Author's response to reviews

Title: Wrist flexion and extension torques measured by highly sensitive dynamometer in healthy subjects from 5 to 80 years

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Author's response to reviews: see over
Dear Mr Duckworth,

The co-authors and I thank you for your thorough attention to our manuscript entitled “Wrist flexion and extension torques measured by highly sensitive dynamometer in healthy subjects from 5 to 80 years” by Decostre et al. We are grateful to the reviewers for their positive review and constructive comments that have helped us to improve the manuscript. Your will find here below our answers to their questions and comments. All the authors agree with the updated content of the manuscript.

We hope that you will find this new version is improved and are looking forward to hearing from you.

Yours Sincerely,

Valérie Decostre
Corresponding author
Answers to reviewer’s report

Title: Wrist flexion and extension torques measured by highly sensitive dynamometer in healthy subjects from 5 to 80 years

Reviewer: Peter Hamer

A) Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. I found the manuscript easy to read, was appropriate in management and analysis of the data collected and did not overstate the results. However, I do question whether the data can be considered as norms. While the total number of healthy people tested initially looks admirable, review of Table 1 indicates relatively small numbers per age grouping and often a different proportion between genders than is found in the general population. There is no indication of the demographics of the sample of the population e.g. socio economic status, blue or white collar workers, metropolitan versus rural or other descriptions related to how well the sample represented the population from which the participants were recruited. The sample is a sample of convenience and may be affected by self-selection bias and it is unclear whether those who volunteered may have different attributes than those who did not volunteer.

Line 77. The sentence was completed by the following italic text:
“Healthy male and female subjects aged between 5 and 80 years old were recruited by advertisements in newspapers, websites, posters and open access animation for the French Telethon. The socio economic status, blue or white collar worker and urban or rural environment of the subjects were not recorded, but since all the measurements took place in Paris, the urban middle class white collar profile is probably over-represented. Therefore, the results presented in this study are not representative of the French population and the terms “norms” or “normative data” used here only refer to our tested sample.”

2. Were the data tested for normality? This would be important if the values reported in Table 1 or predictive equations in Table 3 &4 are intended to be used as norms (as indicated in the manuscript) allowing the reader the confidence to use the mean (±SD) as the best measure of central tendency. Data representation using confidence Intervals (CI) would also be of value – particularly if the data in Table 1 are to be considered as norms. I have calculated some of the confidence intervals and this reveals that many of the age groupings have overlapping CI. As CI are affected by the size of the sample, it may be possible to analyse the different age groups and determine different age groupings based on clear separation of results – if the values presented in Table 1 are intended to be used by readers. I make this comment as the data for torque are presented in Table 1 for different age groups and it is likely that the clinician is more likely to use the values in this Table 1 rather than calculate the predicted value from the equations presented in Tables 3 & 4.

This is a very good point. Normality could not be tested in each age category because of insufficient number (n<30) in some age categories. Different age grouping is a solution. However, we prefer not to enlarge the age range of the different categories as the interest of the corresponding torque would become lower. Indeed, we think that presenting the mean torque of a 5 to 9 years old category may be more useful than the mean torque of a 5 to 14 years old category, although some age groupings have overlapping torque CI.
Table 1 aims to present the subjects characteristics of this study, while the model is expected to be used as healthy control values of wrist flexion and extension. Following the reviewer’s remark that table 1 might be preferentially used instead of the model, we propose in this revised version of the manuscript to add the following paragraph at the end of Discussion – Predictive model (line 310):

“The interest of the predictive models compared to the use of mean values as those presented in Table 1 for the prediction of the expected wrist torque of a subject is the precision and the number of subjects used for the prediction. As an example, the left wrist flexion torque of a 27-years old female 164 cm high can be precisely predicted from the model to 7.5308 N.m (=\text{EXP}(0.761+0.008*164-0.002*27+0.432*0)), while Table 1 reports the 9% higher value of 8.2 N.m for females between 20 and 29 years old with a mean height of 167.2 cm. Moreover, in this example, the model prediction is based on an analysis of the results of 286 subjects, while the experimental mean value in Table 1 was obtained on 32 subjects. However, the fit of the model through the experimental torques is better for children than for adult data as the adjusted $R^2$ is higher for the fit of children than for the fit of adult results (Tables 3 and 4). Using a model or the mean value from a normative table always remains a prediction with its imprecision. However, to determine the predicted torque value of a given subject, we favour calculation from the model with its fit imperfection rather than using the mean torque corresponding to an age category with a mean height as exampled in table 1. First, this limits the effect of confounding variables such as stature, which is included in the model. Second, the model enables the expression in percentage of predicted value for the results of patients, allowing the quantification of a deficit and its evolution.”

B) Minor Essential Revisions (such as missing labels on figures or the wrong use of a term which the author can be trusted to correct)

1. With the addition of line numbers the Reference list has been difficult to follow as the number reference has been overtyped by the line number. This will not be a problem once the manuscript is finalised.

Line numbering now stops before the Reference section so that overtyping of line number on reference number is solved. Sorry for this problem in the initial version.

2. Anthropometric measures – sentence 1 – line 95. The SI correct terminology is Body Mass (kg) rather than weight (SI measurement in Newtons). However, it is acknowledged that the term of weight is commonly used. My preference is to use Body Mass (kg). Please search the manuscript and change each use of weight to mass, including Table 1 and Table 6.

“Weight” was replaced by “body mass” throughout the manuscript and Table 1.

3. Delete “ in line 98 – Anthropometric measurements

“ was deleted (in line 98 now become line 103)

4. In Statistical analyses, line 4 (line 153 in manuscript) change was to were

“was” was replaced by “were” (now in line 158 instead of line 153)
5. Normative data, line 6 (line 193 of manuscript) change systemically to systematically

“systemically” was replaced by “systematically” (now in line 197 instead of line 193)

6. Figure 4, please change Nm to N.m as has been done in all other figures eg. Figure 3

“Nm” was changed to “N.m” in figure 3.

C) Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. Reliability assessment, line 6 (line 221 of manuscript). Suggest change brought out to revealed

“brought out” was replaced by “revealed” (now in line 225 instead of line 221)

2. To encourage the use of the predication equations rather than direct use of numbers presented in the Table, the authors could include a discussion of the value of using the predictive equations (and even consider an example calculation) as I suspect most clinicians will use the table. As the predictive equations have been shown by the authors to have a better fit for children than adults there may need to be further discussion on the limitations of the generalizability of the results from either the torque values in Table 1 or the values obtained from the predictive equations in Table 3 & 4.

As already indicated above ((A) 2), the following paragraph was added at the end of Discussion – Predictive model (line 310):

“The interest of the predictive models compared to the use of mean values as those presented in Table 1 for the prediction of the expected wrist torque of a subject is the precision and the number of subjects used for the prediction. As an example, the left wrist flexion torque of a 27-years old female 164 cm high can be precisely predicted from the model to 7.5308 N.m (=EXP(0.761+0.008*164-0.002*27+0.432*0)), while Table 1 reports the 9% higher value of 8.2 N.m for females between 20 and 29 years old with a mean height of 167.2 cm. Moreover, in this example, the model prediction is based on an analysis of the results of 286 subjects, while the experimental mean value in Table 1 was obtained on 32 subjects. However, the fit of the model through the experimental torques is better for children than for adult data as the adjusted $R^2$ is higher for the fit of children than for the fit of adult results (Tables 3 and 4). Using a model or the mean value from a normative table always remains a prediction with its imprecision. However, to determine the predicted torque value of a given subject, we favour calculation from the model with its fit imperfection rather than using the mean torque corresponding to an age category with a mean height as exampled in table 1. First, this limits the effect of confounding variables such as stature, which is included in the model. Second, the model enables the expression in percentage of predicted value for the results of patients, allowing the quantification of a deficit and its evolution.”
The authors have presented results of a study using a highly sensitive dynamometer specifically for use in the measurement of wrist flexion and extension, in a large group of normal subjects, and in a small group of patients with a limb girdle muscular dystrophy. The paper is well written and relatively easy to understand. The methods are appropriate and well defined and illustrated. I have made no comments on the reliability of the statistics in this paper, as I have no experience in this field. I found the discussion stimulating, and conclusions appear well supported by the data.

**DISCRETIONARY REVISION POINTS**

There are 2 particular points of interest here. Firstly, the authors report a ‘session’ effect, with a small but quantifiable difference in the wrist flexion and extension measurements on testing a second time. They have explained this effect as subjects having less anxiety and familiarity with the device second time around. Did the number of attempts at session 1 influence the reproducibility during session 2? Do the authors think that allowing the subjects more attempts and more time at session 1 will decrease the sessional difference?

Line 230: The following paragraph was added:

> We examined whether the number of trials at the test session influenced the reliability at the retest session. Among the 75 subjects who performed the retest session, about 60%, 30%, 8% and 1% needed respectively 2, 3, 4 and 5 trials at the test session to meet the criteria of 10% reproducibility between 2 trials within a maximum of 5 trials. No relation or significant difference (ANOVA) could be evidenced between the test-retest reliability of the subjects who needed 2, 3, 4 or 5 trials at the test session.

Secondly, the authors have shown that in their subgroup of 9 patients with LGMD, the dominant side produces less torque that the non-dominant side, and conclude that overuse of the dominant arm may be detrimental. Could the authors perhaps expand on this? As a non neurologist, a short discussion of any other supporting evidence here would be useful.

The sentence “This suggests that overuse might be deleterious for skeletal muscles of patients with LGMD2C” was moved from the Results section to Discussion.

The following paragraph was added at the end of Discussion - Feasibility in a small patient group (line 365):

> “Moreover, the dynamometer detected in our group of LGMD2C patients a wrist extension torque systematically weaker in the dominant side than in the non-dominant side. The mean difference and SD represented 1.06 ± 0.52 N.m or 17.61 ± 9.13 % of the predicted value. First, this indicates that differences as small as ~1 N.m can be discriminated by the device. Second, this suggests that overuse might be deleterious for skeletal muscles of patients with LGMD2C. We found no data in the literature on the effect of exercise on muscle contraction in the specific LGMD2C subtype. Nevertheless, a similar conclusion was obtained for ankle dorsi- and plantarflexors of patients with limb girdle muscle dystrophy as their preferred side was more affected (Belanger 1991), even if the preferred side has probably less impact on the lower limbs than on the upper limbs. Other studies reported, however, increased strength and endurance in wrist flexion and extension (Sveen 2013) and no abnormal
creatine kinase level in response to high intensity exercise in patients with LGMD2 (Anderson 2013). The beneficial or deleterious effect of muscle contraction in LGMD2C still needs to be further investigated.”

Finally, the PDF file I received did not have any ‘key’ or figure numbers, although the tables were clearly titled, and I wonder if this is a mistake, or if I have received a corrupted version.

Figures have now been numbered within the file. They were previously numbered within their filename, but unfortunately this did not appear in the file sent to the reviewers.