Neuromuscular fatigue is commonly defined as “any exercise-induced reduction in the ability of skeletal muscle to produce force or power irrespective of task completion” (11). Historically, potential factors involved in neuromuscular fatigue were classified into two categories: 1) central factors involving the CNS and neural pathways and 2) peripheral factors occurring within the muscle beyond the neuromuscular junction (11). It has been shown in adults that peripheral factors account for a larger part of fatigue after repeated maximal contractions compared with prolonged exercise where central fatigue is prominent (27). However, it is still unclear whether the relative contributions of central and peripheral factors to the development of fatigue induced by repeated maximal contractions differ between children and adults. In particular, the role of central factors in the development of fatigue in children is still being debated.

Until now, it has been widely demonstrated that prepubertal children fatigue less than adults when performing maximal isometric (5,15) or isokinetic contractions (8) or dynamic whole-body activities, such as maximal cycling (36,39) and short running bouts (40). We (38,46) and other research groups (21) attributed this phenomenon to the children’s metabolic profile, which is better designed for oxidative than for anaerobic metabolism during high-intensity exercise. This metabolic profile in children could explain their lower muscle fatigue through lower depletion of phosphocreatine, lower muscle accumulation of phosphomonesters (i.e., glucose-6-phosphate), inorganic phosphate, and H+ ions during high-intensity exercise (21). Other contributing factors such as lower muscle force/power capacity (22,45) and higher percentage of fatigue-resistant slow-twitch fibers (23) could also account for these differences. Taken together, all these factors should minimize the development of peripheral fatigue in children. Such lower

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**ABSTRACT**

RATEL, S., V. KLUKA, S. G. VICENCIO, A. JEGU, C. CARDENOUX, C. MORIO, E. COUDEYRE, and V. MARTIN. Insights into the Mechanisms of Neuromuscular Fatigue in Boys and Men. *Med. Sci. Sports Exerc.*, Vol. 47, No. 11, pp. 2319–2328, 2015. **Purpose:** The aim of the present study was to investigate the role of central and peripheral factors in neuromuscular fatigue induced by repeated maximal contractions in children and adults. **Methods:** Eleven boys (9.9 ± 1.2 yr) and 12 men (23.9 ± 3.5 yr) completed a fatigue protocol consisting in a repetition of 5-s maximal isometric voluntary contractions (MVC) of the knee extensors separated by 5-s passive recovery periods until the generated torque reached 60% of its initial value. Single magnetic stimulations were delivered to the femoral nerve every five MVC to follow the course of voluntary activation level and the amplitude of the potentiated twitch torque (Qtwpot) and vastus lateralis and rectus femoris concomitant M-waves (Mmax). **Results:** Torque reached 60% of initial value after 49.5 ± 16.8 and 34.0 ± 19.6 repetitions in boys and men, respectively (P < 0.05). Furthermore, men showed significantly higher knee extensor MVC decline than boys between 50% and 90% of total repetitions (P < 0.05). Voluntary activation remained unchanged in men, whereas it decreased significantly in boys (P < 0.05). In contrast, whereas Qtwpot remained unchanged in boys, Qtwpot decreased progressively up to 60% of total repetitions in men (P < 0.001). Finally, Mmax remained unchanged for vastus lateralis and rectus femoris muscles in both groups. **Conclusions:** Children experienced no apparent peripheral fatigue and higher central fatigue than adults. The greater fatigue resistance in children could be related to a strategy of the CNS aimed at limiting the recruitment of motor units to prevent any extensive peripheral fatigue. **Key Words:** GROWTH, CENTRAL FATIGUE, PERIPHERAL FATIGUE, ELECTROMYOGRAPHY, PERIPHERAL MAGNETIC STIMULATION
Peripheral fatigue in children was reported by Streckis et al. (42) and more recently by Hatzikotoulas et al. (15) and Murphy et al. (31). These studies showed lower twitch torque decrement after sustained or repeated maximal voluntary contraction (MVC) in children compared with that in adults. Furthermore, after repetitive stretch shortening cycles, Gorianovas et al. (12) showed lower low-frequency fatigue, as evaluated by the low-to-high frequency tetanic force ratio, in children compared with that in adults, suggesting smaller alteration of the excitation–contraction coupling. The contribution of sarcolemmal excitability changes to peripheral fatigue in children is much more debated. Although some authors reported lower decrement of the M-wave in response to exercise in boys compared with that in men (15), others showed increase in boys and significant decrease in men (31). However, in the previously mentioned studies, the M-wave changes were only investigated before and after fatigue. These discrepancies could result from a different balance of potentiation and fatigue on the M-wave during exercise between boys and men. Therefore, to check this assumption, the time course of the M-wave should be described during the course of the fatiguing test and compared between children and adults. Although the underlying factors are not all fully identified, there is thus a consensus on the fact that children develop lower peripheral fatigue compared with adults.

At the central level, this lower peripheral fatigue should theoretically translate into reduced afferent inhibitory feedback to the CNS and therefore into reduced central fatigue (2). Accordingly, Gorianovas et al. (12) reported significantly lower levels of central fatigue on the knee extensor (KE) muscles in children as compared with those in adults after a fatigue protocol involving 100 drop jumps (12). However, the same research team reported opposite results in another study where the maximal voluntary activation (VA) of the KE muscles, as determined by the twitch interpolation technique, decreased to a greater extent during a 2-min MVC in 12- to 14-yr-old children compared with that in adults (42). This larger central fatigue observed in children could represent a safety mechanism acting during high-intensity contractions to limit the force output and therefore maintain homeostasis, protect vital functions, and limit peripheral fatigue (2). The theoretical existence of such a protective mechanism has been frequently proposed in adults (33), but it is currently unknown whether its effect is greater in children than that in adults. Interestingly, Hatzikotoulas et al. (15) recently reported a comparable amount of central fatigue in boys and men but lower peripheral fatigue in boys. This result also supports the idea of greater protection by the CNS and/or higher sensitivity of the III–IV afferent fibers in boys to limit the force output and therefore delay peripheral fatigue (2). Beyond the influence of this potential central regulation of force output during a fatiguing task, the exercise duration could promote development of central fatigue in children (5). Indeed, the lower fatigability in children translates into longer exercise duration when repeating maximal contractions (5). Therefore, when matching the level of exhaustion in children and adults, greater central fatigue should be observed in children.

However, these age-related differences in the extent and etiology of neuromuscular fatigue could be confounded by the effect of the absolute force level developed at the beginning of the exercise. Indeed, studies that have compared neuromuscular fatigue between men and women showed that men, who are stronger, are more fatigable than women (17), but these differences are abolished when populations are matched for their absolute force or if absolute force is used as covariable in statistical analysis (19).

The objective of the present study was to investigate the effects of growth on the development and etiology of neuromuscular fatigue. We formulated the hypotheses 1) that children would experience less peripheral fatigue and more central fatigue than adults during a fatiguing task conducted until a given level of exhaustion, matched between the two populations, 2) but that these age-related differences of peripheral and central fatigue would be reduced when the confounding effect of the absolute force is taken into account in the analysis.

**MATERIALS AND METHODS**

**Subjects.** A total of eleven 8- to 11-yr-old healthy boys (Tanner stages I–2) and twelve 18- to 30-yr-old healthy men were recruited. All the subjects were involved in different physical activities such as rugby, basketball, swimming, etc. To be included, they had to exercise less than 4 h wk⁻¹ and be free of any medical contraindication to physical activity. The present study was approved by the local ethics committee (Protection Committee of People for Biomedical Research South East VI; authorization number, AU929). All the participants were fully informed of the experimental procedures and gave their written consent before any testing was conducted. In addition, the written consent of the parents/guardians was also obtained for the children participants.

**Experimental procedure (design).** All subjects were tested on three experimental sessions separated by at least 1 wk. The first session was dedicated to collecting subjects’ physical characteristics (anthropometrical measurements, body composition, and maturation assessment), familiarization with the experimental procedures, and clinical examination by a medical practitioner (pediatrician for the children). During the second session, participants were asked to perform MVC of the KE muscles at different knee angles (20°, 40°, 60°, 70°, 80°, 90°, and 100°; 0°, full extension) to determine the optimal angle for maximal torque production. Finally, during the third session, all the subjects performed the intermittent voluntary fatigue protocol.

**Anthropometric measurements.** Body mass (BM) was measured to the nearest 0.1 kg using a calibrated scale, and height was determined to the nearest 0.01 m using a standing stadiometer. Height and BM were measured without shoes and while wearing underwear. Sitting height was also measured while the participants sat on the floor against...
During each test, the subjects were instructed to grip the seat which was aligned with the lateral femoral condyle of the right femur. This configuration was chosen to reduce the risk of peripheral fatigue. A high-density foam pad was placed against the posterior aspect of the leg, and a Velcro strap was positioned over the anterior malleolus. The lever arm was home built with the hip joint flexed at 30°. Subjects were comfortably positioned on an adjustable chair with visual feedback of torque output during the exercise. How- ever, they were strongly encouraged by the investigators during the entire task and during the preceding and following test sessions. The knee joint was fixed at the optimal angle for maximal torque production, which was determined from the torque–angle relation during the second visit. To follow the recovery process, the participants performed one 5-s MVC 3, 6, and 15 min after the end of the protocol. Single magnetic stimulations were delivered to the femoral nerve every five MVC and during the recovery period to determine the maximal level of VA using the twitch interpolation technique (see following section for more details). The EMG activity of the KE muscles was recorded during the entire fatigue protocol. The amplitude of the potentiated twitch torque (Qtwpot) (see following section) and vastus lateralis (VL) and rectus femoris (RF) concomitant compound action potential amplitudes (Mmax) were considered as indicators of peripheral fatigue. The time course of VA and normalized EMG (see following section) of the VL and RF muscles throughout the protocol was considered as an index of central fatigue.

Torque measurements. Voluntary and evoked contractions were assessed in isometric condition with an isokinetic dynamometer (Cybex NORM; Lumex, Ronkonkoma, NY). Subjects were comfortably positioned on an adjustable chair with the hip joint flexed at 30° (0°, neutral position). The dynamometer lever arm was attached 1–2 cm above the lateral malleolus with a Velcro strap. This lever arm was home built with a high-density foam pad placed against the posterior aspect of the leg and a Velcro strap positioned over the anterior aspect of the leg. This configuration was chosen to reduce cushioning and improve torque transmission and resolution, which is critical when evaluating twitch contractile properties and the VA level. The axis of rotation of the dynamometer was aligned with the lateral femoral condyle of the right femur. During each test, the subjects were instructed to grip the seat during the voluntary contractions to stabilize the pelvis. Strong verbal encouragements were given by the investigators during each contraction. Torque data were corrected for gravity using the Cybex software and were digitized and exported at a rate of 2 kHz to an external analog-to-digital converter (PowerLab 8/35; ADInstruments, New South Wales, Australia) driven by the LabChart 7.3 Pro software (ADInstruments, New South Wales, Australia).

Femoral nerve stimulation. Evoked contractions of the KE muscles were triggered by a single magnetic stimulus delivered to the femoral nerve using a 45-mm figure-of-eight coil connected to a magnetic stimulator (Magstim 2002; peak magnetic field strength, 2.34 T; stimulation duration, 0.1 ms; Magstim Co., Whiteland, Dyfed, United Kingdom). The coil was placed high in the femoral triangle in regard of the femoral nerve. Small spatial adjustments were initially performed to determine the optimal position where the greatest unipolar KE twitch amplitude (Qtwpot) and the greatest VL and RF Mmax were evoked. The optimal stimulation intensity, i.e., the intensity where maximal twitch and concomitant M-waves amplitudes started to plateau, was determined from a recruitment curve. Briefly, two single stimulations were delivered every 30 s at 70%, 80%, 85%, 90%, 95%, 97%, and 100% of the maximal stimulator power output. Qtwpot and Mmax plateaued at 85.0% ± 4.3% and 85.0% ± 6.7% of the stimulator power output for boys and men, respectively. This optimal intensity of stimulation was not statistically different between groups. To overcome the potential confounding effect of axonal hyperpolarization (7), the stimulation intensity was set to 100% of the stimulator output during the subsequent testing procedures (i.e., voluntary intermittent fatigue protocol). This intensity corresponded to 117.9% ± 6.0% and 118.4% ± 10.1% of the optimal intensity in the boys and men, respectively. This supramaximal intensity of stimulation (approximately 120%) has been demonstrated as being optimal for adequate assessment of central and peripheral fatigue of the KE muscles (32).

VA level. To determine VA, the twitch interpolation technique was used. Briefly, a superimposed (Qtww) and a potentiated (Qtwpot) single twitch were delivered during MVC after the torque had reached a plateau and 3 s after the cessation of the contraction, respectively. This provided the opportunity to obtain a potentiated mechanical response and hence reduce the variability of VA values. These superimposed and potentiated mechanical amplitudes allowed the quantification of VA (%VA) as proposed by Merton (28) in equation 1:

\[
\%VA = \left(1 - \frac{Qtww \times Qtwpot^{-1}}{}\right) \times 100
\]  

[1]

EMG recordings. The EMG signals of the VL, RF, and biceps femoris (BF) muscles were recorded using bipolar silver chloride surface electrodes (Blue Sensor N-00-S, 30 × 22 mm; Ambu, Denmark) during voluntary and evoked contractions. The recording electrodes were taped lengthwise on the skin over the muscle belly, as recommended...
by the Surface Electromyography for the Noninvasive Assessment of Muscles, (16) with an interelectrode distance of 20 mm. The position of the electrodes was marked on the skin in case they needed to be repositioned during the experiment (which occurred in two of 23 subjects during the recovery period). The reference electrode was attached to the patella. Low impedance (Z < 5 kΩ) at the skin–electrode surface was obtained by shaving, gently abrading the skin with thin sandpaper, and cleaning with alcohol. EMG signals were amplified (Dual Bio Amp ML 135; ADInstruments, New South Wales, Australia) with a bandwidth frequency ranging from 10 to 500 Hz (common mode rejection ratio > 85 dB; gain, 1000) and simultaneously digitized together with the torque signals. The sampling frequency was 2 kHz. During the course of the fatigue protocol, root mean square (RMS) values of the VL and RF EMG activity were calculated during the MVC trials over a 0.5-s period after the torque had reached plateau and before the superimposed stimulation was evoked. This RMS value was then normalized to the maximal peak-to-peak amplitude of the potentiated VL and RF M-waves (RMS/M<sub>max</sub>).

**Antagonist coactivation.** The level of antagonist coactivation (%CoAct<sub>BF</sub>) of the BF muscle was computed as the BF EMG activity during knee extensions (Kext), normalized to the maximal BF EMG activity recorded during a maximal knee flexion (Kflex) (equation 2). To record this maximal BF RMS value, the participants were asked to perform 3-s maximal voluntary isometric contractions of the knee flexors before the fatigue protocol. This measurement was repeated twice at a 90° knee angle. The best trial was used for subsequent analysis.

\[
\%\text{CoAct}_{\text{BF}} = \left(\frac{\text{RMS}_{\text{Kext}}}{100}\right) \times \frac{\text{RMS}_{\text{Kflex}}}{\text{RMS}_{\text{Kmax}}} \tag{2}
\]

**Statistical analysis.** Data were screened for normality of distribution and homogeneity of variances using a Shapiro–Wilk normality test and the Bartlett test, respectively. Student’s t-tests for unpaired samples were used to compare age, APHV, and anthropometric characteristics between both groups. Maturation status (Tanner staging) was compared between groups using a chi-squared test for qualitative variables. Differences in absolute values and in percent changes relative to the prefatigue values were analyzed by a two-way (group × percentage of repetitions) ANOVA with repeated measures. When the ANOVA revealed significant effects or interactions between factors, a Fisher least significant difference post hoc test was applied to test the discrimination between means. Moreover, to discriminate the effect of MVC torque on fatigue, we used a mixed general linear model: the initial MVC torque was used as a continuous predictor variable (= covariable), the group as a categorical independent variable, and the MVC torque during exercise, Qt<sub>w<sub><sub>pot</sub></sub>, or VA as dependent variables. Pearson correlation coefficients were used to determine linear correlations between the initial MVC torque, the total number of repetitions, and relative Qt<sub>w<sub><sub>pot</sub></sub> and VA variations over the fatigue protocol. The relative changes of Qt<sub>w<sub><sub>pot</sub></sub> and VA were calculated as shown in equation 3:

\[
\left[\frac{\text{final value} - \text{initial value}}{\text{initial value}}\right] \times 100 \tag{3}
\]

The limit for statistical significance was set at \( P < 0.05 \). Statistical procedures were performed using the Statistica 8.0 software (StatSoft, Inc.). Results were presented in the text and tables in absolute values (mean ± SD). For the sake of clarity, data presented in figures were expressed as a percentage of their initial values (mean ± SD).

**RESULTS**

**Participants’ characteristics.** Subjects’ characteristics are described in the Table 1. As expected, the boys showed significantly lower values for BM, height, and BMI compared with men \( (P < 0.001) \). However, no significant difference was observed for the percentage of body fat between the two groups. In children, age at the peak height velocity was 14.1 ± 1.0 yr, and their chronological age was approximately – 3.6 ± 0.7 yr from APHV.

**MVC torque.** The peak MVC torque was produced at a knee angle of 77.3° ± 6.5° and 80.8° ± 7.9° in boys and men, respectively. No significant difference for the optimal angle was observed between groups. Task failure, corresponding to the predetermined 60% decrement of MVC was reached after 49.5 ± 16.8 and 34.0 ± 19.6 repetitions in boys and men, respectively, and this difference was statistically significant \( (P < 0.05) \). MVC torque varied as a function of group and percentage of repetitions during the fatigue test \( (P < 0.001) \). Boys produced significantly lower absolute MVC torque values than men \( (P < 0.001) \). Initial values were 86.0 ± 28.3 and 292.7 ± 52.0 Nm in boys and men, respectively. Furthermore, when percent MVC changes (relative to initial values) were calculated, men showed significantly earlier reduction of MVC torque than boys (Fig. 1). Significant child–adult differences in relative MVC changes were observed between 50% and 90% of total repetitions \( (P < 0.05) \). At failure, relative MVC, expressed as a percentage of its initial value, was not different between groups. During the recovery period, the boys’ group showed significantly faster recovery of the MVC torque compared with men \( (P < 0.05) \). Whereas MVC torque had fully recovered after 3 min in boys, men did not recover their initial KE MVC torque even after 15 min of recovery.

**TABLE 1. Physical characteristics of the experimental groups.**

<table>
<thead>
<tr>
<th></th>
<th>Boys (n = 11)</th>
<th>P Value</th>
<th>Men (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>9.9 ± 1.2</td>
<td>&lt;0.001</td>
<td>23.9 ± 3.5</td>
</tr>
<tr>
<td>APHV (yr)</td>
<td>14.1 ± 1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Years to APHV</td>
<td>−3.6 ± 0.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tanner stages (pubic hair)</td>
<td>I–II</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tanner stages (testicular size)</td>
<td>I–II</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.39 ± 0.09</td>
<td>&lt;0.001</td>
<td>1.75 ± 0.07</td>
</tr>
<tr>
<td>BM (kg)</td>
<td>33.2 ± 8.3</td>
<td>&lt;0.001</td>
<td>76.3 ± 8.2</td>
</tr>
<tr>
<td>BMI (kg·m&lt;sup&gt;−2&lt;/sup&gt;)</td>
<td>17.2 ± 3.7</td>
<td>&lt;0.001</td>
<td>24.9 ± 2.8</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.
However, when the initial MVC torque was used as covariable, no significant interaction or main effect on the time course of MVC was observed.

### Potentiated twitch torque

Twitch potentiation after the first MVC did not differ between groups (men, +31.7% ± 16.9%; vs boys, 21.3% ± 32.0%; \(P = 0.34\)).

During the fatiguing exercise, ANOVA revealed significant interaction of group–percentage of repetitions for \(\text{Qtwpot}^{\text{pot}}\) (\(P < 0.001\)). Men showed greater absolute \(\text{Qtwpot}^{\text{pot}}\) values than boys over the entire fatigue protocol (\(P < 0.001\)). Initial values were 23.3 ± 8.3 and 78.5 ± 26.8 Nm and in boys and men, respectively. Furthermore, significant interaction of group–percentage of repetitions was observed for relative \(\text{Qtwpot}^{\text{pot}}\) changes (\(P < 0.001\)). In boys, the potentiated twitch torque remained unchanged over the fatigue test and during the subsequent recovery period. In contrast, in men, \(\text{Qtwpot}^{\text{pot}}\) decreased progressively up to 60% of the total number of repetitions and then remained unchanged until the end of the fatigue protocol (Fig. 2). \(\text{Qtwpot}^{\text{pot}}\) partly recovered at the 15th minute of recovery in men. Significant child–adult differences in relative \(\text{Qtwpot}^{\text{pot}}\) changes were observed between 20% and 100% of total repetitions (Fig. 2).

However, when the MVC torque was used as covariable, no significant interaction or main effect on the time course of \(\text{Qtwpot}^{\text{pot}}\) was observed.

### VA level

ANOVA revealed a significant interaction of group–percentage of repetitions for VA (\(P < 0.001\)). Absolute VA values were significantly higher in men over the fatigue test except for the first MVC where no difference was observed between the two groups (86.9% ± 7.6% vs 91.2% ± 2.6% in boys and men, respectively). Furthermore, a significant interaction of group–percentage of repetitions for relative VA changes was observed (\(P < 0.001\)). Whereas no significant change of VA was observed in men throughout the fatigue protocol, boys displayed significant and progressive VA decrement until the end of the test (\(P < 0.05\)). At the end of the fatigue test, VA represented 73.2% ± 19.8% of the initial value in boys. Afterwards, VA returned to its initial value after 3 min of recovery in boys (Fig. 3). Significant child–adult differences in relative VA changes were observed between 60% and 100% of total repetitions (Fig. 3).

However, when the MVC torque was used as covariable, no significant interaction or main effect on the time course of VA was observed.

### EMG activity

ANOVA revealed no significant interaction or main effect for the \(M_{\text{max}}\) for VL and RF muscles. The \(M_{\text{max}}\) remained unchanged throughout the fatigue protocol for VL and RF in boys and men. Similarly, no significant interaction was observed for the RMS/\(M_{\text{max}}\) ratio of the VL and RF muscles. However, ANOVA revealed significant differences across repetitions and between groups. The RMS/\(M_{\text{max}}\) ratio was higher in men for the VL and RF muscles (\(P < 0.05\) for both muscles) and significantly decreased over the fatigue protocol (\(P < 0.001\) for both muscles).

### Antagonist coactivation

No significant effect of group was observed for \(\%\text{CoAct}_{\text{BF}}\). Initial \(\%\text{CoAct}_{\text{BF}}\) values of the fatigue test were 15.5% ± 2.8% and 16.3% ± 3.9% in boys and men, respectively. However, ANOVA revealed significant interaction of group–percentage of repetitions regarding \(\%\text{CoAct}_{\text{BF}}\) (\(P < 0.001\)). \(\%\text{CoAct}_{\text{BF}}\) values
remained unchanged in men throughout the fatigue protocol, whereas in boys, it decreased significantly from 30% to 100% of total repetitions ($P < 0.01$) (Fig. 4).

**Correlations.** When both groups were pooled in the analysis, the first MVC of the fatigue protocol was inversely correlated to the number of repetitions ($r = -0.52, P < 0.05$) and relative VA changes ($r = -0.64, P < 0.001$). In contrast, a significant positive relation was found between the first MVC and the relative Qtwpot decrement ($r = 0.66, P < 0.001$). Furthermore, the number of repetitions was positively correlated to the relative VA decrement ($r = 0.54, P < 0.05$) and negatively related to the relative Qtwpot decrements

![FIGURE 2](http://www.acsm-msse.org)

**FIGURE 2**—Time course of the Qtwpot of the KE muscles (expressed as a percentage of the initial value) during the fatigue protocol and subsequent recovery period in boys (■) and men (□) (mean ± SD). *Significantly different between boys and men, $P < 0.05$. **Significantly different between boys and men, $P < 0.01$. §§Significantly different from the first MVC, $P < 0.001$. $$$Significantly different from the last MVC of the fatigue test, $P < 0.001$.}

![FIGURE 3](http://www.acsm-msse.org)

**FIGURE 3**—Time course of the level of VA of the KE muscles (expressed as a percentage of the initial value) during the fatigue protocol and subsequent recovery period in boys (■) and men (□) (mean ± SD). *Significantly different between boys and men, $P < 0.05$. **Significantly different between boys and men, $P < 0.01$. §§Significantly different from the first MVC, $P < 0.001$. $$$Significantly different from the last MVC of the fatigue test, $P < 0.001$.}
Finally, the VA decrement was positively correlated to the %CoActBF decrement in boys ($r = 0.61, P < 0.05$). However, such correlation was not observed in men.

**DISCUSSION**

The purpose of the present study was to investigate the effects of growth on neuromuscular fatigue induced by repeated MVC of the KE muscles and to assess the contributions of central and peripheral factors to the fatigue development in children and adults. The main results showed that prepubertal boys fatigue less than men during repeated maximal contractions. The greater fatigue resistance in boys is associated with 1) no apparent peripheral fatigue, as evidenced by the lack of change in the potentiated twitch torque and $M_{\text{max}}$ values for VL and RF muscles, and 2) higher central fatigue than men, as illustrated by a higher VA deficit of the KE muscles. However, when MVC was used as covariable in the statistical analysis, differences of central and peripheral fatigue between groups were abolished, suggesting that initial MVC is a greater contributor to fatigability than age.

The results of the present study confirmed that children fatigue less than adults over repeated MVC. The MVC torque of the KE muscles declined more slowly in boys, and the number of repetitions to task failure was higher in boys. Our results agree with the data published by Armatas et al. (5), showing a greater number of repetitions in prepubertal boys compared with men during a similar intermittent isometric fatigue protocol involving the KE muscles. The results of the present study are also consistent with other studies comparing boys and men during fatigue tests with other muscle groups (i.e., elbow flexors (13)), contraction modes (i.e., isokinetic contractions (8)), and other dynamic whole-body actions, such as maximal cycling (36,39) and short running bouts (40).

Although scientific evidence supports greater fatigue resistance in children during high-intensity intermittent exercise, the mechanisms explaining this phenomenon remain debated, especially the role of central factors (37). To gain insight into the origin of lower fatigability in children, we assessed the contribution of central and peripheral factors to fatigue. Whereas peripheral factors were mainly involved in men, central factors mainly accounted for fatigue in prepubertal boys.

**Peripheral mechanisms.** The absence of alteration of Qtwpot in boys suggests that contractile properties and/or excitation–contraction coupling were preserved in prepubertal boys, in contrast to men. Our results agree with the results recently published by Murphy et al. (31), showing no Qtwpot alteration of the KE muscles in 10-yr-old boys after three sets of resistance exercise despite significant MVC decrease. The results of the current study are also consistent with previous studies showing lower alteration of the potentiated twitch torque during fatigue in children compared with that in adults (12,15,42). However, our data regarding the time course of $M_{\text{max}}$ are inconsistent with the literature. Whatever the population considered, no alteration of $M_{\text{max}}$ was observed in the current study, while others reported either lower decrement in boys compared with that in men (15), or increase by potentiation in boys and...
significant decrease in men (31). Further studies are therefore required to elucidate the growth- or maturation-related changes in the excitability of the sarcolemma associated with fatigue.

Among the factors that may account for the difference of peripheral fatigue between boys and men are the MVC torque, muscle fiber type composition, muscle metabolism, and musculotendinous stiffness. Indeed, in the present study, the first MVC of the fatigue test was positively correlated to the twitch torque decrement. Furthermore, when the initial MVC torque was used as covariable, no significant difference in the time course of the potentiated twitch was observed between groups. This suggestion is consistent with other studies that showed that the larger fatigue seen in men versus women was eliminated when subjects were matched for absolute strength (19). Furthermore, in a study reporting greater fatigue in men versus women, Russ (41) found that subsamples of strength-matched men and women exhibited similar changes in peripheral fatigue.

Muscle phenotype could also account for the differences of peripheral fatigue between boys and men. It has been previously shown that individuals with predominantly fast-twitch fibers develop greater peripheral fatigue compared with subjects with higher proportion of slow-twitch fibers (14). It has been suggested that adults have a lower percentage of fatigue-resistant slow-twitch fibers than children (23). However, the influence of muscle typology on fatigue resistance in children remains to be demonstrated because other studies showed no significant difference in muscle fiber type composition between children and adults (6).

Furthermore, several studies using 31P phosphorus magnetic resonance spectroscopy provided evidence that children rely more on oxidative than anaerobic metabolism during high-intensity intermittent exercise (38,46). This specific metabolic profile in children could lead to lower accumulation of metabolic byproducts (i.e., H+ ions and inorganic phosphate) and lower phosphocreatine depletion during exercise compared with adults (21). As these metabolic byproducts promote peripheral fatigue through alteration of the contractile processes (1) and the excitation–contraction coupling (1), lower accumulation of metabolites could translate into reduced peripheral fatigue, as observed in children.

Finally, recent reports suggest that compliant tendinous tissues may act as a “mechanical buffer” that may protect the muscle from extensive damage and fatigue (18,24). As the musculotendinous stiffness has been reported to be lower in children (47), part of the constraints imposed on the muscle–tendon unit could be better absorbed by the tendon itself in children and explain their lower peripheral fatigue during repeated maximal contractions. Nevertheless, these results were obtained from adult and animal models during dynamic contractions (18,24) and need to be confirmed in children for isometric and dynamic contractions. Alternatively, one may argue that greater compliance puts the muscle in a less productive force condition. This effect results in a rightward shift of the force–length relation (25). In the current study, both groups exercised and were tested at their optimal joint angle, which was similar between groups. However, greater tendon compliance would result in a greater shortening of the muscle fibers, even at the optimal muscle–tendon length. The consequence would be that the children, who have greater musculotendinous compliance (47), would exercise at a shorter relative muscle fiber length than adults. Such conditions could reduce peripheral fatigue (10) and increase central fatigue (9). This is thus consistent with our findings and those of Streckis et al. (42), which show lower peripheral fatigue and greater central fatigue in children.

Central mechanisms. Regarding neural factors, boys showed significant VA decrement during the fatigue test, whereas no significant change of VA was observed in men. This suggests that in addition to the lack of peripheral fatigue, the larger central fatigue in boys may also be responsible for their lower fatigability. The interplay of central and peripheral mechanisms of fatigue as a function of age remains to be elucidated; however, on the basis of our results, it could be suggested that the greater central fatigue in boys accounted for their lower peripheral fatigue. Indeed, according the central governor theory, the CNS could limit the recruitment of motor units to prevent any extensive homeostasis disturbance, muscle damage, and biological harm (33). As such, Amann and Dempsey (3) proposed the existence of a “critical threshold” of peripheral fatigue and demonstrated that when the inhibitory feedback from group III/IV afferents was reduced by pharmacological blockade, the exercising adult subjects “tolerated” the development of peripheral muscle fatigue substantially beyond their critical threshold (2). It is currently unknown whether this critical threshold is different in children and adults, but the lower peripheral and the higher central fatigue reported here and previously by Streckis et al. (42) suggest that the critical threshold could be centrally set at a higher level in children. Interestingly, Hatzikotoulas et al. (15) recently reported a comparable amount of central fatigue in boys and men but lower peripheral fatigue in boys. This finding also supports the idea that the CNS could not tolerate the development of an extensive peripheral fatigue in children, contrary to adults. Whether a higher limitation is set at a supraspinal level (29) and/or whether the sensitivity of the III–IV afferent fibers differ between boys and men remain to be determined. Furthermore, as the nature of the regulation (i.e., inhibitory or facilitatory) of the neural drive by the group III–IV afferents may vary across muscles (26), other muscles should be investigated before generalization of these findings. Finally, we cannot exclude the additional contribution of other regulatory mechanisms, acting extrinsically or intrinsically on the motoneuron pool (11), to the difference of central fatigue between boys and men. Thus, other nervous adjustments could also account for the lower fatigability in boys, but these remain to be identified.

The higher implication of central factors in the development of fatigue in boys could also be ascribed to their lower

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absolute MVC torque and consequently to the concurrent longer exercise duration. Indeed, in the present study, the relative VA loss was inversely correlated to the first MVC of the fatiguing task and positively correlated to the number of repetitions. Furthermore, we showed no significant difference in the time course of VA between groups when the MVC torque was used as covariable. This concurs with previous studies, which showed that central fatigue is mainly involved during prolonged exercise (27). These results also agree with those published by Russ (41), which reported similar changes in MVC decrements and central activation in strength-matched men and women.

The time course of the level of coactivation during the fatiguing task showed opposite patterns in both groups, as it decreased in boys whereas it remained unchanged in men. The progressive decrease of the coactivation level observed in boys may have contributed to limit the loss of torque and therefore delay the level of fatigue. Furthermore, in the present study, the decrement of VA was positively correlated with the decrement of coactivation in boys, which is in accordance with the theory of “common drive.” Such a phenomenon could have served to maintain the balance between agonist and antagonist joint torque in boys to preserve their joint integrity (35).

During recovery, the results of the torque output are in accordance with previous studies showing that boys recover faster than men (5). In our study, boys reached their initial torque values after 3 min of recovery whereas men’s torque did not reach initial values even after 15 min. This fast recovery in boys was associated with the complete recovery of the VA level, suggesting that central fatigue withdrawal mainly accounted for the torque recovery. Similarly, Armatas et al. (5) showed that the faster torque restoration in boys was related to faster recovery of the agonist EMG activity of the KE muscles. In contrast, in men, the incomplete restoration of torque is probably attributed to peripheral factors, as the VA level remained unchanged during fatigue. It is likely that the excitation–contraction coupling and/or contractile activity had not fully recovered in men after 15 min of recovery, but direct evidence to support this assumption is still lacking.

A few limitations of our study could be noted. First, there was a lack of agreement between the time course of the VA and normalized EMG data (i.e., the RMS/M_{max} ratio), the latter being comparable between boys and men whereas the former differed. This discrepancy between the results of EMG and the interpolated-twitch method probably originates from the fact that surface EMG is not sufficiently sensitive to measure small differences in VA level (20). Other studies previously reported this lack of consistency between EMG and the twitch interpolation data (22,43). Another difference between the two methods is that the twitch interpolation technique reflects the activation of the entire KE muscle group whereas EMG assesses the activity of individual muscles. Therefore, in the present study, we cannot rule out the possibility that greater reduction of normalized EMG activity could have been observed during exercise in boys on other KE muscles (i.e., on the vastii medialis and intermedius muscles). Finally, a limitation of the study is the absence of evaluation of the maximal twitch potentiation capacity. As the time course of the potentiated twitch reflects the balance between the peripheral fatigue and the twitch potentiation mechanisms, any difference in potentiation between groups may have affected the time course of the twitch amplitude and potentially hidden part of the peripheral fatigue. However, we measured the twitch potentiation after the first MVC and it did not differ between groups. This is consistent with the results of Pääsuo et al. (34), which showed no significant age-related difference in twitch potentiation between prepubertal boys and men. Conversely, Arabatzi et al. (4) have reported higher potentiation in men compared with that in boys but these results were obtained during voluntary explosive contractions, such that they do not fully apply to twitch potentiation. Should they fully apply, it would mean that the actual amount of peripheral fatigue is much greater in men. Thus, it is not contradictory with the finding that the peripheral fatigue is lower in children.

To conclude, the results of the present study show that boys fatigue less and more slowly than men during repeated MVC. The contribution of central and peripheral mechanisms to the development of neuromuscular fatigue differed between the two groups. Peripheral factors mainly accounted for fatigue in men, whereas central factors were mainly involved in boys. Therefore, it is likely that the lower fatigability in children is accounted for by the lack of peripheral fatigue. Moreover, the greater central fatigue observed in boys could reflect a strategy of the CNS aimed at limiting the recruitment of motor units to prevent any extensive peripheral fatigue. However, these age-related differences in the extent and etiology of neuromuscular fatigue disappear when the initial MVC is used as covariable, suggesting that initial MVC is certainly the main contributor to the observed differences between children and adults.

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