Neuromuscular Reflexes Contribute to Knee Stiffness During Valgus Loading

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Submitted 6 September 2004; accepted in final form 16 December 2004

INTRODUCTION

Joint stability has been classically attributed to four major factors: bone/cartilaginous contact forces (Blankoveet al. 1991), ligament and capsule stiffness (Hull et al. 1996; Renstrom et al. 1986), intrinsic stiffness of active muscles (Olmstead et al. 1986), and reflexively mediated muscle stiffness (Kearney and Hunter 1990). Reflex action may be mediated by muscle and mechanoreceptors originating in periarticular tissues (e.g., skin, ligaments, and joint capsule). Palmer (1958) proposed that neuromuscular control of the knee is made possible by ligaments that supply the CNS with afferent input. Since this early study by Palmer, several authors have focused on investigating periarticular tissue afferents and their specific neuromuscular pathways. For example, Hongo et al. (1969) showed that activation of the ligament’s mechanoreceptors directly increased the activity of the α-motorneurons, and Sojka et al. (1989) showed a direct association between the neuronal discharge of posterior cruciate ligament mechanosensitive afferents and the γ-motorneuron system in the cat’s knee. These findings suggest that the ligament’s mechanoreceptors are involved in a neuronal pathway that may play a direct as well as indirect role in mediating muscle contractions. A number of investigators have reported that contractions of knee muscles can increase joint stiffness well beyond that provided by the joint’s passive tissues (Baratta et al. 1988; Draganich et al. 1989; O’Connor 1993; Schipplein and Andrich 1991; Solomonow et al. 1987; Yasuda and Sasaki 1987). Such muscle contractions can be elicited either through reflexive or voluntary means. Animal experiments have shown that the reflexive activity of muscles crossing a joint can change if the joint’s capsule is mechanically stimulated (Baxendale et al. 1987; Greenfield and Wyke 1966). This altered activity has been postulated to increase joint stiffness providing a measure of joint protection. Therefore it seems that knee joint mechanoreceptors may potentially play a role in promoting joint stability by providing sensory feedback that facilitates protective patterns of muscle activity (Draganich et al. 1989; Johansson et al. 1991; O’Connor and Brandt 1993; Solomonow and Krosggaard 2001; Solomonow et al. 1987). The breakdown of such a protective stabilizing mechanism may initiate or contribute to the progression of osteoarthritis (OA) in the joint. Experiments on animal model have recently shown that selective joint denervation appears to dispose the joint to osteoarthritic changes (Salo et al. 2002). It is hypothesized that such an absence of appropriate sensory input from the joint’s periarticular structures reduces joint stiffness, potentially resulting in joint damage.

In an earlier study, we reported that reflex activity was consistently elicited in knee joint muscles by applying abduction angular perturbations to the human knee (Dhaher et al. 2003). This reflex seems to be mediated by periarticular tissue afferents. Unlike the muscle spindle-mediated stretch reflex, the perturbation-induced reflex was characterized by a longer latency response (t>70 ms), which consisted of a “diphasic” EMG pattern. This response consisted of an initial EMG peak, followed by a sustained reflex response that lasted throughout the duration of the mechanical perturbation. Wyke (1973) attributed the initial brief reflex burst to the type II (fast adapting) receptors, while proposing that the prolonged reflex activity is due to the type I (slow adapting) receptors. Recent microneurographical recordings from slow and fast adapting cutaneous afferents from the skin overlaying the human knee...
joint indicated that these mechanoreceptors respond both pha-
sically as well as tonically to flexion/extension movements
(Edin 2001), results that are consistent with the “diphasic”
responses reported in Wyke (1973) and Dhaher et al. (2003).

Although a protective and stabilizing role for periarticular
structure selection criterion.
tissue afferents and their muscular connections is widely pro-
posed, we are unaware of any in vivo quantitative studies in a
human model describing the contribution of the joint’s periar-
ticular tissue sensory systems to the regulation of joint stiffness
(Sjolander et al. 2002). Accordingly, the purpose of this study
was to assess joint stiffness, mediated by this sensory system as
a function of preactivation levels of the knee muscles. We
propose that the knee joint mechanoreceptors located in medial/
lateral periarticular tissues play a major role in preserving joint
integrity by providing sensory feedback that promotes the
activation of key knee stabilizer muscles, resulting in a signif-
ificant increase in frontal plane joint stiffness. A parametric,
linear, delayed, second-order, dynamic model was used to
model knee joint mechanics under an abduction loading con-
dition. Three levels of qualifiers were used to validate success-
fully the parametric model proposed in this study: the overall
variance accounted for by the reflex components and a model
structure selection criterion.

**METHODS**

**Experimental protocol**

Ten male subjects (mean age, 26 ± 4 yr; height, 180 ± 5 cm; 
weight, 83.8 ± 11.5 kg), with no history of neurological or muscu-
loskeletal disorders, were tested. All subjects had moderate level of
activity (2–3 days/wk exercise), mostly running/jogging or playing
basketball. All experimental procedures were approved by the Insti-
tutional Review Board of Northwestern University and complied with
the principles of the Declaration of Helsinki. Informed consent was
obtained prior to testing. Subjects were seated with the right limb secured in a single-degree
of freedom servomotor system (Fig. 1). The fully extended right knee
joint was preloaded in the abduction direction to ensure initial stretch
of the medial aspect of the joint’s periarticular tissues (Dhaher et al.
2003). To identify the abduction angle necessary to stretch the medial
periarticular tissues, torque-angle relationships were obtained by
stretching the joint in the abduction-adduction direction starting from the
neutral position (0° abduction/adduction angle) at a constant velocity (3°/s) under a volitionally relaxed state (inactive knee mus-
cles; Fig. 2). These relationships obtained at low loading rates have
been used to describe the quasi-static properties of the joint, e.g.,
linear to nonlinear angular transitions (Olmstead et al. 1986). In vitro
knee preparations have attributed loading of the joint’s ligamentous
structure to the nonlinear component of the torque-angle relationship
(cf. Markolf et al. 1981). In this study, the angular onset of the
nonlinear portion of the curve was estimated by fitting the mean of the
hysteresis loop representing the joint torque-angle relationship at the
volitionally relaxed state (Fig. 2, inset) with a piecewise continuous
function as outlined in Audu and Davy (1985). The piecewise con-
tinuous function proposed by Audu and Davy (1985) was slightly
modified with the addition of a linear term. Hence the three com-
ponents of the piecewise continuous function consisted of a linear term for small angles ($\theta_1 < \theta < \theta_2$) and two exponential terms to fit the portion of the mean torque-angle curve at the larger angles both in the
adduction ($\theta > \theta_2$) and abduction ($\theta > \theta_1$) directions (Fig. 2, inset). The coefficient of the linear (2 parameters) and the exponential (2
parameters per exponent; Audu and Davy 1985) terms, together with the
angular onsets ($\theta_1, \theta_2$) were identified using a least square fit
subjected to continuity constraints at the angular onsets. For example,
the nonlinear angular onsets for the torque-angle relationship shown in Fig. 2 (solid line) were $\theta_1 = -2^\circ$ and $\theta_2 = 3^\circ$. Our preliminary
results showed that the onset of the nonlinear portion of the torque-
angle relationship in the abduction direction occurred at knee abduc-
tion angles less than $-2^\circ$, and thus a $-4^\circ$ abduction offset was used
across all subjects. Loading of the knee’s periarticular tissues as result of the angular offset ($-4^\circ$ of abduction) ensured an instantaneous
resistance by these tissues to an additional mechanical perturbation,
hence eliminating the potential for mechanical delays.

With the knee joint placed in full extension, and preloaded to $4^\circ$
of abduction, subjects were instructed to *volitionally co-contract* their
knee muscles (flexors and extensors) to increase the joint adduction
torque output to match a prespecified target level prior to the angular
perturbation. The reason for using a co-contraction paradigm is based
on preliminary results that indicated that target matching to either a
flexion (activation of flexors only) or an extension (activation of
extensors only) moment in this abducted and fully extended knee
joint was an unreliable measure and difficult to achieve. Instead,

![FIG. 1. Overview of the experimental set-up.](http://jn.physiology.org/)

Subjects were seated in a BIODEX chair, with the trunk supported under the ischial tuberosities and arms crossed in front of the subject’s chest. Apex of the patella served to align the motor axis of rotation with the right knee joint’s adduction/abduction axis of rotation. Left leg of the subjects rested on a fixture, which introduced a knee flexion angle of 60° (from full extension) and a hip flexion angle of 120°. Right leg was fixed within a coupling ring with a cast placed around the ankle joint. Coupling ring was fixed to a servomotor actuator with a precision potentiometer and tacho-
meter. Knee was fitted within a bracket mounted firmly at the medial and lateral femoral epicondyles. Together with a thigh strap, brackets isolated the knee adduction-abduction movement from the abduction/adduction movement of the hip joint. Figure modified from Dhaher et al. (2003).
subjects were asked to maintain different knee muscle co-contraction levels because co-contraction of both flexors and extensors in this abducted posture results in knee adduction torque. The resulting adduction torque was used as a measure of the subject’s co-contraction level. To ensure that the required levels of knee adduction torque were a result of activation of the knee flexors and extensors only, special attention was given to the potential recruitment of the hip abductor/adductor muscles during the target-matching scheme. While involvement of hip abductors and/or adductors would have been detected by monitoring their EMG activity, the limited number of EMG units available in our laboratory prevented us from collecting EMG from all hip and knee muscles simultaneously. Our preliminary data (unpublished), instead, indicated that involvement of any of the hip adductors or abductors during this target-matching scheme were reflected by the development of in-plane forces normal to the knee joint (in the medial-lateral direction).

The volitionally co-contracted state was performed for five different co-contraction target levels identified as a percentage of the torque associated with both the volitionally co-contracted and relaxed states (Fig. 1). A visual display of the target levels of the 30 – 40, and 40 – 50% of APT as measured with a six-degree of freedom load-cell (Fig. 1). The %APT was equal to the difference between the joint’s preloaded position (−4° of abduction; see Fig. 2). The %APT was used to compute the %APT required for the subject at the volitionally relaxed (solid line) and the 1st volitionally co-contracted state (η1; dashed-dotted line). As shown in the figure, co-contraction of both medial and lateral muscles resulted in an increase of the knee adduction torque at the −4° abduction offset angle. Inset: 3 components of the piecewise continuous function used to describe the mean of the hysteresis loop representing torque-angle relationship in the abduction/adduction direction in the voluntarily relaxed state. The 3 components consist of a linear part, defined between the angles θ1 and θ2 (thick solid line) 2 nonlinear parts defining the joint quasi-static properties in the abduction (angles < θ1) and adduction (angles > θ2) directions (thin solid line). Dashed gray line shown in the inset is an extrapolation of the linear fit of torque-angle data between θ1 and θ2. Extrapolation shows deviation of the linear fit from the measured data at estimated nonlinear angular onsets (θ1 and θ2).

As shown in Fig. 3, the abduction perturbations occurred at −4° abduction offset angle on the nonlinear portion of the joint quasi-static property (the torque angle relationship obtained at low loading rate of 3/s). This indicates that the medial aspect of the joint’s periarticular tissues was stretched prior to perturbation. The perturbation onset was randomly triggered after the detection of a stable background adduction torque developed with co-contraction. This stable background adduction torque was then used to compute the %APT required for the...
target matching protocol (see Fig. 2). The background adduction torque onset (t\text{onset}) was identified when 10 consecutive points (a total of 10 ms obtained at 1-KHz sampling rate) in the torque trace were within 2 SD of the mean of the preceding torque signal taken over a 200-ms sliding time window.

Preamplified surface EMG electrodes (Delsys Bagnoli 3.2) were used to record in three medial muscles, rectus femoris (RF), vastus medialis (VM), and semitendinosus (ST), and two lateral muscles, vastus lateralis (VL) and biceps femoris (BF), using preamplified surface electrodes (Delsys) before and during the mechanical perturbation at 1-KHz sampling frequency. Medial muscles are defined as muscles that lie on the medial aspect of the thigh’s anterior and posterior compartments. Lateral muscles are defined as muscles that lie in the lateral aspect of the thigh’s anterior and posterior compartments. The RF, however, is very difficult to classify based on its anatomical location since it lies in on the mid-line separating the medial and lateral parts of the thigh’s anterior compartment. Based on electrical stimulation data from our laboratory (Dhaher and Kahn 2002), selective activation of the RF in the fully extended knee in four subjects resulted in an adduction action at the tibia; hence we classify RF as a medial muscle.

Subjects were asked to report any discomfort or pain during the abduction perturbation to reduce any possibility of eliciting reflex responses from nociceptors (Aδ fibers or C fibers). To assess potential variations in reflex contribution to the measured torque attributable to muscle fatigue, subjects were asked to generate 15% APT before and after the perturbation experiments. The frequency spectrum of the resulting volitional EMG signal from all muscles was obtained, and the median frequency was calculated. Significant variation of mean frequency is used as a measure of muscle fatigue (cf. Hagg 1992). After the completion of the mechanical perturbation experiments, the cast was removed, the subject was taken out of the chair, and flexion and extension maximum voluntary contraction levels (MVC) were recorded for each subject at a knee flexion angle of 60° (less than full extension). MVC data were collected at this knee-flexed posture and fully extended knee postures used during the mechanical perturbation experiments. Including subject set-up, collection of the subject’s joint adduction/abduction torque at the voluntarily relaxed state, target matching training trials, and finally the mechanical perturbations trials performed at all required co-contraction levels, the experimental session lasted between 4 and 6 h.

**Data analysis**

To eliminate high-frequency noise (>250 Hz) associated with the servomotor system seen during the perturbation experiments, the EMG and load cell signals were on-line filtered with an eighth-order Butterworth, low-pass, zero-phase digital filter with a 220-Hz cut-off frequency to prevent aliasing and sampled at 1 KHz. Similar on-line filtering parameters have also been used in earlier reflex studies that involved the use of servomotor systems (Kearney et al. 1997; Stein and Kearney 1995; Zhang and Rymer 1997).

The load cell signals recorded during the mechanical perturbation protocol and used in the estimation process (see Eq. 1) were filtered off-line using an eighth-order Butterworth, low-pass, zero-phase digital filter with a 50-Hz cut-off frequency. The background adduction torque developed as a result of co-contraction (the horizontal axis in Figs. 5 and 6) before perturbation was calculated as the mean of the torque values taken over an 80-ms time window preceding the movement onset t\text{onset}.

A second-order delayed differential equation was used to characterize the co-existence of intrinsic properties and reflex action of the lower limb under dynamic conditions. In general, measured knee adduction/abduction torque is determined by intrinsic and reflex responses to an applied perturbation. The intrinsic torque arises from the initial muscle force response as well as from the forces and torques generated by stretching the passive tissues surrounding the muscles and the knee joint. The reflex response represents the involuntary change in muscle activation due to the stretch-evoked afferent response. The major difference between the intrinsic and reflex components is that the intrinsic response starts immediately after perturbation while the reflex response is significantly delayed by the time taken for the signals to travel from the afferent sites to spinal cord motoneuron, (and potentially supraspinal), and back to the knee muscles. Hence, the second-order system describing the knee and lower limb musculoskeletal dynamics took the following form (Zhang and Rymer 1997).
\[ I \times \theta + [B(\eta_i) + B_i(t \geq t_i; \eta_i)] \times \theta + [K(\eta_i) + K_i(t \geq t_i; \eta_i)] \times \theta = T \]

where \( \eta_i \) indicates the different \%APT \( (i = 0 \) for the voluntarily relaxed and \( i = 1, \ldots, 5 \) for the 5 voluntarily co-contracted states); \( t_0 \) is the average periarticular reflex delay, estimated as the minimum reflex delay observed across all muscles for each subject; \( t_d \) is the average periarticular reflex delay, estimated as the minimum reflex delay observed across all muscles for each subject (see data reported in Dhaher et al. 2003); \( T \) is the joint’s measured adduction/abduction torque (output); and \( \theta \) is the knee adduction/abduction angle (input). In this model, the intrinsic and reflex based musculoskeletal adduction/abduction dynamic properties are separated. The inertia, \( I \), dynamic stiffness, \( K(\eta_i) \), and dynamic damping, \( B(\eta_i) \), are the intrinsic joint properties under dynamic conditions, including the initial muscle contractions, as a function of the voluntarily co-contracted state prior to perturbation. \( K_i(t \geq t_i; \eta_i) \) and \( B_i(t \geq t_i; \eta_i) \) are the stiffness and damping reflex contributions, also as a function of the voluntarily co-contracted state prior to perturbation, respectively. The major difference between the intrinsic \( [I, K(\eta_i), B(\eta_i)] \) and reflex \( [K_i(t \geq t_i; \eta_i), B_i(t \geq t_i; \eta_i)] \) parameters is that the intrinsic parameters take values immediately after the perturbation and remain constant thereafter, whereas the reflex parameters are significantly delayed with zero values before the periarticular reflex delay \( (t_d) \).

In this study, a sequential linear and quadratic programming method (QP) was used to estimate five parameters at the relaxed and co-contracted states \( (\eta_0, \eta_1, \eta_2, \eta_3, \eta_4, \text{and} \eta_5) \), specifically, the Levenberg-Marquardt algorithm (Gill et al. 1981), which is available in Matlab (MathWorks, Natick, MA). This method is a generalization of Newton’s method in that it finds the optimal step size from the current point (in search for the optimal solution) by minimizing a quadratic model of the problem. The model was cross-validated with simulations based on data not used in the estimation procedure. To test the effectiveness of including the two additional parameters to account for the presence of both reflex stiffness, \( K_i(\eta_i) \), and damping, \( B_i(\eta_i) \), a model structure selection criterion known as the MDL factor will be used as follows (Ljung 1987)

\[
\text{MDL} = \log \left( 1 + \frac{2 + d}{M} \right) \times \frac{1}{M} \sum_{k=1}^{\infty} e^2(k)
\]

where \( M \) is the number of data points, \( e(k) \) is the error at point \( k \), and \( d \) is the number of parameters used in the estimation procedure \( (d = 3 \) for using 3 terms in the estimation procedure (inertia and passive stiffness and damping) and \( d = 5 \) when the 2 delayed components (reflex stiffness and damping) are included in the estimation procedure). A reduction in the MDL indicates the significance of including the two reflex terms in the second-order model (Ljung 1987).

A portion of the recorded adduction/abduction torque will result from the inertia of the fixture (the cast, the coupling ring, and the cantilever beam). Thus at the end of the experiment, the impulse response of the fixture was obtained to identify the fixture torque contribution. Specifically, an angular impulse (2° and 70 ms wide) was applied to the fixture, and the corresponding torque was measured. Assuming that the stiffness and damping of the fixture are negligible, the fixture inertia was estimated by cross-correlating the measured torque and the second derivative of the impulse position perturbation. The mean of the fixture inertia across all 10 subjects was 0.233 ± 0.024 (SD) kg m²/s. The estimated fixture inertia was used to compute the fixture torque contribution during the abduction positional perturbations (the estimated inertia times the second derivative of the position signal). The fixture torque is subtracted from the measured torque to yield the torque due to the knee and lower limb musculoskeletal dynamics \( (T, \text{see Eq. 1}) \), which was the signal used for further analysis.

The linear association between \( K \) and \%APT and between \( K \) and \%APT across all subjects was estimated using repeated measures linear regression to account for the multiple measurements taken from each subject (PROC MIXED, SAS version 8.02, Cary, NC) and took the form

\[
K = a_1 \times \eta + a_o
\]

where \( \eta \) represents the \%APT (dimensionless), \( a_1 \) (N m/rad) is the joint stiffness at the voluntarily relaxed state, and \( a_o \) (N m/rad) represents the rate of increase of joint stiffness as a function of the percent passive torque level. For the intrinsic joint stiffness estimates, \( a_o \) represents the joint stiffness when muscles surrounding the knee are inactive, and \( a_i \) represents the part of the intrinsic stiffness that arises from muscle contractions prior to perturbation. A one-sample \( t \)-test was used to test if the background levels were different from zero. The method used to fit the data was restricted maximum likelihood (REML) with an unstructured covariance structure.

While position and torque are the only important signals that are used in the system identification method proposed here, EMG of muscles surrounding the knee joint provide an indirect measure of the neural input to the muscle that can be correlated to the estimated reflex stiffness. Hence to assess the effect of the reflex intensity on the estimated reflex stiffness, a multilevel hierarchical linear model relating reflex intensity to reflex stiffness was created using the Mixed Models procedure of SPSS 11.5 (SPSS, Chicago, IL). The hierarchical model correlates the reflex intensity recorded in all muscles and the estimated reflex stiffness. For this analysis, the acquired EMG signals were rectified and smoothed off-line using an eighth-order Butterworth, low-pass, zero-phase digital filter with a 20-Hz cut-off frequency (see dark line in Fig. 4 for an exemplar signal). To quantify the intensity of the reflex response, a normalized reflex (NR) measure was used for all muscles following the procedure (Dhaher et al. 2003)

\[
NR = \frac{EMGrms_{\text{reflex}} - EMGrms_{\text{background}}}{EMGrms_{\text{MVC}} - EMGrms_{\text{background}}}
\]

where \( EMGrms_{\text{reflex}} \) was the time average of the rectified and smoothed EMG activity during the reflex activity period, \( EMGrms_{\text{MVC}} \) was the time average of the muscle’s background activity calculated over a time window between the onset of a stable background torque signal and 80 ms before the onset of the mechanical perturbation \( (t_1) \), and \( EMGrms_{\text{background}} \) was the time average of the EMG activity recorded over 200 ms at MVC in flexion or extension. To minimize the potential for voluntary response in corrupting the reflex signal, \( EMGrms_{\text{reflex}} \) was calculated over a 150-ms time window after the onset of the reflex response, which includes the “dynamic” increase in muscle activity (DR) after the onset of perturbation. The choice of the 150-ms time window was guided by the reported voluntary contraction onset times of knee muscles following mechanical perturbations (~250 ms) (Pope et al. 1979; Wojtys and Huston 1994). A muscle reflex response was defined as an NR significantly \( (P < 0.05) \) greater than zero at the abduction angular perturbation and the targeted volitional co-contraction level (Dhaher et al. 2003). The mean and SD of muscle activity over the same time window was used to represent the corresponding EMG preactivation level prior to the onset of the mechanical perturbation \( (EMGrms_{\text{MVC}} + EMGrms_{\text{background}}) \) given in Eq. 4.

In the hierarchical model, intersubject differences were modeled by treating subjects as random effects, each with their own error structure. The temporal effect of time and resulting dependency created by assessing muscle activity during different trials at the same background adduction torque level was modeled using a first-order autoregressive process. The linear association between \( K \) and the knee muscle NRs were entered simultaneously into the model. Essentially a multiple regression analysis, a linear combination of muscles was created that maximized the prediction of \( K \). Simultaneous entry into the equation relegates the parameters (the regression weights) to reflect the unique contribution of each muscles reflex activity on stiffness. These weights can be directly compared with the weights from each muscle when entered alone into the equation, which
essentially reflect the correlation of that muscle’s activity with stiffness (ignoring the effects of the other muscles). In this way, the unique effect of each muscle (in comparison to other muscles) on stiffness can be compared with its independent effect (when considered by itself) on stiffness.

RESULTS

Muscle reflexes are elicited by the application of a mechanical abduction stimulus. The reflex EMG response elicited by a constant velocity abduction stimulus (7°, at 60°/s; i.e., “loading phase”), exhibited two components (Fig. 4). The first component was a “dynamic” increase in muscle activity (DR), followed by a second component of SR that appeared throughout the sustained step perturbation followed by an EMG increase during the unloading phase. This overall (dynamic-static) pattern of activity was also routinely observed for other preactivation levels of perturbation.

The intrinsic dynamic stiffness increased monotonically with the levels of the volitional co-contraction, as measured by the increase in the %APT, across all subjects (Fig. 5, bottom). While the effect of the volitional co-contraction levels prior to perturbation on knee intrinsic dynamic stiffness is similar across subjects, there was considerable intersubject variability. Specifically, at the volitionally relaxed state (η₀; 0% APT), the stiffness estimates across all 10 subjects ranged from a minimum of 219.5 N · m/rad to a maximum of 468.05 N · m/rad, with a mean of 398.2 ± 69.9 N · m/rad.

The linear association between $K(\eta)$ and %APT across all subjects was estimated using repeated measures linear regression to account for the multiple measurements taken from each subject as defined in Eq. 4 (Fig. 5). We observed that the intrinsic joint adduction-abduction stiffness due to the voluntary muscle contractions (the part of the intrinsic stiffness that arises from muscle contractions prior to perturbation) increased moderately with the increase in muscles co-contraction levels across all subjects (Table 1). The model data shows that the intrinsic dynamic stiffness increased from 0 N · m/rad at the volitionally relaxed state (η₀) to 60.0 N · m/rad at the largest adduction/abduction torque level as a %APT. The overall increase accounted for ~13% of the increase in the overall joint intrinsic dynamic stiffness due to muscle contractions (60 N · m/rad divided by the intrinsic dynamic stiffness estimated at the volitionally relaxed state, see Table 1).

Knee joint reflex stiffness in the adduction/abduction direction increased as the volitional co-contraction levels were increased. Considerable intersubject variability was observed in the rate of increase of the reflex stiffness as a function of the %APT. For example, based on a simple linear regression model of subject S1 data (\(\triangledown\) label in Fig. 5; top), the reflex stiffness increased an average of 8.5 N · m/rad for every 10% increase in %APT. This rate of increase was larger for subject S8 (\(\triangledown\) label in Fig. 5; top; 12.2 N · m/rad for every 10% increase in the volitional co-contraction level). The linear association between $K_r$ and %APT across all subjects (Fig. 5, dashed line)
Reflex stiffness ($K_r$) was estimated using Eq. 4, where $\%APT$ was represented in terms of the independent variable $\eta$ (Table 1). Reflex stiffness ($K_r$) was significantly greater than zero (mean = 82.2 N · m/rad; 95% CI: 67.7, 96.8) at relaxed conditions and increased on an average of 5.3 N · m/rad for every 10% increase in the $\%APT$ ($P = 0.015$).

To investigate if the increase of reflex stiffness with increasing levels of the percent addition passive torque ($\%APT$), as a result of changing the background co-contraction levels, was associated with an increase in the reflex intensity, statistical analysis was conducted to examine the effects of repeated trials, NR, and the interaction between repeated trials and NR levels on joint reflex stiffness. Stiffness was not independently influenced by repeated trials, because no changes in joint stiffness were observed over the course of the different trials [$F(3,68.8) = 1.1, P = 0.35$]. The level of the NR did influence joint stiffness, because increased levels of NR produced greater joint stiffness [$F(5,49.7) = 5.87, P < 0.001$]. No interaction between NR levels and trial number was observed, such that increases in NR did not produce differential amounts of reflex joint stiffness as a function of trial [$F(15,17.6) = 0.78, P = 0.69$]. Accordingly, we concluded that the observed increase in reflex stiffness was indeed associated with increased intensity of the reflex activity in all subjects. We also concluded that, while the number of trials per subject varied slightly, this variation had no effect on the estimated stiffnesses and their linear association with reflex activity in all subjects.

The magnitude of the reflex torque contribution to the overall torque was significant ($P < 0.05$) for all of the co-contraction levels used in this study. This is shown in Fig. 6, where the percent of variance accounted for of the reflex component ($\%VAF_r$) is plotted against the $\%APT$ defined as

$$\%VAF_r = 100 \cdot (1 - \frac{\text{var}_s}{\text{var}_t}),$$

where $\text{var}_s$ and $\text{var}_t$ are the variances of the total torque and reflex torque, respectively. The reflex torque was estimated by subtracting the estimated passive torque from the total torque measured at the load cell. The reflex contribution ranged from 10 to 45% depending on the subject and the level of the $\%APT$.

The validity of the delayed second-order model used in this study is given in terms of the percent variance accounted for defined as

$$\%VAF_e = 100 \cdot (1 - \frac{\text{var}_e/\text{var}_s}{\text{var}_e/\text{var}_s}),$$

where $\text{var}_e$ and $\text{var}_s$ are the variances of the simulated error and signal, respectively. The $\%VAF_e$ was >95% for all subjects across all trials and preactivation conditions. In addition, to indirectly evaluate the effectiveness of the estimation procedure used in this study, the lower limb inertial estimates were compared with those reported in the literature. The mean attributed to the estimated

![Fig. 5. Mean and SD across trials of the intrinsic and reflex adduction-abduction joint stiffness for all 10 subjects. Dashed lines shown in the figures are the intrinsic ($K$) and reflex ($K_r$) stiffness group fit determined using the parametric model described in Eq. 4 for all subjects as a function of the percent addition passive torque ($\%APT$) levels ($\eta$).](http://jn.physiology.org/)

### Table 1. Regression coefficients and the corresponding statistical measures for the mixed linear model fit of the association between $K_i$ and $K$ with percent addition passive torque levels ($\%APT$) ($\eta$) using the stiffness estimates of all 10 subjects shown in Fig. 5 using Eq. 4

<table>
<thead>
<tr>
<th>Stiffness</th>
<th>$a_o$ (N.m/rad)</th>
<th>$a_i$ (N.m/rad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrinsic $K$</td>
<td>440.41 (P &lt; 0.0001)</td>
<td>1.2714 (P &lt; 0.0024)</td>
</tr>
<tr>
<td>Reflex $K_r$</td>
<td>86.3425 (P &lt; 0.0001)</td>
<td>0.5297 (P &lt; 0.0133)</td>
</tr>
</tbody>
</table>

The stiffness values at $\eta = 0$ defined in Eq. 4 as $a_o$ are intrinsic and reflex stiffness estimates determined when knee muscles were quiescent prior to the mechanical perturbation (the volitionally relaxed state, $\eta_o$). For the intrinsic stiffness component, $a_o$, represents the combined stiffness of the joint’s periarticular tissues and passive tissues surrounding the noncontracted knee muscles and and $a_i$ represents the part of the intrinsic stiffness that arises from muscle contractions prior to perturbation.
Our results revealed that reflexive muscle contractions are mediated by periartrial tissue afferents and can result in a significant increase in the joint’s adduction-abduction stiffness with the joint in the fully extended posture. Our data also indicated that the reflex mediated stiffness was moderately dependent on the activation state of the muscles prior to the perturbation.

There have been numerous studies that used two different mathematical formulations to estimate reflex contribution to joint mechanics from data that include the intrinsic as well as the reflex contributions: parametric (cf. Zhang and Rymer 1997) and nonparametric (cf. Kearney et al. 1997) methods. Unlike the nonparametric approaches, parametric methods require a priori knowledge of the structure. In this study, a parametric linear delayed second-order dynamic model was used to model knee joint mechanics under the adduction/abduction loading conditions. Three levels of qualifiers were used to validate this assumption: the overall variance accounted for, variance accounted for by the reflex components, and a model structure selection criterion (MDL). The validity of the delayed second-order dynamic model choice was shown by the high levels of the VAF (%VAF >95%) and the substantial contribution of the reflex component to the total torque output (as high as 45%). The addition of the delayed component to the model structure was further justified with the significant drop in the MDL factor as a result of the addition of the two extra parameters to account for the reflex components (≈90% reduction).

During the volitionally relaxed state, our data show that active modulation of the joint’s frontal plane stiffness can be achieved by muscle contractions elicited by periartrial tissue afferents. These data indicate that this modulation is substantial when related to the joint intrinsic dynamic stiffness attributed to the passive compliance of the joint’s periartricular tissues and the relaxed muscles. The relative contribution of the reflex modulation to the overall joint stiffness when no muscle contraction is present is ~20% (~86/440; see Table 1). More importantly, however, is the finding that the reflex mediated stiffness was substantial in relation to the stiffness contribution of the precontracted muscle, suggesting that the reflexive contraction may be used to increase joint stiffness during a functional movement. Over the range of preactivation levels that were tested, the volitionally co-contracted states increased the joint stiffness an average of 60 N · m/rad, while the reflex component increased the joint adduction/abduction stiffness by 27 N · m/rad. This indicates a relative increase of 45% of active knee joint stiffness as a result of the reflexive contractions. This ratio is consistent with findings obtained from studies on
muscle stretch reflex contributions to joint stiffness. For example, Zhang and Rymer (1997) reported a stiffness increase of 10–50% of the overall joint stiffness due to reflex contractions in the human elbow computed over a range of preactivation levels.

The intrinsic dynamic stiffness data estimated at the voluntarily relaxed state represented the joint’s periarticular tissue stiffness. The mean value of this stiffness was 413.2 N · m/rad, which is substantially larger than the mean passive adduction/abduction joint stiffness (236 N · m/rad) reported by Bryant and Cooke (1988). Although obtained at the same posture, the difference in the joint stiffness between our results and those of Bryant and Cooke (1988) may be attributed to the difference in the loading rate used. They estimated knee joint quasi-static stiffness by computing the slope of the torque-angle relation obtained at a loading rate of 13°/s while our estimates of joint stiffness were obtained using a dynamic model of the joint subjected to a significantly larger loading rates (60°/s). The increase of joint stiffness with increasing loading rate has been illustrated in experiments conducted under reduced preparation on passive tissues (Mow and Hayes 1991). This increase in loading rate has a significant effect on the nature of the torque-angle relationship, due to inertial and damping contributions, as shown in Fig. 3.

We were interested in investigating the joint mechanics using loading rates similar to those encountered during functional tasks. For example, derived from data reported by Lafortune et al. (1992), loading rates in the adduction-abduction direction during over ground walking was found to be in the range of 40–80°/s (which includes the 60°/s used in this study). Given that passive tissues stiffness is highly dependent on loading rates (Mow and Hayes 1991), estimation of knee intrinsic stiffness using a dynamic model of the limb is advantageous because it provides a more realistic insight into the modulation of knee joint stiffness at loading rates observed during normal functional tasks. However, it could be argued that joint stiffness can be calculated from the slope of the torque-angle relationship obtained at these higher loading rates. In that case, it is difficult to decouple intrinsic stiffness effects from inertial and damping contributions, an issue that is accounted for with the use of a second-order dynamic model.

The contribution of the contracted muscle intrinsic stiffness is apparent during the voluntarily co-contracted states. Overall, our estimates of intrinsic joint stiffness were consistent with previous findings (Markolf et al. 1978). However, the increase in joint stiffness due to muscle contraction seen here (~13%: the largest stiffness increase due to muscle contractions divided by the joint passive stiffness estimates at the voluntarily relaxed state) were significantly lower than some of the reported data (Bryant and Cooke 1988; Goldfuss et al. 1973). This difference may have been in part due to the difference in joint adduction/abduction posture at which the joint stiffness was calculated and the muscle activation levels. Previously, joint stiffness increase was assessed at the neutral position while our values were measured at an abduction offset angle of ~4°. Olmstead and colleagues, however, reported a 20% increase in joint stiffness as a result of muscle contractions when measuring at the terminal point of the torque–angle curve (adduction angle ~5°) (Olmstead et al. 1986). This value is comparable with the increase observed in our subjects.

Considering the stiffness estimates reported previously in the sagittal plane (Tai and Robinson 1999), muscle contractions resulted in a substantially smaller contribution to the overall joint stiffnesses in the adduction/abduction direction (~13%) compared with the flexion/extension directions (~50%). This substantial difference is due in part to the fact that in the mid-range of the flexion/extension degree-of-freedom, most of the stiffness is attributed to active muscle intrinsic stiffness (Zhang et al. 1998). In contrast, the main components that contribute to the overall joint adduction/abduction stiffness are the joint’s periarticular tissues. As a result of the mixed model fit of the intrinsic dynamic stiffness, the passive component of joint stiffness accounted for ~440 N · m/rad of the overall joint stiffness. The full range of preactivation muscle contractions resulted in an ~60 N · m/rad (~13%) increase in the joint intrinsic adduction/abduction stiffness. This modest contribution of muscle contractions to the adduction/abduction stiffness is consistent with earlier findings with regard to the volitional contribution of knee muscles in support of adduction or abduction loads. Lloyd and Buchanan (2001) reported an average volitional muscle contraction contribution (relative to that at the voluntarily relaxed state and expressed as a percent of the total targeted load) in the adduction and abduction direction of 9 and 18%, respectively.

The reflex-induced stiffness showed a proportional dependence on the levels of the volitional co-contraction states prior to perturbation, represented by different percentages of the adduction passive torque (%APT). Results from the multilevel hierarchical model showed that this increase in reflex stiffness was also associated with increased EMG intensity of the reflex activity [F(5,49.7) = 5.87, P < 0.001] in all subjects. This trend is consistent with the observations of Carter et al. (1990) and Zhang and Rymer (1997) who showed that muscle reflex stiffness mediated by muscle spindle afferents increased with an increase in background muscle activation levels. In our study, the stiffness behavior may depend on modulation of motoneuron pool excitability, which is altered as a result of varying preactivation levels. An increase of the preactivation level provides additional excitatory input to the motor pool and causes more motoneurons to fire (Fuglevand et al. 1993; Matthews 1986), resulting in increased EMG intensity of the reflex activity, compared with lower preactivation levels. An alternative explanation for the proportional stiffness increase is the alteration in passive strain of tissues surrounding the knee and their afferent innervation. Co-contraction of the knee muscles at different preactivation levels in the abducted posture may alter the tension in medial periarticular tissues, thereby changing the afferent discharge to the spinal motor pools prior to and during the abduction perturbations. In reduced preparations, mechanically sensitive afferents in the cat knee joint capsule showed a strong association between the neural discharge rate and the amplitude of the sustained tension applied to the capsule (Hoffman and Grigg 1989). In our experimental study, however, the change in tension in periarticular structures due to muscle contractions is unknown, and further experimental studies would be necessary to determine whether there was, indeed, a significant alteration in periarticular tissue tension as a result of co-contraction in the abducted position. Such futures studies would help distinguish the precise mechanisms underlying changes in reflex stiffness.
Group Ia muscle spindles may have been activated by the abduction mechanical perturbation, although the absence of any short latency response (25 ms, see Dhaher et al. 2003) in the perturbation-induced EMG activity observed at the different preactivation levels indicates that the mechanical stimulus did not directly manifest itself in a muscle contraction. However, spindle activation, with changing sensitivity as a result of muscle contraction (Kandel et al. 2000), may have contributed indirectly to the observed reflex by providing subthreshold excitation of the motor pool, thereby altering the observed long-loop reflex behavior following stimulation of periarticular afferents. To clearly establish that these reflexes are indeed due to periarticular tissue afferents, experiments that involve the anesthesia of nerve branches known to contain most of the afferent nerves from the knee joint passive tissues (Kennedy et al. 1982) should be conducted. A significant modulation of the reflex following afferent blockade would indicate that a substantial component of the observed reflex could be attributed to the periarticular tissue receptors. Moreover, reflex stiffness estimates based on such afferent blockade experiments are most convincing and are the ultimate validation tool to the mathematical formulation used here to estimate reflex contributions to joint mechanics. However, nerve blockade experiments are lengthy and require the careful matching of the operating points, background activation levels and the initial joint abduction offset angle, before and after the nerve block procedure.

A key to the functional significance of the reflex stiffness is the existence of a mechanical stimulus during natural movement that would elicit a timely response from the periarticular tissue afferents. Under many naturally occurring conditions (Besier et al. 2001a,b; Hull 1997; Quinn and Mote 1992) where sustained adduction/abduction loading arises, reflex action may be used to help protect the joint through a continuous modulation of joint stiffness. Neptune et al. (1999) reported that the stance phase of a side-stepping cutting maneuver (average running speed of 4.0 m/s) can last ≥270 ms, a sufficient time for the periarticular tissue-muscular reflex to be significant. Under a similar experimental paradigm, McLean et al. (1999) reported a 5–8° range of abduction angle between the tibia and femur during the stance phase of the side-stepping movement and Besier et al. (2001b) reported that ~40 N · m of applied abduction loading was applied to the knee during the weight acceptance portion of the same movement. This indicates that mechanical perturbations during natural movements do exist to potentially elicit response form periarticular tissue afferents (Dhaher et al. 2003).

The potential contribution of any reflex action to the overall joint stability during a functional movement like the side-stepping maneuver can therefore be estimated using previously reported angular (~8°; McLean et al. 1999), and loading (40 N · m; Besier et al. 2001b) levels and our estimates of joint reflex stiffness. A reflex stiffness of 87 N · m/rad, estimated here during the volitionally relaxed state, would result in a potential reflexive increase in joint adduction torque of ~12 N · m for an 8° abduction deformation at the knee. This increase when compared with the hypothetically applied abduction loading at the knee (40 N · m) accounts for ~30% of the applied torque at the joint, a substantial reflex adduction torque for the maintenance of joint integrity in the frontal plane. While the scenario presented here is one of the many possibilities to show the potential mechanical significance of this class of reflex, further experiments are necessary to examine the exact contribution of the periarticular tissue afferents to joint stiffness under load bearing conditions commonly encountered during “real life” functional tasks.

Considering the late onset of the reflex observed here, reflex action might not be fast enough to provide the necessary constraint to protect the joint from damaging loads occurring at high loading speeds (Dyhre-Poulsen and Krosggaard 2000). This presents a significant limitation of such reflex compensatory mechanisms in protecting the knee joint during a rapid injury-inducing load. In these cases, an alternative hypothesis would be that reflexes elicited from periarticular tissues mechanoreceptors contribute to knee joint stability because they help the nervous system establish predictive motor patterns in key neural structures (Dhaher et al. 2003). Due to the late onset of the reflex observed (>70 ms), sufficient time for a transcortical transmission (Christensen et al. 2000), it is possible that this reflex may be involved in the establishment of predictive motor patterns in key neural structures. Neurophysiological and motor control findings reported in the literature further support this conclusion. For example, activity in the cerebellum, which is intricately involved in motor learning (Leiner et al. 1986; Thach 1998), can be elicited from muscle and joint mechanoreceptors (Gellman et al. 1983, 1985). To this end, loading of periarticular tissues can allow the nervous system to develop postural control strategies that resist excessive strain seen during various biomechanical conditions. Although the origins of such strategies are unclear, it is likely that the muscle patterns elicited by adduction or abduction loading may emerge during natural rapid movements through growth and development.

One could argue that various load bearing and postural conditions of the knee joint, as seen during many functional tasks, may affect the reflex contribution to joint stiffness reported here under isolated conditions. However, the choice of using the extended knee only to assess the effect of abduction loading on the periarticular tissue afferents reflex contribution to joint stiffness proves advantageous in several respects. There is less likelihood that muscle proprioceptors will contribute to reflex activation in these directions, allowing a clear examination of the ligament/capsular mechanoreceptor contribution to joint stiffness. Loading a slightly flexed knee into adduction/abduction rotation, a posture often associated with knee injuries, will induce hip rotation. This rotation would result in an EMG response with a significant component originating from muscular and passive tissue afferent surrounding the hip. Thus the choice of full extension during the adduction/abduction loading was required to isolate knee passive tissue afferent responses from hip afferent contributions.

Given the linear association between the reflex intensity and stiffness reported here (see the mixed model results), one would expect that modulation of joint stiffness via this class of reflex can be closely associated with the modulation of reflex intensities as a function of the amplitude of the mechanical stimulus. In our earlier study, we have reported a nonlinear reflex trend as a function of perturbation amplitude per muscle with a consistent reflex pattern across all muscles for the different levels of stimuli (Dhaher et al. 2003). Considering the linear association between reflex intensity and stiffness along with the nonlinear relationship between reflex intensity and...
perturbation amplitude, it is possible that reflex stiffness is associated nonlinearly with the angular perturbation amplitude. Further experiments are necessary, however, to investigate the effect of altered amplitude of perturbation on the associated reflex stiffness. Such findings would establish whether this reflex stiffness and its protective role indeed hold true for all or a limited physiological range of angular perturbations.

Finally, previous studies have shown that reflex is task dependent (cf. Hultborn 2001 for an extensive review). Thus the contribution of the periarticular tissue afferents reflects to joint stiffness obtained using the seated posture described in this study may change during other functional tasks, like walking or standing. Attempts to load ligaments during functional tasks are certainly feasible, but are technically demanding, and would divert our efforts from understanding the properties of the mechanoreceptor-based knee joint reflex stiffness contribution, a necessary prerequisite. Moreover, investigation of the knee joint’s medial-lateral stability and the role of the periarticular tissue afferents in joint’s stiffness modulation provide an important model for understanding joint stability in other single degree-of-freedom joints, such as the radio-ulnar joint of the elbow and the interphalangeal joints of the hand and foot, that also rely on collateral ligaments to provide medio-lateral stability.

Acknowledgments

The authors thank Michael Lewek for critical editorial and scientific review of this manuscript.

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Grants

The authors gratefully acknowledge Dr. Ralph and Marian C. Falk Medical Research Trust and National Institute of Arthritis and Musculoskeletal and Skin Diseases Grants AR-46422-02 and 1 R01AR-049837-01 and the Whittaker Foundation for support of this research.

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J Neurophysiol • VOL 93 • MAY 2005 • www.jn.org

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