic the puncture during the Xylocaine injection. This injection was necessary in order to evaluate the effect of a needle stick on our dependent measures. The Xylocaine injection was then performed following by injection of 60 mL of saline into the superolateral joint capsule [13]. Xylocaine was advanced between the articular surface of the patellofemoral joint at the midpoint of the patella [13]. Hmax, Mmax, and blood samples were recorded after the first needle insertion, Xylocaine injections at 25 and 45 min post-saline injection.

The protocol for the control condition was time matched to the effusion condition. No injections took place during this condition.

Blood samples (10 mL) were collected in pre-chilled vacutainer tubes. Plasma was kept on ice until separated in a refrigerated centrifuge within 30 min of collection and then frozen immediately at −20 °C in plastic vials. The determination of plasma epinephrine and norepinephrine was performed using high-pressure liquid chromatography (HPLC) with electrochemical detection. This assay involves extraction of plasma with alumina followed by HPLC. HPLC has been shown to be highly sensitive (1 pg) and have good precision (CV = 6%) in detecting epinephrine and norepinephrine [15].

An a priori power analysis based on our previous work using the H-reflex revealed an average effect size of 1.77 mV and an average standard deviation of 1.38 mV. Using these values, we calculated a minimum detectable effect size of 1.71 mV as the smallest within-subject change that would lead one to reject the null hypothesis, assuming a two-sided type I error rate of 0.05 and a power of 0.80. A 2 × 5 repeated measures ANOVA was used to analyze each dependent variable. The model parameters were estimated by restricted maximum likelihood. The covariance matrix was lead one to reject the null hypothesis, assuming a two-sided type I error rate adjustment was based on a Fisher’s least significant difference criterion with a type I error rate of 0.05.

Means and standard deviations for all dependent variables can be found in Table 1. An interaction was observed between measurement interval and condition for the H-reflex (F4,72 = 8.62; P < 0.0001). Hmax during the effusion admission was smaller at baseline compared with measures taken post-needle stick (P = 0.015), 25 min (P < 0.0001), and 45 min (P < 0.0001) post-knee effusion. No differences in Hmax were noted during the control condition at any measurement interval (P > 0.05; 1 − β = 0.52; δ2 = 0.25). No significant effect for measurement interval (F4,72 = 0.97, P = 0.4278; 1 − β = 1.0, δ2 = 0.90), condition (F4,72 = 1.03; P = 0.3364; 1 − β = 1.0; δ2 = 0.91), or measurement interval × condition (F4,72 = 0.27; P = 0.8989; 1 − β = 1.0; δ2 = 0.90) was detected for Mmax.

No differences in plasma epinephrine levels for measurement interval (F6,88.7 = 0.23; P = 0.92; 1 − β = 0.18; δ2 = 0.11), condition (F4,4.3 = 0.57; P = 0.47; 1 − β = 0.43; δ2 = 0.35), or measurement interval × condition (F4,88.7 = 1.09; P = 0.37; 1 − β = 0.28; δ2 = 0.18). Likewise, no changes were noted for plasma norepinephrine when compared for measurement interval (F4,30.3 = 1.86; P = 0.13; 1 − β = 0.64; δ2 = 0.35), condition (F4,4.8 = 1.04; P = 0.34; 1 − β = 0.88; δ2 = 0.87), or measurement interval × condition (F4,30.4 = 0.58; P = 0.68; 1 − β = 0.23; δ2 = 0.15).

Knee effusion has been shown to result in soleus facilitation, our data support these findings [9,11]. We can go a step further with our results and suggest that the facilitation is not the result of a sympathetic response. We felt that the introduction of the effusion may be perceived as a stressor by the body and result in an increased release of epinephrine and norepinephrine potentially increasing motor output to the soleus muscle and contributing to the H-reflex facilitation. An additional finding is that decreased cutaneous feedback from receptors surrounding the knee joint (that resulted from the introduction of Xylocaine) did not appear to alter the soleus H-reflex amplitude. Together, these two findings suggest that the joint effusion is indeed responsible for the increased soleus output and probably is due to increased capsular tension and stimulation of joint mechanoreceptors [7].
The amplitude of the H-reflex did increase after a simple needle stick indicating motoneuron excitability was altered due to the subcutaneous injection. Three possible explanations can account for this increase: (1) stimulation of pain receptors, (2) damage to subcutaneous tissue, or (3) a sympathetic response to the injection. Stimulation of cutaneous pain receptors is known to result in a decrease in both the H-reflex and motor(evoked potentials and therefore their influence is an unlikely explanation for the facilitation of the H-reflex seen here [12,14,18]. Damage to subcutaneous tissue caused by the needle puncture also needs to be considered as a potential influence on the H-reflex. Intuitively, damage to tissue would result in a decrease rather than an increase in the H-reflex. Although no data are available directly supporting this notion, a study where 0.2 mL of isotonic saline was injected into the subcutaneous tissue over the abductor digiti minimi no differences were detected in the flexor carpi radialis H-reflex or in the motor evoked potential from the abductor digiti minimi [14]. If damage to subcutaneous tissue was responsible for the facilitation of the H-reflex seen in our study, we would expect to see similar results in the above described investigation.

With damage to subcutaneous tissue and stimulation of pain receptors ruled out as contributing factors, the most reasonable explanation would be activation of the stress response due to the introduction of the needle. This hypothesis appears to contradict our results as we did not see a heightened level of plasma catecholamines post-needle stick. In general, evidence suggests that needles and injections are perceived negatively and are a fearful stimulus for patients [5,17] which may result in activation of the stress response. The facilitation of the H-reflex could also be due to the release of other secreted hormones such as cortisol or may have been the result of a local effect that did not manifest systematically. Another possibility for why no differences were detected in plasma catecholamine levels is that we failed to capture the increase in epinephrine and norepinephrine due to their short half-life. Blood was drawn after H-reflex measurements and the half-life of catecholamines is 1–2 min; therefore, it is possible we missed their peak if the stress response was indeed activated. It should be mentioned that if we failed to capture a change due to the quick removal of the catecholamines, then their presence is inconsequential and does not influence the results of measures seen using our model.

When Xylocaine was introduced, the H-reflex amplitude returned toward the baseline value. This could be due to an inhibitory effect of the Xylocaine arising from decreased or altered input from cutaneous mechanoreceptors and/or the increased excitability that resulted from the needle stick was “wearing off”. We contend the latter to be the more likely explanation. In previous experiments where the skin was numbed with Xylocaine, either no change [1] or a facilitation [3] was noted in the H-reflex amplitude.

No changes were noted in plasma epinephrine and norepinephrine levels at 25 and 45 min following the effusion. This preliminary evidence suggests that induced joint swelling does not influence catecholamine release. Increased secretion of norepinephrine and epinephrine are associated with the inflammatory response [2,8]. Perhaps, the sympathetic response to injury occurs due to the presence of inflammatory mediators and since our model is non-inflammatory in nature, it does not elicit stimulation of the hypothalamic–pituitary-adrenal axis causing increased release of catecholamines.

Non-noxious stimulation of articular afferents has been shown not to alter adrenal catecholamine secretion in cats [19]. Passive flexion, extension, internal rotation, and external rotation of the knee within normal ranges did not cause increased secretion of catecholamines. This evidence suggests that pain may be involved in the sympathetic response to joint injury. The knee effusion model is not perceived as painful by subjects [10] and may account for the failure to detect an increase in the release of catecholamines.

In conclusion, our data suggests that stimulation of joint mechanoreceptors due to the induction of an
experimental knee joint effusion does not activate the hypothalamic–pituitary adrenal axis. Future research should be conducted to determine if the presence of joint pain and inflammation associated with knee joint injury influences the sympathetic nervous system and if the sympathetic response relates to the amount of AMR present following injury.

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References