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Increase in Volitional Muscle Activation from Childhood to Adulthood: A Systematic Review and Meta-analysis

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ABSTRACT

WOODS, S., C. O'MAHONEY, J. MAYNARD, R. DOTAN, G. TENENBAUM, E. FILHO, and B. FALK. Increase in Volitional Muscle Activation from Childhood to Adulthood: A Systematic Review and Meta-analysis. *Med. Sci. Sports Exerc.*, Vol. 54, No. 5, pp. 789–799, 2022. **Introduction:** Children's maximal muscle strength is consistently lower than adults', even when normalized to body size. Lower volitional muscle activation (VA) in children is often considered one of the main reasons for age-related differences in muscular performance. However, some recent studies have reported similar VA in children and adults, bringing into question whether there is indeed an age-related increase in VA. The purpose of this review was to determine the effect of age on VA during maximal isometric contractions. **Methods:** Literature examining VA differences, using twitch interpolation in children (7–14 yr) and adults (16–28 yr), was systematically reviewed. Of the 1915 studies initially identified, 19 data sets were eligible for inclusion in the qualitative analysis and 14 in the quantitative meta-analysis (comprising 207 children and 193 adults). **Results:** Significantly lower VA in children was reported in 9/19 (47%) studies. A random-effects meta-analysis found a strong effect of age on VA, supporting lower VA in children compared with adults (Hedges' $g = 1.55$; confidence interval: 0.9–2.13). Moderator analysis included muscle group, sex, children's age, stimulation number (singlet, multiple), type (electric, magnetic), and location (muscle, nerve), of which only muscle group was significant ($P < 0.001$). A significant Egger's regression test and asymmetrical funnel plot suggest that publication bias may be present. **Conclusions:** Overall, these findings suggest that compared with adults, children activate their motor-unit pool less compared with adults. Moreover, that the degree of VA increase with age may be influenced by the muscle examined (upper vs lower extremity). However, more research is needed to elucidate the influence of this possible factor, as the current review contains limited data from upper body muscles. The developmental mechanism responsible for children's lower VA requires further research. **Key Words:** VOLUNTARY ACTIVATION, INTERPOLATED TWITCH, MUSCLE ACTIVATION, MAXIMAL VOLUNTARY CONTRACTION, MATURATION

BASIC SCIENCES

Children's muscle performance is consistently lower than adults' (e.g., lower maximal strength and rate of force development), even after accounting for differences in body size (1–4). Based on differences in growth rate versus the rate of strength gain, Asmussen and Heeboll-Nielsen (5) suggested, already in 1955, that beyond body size, lower volitional muscle activation (VA) in children can explain their lower muscular performance. This notion has been supported by subsequent studies demonstrating lower size-normalized maximal strength and lower rate of force development (2,5–7), as well as differences in the electromyographic (EMG) pattern during various contraction tasks (8,9). Several studies have also demonstrated lower VA in children, compared with adults, during maximal volitional contractions (MVC) of various muscle groups (e.g., quadriceps, biceps bracii, adductor pollicis) (4,10–14). However, several recent studies have failed to identify child–adult VA differences (15–21). These inconsistent findings have clouded our understanding of the maturational changes in muscle performance and the influence that possible changes in VA may have on performance, specifically maximal strength.

VA is typically assessed and quantified using twitch interpolation (interpolated twitch technique, or ITT), where an electric or magnetic pulse is applied to the muscle or motor nerve during MVC. This technique was first introduced by

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Submitted for publication July 2021.
Accepted for publication December 2021.

0195-9131/22/5405-0789/0
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DOI: 10.1249/MSS.0000000000002853

Merton (22), who argued that when an electrical stimulus is applied to the muscle or associated motor nerve during an MVC and additional force is evoked (superimposed twitch), there is incomplete volitional activation of the muscle (i.e., activation deficit). Neural mechanisms resulting in activation deficit include submaximal motor-unit recruitment and/or suboptimal firing rates during volitional contractions.

Using twitch interpolation, there are currently two approaches for calculating VA. The more traditional approach is the "central activation ratio" (VA_{CAR}), which quantifies VA as percentage fraction: MVC/(MVC + superimposed twitch) × 100 (22). At present, a more commonly used variant of VA_{CAR} adds a resting twitch after the MVC, to account for peripheral phenomena such as potentiation, and is often termed "VA" or "VA_{ITT}" to distinguish it from VA_{CAR}. VA_{ITT} is calculated as follows: (1 − superimposed twitch/resting twitch) × 100 (23). Both calculations have been used to quantify VA mainly during maximal isometric contractions in various populations (e.g., children, adults, elderly, and those with chronic conditions).

There are several methodological and physiological factors that may affect VA determination by affecting the muscle's mechanical output. For instance, stimulation intensity, number of stimuli (single vs multiple stimuli), stimulation frequency (when multiple stimuli are used), musculotendinous stiffness, muscle potentiation, and coactivation, are all factors found to affect VA in adults (24–26). More specifically, these factors influence the accuracy and reliability of VA determination. For the purpose of this review, it is also important to note that some of these factors are also affected by maturation. For example, coactivation is often found to be greater in children than in adults, whereas musculotendinous stiffness and muscle potentiation may be lower in children (27, 28). Nevertheless, most studies have used either the VA_{ITT} or VA_{CAR} approach similarly in children and adults.

Therefore, the purpose of this review was to systematically examine child–adult differences in VA during maximal isometric contractions and possible related mediators. The published research, which examined VA (by estimating VA_{ITT} or VA_{CAR}) in both children and adults, was systematically reviewed and integrated in a meta-analysis. We hypothesized that VA in children would be lower than in adults. We also hypothesized that factors such as stimulation methods (stimulation number, type, and location), muscle group examined (upper or lower limb), and age of the child participants would influence the observed age effect.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used to guide our investigation and present the systematic review (http://www.prisma-statement.org/). Furthermore, before data extraction, the methods and analysis procedures of the systematic review were disclosed publicly on the International Prospective Register of Systematic Reviews (209907).

Literature search. An initial search of MEDLINE (OVID), MBASE (OVID), SPORTDiscus (EBSCO), and Web of Science databases was performed on August 11, 2020, to identify relevant studies. The combination of keywords and/or phrases (mp), and MeSH terms (/) pertinent to "children" (Child/, child*mp, adolesc*mp, youth*mp, boy*mp, girl*mp), "adults" (Adult/, *adult/, *middle age/, *young adult/, Adult*mp, men mp, man mp, women mp, woman mp, female*mp, male*mp) and "voluntary muscle activation" (voluntary activation mp, muscle activation mp, central fatigue mp, central activation mp, volitional activation mp, motor unit activation mp) were used to search for relevant articles. This search was repeated on April 22, 2021, to check for additional articles published in the intervening period. One additional article was found (23).

Once the search was complete, all the identified publications were uploaded into screening and citation management software (Covidence and Zotero, respectively). After duplicates were removed, three reviewers (B.F., J.M., C.O.) independently screened titles and abstracts for relevant articles. Conflicts among reviewers were resolved by an additional reviewer (R.D.). Next, article eligibility was further assessed by two reviewers (B.F., S.W.), independently, by screening the full text of all the remaining articles. Also, at this stage, the reference lists were screened to identify any relevant articles that were missed in the search. Conflicts between reviewers were resolved by an additional reviewer (R.D.). See Figure 1 for a PRISMA flowchart of the articles included and excluded throughout the screening process.

Identification and selection of studies. Studies were included in the review if they assessed VA in healthy children and adolescents or young adults during maximal isometric contractions, using VA_{ITT} or VA_{CAR}. If an intervention (e.g., fatiguing contractions) was part of the study design, baseline values were extracted. If data were presented in the article as figures, authors were contacted, and the relevant data requested. If data could not be provided, group means and SDs were estimated using WebPlotDigitizer (29), which is well accepted and has been shown to be a valid tool for extracting data from figures (30). No limits were placed on the year of publication, and only full-text articles published in English were identified. Studies were excluded from the meta-analysis if effect sizes (ES) could not be calculated (10).

Quality assessment. Risk of bias was assessed using a combination of the Appraisal tool for Cross-Sectional Studies (AXIS tool) (31) and Quality Assessment Tool for Quantitative Studies (32). Some items were removed, as they were not relevant for cross-sectional studies with no intervention. The assessment tools were used to evaluate the following qualities: 1) sampling/target population, 2) design, 3) procedures, 4) statistical analysis, 5) reporting of findings, 6) reporting withdrawals/nonresponders, and 7) possible bias from funding sources. The risk of bias assessment was completed for all studies by two researchers independently (B.F., S.W.), and disagreements were resolved by consensus. Publication bias was also assessed using a funnel plot and Egger's regression test.

Data extraction and analysis. From the included studies, participant characteristics (sex, age, and pubertal stage or maturational status for the children), muscle group examined,

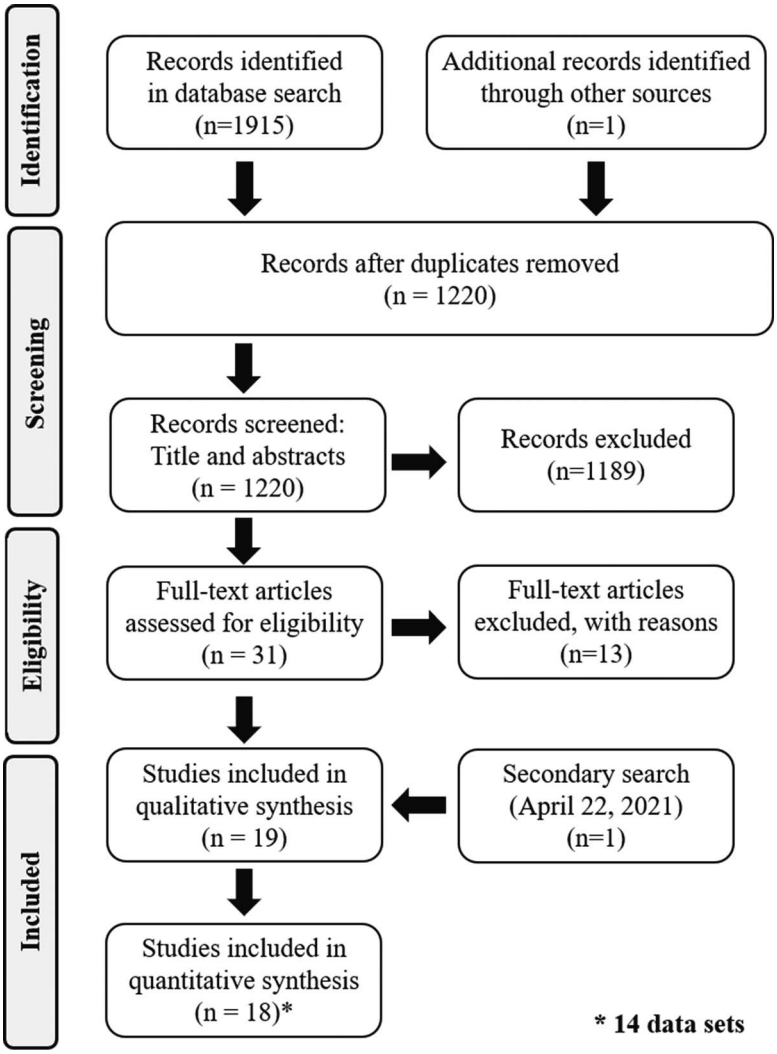

FIGURE 1—PRISMA flowchart of study selection.

calculation method (VA_{ITT} or VA_{CAR}) for estimating VA, stimulation number (singlet, doublet, train), technique (electric or magnetic), location (muscle or nerve), and estimated VA (group mean and SD) were extracted by two authors independently (B.F., S.W.). Conflicts were resolved by consensus.

Narrative synthesis. For the narrative synthesis, extracted data were compiled into a table where each comparison is listed separately (Table 1). Comparisons are organized so that those who report a significant difference in VA between children and adults are listed first, then by muscle examined, and lastly, in alphabetical order.

Meta-analysis of pooled data. A meta-analysis of the pooled data was used to further examine age-related differences in VA between children and adults. We used Campbell's Collaboration calculator (www.campbellcollaboration.org/resources) to compute Hedges' g ES. A mixed-effects model was used to examine main effect of age on VA. This model was appropriate, as ES values vary considerably because of between-study differences (e.g., methodological procedures, participants' demographic characteristics), and we aimed to generalize our findings beyond the sampled studies (39). After the calculation of confidence intervals, Cochran's Q statistic was used to test the heterogeneity of the pooled distribution. Since the Q statistic maintained a low power (limited studies in meta-analysis), the $I^2_{average}$ was also computed (40). Moreover, computation of I^2 is required to assist with the interpretation of the Q test, because the Q test does not indicate the extent of true heterogeneity, but rather just that the effect is significant. To further explore the origins of heterogeneity, a moderator analysis was conducted, with muscle group, sex, stimulus type, number and location, and age of child participants. All statistical procedures were performed in Comprehensive Meta-Analysis program (version 3.0). Significance of ES was determined at $P < 0.05$.

RESULTS

Study Selection

A total of 1915 studies were identified in the initial search (Fig. 1). An additional study was identified in paper records, and another study was identified in the secondary search (see

TABLE 1. Studies reporting VA in both children and adults.

Reference	Sex	Participant Number and Age, *n* (Age in Years)		Muscle	Stim Type/Location	VA Calculation	Stim No.	VA Results (%)		Significant Difference
		Children	Adults					Children	Adults	
Blimkie (10)	Male	25 (~10)	10 (~16)	KE	ES/M	VA_{ITT}	Single	77.7	95.3	Yes
Kluka et al. (14)	Male	13 (10.2 ± 1.1)	10 (23.9 ± 2.9)	KE	MS/N	VA_{ITT}	Single	88.0 ± 8.0	94.0 ± 4.0	Yes
O'Brien et al. (12)[a]	Female	10 (9.3 ± 0.8)	10 (27.4 ± 4.2)	KE	MS/M	VA_{ITT}	Doublet	66.9 ± 13.0	86.6 ± 6.6	Yes
O'Brien et al. (4)[a]	Female	10 (9.3 ± 0.8)	10 (27.4 ± 4.2)	KE	MS/M	VA_{ITT}	Doublet	68.0 ± 11.6	86.6 ± 6.6	Yes
Streckis et al. (33)[b]	Female	7 (13.6 ± 0.2)	7 (20.8 ± 0.5)	KE	ES/M	VA_{ITT}	Train (500 ms)	83.2 ± 2.6	94.4 ± 1.1	Yes
Grosset et al. (13), 7 yr	Male	6 (7)	9 (21.0 ± 2.3)	PF	ES/N	VA_{CAR}	Single	87.0 ± 4.7	98.5 ± 0.2	Yes
Kluka et al. (34)	Male	14 (10.0 ± 1.0)	15 (24.6 ± 4.2)	PF	MS/N	VA_{ITT}	Single	87.6 ± 1.6	92.4 ± 1.7	Yes
Gillen et al. (35)	Male	10 (9.8 ± 0.5)	10 (17.6 ± 0.8)	EF	ES/M	VA_{ITT}	Doublet	72.6 ± 4.9	89.8 ± 5.5	Yes
Gillen et al. (35)	Female	10 (9.8 ± 0.6)	10 (16.9 ± 1.0)	EF	ES/M	VA_{ITT}	Doublet	67.2 ± 6.7	90.3 ± 3.5	Yes
Martin et al. (11)	Male	13 (11.6 ± 0.1)	8 (25.6 ± 1.5)	ADP	MS/N	VA_{ITT}	Single	85.0 ± 2.7	94.8 ± 1.4	Yes
Bontemps et al. (15)	Male	18 (10.4 ± 0.8)	19 (21.7 ± 3.4)	KE	MS/N	VA_{ITT}	Single	90.1 ± 6.3	92.8 ± 3.9	No
Chalchat et al. (16)	Male	11 (10.3 ± 0.7)	13 (23.8 ± 3.1)	KE	MS/N	VA_{ITT}	Single	93.2 ± 2.9	94.9 ± 2.4	No
Gorianovas et al. (36)[b]	Male	11 (11.8 ± 0.9)	11 (20.8 ± 1.9)	KE	ES/M	VA_{ITT}	Train (250 ms)	87.5 ± 7.8	93.3 ± 6.2	No
O'Brien et al. (12)[a]	Male	10 (8.9 ± 0.7)	10 (28.2 ± 3.6)	KE	MS/M	VA_{ITT}	Doublet	75.1 ± 12.8	85.6 ± 8.5	No
O'Brien et al. (4)[a]	Male	10 (8.9 ± 0.7)	10 (28.2 ± 3.6)	KE	MS/M	VA_{ITT}	Doublet	75.1 ± 12.8	86.7 ± 9.3	No
Piponnier et al. (17)[c]	Male	21 (10.4 ± 0.7)	24 (21.4 ± 3.2)	KE	MS/N	VA_{ITT}	Single	90.4 ± 6.0	92.7 ± 4.1	No
Piponnier et al. (18)[c]	Male	22 (10.3 ± 0.7)	22 (21.6 ± 3.3)	KE	MS/N	VA_{ITT}	Single	90.9 ± 5.6	92.6 ± 4.3	No
Piponnier et al. (19)[d]	Male	9 (9.9 ± 1.3)	11 (23.6 ± 3.0)	KE	MS/N	VA_{ITT}	Single	87.1 ± 7.6	92.2 ± 3.2	No
Streckis et al. (33)[b]	Male	7 (13.9 ± 0.3)	7 (22.2 ± 0.9)	KE	ES/M	VA_{ITT}	Train (500 ms)	91.5 ± 2.4	92.8 ± 1.3	No
Ratel et al. (21)[d]	Male	11 (9.9 ± 1.2)	12 (23.9 ± 3.5)	KE	MS/N	VA_{ITT}	Single	86.9 ± 7.6	91.2 ± 2.6	No
Belanger and McComas (37)	Male	10 (11.0 ± 2.3)	8 (16.5 ± 0.9)	PF	ES/N	VA_{ITT}	Single	94.0 ± 11.3	99.4 ± 1.8	No
Grosset et al. (13), 10 yr	Male	11 (10)	9 (21.0 ± 2.3)	PF	ES/N	VA_{CAR}	Single	95.6 ± 1.0	98.5 ± 0.2	No
Grosset et al. (13), 11 yr	Male	5 (11)	9 (21.0 ± 2.3)	PF	ES/N	VA_{CAR}	Single	96.7 ± 0.3	98.5 ± 0.2	No
Hatzikotoulas et al. (38)	Male	11 (10.7 ± 0.2)	11 (26.4 ± 0.7)	PF	ES/N	VA_{CAR}	Single	98.1 ± 0.4	98.5 ± 0.5	No
Piponnier et al. (17)[c]	Male	21 (10.4 ± 0.7)	24 (21.4 ± 3.2)	PF	MS/N	VA_{ITT}	Single	95.2 ± 3.9	95.4 ± 4.5	No
Piponnier et al. (20)[c]	Male	19 (10.2 ± 0.6)	23 (21.5 ± 3.3)	PF	MS/N	VA_{ITT}	Single	93.6 ± 5.1	94.4 ± 3.9	No
Belanger and McComas (37)	Male	10 (11.0 ± 2.3)	8 (16.5 ± 0.9)	DF	ES/M	VA_{ITT}	Single	100 ± 0	100 ± 0	No
Blimkie (10)	Male	26 (10)	10 (16)	EF	ES/M	VA_{ITT}	Single	89.4	89.9	No

Note that some studies report volitional activation of multiple groups (age groups, male/female). Each comparison is listed separately.
[a]Data reported in O'Brien et al. (12) and (4) come from the same participants' data set.
[b]VA data estimated from a figure using WebPlotDigitizer (35).
[c]Data reported in Piponnier et al. (17), (18), and (20) come from the same participants' data set.
[d]Data reported in Piponnier et al. (19) and Ratel et al. (21) come from the same participants' data set.
ES, electrical stimulation; M, muscle; MS, magnetic stimulation; N, nerve; VA_{CAR}, volitional activation, calculated the central activation ratio approach; VA_{ITT}, volitional activation, calculated using the traditional ITT.

Literature search). After the removal of duplicates (n = 695), 1189 additional studies were excluded after title and abstract screening. Full-text screening was conducted on 32 studies, and 19 were included in the final qualitative analysis. Of the 19 studies, 18 were included in the meta-analysis (see Selection criteria). After communication with some of the authors, it was determined that some of the studies reported results from the same participant data set. These studies were pooled, leaving a total of 14 separate participant sets in the final meta-analysis.

Study Characteristics: Narrative Synthesis

Table 1 summarizes the 19 studies included in the qualitative review. The studies included were published between 1989 and 2021 and comprised a total of 233 children (7–14 yr) and 203 young adults (16–28 yr). Some participants were included in more than one study (see Table 1 footnotes). The mean sample sizes were 16 (range, 7–37) and 14 (range, 7–24) for children and adults, respectively. All but four studies (79%) examined males only. A statistically significant lower VA in children was reported in 47% (9/19) of the studies. However, in all but one case, children's reported VA values were lower than in adults. In this single case, dorsiflexor VA was identical in children and adults (37).

Eighty-four percent (16/19) of the studies examined VA only in lower-extremity muscles. Some of these studies examined two lower-extremity muscle groups (10,17,37) (one tested dorsiflexors (DF), 6 tested plantar flexors (PF), 12 tested knee extensors (KE)). One of 19 studies examined both lower and upper extremity muscles (elbow flexors (EF) and KE) (10), and 2 of 19 studies examined only an upper extremity muscle (adductor pollicis (ADP) or EF) (11,35). In the lower extremity muscles, VA was significantly lower in children in 7/17 (41%) of the studies (4,10,12–14,33,34). Although motor units are typically classified along a spectrum from low to high threshold, it is presumed that high-threshold motor units are primarily composed of fibers with type II metabolic and mechanical characteristics (41,42). It is hypothesized that children activate their high-threshold motor units to a lesser extent, during maximal contractions, compared with adults (43). Thus, child–adult differences in VA may be influenced by the relative type-II composition of the tested muscle. The PF muscle group, which plays a chronic postural role, is predominantly composed of endurance-oriented muscle fibers of the type-I fiber characteristics. This group was examined in 32% (6/19) of the studies included in the qualitative analysis (13,17,20,34,37,38). Of these studies, a significant child–adult VA difference was reported in two (33%) of the studies (13,14). Fifteen of the studies examined muscles, which could be classified as having a "mixed" fiber type, containing similar proportion of type-I and type-II muscle fibers (4,10–12,14–19,21,33,35–37). Of these studies, 47% (7/15) reported VA to be significantly lower in children than in adults (4,10–12,14,33,35).

The age range of the children who participated in the included studies was 7–14 yr. In 32% (6/19) of studies, the mean age of the children was less than 10 yr (4,12,13,19,21,35). Sixty-seven percent (4/6) of these studies reported lower VA in children compared with adults (4,12,13,35). Of the studies investigating "older" children (>10 yr, $n = 14$), 35% (5/14) reported significantly lower VA in children compared with adults (10,11,14,33,34).

Most of the studies (74%) used a single stimulus (singlet) when evoking a muscle twitch for the assessment of VA. Five studies (26%) used multiple stimuli, where 60% (3/5) utilized doublet stimuli (4,12,35). The other two studies using stimuli trains of 250–500 ms (33,36). Of the studies using multiple stimuli, 80% (4/5) reported significantly lower VA in children compared with adults (4,12,33,35).

Thirty-seven percent (7/19) of studies evoked twitches using electrical stimulation (10,13,33,35–38), where the remaining used magnetic stimulation. Of the studies using electrical stimulation, 57% (4/7) reported significant differences in VA between children and adults (10,13,33,35). Of the studies using magnetic stimulation, 42% (5/12) reported significant child–adult differences in VA.

Thirty-two percent (6/19) of studies applied the stimulus (electrical or magnetic) directly to the muscle (4,10,12,33,36,37). Of these studies, 67% (4/6) reported significantly lower VA in children compared with adults (4,10,12,33). Of the studies that applied the stimulus (electrical or magnetic) to the nerve, 36% (5/14) reported significantly lower VA in children than in adults (11,13,14,34,35).

Risk of bias

A subset of questions from two validated questionnaires were used to assess risk of bias among the studies included (31,32). For the Thomas et al. (32) assessment, studies were ranked "strong," "moderate," or "weak." For the Downes et al. (31) assessment, studies were classified as either "meeting" the criteria ("yes") or "not meeting" the criteria ("no").

Using Thomas et al.'s (32) assessment tool, 18 studies were classified as "strong" and 1 "moderate" in terms of the validity of the data-collection method. Selection bias was rated as "strong" for 1 study, "moderate" for 15 studies, and "weak" for the remaining 3. Seven studies were rated as "strong," 8 as "moderate," and 4 as "weak," in terms of controlling for confounding variables (e.g., training status). All studies but one were rated as "weak" for reporting of participants who withdrew from the study. Lastly, all studies were given a "weak" rating for "blinding" the data reduction and analysis.

Quality ratings using the Downes et al.'s (31) assessment tool are as follows: Only two studies provided justification for sample size. Sixteen of the studies clearly defined the target population, and it is likely that the selection processes resulted in recruiting representative participants. However, in most studies, little information was provided about recruitment strategy, which made the representativeness of the population difficult to evaluate. Eighteen studies defined the procedures, protocols, and statistical procedures clearly enough for them to be repeated. None of the studies had funding where a conflict of interest would be of concern. Finally, none of the studies disclosed whether there were "nonresponders" or any participants where VA could not be assessed.

Meta-Analysis of Pooled Data

Main analyses. The meta-analysis was performed on 14 data sets, including 207 children and 193 young adults. Hedges' g, 95% confidence intervals, and Q statistics for the studies included in the meta-analysis are presented in Table 2 and illustrated in Figure 2. The test of heterogeneity Q revealed that the observed ES across the studies was large (Hedges' $g = 1.55$; confidence interval: 0.96–2.13) and that approximately 85% of the variance observed is a true effect rather than sampling error ($I^2_{average} = 85.20$).

A funnel plot based on the Hedges' g ES (x axis) and standard errors (y axis) for each study is presented in Figure 3. Because the funnel plot is asymmetrical, the possibility of publication bias was further explored using Egger's regression test. The intercept of Egger's test was significant ($t = 4.41$, $P < 0.001$), suggesting presence of publication bias. However, Rosenthal's fail-safe N test revealed that 529 studies would be needed to nullify (i.e., nonsignificant result; $P > 0.05$) these findings, and Owrin's fail-safe N test revealed that 159 additional studies with a null effect ($g = 0$) would be needed to bring the observed ES values to a trivial value of Hedges' $g = 0.10$. Overall, these results suggest that there is an effect of age on VA. That is, VA is lower in children compared with adults.

Moderator analyses. Six moderators were examined for their contribution in accounting for the ES heterogeneity, namely, muscle group (upper or lower body), sex (male or female), age category (young or older children), stimulation type (electric or magnetic), stimulation location (muscle or nerve) and number of stimulations (single or doublet/train). The only moderator found to be significant was muscle group (upper vs lower extremity; Table 3).

DISCUSSION

This meta-analysis is the first to review differences in VA between children and adults. Overall, less than half the individual studies reported significantly lower VA in children. However, once pooled, the meta-analysis of 14 data sets, including 207 children and 193 young adults, showed that VA is lower in children compared with adults, regardless of sex. This effect was also independent of the stimulation methodology used (i.e., magnetic vs electrical, single vs multiple impulses) and age of the child participants. Overall, these findings suggest that children activate their motor-unit pool to a lesser extent than adults. Lower VA in children can explain children's lower body size–normalized maximal and explosive strength (4,44).

Although the pooled analysis showed a strong effect of age on VA, many of the individual data sets included in the meta-analysis concluded that VA did not differ between children and adults, based on lack of statistical significance (64% of

TABLE 2. Random-effects meta-analysis results.

	Statistics for Each Study						
Reference	**Hedges' *g***	**SE**	**Variance**	**Lower Limit**	**Upper Limit**	***Z***	***P***
Belanger and McComas (37)	0.425	0.457	0.209	–0.471	1.321	0.929	0.353
Bontemps et al. (15)	0.507	0.327	0.107	–0.134	1.149	1.551	0.121
Chalchat et al. (16)	0.622	0.406	0.165	–0.173	1.417	1.533	0.125
Gillen et al. (35),	3.709	0.518	0.268	2.694	4.723	7.164	<0.001
Grosset et al. (13)	2.403	0.471	0.222	1.480	3.326	5.102	<0.001
Gorianovas et al. (36)	0.816	0.428	0.183	–0.024	1.655	1.905	0.057
Hatzikotoulas et al. (38)	0.962	0.445	0.198	0.090	1.834	2.161	0.031
Kluka et al. (14)	0.878	0.426	0.181	0.043	1.712	2.062	0.039
Kluka et al. (34)	2.823	0.518	0.268	1.809	3.837	5.455	<0.001
Martin et al. (11)	4.076	0.763	0.582	2.582	5.571	5.345	<0.001
O'Brien et al. (4,12)	1.431	0.349	0.122	0.747	2.114	4.102	<0.001
Piponnier et al. (17,18,20)	0.260	0.298	0.089	–0.323	0.844	0.874	0.382
Piponnier et al. (19) and Ratel et al. (21)	0.817	0.430	0.185	–0.026	1.660	1.901	0.057
Streckis et al. (33)	3.075	0.551	0.303	1.995	4.155	5.581	<0.001
Overall	1.545	0.300	0.090	0.958	2.133	5.156	<0.001

comparisons; Table 1). The apparent discrepancy between the findings of some individual study comparisons and the current meta-analysis may have resulted from the small, convenience samples used in most studies (mean sample sizes of studies included in the meta-analysis, respectively). With such sample sizes and given the modest between-group differences and potentially large within-group variability, the individual studies may not have had the statistical power to detect a significant age effect, as was demonstrated in the present meta-analysis (45,46). Moreover, this sampling strategy can be problematic as the participants assessed may not be completely representative of the target population (47,48). For example, it is not clear whether participants in many of these studies were sedentary, physically active, or highly trained. In studies involving exercise, there may be a selection bias, as volunteers are likely to favor exercise or sports training. Assuming training increases VA, specifically in children (49–51), such a bias may decrease the likelihood of detecting a true difference between samples. Furthermore, small sample sizes may exaggerate this problem (52). Thus, studies with small sample sizes should be interpreted with caution. For this reason, meta-analyses are essential to compile findings from quality research and allow for a more robust examination of the research question.

The funnel plot and Egger's regression test revealed that the meta-analysis may have been impacted by publication bias. Given our meta-analysis involved only 14 data sets from relatively small studies, publication bias may not be reliably detected by statistical tests (53). Moreover, an asymmetrical funnel plot and significant Egger's test are attributed to "true heterogeneity" rather than publication bias (54,55). True heterogeneity among studies may have resulted from the different study designs, participant characteristics, or techniques used. More specifically, these factors could cause the precision of measurement to be dissimilar among studies, which consequently leads to the underlying effect examined by studies to be different. In the present review, we pooled data from cross-sectional studies comparing children and adults where participants' age, training history, habitual activity level, testing protocols and techniques, as well as the muscles evaluated among studies were different. Therefore, we suggest that the observed funnel plot asymmetry and significant Egger's regression test reflect a true difference among studies (i.e., true heterogeneity), rather than publication bias.

Factors that may affect child–adult VA differences. Based on the current literature, VA in adults seems to be >90%, whereas it varies widely in children (67%–100%). For example, O'Brien et al. (4,12) reported boys' KE VA to be 75.1%, whereas

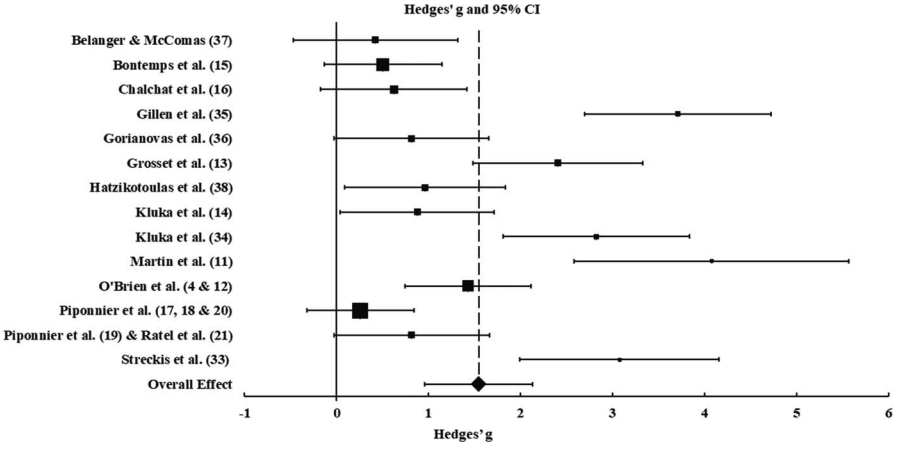

FIGURE 2—Forest plot of mean, overall, and individual study effects. Diamond and dashed line indicate the mean over all random effect for differences in VA between children and adults. Squares indicate the individual study effect, with the size indicating the weighting, and 95% confidence intervals are indicated by horizontal lines. Effects to the right of the 0 indicate VA greater in adults than in children.

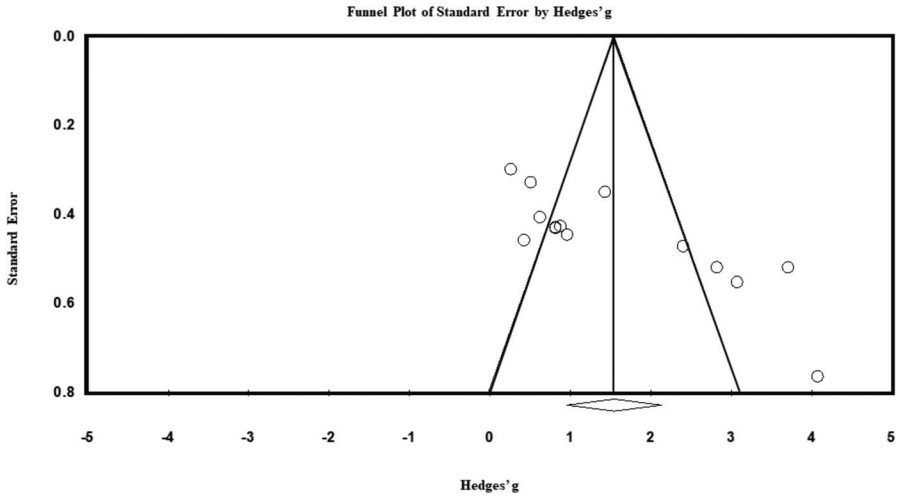

FIGURE 3—Funnel plot of standard error by Hedges's *g*.

Piponnier et al. (17) reported it to be 90.4%. In an attempt to provide some insight into this observation, we conducted a moderator analysis. The discussion hereinafter highlights our findings and discusses factors that may influence child–adult differences in VA.

Of the moderators included in the analysis, muscle group was the only one that was statistically significant (Table 3), suggesting that the effect of age on VA may differ between upper and lower extremity muscles. However, only two studies examined upper extremity muscles (ADP and EF) (11,35). These studies also exhibited the largest ES (g = 4.076 and 3.709). Therefore, the finding of greater child–adult VA differences in upper extremity muscles should be treated with caution. More studies are needed to elucidate whether child–adult VA differences vary between upper and lower extremity muscles and those with functional differences.

Child–adult differences in VA may also depend on the functionality and composition of the examined muscle or muscle group. It has been suggested that children activate their high-threshold motor units to a lesser extent compared with adults (43). We hypothesized that, under such conditions, child–adult VA differences would be smaller in muscle groups known to have a high percentage of low-threshold, type-I fibers (e.g., PF) (53,54). Such age-related differences are not clearly observed in the present review, although they are in the expected direction. That is, child–adult VA differences in the pooled data were ~4% (~93% vs 97%) in the PF and ~7% in mixed-composition muscles (~86% vs 93%). Although the observed VA values and child–adult differences thereof might not reflect the true values, it should be highlighted that these findings are congruent with children's proposed lower capacity to activate higher-threshold motor units. Indeed, it is also

TABLE 3. Results of moderator analysis.

Moderator	No. Data Sets	Point Estimate	SE	Lower Limit	Upper Limit	*Q*	*P*
Age							
Young children <10 yr	4	2.056	0.583	0.913	3.199		
Older children >10 yr	10	1.328	0.336	0.670	1.986		
Total between						1.169	0.280
Stimulation type							
Muscle	6	1.873	0.537	0.821	2.925		
Nerve	8	1.283	0.344	0.609	1.957		
Total between						0.857	0.354
Stimulation number							
Single	10	1.262	0.315	0.645	1.880		
Multiple	4	2.217	0.652	0.940	3.495		
Total between						1.741	0.187
Stimulation location[a]							
Muscle	3	1.719	0.583	0.576	2.862		
Nerve	10	1.617	0.386	0.859	2.374		
Total between						4.802	0.091
Muscle group							
Lower body	12	1.196	0.250	0.707	1.686		
Upper body	2	3.825	0.428	2.985	4.664		
Total between						28.106	<0.001
Sex							
Male	11	1.271	0.304	0.675	1.866		
Male and female	3	2.472	0.664	1.170	3.775		
Total between						2.705	0.100

[a]Belanger and McComas (37) was not included because stimulus was evoked to the muscle (DF) and nerve (PF).

possible that differences in muscle functionality (e.g., muscles used extensively vs those used irregularly), or in the muscles' motor-unit recruitment range, may contribute to differing VA between muscles. Thus, it is possible that VA response may be muscle-specific, and that future studies should further examine how muscle characteristics, such as muscle composition, function, or recruitment range, affect VA in general and child–adult differences thereof, in particular.

Processes (e.g., myelination and synaptic pruning) involved in neuromotor maturation (e.g., myelination and synaptic pruning) seem to become heightened before and during puberty (11–14 yr; (36,44,45); see discussion hereinafter for more details). Implications of such changes can be observed by Grosset et al. (13), who examined PF VA and reported a linear decrease in activation deficit with increasing age (7–11 yr), with a significant child–adult difference only between 7-yr-old children and adults. These finding suggests that child–adult VA differences are age-dependent, with larger differences in studies of younger children. Thus, in the present analysis, we categorized studies that examined "younger" (<10 yr) or "older" children (≥10 yr). The qualitative narrative synthesis of studies (Table 1) suggests that child–adult differences in VA may be greater when younger children are examined. Specifically, child–adult differences seem to be more than twice as large in studies that examined "younger" than in those that tested "older" children (~14% vs ~4%, respectively). Nevertheless, the moderator analysis revealed that age group was not statistically significant (Table 3), indicating that children's age did not influence the main effect of age (child vs adult) on VA. It is possible that statistical significance was not reached because there were only four data sets that included younger children. Thus, although examining VA in young children may be technically difficult, studies examining cohorts of multiple maturity levels (including young children) are necessary to further explain the nature of VA changes with maturation.

There is a lack of research regarding sex-related differences in neuromotor performance in adults and more so in children. Indeed, only 4/19 studies included in this review had a female participant group. During growth, sex-related differences in muscle performance are typically not observed until puberty (e.g., anaerobic power, muscular strength) (1,56–58). Moreover, age-related changes in muscle performance may be different in females compared with males and with a different timeline (2,7). Likewise, Long et al. (59) found cycling EMG threshold difference between girls and women (5.4%) to be smaller than the difference observed between boys and men (11.5%) (60). On the other hand, sex-related differences were not observed in isometrically determined EMG threshold (61). Furthermore, O'Brien et al. (4,12), Streckis et al. (33), and Gillen et al. (35) reported larger child–adult VA differences in females compared with males. Although the data are limited, it is important to note that in all cases in which VA was examined in females (4,12,33,35), it was found to be significantly lower in girls than in women. In the present analysis, sex was not found to be a statistically significant moderator (Table 3), suggesting that sex of the participants did not influence the observed child–adult differences in VA. In view of the limited data in females, more female–male comparative research is needed to understand whether there are sex-related differences in neuromuscular function, specifically during maturation.

Twitch interpolation (i.e., VA_{ITT} and VA_{CAR}) is a commonly used technique. Its validity and reliability in estimating VA have recently been questioned (26,62), because its results may be influenced by factors such as muscle length, composition, potentiation, or technical application. Specifically, these factors seem to influence the mechanical properties or output of the muscle and consequently affect superimposed-to-resting twitch ratios used to estimate VA (26) Notably, children have lower musculotendinous stiffness compared with adults (27,63), which can affect the resting twitch force (i.e., length–tension relationship). As was demonstrated by Hill (64), lower stiffness (or greater compliance) will result in dampened twitch torque and a delay in twitch onset. Potentially, this could result in a larger superimposed-to-resting twitch ratio in children and an underestimation of VA. More studies are needed to investigate how age-related differences in the muscle's mechanical properties influence the superimposed-to-resting twitch ratio and therefore child–adult differences in VA. Possibly a child-specific, or a more sensitive VA test should be developed.

Methodological factors related to the stimulation can also influence the estimation of VA when using twitch interpolation. The studies within this review differ widely with respect to stimuli number, type, location, frequency, and timing. These differences make it difficult to directly compare studies and may explain the high inter-study variability in reported VA. In adults, it has been argued that using doublets or train stimulations may result in a more accurate estimate of VA (62,65), as such stimulation reduces the slack of series elastic components, resulting in a larger, better detectable superimposed twitch (66,67). As mentioned previously, children have lower musculotendinous stiffness than adults (27,63). Therefore, multiple stimulations may be required to estimate VA more accurately in children. Among adults, doublet stimulations have been shown to result in greater superimposed twitch torques than singlet stimulations (68), resulting in larger superimposed-to-resting twitch ratios and lower VAs. Although this seems congruent with greater motor-unit activation by doublet versus singlet stimulation, the notion has never been proven or refuted in adults. This may also be the case in children. Based on the pooled data, child–adult VA differences were larger (~8%) in studies using multiple stimulations than in those using singlets. Moreover, studies using multiple stimulations reported lower VA in both children and adults (by ~12% and ~5%, respectively) than studies using singlet stimulation. Considering children's suggested greater activation deficit, stimulation number seems to be an important factor explaining why VA is overestimated by singlet stimulations. Although the use of doublets or train stimulation may be advantageous, we and others (15) have found that it is uncomfortable and not well tolerated by children. As observed in adults (69), this discomfort and anticipated pain may result in underperformance during MVC, thus affecting the SI_{tw}, resulting in an underestimation of VA. In children, the effect of the anticipated pain and discomfort

may be further accentuated, explaining the apparent reliance on singlet stimulation in the studies reviewed (14/19 studies). The moderator analysis revealed that technical factors (e.g., stimulation number) were nonsignificant (Table 3), suggesting that child–adult differences in VA were not influenced by the stimulation procedures. However, it is possible that statistical significance was not reached because of the small number of studies and the large variability in VA. Future studies should examine the effects of different stimulation methodology on VA determination in children. Moreover, other techniques that do not involve electrical stimulation (e.g., magnetic resonance imaging) should be explored for the assessment of VA in children (70).

Possible mechanisms underlying child–adult VA differences. Much of the literature examining child–adult differences in VA focuses on peripheral factors that may affect VA, as reflected in the moderator analyses within this study. However, age-related increases in VA may be attributed to maturational changes occurring within the central nervous system. Cortical white matter (myelin) allows for fast and saltatory conduction of action potentials. Total cortical white matter volume increases from birth until ~30 yr of age (71–74), with accelerated myelination occurring in specific regions at different stages of development (75,76). Increased myelination, essential for high-quality interregional cortical communication, is observed with progressing maturation (77). Motor evoked potential thresholds (MEP_{Th}) provide insight into the degree of cortical connectivity (e.g., myelination) and excitability of the corticospinal tracts, with a high MEP_{Th} indicating lesser development (78). Several studies report MEP_{Th} decreases with age during childhood, reaching adult levels by adolescence (78,79). Therefore, it is possible that enhanced myelination and connectivity lead to greater muscle activation, specifically of higher-threshold motor units.

Synaptic pruning is another process in the maturing cortex in which unused or "weak" synaptic connections are eliminated to create more efficient neural networks (80). Pruning may increase the strength of neuronal connections sufficiently to facilitate the depolarization of neurons (particularly neurons of higher-threshold motor units), which previously could not be depolarized, or allow them to depolarize at more optimal rates (81). As reflected from autopsy and magnetic resonance imaging studies, pruning seems to peak around the transition from childhood to adolescence (82–84). This is in line with the suggestion that child–adult differences in VA are more prominent when children are <10 yr old (13). That is, the timing of myelination and synaptic pruning may be related to the increasing VA in maturing children.

CONCLUSIONS

The present review compiled data from 19 studies and performed a meta-analysis on 14 data sets. The qualitative synthesis of the data shows that in all the studies but one, VA is lower in children compared with adults. However, likely because of the small sample sizes and the inherent variability associated with VA determination, many of the comparisons were not found to be statistically different. The quantitative meta-analysis found a strong main effect of age on VA, with lower VA in children compared with adults. Lower VA in children can explain their lower body-size–normalized maximal and explosive strength (4,44). This may also partly explain children's strength improvements after resistance training without concomitant hypertrophy (49,50), but more research is needed to elucidate the possible resistance training effect on children's VA. The age effect was found independent of physiological or methodological factors. However, because of the small number of available studies, more research is needed to provide better insights into these factors. Most of the studies to date examined mainly lower extremity muscles in males only. To attain a more comprehensive understanding of VA and maturation, future studies should compare lower versus upper extremity muscles, as well as males versus females. Mechanisms underlying an age-related increase in VA are unclear, but centrally regulated processes such as myelination and synaptic pruning are likely involved.

This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC grant to B. Falk). S. Woods holds an Ontario Graduate Scholarship, and C. O'Mahoney received an NSERC Undergraduate Student Research Award. The authors would like to thank Brock University Librarians Evelyn Feldman and Elizabeth Yates providing invaluable assistance with the systematic data search.

The authors declare no conflict of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine. All results presented here are done so clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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