Ecological validity of biomarkers in drug research

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CHAPTER 6

POWERJAR, A NOVEL DEVICE FOR QUANTITATE ASSESSMENT OF JAR OPENING: AN EXPLORATORY TECHNICAL VALIDATION STUDY.

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ABSTRACT

Grip strength, assessed with a handheld dynamometer, is commonly used to monitor disease progression and evaluate healthcare interventions. However, grip strength alone does not fully reflect the complexity of daily tasks, which require a combination of strength, coordination, and fine motor control. This study introduces the PowerJar, a novel device designed to quantify grip and rotational forces during simulated jar-opening tasks, providing a more complete assessment of hand function.

This observational study included healthy volunteers and patients with neuromuscular diseases. Healthy participants performed PowerJar tasks four times at 60-minute intervals, while patients performed tasks once during each of two visits. Usability was assessed through a questionnaire after each visit. Grip strength was measured using both the PowerJar and a handheld dynamometer. Repeatability was evaluated by assessing the consistency of PowerJar measurements across multiple sessions.

The study included 62 healthy participants and 18 patients. Usability assessments indicated that the PowerJar tasks were reasonably challenging but manageable. A strong positive correlation was found between handheld dynamometer and PowerJar measurements, although the dynamometer recorded on average higher grip strength values. Repeatability analysis showed moderate to good repeatability for both grip and angle parameters.

The PowerJar demonstrated usability across different populations and provided additional information beyond standard grip strength assessments. The device's moderate repeatability suggests its potential for early-phase drug development and clinical trials. However, further research is needed to explore the PowerJar's sensitivity to changes in neuromuscular diseases and responses to interventions.

INTRODUCTION

Neuromuscular diseases often lead to progressive impairments in muscle strength and functional independence, reducing the patients' quality of life. Clinical research frequently uses grip strength assessed with a handheld dynamometer to monitor disease progression. Additionally, it is used to evaluate the efficacy of healthcare interventions such as drugs and physical therapy.[1-5] Grip strength is an appealing procedure to be used in both clinical and research settings due to its simplicity, reliability, and validity.[5]

While grip strength is often used to assess muscle function, it provides an isolated measure of force which does not fully reflect the complexity of daily life tasks. These tasks often require a combination of strength, coordination, and fine motor control.[6] As a result, grip strength does not fully reflect the challenges patients face in their daily activities or the true impact of neuromuscular disease. This discrepancy can lead to situations where grip strength improves, yet patients might experience no significant improvement in daily functioning. In drug development, enhancing daily life quality is essential for regulatory approval. Consequently, quality of life is frequently used as a clinical outcome measure in registration trials to assess the effect of treatments on patients' everyday activities.

To increase efficiency and minimize costs and risks, predictive biomarkers are often utilized in early-phase trials to identify potential outcomes before progressing to registration trials. Such a biomarker should quantify a daily task that impacts daily life of patients. Functional tasks, such as opening jars or bottles, represent a critical aspect of daily living and require both grip strength and rotational force. These tasks are significant challenges for individuals with neuromuscular diseases, and easy relatable to daily life function. Approximately 14% of the elderly were found unable to open a screw cap bottle containing their medication.[7]

Unlike isolated strength measurements, assessing the ability to perform such tasks can provide deeper insights into the daily life burden of the disease and the efficacy of (drug) interventions. Earlier attempts to assess daily life activities considering hand function resulted in the Jebsen hand function test and the Duroz hand index. These assessments include tying shoelaces, cutting putty with knife and fork, manipulating coins into a slot or pouring a glass of water and showed differences between healthy volunteers and patients suffering from conditions like stroke and arthritis.[8-10] The outcome parameters of these tests are not ideal as these often rely on observer ratings, making them dependent on individual observers. Additionally, these tests are labour-intensive and have relatively low resolution compared to the possibilities of computerized tests.

This contrasts with biomarkers used in clinical trials as part of early phase drug development, which should be quick, easy to assess, sensitive, and repeatable to ensure its reliability in placebo-controlled clinical trials with possible small dose-dependent effects. To bridge this gap in biomarkers, the PowerJar was developed, a novel device designed to quantify grip and rotational forces during simulated jar-opening tasks. By replicating this daily activity, the PowerJar provides an opportunity to measure outcomes that are more reflective of everyday challenges and closer related to clinical outcome assessments collected in drug registration trials.[11]

This study addressed two objectives. First, we evaluated the usability of the PowerJar device in both healthy volunteers and patients with neuromuscular diseases. The usability was evaluated by determining whether the device can be effectively utilized and integrated into clinical studies. Furthermore, the PowerJar's capability to capture grip and rotational forces in a standardized manner was assessed. Second, we investigated the repeatability and reliability of the PowerJar measurements in healthy volunteers. Repeatability was assessed by assessing the consistency of measurements across four sessions in one visit. Reliability was assessed by comparing grip strength assessments of the PowerJar to those recorded with a handheld dynamometer. Combined with usability, the repeatability and reliability were used for an evaluation of the endpoints generated by the PowerJar as possible biomarkers in early phase drug development clinical trials.

METHODS

This was a two-part, observational study in healthy volunteers and patients with a neurological disease and self-reported hand weakness. The study was approved by the BEBO Ethics Committee located in Assen (The Netherlands). All participants provided written informed consent prior to any study related activities. The first part of the study, part A, included healthy male and female participants who performed all tasks of the PowerJar (see methods section) four times at 60-minute intervals. The second part, part B, included male and female patients with a neurological disease and self-reported hand weakness who performed all tasks of the PowerJar once during each of two visits. There were at least 6 days between the visits.

Participants

Part A: Healthy male and female participants were invited to join the study and were assigned to one of three age groups. Each of the three age groups (between 21-40, 41-60, and 61-80 years old) consisted of 10 male and 10 female participants. After signing of the informed consent form, participants underwent medical screening consisting of a physical examination and recording of their medical history, height, and weight. When included in the study, participants were not allowed to consume alcohol within 24 hours of the study visit, use any form of medication or supplements during the study, and had to refrain from heavy physical exercise at least 48 hours prior to the study visit.

Part B: Male or female patients with a neurological disease, including Myasthenia Gravis, Myotonic Dystrophy, Parkinson's Disease, and Inclusion Body Myositis were invited for a brief medical screening. After signing of the informed consent form, participants underwent a brief medical screening consisting of recording medical history and current medication. Eligibility was limited to patients who self-reported hand weakness, assessed through the question: 'Do you have difficulties opening a jar, or has this task become more challenging than it was in the past?'. Patients with medical conditions that might interfere with the study results and/or inability to use the PowerJar device were excluded.

Assessments

Usability assessment of PowerJar

The usability of the PowerJar device was assessed by observing participants as they interacted with the device. Furthermore, after completing all PowerJar assessments, participants completed a questionnaire addressing fatigue and discomfort. Fatigue was assessed using a 15-point Likert scale, where 6 indicated very light fatigue and 20 indicated very heavy fatigue. Participants were asked to specify the task that induced the fatigue and the location in their body where they experienced it. Additionally, the participants reported any discomfort experienced with the PowerJar and if applicable the location of the discomfort.

Handheld Dynamometer

A handheld dynamometer (Smart Hand Dynamometer, Jamar) was used as the gold standard to measure maximum voluntary grip strength (i.e., the maximum amount of grip force exerted by the participant in kg). Assessments were performed as recommended by Roberts et al.[3] The participant was seated in a chair with their forearms on the chair's fixed armrests, ensuring that the wrists were able to be moved freely just beyond the ends of the armrests. The participant's wrists were to be maintained in a neutral position with the thumb facing upwards. The participant held the dynamometer in the tested hand. See Figure 3 for a side view of the assessment. The participant was then encouraged to squeeze the dynamometer as tightly as possible. This was repeated three times for each hand.

PowerJar

The PowerJar (UsinLife LLC, Edison, NJ, USA) combines resistive torque producing electronics with an isometric grip measurement device that is shaped in a jar-and-lid configuration (Figure 1). The lid of the PowerJar has a diameter of 6.5cm and was designed to have similar dimensions as the lid of a typical jar. The PowerJar is connected to a computer that enables measurement of the grip force with a resolution of 0.06 kg and the rotation of the lid with a resolution of 0.01 degrees with a sample rate of up to 13Hz. Additionally, the computer is used to configure the resistive torque of the lid Nm. The resistive torque is generated by an electric motor combined with adjustable gearings rated to generate 0 – 5.7 Nm with a resolution of 0.01 Nm. The PowerJar kept the resistive torque at a constant level throughout the measurement.

As part of the PowerJar assessments, electromyography (EMG) was recorded with surface electrodes. As we found these data not to be useful in the assessment of muscle fatigue these data will not be further discussed in this report.

POWERJAR TASKS Participants were to complete a total of 6 different tasks using the PowerJar. For all these tasks, participants were to use both hands. In part A, the participant's dominant hand was put on the lid and the non-dominant hand was placed around the body of the device, with the thumb wrapped around one side and the remaining fingers wrapped around the opposite side (See Figure 2). In part B, the participant was free to choose which hand is placed on the lid and which hand was placed on the body. The observer used the connected laptop to run six different tasks. The laptop was also connected to an external monitor where the participants could receive live feedback on their performance. The exerted grip force in kg and rotation of the lid in degrees were sampled with a non-uniform sampling frequency ranging between 7.5 and 13 Hz.

Prior to the assessments, the participant was shown how to use the PowerJar. Additionally, the highest resistive torque a participant could withstand was determined by stepwise increasing the resistive torque. In case the highest possible resistive torque that the participant could withstand was lower than the expected highest level of resistive torque based on the age group (see Table 1), this resistive torque was used for the next tasks.

In each round of assessments, participants performed six distinct tasks. Tasks 2, 3, and 4 were designed to induce fatigue which should have been primarily assessed with the EMG analysis. However, upon data review and exclusion of the EMG results, these tasks were found less informative as addition to the standard grip strength assessment for the aim of this research. Therefore, the data of tasks 2, 3, and 4 were excluded from the primary analysis but added as supplementary materials.

TASK 1 Angle Control (20 degrees). Participants were instructed to rotate the lid to an angle of 20 degrees and maintain this position for as long as possible. Real-time feedback was provided on a monitor, allowing participants to track the rotational position of the lid. The non-rotating hand was placed on the body of the jar to provide stability, applying grip force when necessary. Participants were instructed to release the lid if the angle dropped below 15 degrees. This task was performed at three resistive torque levels (see Table 1).

TASK 2 Rhythmic Rotation (15–25 degrees). Participants rotated the lid between 15 and 25 degrees in sync with a 2 Hz metronome. This task was performed at three resistive torque levels (see Table 1) for a duration of 30 seconds.

TASK 3 Rhythmic Grip. Participants were instructed to grip the body of the jar as hard as possible and then release it in sync with a 2 Hz metronome for a duration of 30 seconds.

TASK 4 Rapid Grip-and-Release. Participants gripped and released the body of the jar as hard and as quickly as possible for a duration of 30 seconds.

TASK 5 Rapid Opening and Closing (40 degrees). Participants rotated the lid between 0 (open) and 40 (closed) degrees as frequently as possible within 30 seconds. Real-time feedback was displayed on an external monitor to guide rotational positioning. Participants used their non-rotating hand to stabilize the bottle, applying grip force when necessary. This task was performed at three resistive torque levels (see Table 1).

TASK 6 Maximal Grip. Participants were instructed to grip the body of the jar as hard as possible and maintain this grip for as long as possible. Participants were allowed to release the jar when their grip strength dropped below 75% of the initial maximum or after reaching a 60-second time limit.

Data analysis

Handheld Dynamometer

Participants performed three maximum grip strength measurements per hand using the handheld dynamometer. Only the highest value obtained from the non-dominant hand, which was the hand used during the maximal PowerJar grip assessment, was used for further analysis.

PowerJar

DATA PROCESSING To ensure a constant sampling rate, data is resampled to the average sampling rate of 11.11 Hz. After resampling, missing data points were filled using a linear interpolation. Additionally, the grip data was smoothed using a moving average with a window of 6 samples (i.e., approximately 0.54s).

PARAMETERS The parameters listed in Table 2 were computed for the assessment during the analysis. For Task 1, the computation window was defined as follows: from the point when the angle exceeded 15 degrees to when the angle dropped below 15 degrees. The following grip features were calculated: area under the curve, maximum value, linear term and root mean square error of a first order polynomial fit. The angle of the lid was characterized by the linear term and root mean square error of a first order polynomial fit. Furthermore, the total hold time was determined.

For Task 5, all features were computed between the first and last closing cycle of the lid. The following grip features were calculated: dominant frequency, frequency dominance, and power of the dominant frequency. Angle features included the quadratic and linear terms of a second order polynomial fit, dominant frequency, frequency dominance, and power at the dominant frequency. The combination of grip and angle was characterized by the correlation between their values and the number of successful openings. Peak-to-peak features consisted of the linear term of a first order polynomial fit, intercept, and root mean square error.

For Task 6, the computation window was defined from the point of maximum grip strength to when the grip strength decreased to 75% of the maximum value. The following grip features were calculated: area under the curve, maximum value, and linear term of a polynomial fit. Furthermore, the total hold time was determined.

Statistical analysis

Statistical analysis was performed in R statistical software (v4.4.1; R Core Team 2025) using the DPLYR (v1.1.4), TIDYR (v1.3.1), LME4 (v1.1-36), CAR (v3.1-3), EMMEANS (v1.10.6) and LMERTEST (v3.1-3) package.

Comparison of grip strength between the handheld dynamometer and the PowerJar

Grip strength performance measured with the handheld dynamometer was compared to the maximum grip strength obtained during Task 6 of the PowerJar assessments. Participants in Part B were free to choose whether to place their weakened or not-weakened hand on the lid and body for each assessment. However, hand placement was not registered for part B, therefore this analysis was limited to healthy participants (Part A). A Pearson correlation coefficient was calculated to assess the relationship between the two measurements, and a paired two-sided t-test was conducted to evaluate differences between the devices.

Repeatability and potential sensitivity task 1, 5 and 6

To assess the repeatability and potential sensitivity, we fitted a random intercept model with measurement as fixed effect for each parameter. Type-III F-statistics were used to assess statistical significance of measurement as fixed effect ($\alpha = .05$). To estimate the repeatability, we derived the intraclass correlation coefficient (ICC) based on the variance components by dividing the between-subject variance by the sum of the between-subject and within-subject variance. The repeatability is considered poor for ICC values below 0.50, moderate for values between 0.50 and 0.75, good for values between 0.75 and 0.90, and excellent for values above 0.90.[12] Furthermore, to assess the potential sensitivity, minimum detectable effect (MDE) values were calculated. The MDE was then calculated by multiplying the effect size by the pooled standard deviation (i.e., the square root of the sum of the within- and between-subject variance). The effect size used to calculate the MDE was based on a paired sample t-test with a power of .80, a significance level of 5% (α = .05), and a sample size of 15 (a typical sample size for a clinical).

Data from Part B was excluded from this analysis. Unlike Part A, patients in Part B were allowed to switch hands between visits, and no quantification of symptom severity was available for each assessment day. As disease progression or variability could influence repeatability measurements, this part of the dataset was deemed unsuitable for inclusion in this analysis.

Resistive torque correction per age group

The resistive torque levels (Table 1) participants had to withstand were to correct for age. To determine whether this age-based resistive torque levels gave the desired results, a random intercept model was fitted with age group and measurements as fixed effects. To ensure normality, the values of the parameters Slope Angle (Task 1) and Quadratic Term Angle (Task 5) were exponentially transformed prior to model fitting. The parameter values were compared between each age group. Due to the explorative nature of this study, no p-value correction was applied.

RESULTS

Participants

In part A, 73 participants were screened, and 62 participants were included in the three pre-defined groups. The main reason for exclusion during screening was a disease or condition that affected upper limb function (n=11). All participants completed the full study, but two healthy female participants did not complete all tasks due to discomfort performing the tasks (one in the youngest age group and one in the middle age group) and were therefore excluded from analysis.

In part B, 21 participants were screened, and 18 patients were included (9 female). Three patients were excluded; two because of multiple interfering diseases in upper limbs and one because the disease did not affect their hands. There were 3 diseases present in the patient group: Parkinson's disease (n=8), Myasthenia Gravis (n=5) and body myositis (n=5). Two participants discontinued participation after the first visit, therefore only the data of their first visit were included in the analysis.

The demographics of the analysis population is summarized in Table 3.

Usability of the PowerJar

The questionnaire on usability was added later to the study, resulting in some missing data. A total of 46 healthy participants completed the questionnaire, and they reported an average (+/- standard deviation) fatigue level of 13.0 (+/- 1.5), which corresponds to reasonably heavy tasks. Task 5 was identified as the most fatiguing activity (n = 32), with fatigue primarily located in the arm (n = 14), hand (n = 10), and thumb (n = 9). Among healthy participants, 16 participants reported no discomfort from using the PowerJar. However, 14 experienced minor thumb pain, 8 developed the beginnings of a blister, and 4 reported hand discomfort during or immediately after the assessments.

Patients reported in their first visit an average fatigue level of 12.9 (+/- 1.5), with task 5 also inducing the most fatigue (n = 13). Fatigue was most commonly experienced in the thumb (n = 9), followed by the hand (n = 4), wrist (n = 3), and arm (n = 2). Regarding discomfort, 6 patients reported none, 8 experienced thumb discomfort, and 3 reported discomfort in other locations.

During their second visit, patients reported an average fatigue level of 12.6 (+/- 1.6). As in the first visit, task 5 was identified as the most fatiguing activity (n = 7). Fatigue was experienced in the hand (n = 6), followed by the thumb (n = 4), arm (n = 3) and other locations (n = 5). In terms of discomfort, 9 patients reported none, 3 experienced thumb discomfort, and 7 reported discomfort in other locations.

Missing and excluded PowerJar data

The number of missing measurements for the highest successfully completed resistive torque level per task were 1, 1, and 0 for task 1, task 5, and task 6, respectively. These measurements were missing due to technical reasons. Several additional measurements were excluded from data analysis to maintain validity of the dataset:

Task 1 (239 initially available measurements): Exclusions were made if participants failed to achieve a 15-degree rotation throughout the measurement (n = 22) or if the measurement was abruptly terminated without the angle dropping below 15 degrees (n = 6). Additionally, measurements with smoothed grip force values ≤ 1 kg were excluded, as these were considered measurement noise (n = 17). After these exclusions, a total of 194 measurements remained for analysis. See Figure S1 for an example of the data from an assessment.

Task 5 (239 initially available measurements): One measurement was excluded due to fewer than two complete opening-closing cycles (n = 1). Grip force data with smoothed values ≤ 1 kg were also excluded as noise (n = 12). After these exclusions, a total of 226 measurements remained for analysis. See Figure S2 for an example of the data from an assessment.

Task 6 (240 initially available measurements): Measurements shorter than 1.5 seconds (n = 8) or those ending abruptly without a sufficient drop in grip strength below 75% of the participant's maximum (n = 2) were excluded. No exclusions were necessary due to low grip force, as smoothed values ≤ 1 kg were not observed (n = 0). After these exclusions, a total of 230 measurements remained for analysis. See Figure S3 for an example of the data from an assessment.

Six healthy participants had difficulties completing measurements at the highest resistive torque levels, resulting in missing data. Consequently, the most challenging resistive torque level varied between participants, with some reaching the second level as their highest and others reaching the third level. To ensure consistent analysis, only data from the highest successfully completed resistive torque level for each participant was included in the analysis.

Comparison handheld dynamometer and PowerJar

Data from 57 healthy participants were analysed. Due to human error, data from 5 participants were not recorded for the handheld dynamometer. A strong positive correlation was found between the handheld dynamometer and PowerJar measurements (Pearson correlation coefficient: $r = .79$). The paired t-test indicated a significant difference between the two methods ($p < .001$), with a mean difference of 16.79 kg (handheld dynamometer larger than PowerJar). See Figure 4 for the scatterplot and boxplot of the results.

Repeatability Task 1, 5 and 6

All calculated ICCs are provided in the supplementary materials. A summary of the ICCs greater than 0.5 is presented in Table 4, the full tables are added in the supplements (Table S1, S2 and S3). For Task 1, the area under the grip curve, maximum grip, and hold time demonstrated moderate repeatability, with ICCs of 0.70, 0.66, and 0.59, respectively. In Task 5, two parameters, number of openings and dominant frequency, showed good repeatability, with ICCs of 0.79. The ratio of successful openings and the correlation between angle and grip demonstrated moderate repeatability, with ICCs of 0.67 and 0.64, respectively. Additionally, the dominant frequency and associated power of the grip, as well as the dominant frequency of the angle, exhibited moderate repeatability, with ICCs ranging from 0.51 to 0.59. For Task 6, maximum grip showed good repeatability and the area under the grip curve showed moderate repeatability, with ICCs of 0.87 and 0.71 respectively.

Resistive torque correction per age group

The correction performed on the resistive torque levels per age group aimed to result in comparable results between each group. In Table 5, the contrasts, 95% confidence intervals (CI) and their corresponding p-value are shown with at least one significant difference between groups (with the cut-off set at $p < .05$). The full tables for both Tasks 1 and 5 are added in as supplementary materials (Table S4). Three out of the seven parameters for task 1 showed a significant difference between age groups, including the Total Grip between 20-40 and 41-60 years (ED: -109 kg*s (-214.24, -5.46)), and the Maximum Grip between 20-40 and 61-80 years (ED: -4.01 kg (-6.38, -1.64)). Nine parameters of task 5 (total of 14) differ significantly between age groups. These nine include both grip and angle related parameters. For example, the dominant frequency of both grip (ED: -0.29 Hz (-0.57, -0.02)) and angle (ED: 0.45 Hz (0.11, 0.80)) showed a difference between the age groups 20-40 and 41-61 years. Whereas the Number of Openings showed a difference between all age groups (ED: 7.50 (0.56, 14.44), ED: 17.46 (10.52, 24.40), ED: 9.96 (3.02, 16.90).

DISCUSSION

In this study, we assessed the usability and repeatability of the PowerJar in a clinical setting. Usability was assessed in both healthy volunteers and patients with a neuromuscular disease, and repeatability was assessed in healthy volunteers only. The tasks selected to assess repeatability were chosen to resemble daily life activities that often require prolonged grip or the combined use of grip and torque. Both grip and torque during jar-opening tasks are often overlooked using handheld dynamometers to assess the grip strength. By including these more relevant tasks, the PowerJar provides valuable additional information beyond standard grip strength assessments.

Usability

Ninety-seven percent of the healthy participants and all patients completed participation in the study, which suggests that the device is easy to use and well-suited for various grip and rotation tasks. The average fatigue levels, 13.0 (i.e., reasonably heavy) for healthy participants and 12.8 for patients, indicated that the tasks were perceived as reasonably challenging. Combined with the fact that nearly all participants successfully completed participation in the study, it suggests that the tasks were challenging, but not excessively demanding. These results are expected, as we aimed to design the tasks to induce fatigue, but not to induce failure to perform the test. Of all tasks, both groups reported the rapid opening and closing task (i.e., task 5) as the most fatiguing task, likely due to the repetitive dynamic movement it requires. Interestingly, while both groups experienced hand fatigue, arm fatigue was reported most frequently among healthy participants, while patients rarely reported arm fatigue. This may hint towards differences in techniques used by both groups. It might be expected that patients, especially those with hand weaknesses, would compensate by using larger muscle groups (e.g., the bigger arm muscles) to assist with the task. However, the data on perceived fatigue indicates that patients primarily relied on the thumb and the hand. This could imply that the rapid opening and closing task assessment can only provide insight in hand function and not accurately reflect lower and upper arm impairment.

Patients reported reduced discomfort during the second visit compared to the first. This may be explained by an increased device familiarity or by patients intentionally performing the task less intensively during the second visit. Regarding the device familiarity, the hand could have been positioned slightly different during the second visit to reduce discomfort. Furthermore, changes in disease symptoms (e.g., off-period for Parkinson) may have influenced the reported discomfort. However, neither the exact hand position nor disease symptom severity were recorded. Future studies would benefit from registering in more detail the hand positioning and symptom severity to improve data consistency and reliability in data collection. Despite this limitation, the PowerJar demonstrated its usability as task in the setting of early phase clinical trials across different populations.

Comparison with handheld dynamometer

The handheld dynamometer is frequently used tool in clinical studies to assess grip strength. The strong correlation between the PowerJar and the handheld dynamometer measurements confirms the PowerJar's potential as a reliable grip strength assessment tool. However, the dynamometer consistently recorded approximately 17 kg higher grip strength values than the PowerJar. This discrepancy is likely due to differences in hand and finger positioning between the two devices, which engage different muscles. This difference underscores the limitations of the handheld dynamometer in reflecting grip strength during everyday tasks, such as gripping a jar. On the other hand, typical handheld dynamometers allow for between-subject variabilities in hand size, a feature not present in the PowerJar. Regardless, given the strong correlation, using the PowerJar-obtained grip strength measurements could be used to determine the effects of interventions.[1-5] Combined with other PowerJar tasks, the PowerJar could provide a more detailed assessment of grip strength. Further research is required to confirm these findings and to explore the potential of the PowerJar in clinical settings.

Repeatability

The study assessed the repeatability of PowerJar tasks. Ensuring a good repeatability is essential for early-phase drug development, particularly in placebo-controlled trials where the pharmacodynamic response to the treatment is quantified. Therefore, the tasks must provide consistent parameters for the same participant within a single visit without any intervention.

The parameters derived from the various PowerJar tasks demonstrated moderate to good repeatability, with ICC values greater than 0.5 for multiple grip-related and angle-related features. In the angle control task, the total grip and maximal grip where the best repeatable parameters. Furthermore, the hold time showed moderate repeatability. For the rapid opening and closing task, parameters associated with the opening frequency and closing frequency showed moderate to good repeatability. In the maximal grip task, the maximum grip parameter showed good repeatability, while total grip showed moderate repeatability. In conclusion, these findings indicate that the PowerJar tasks can repeatably measure various grip and angle parameters, making them of interest for assessing hand function in clinical and research settings.

The repeatability analysis was limited to the highest achieved resistance level, because not all participants were able to perform all three pre-defined resistive torque levels. The pre-defined resistive torque levels aimed to account for possible age-related differences in strength. However, as demonstrated in the age group comparison, this adjustment did not eliminate intergroup differences, suggesting that other factors such as individual physical condition may also play a role in performance. Additionally, it suggests that resistive torque levels may be more effectively determined by participant performance or even standardized for better comparability. Even though intergroup differences were present and only the highest resistive torque was analysed, the PowerJar still demonstrated moderate repeatability. These findings indicate the PowerJar's potential to assess the effects of clinical interventions.

Limitations

This was the first study to use the PowerJar in a clinical setting, and we identified several limitations in both the study design and the interpretation of results. First, due to the exploratory nature of this study, the number of included patients, was moderate. Additionally, no other, clinical, assessment of hand function of the patients was included in the study. This made it difficult to assess the impact of hand function impairment on the performance within and between study visits. The next step would be to perform more studies to relate PowerJar tasks to daily life activities. Future studies can address this by implementing stricter screening criteria and more elaborate clinical assessments of disease severity to create both a well-defined and larger study population. A second limitation is related to the technical issues that resulted in the EMG data not being useful in the assessment of muscle fatigue. Nonetheless, the fatigue questionnaire results provided insight into the effort and experience of the study participants, but future studies should aim to include the EMG for both an objective assessment of fatigue and the identification of possible compensation mechanisms in patients.

CONCLUSION

The current study provides evidence that the PowerJar is moderately repeatable in healthy volunteers under controlled conditions. Furthermore, the study demonstrates the PowerJar's usability across different populations. This makes the PowerJar a promising tool for assessing hand function in a clinical study setting. Further research is required to explore its sensitivity to changes in neuromuscular diseases and responses to drug interventions, and its potential relation to clinical outcomes for patients.

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FIGURE 1 PowerJar setup as used in the study. The computer that is attached and used for controlling the PowerJar is not shown.

FIGURE 2 A) The position of the participant while gripping the PowerJar. B) The grip position of the hands and fingers of a typical participant.

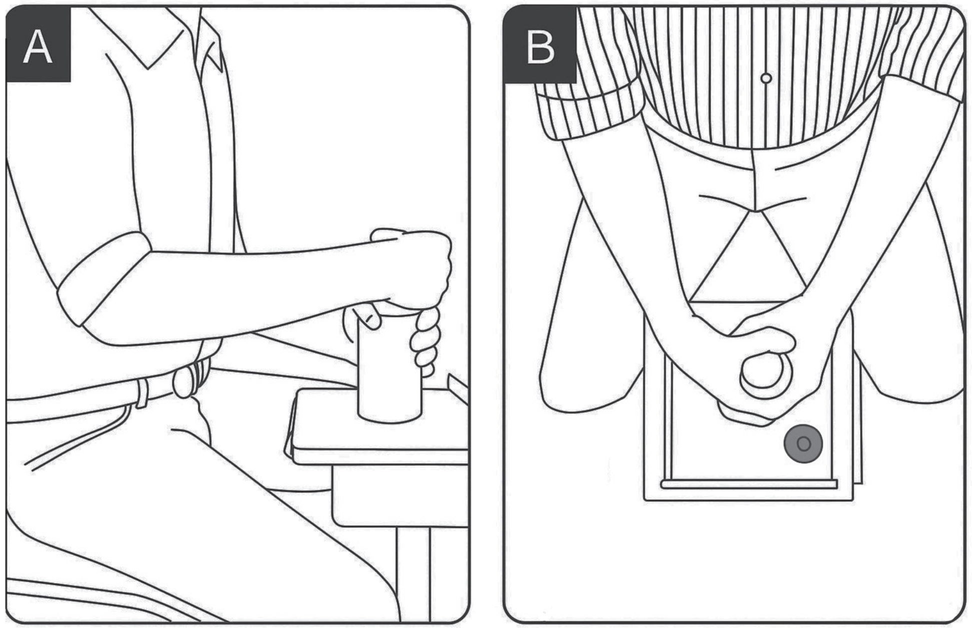


FIGURE 3 Grip position of the handheld dynamometer of a typical participant.

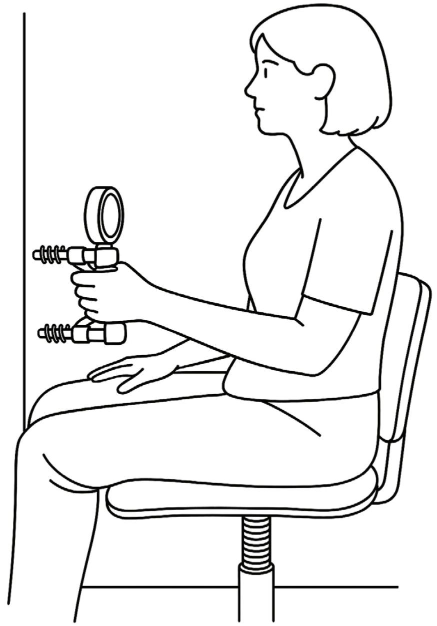


FIGURE 4 A) Boxplots of the Maximum Grip measured with the handheld dynamometer and the PowerJar. B) Correlation plot (r=.79) between the maximum grip values obtained by the handheld

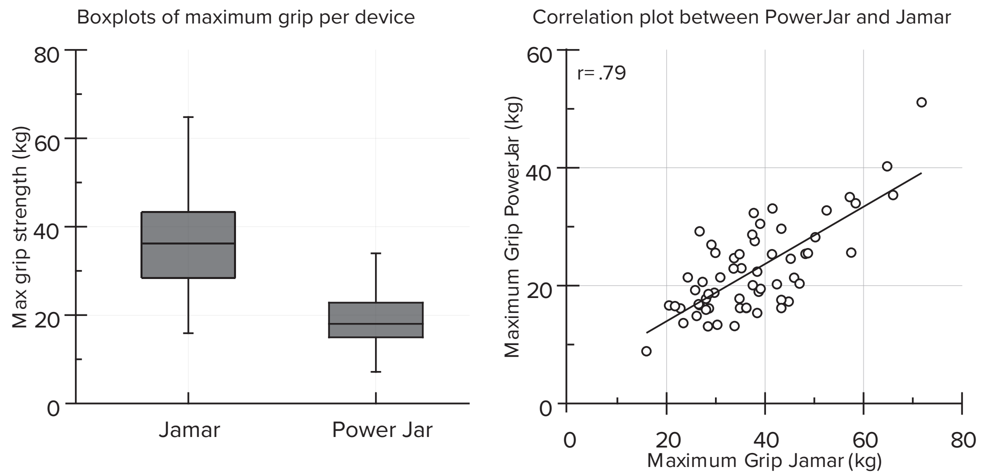


TABLE 1 Pre-determined resistive torques per age group.

Age group	First level	Second level	Third level
20–40 years old	2000 mNm	3500mNm	4991 mNm
41–60 years old	1500 mNm	3000mNm	4991mNm
61–80 years old	1000 mNm	2500 mNm	4000 mNm

TABLE 2 Calculated parameters per task.

Category	Parameter	1	5	6	Definition
Grip	Total [kgs]	X		X	Area under the curve (AUC) in the defined period.
	Slope [kg/s]	X		X	Linear term of a polynomial fit (1st order) of the grip values in the defined period.
	Max [kg]	X		X	Maximum grip value in the defined period.
	RMSE [kg]	X			Root mean square error of the polynomial fit (1st order) of grip values in the defined period.
	Dominant freq. [Hz]		X		Dominant frequency of the grip values.
	Freq. dominance [a.u.]		X		Peak AUC (around dominant frequency +- 0.25Hz) / total AUC (0-10Hz).
	Power frequency [kg^2]		X		Power at the dominant frequency.
Grip & Angle	Hold time [s]	X		X	Time of the defined period.
	Correlation grip and angle [a.u.]		X		Correlation coefficient between angle and grip values.
	Number of openings [#]		X		Opening is defined as angle >40.
	Number of Openings : total peaks [a.u.]		X		Number of successful openings divided by the total peaks.
Angle	Slope [deg/s]	X	X		Linear term of a polynomial fit (1st order task 1, 2nd order task 5) of the angles in the defined period.
	RMSE [deg]	X			Root mean square error of the polynomial fit (1st order) of the angles in the defined period.
	Quadratic term polyfit [deg/s2]		X		Quadratic term of a polynomial fit (2nd order task 5) of the angles in the defined period.
	Dominant freq. [Hz]		X		Dominant frequency of the angle values.
	Freq. dominance [a.u.]		X		Peak AUC (around dominant frequency +- 0.25Hz) / total AUC (0-10Hz).
	Power frequency [deg2]		X		Power at the dominant frequency.
Peak-to-Peak (P2P)	Slope P2P [s/#]		X		Linear term of a polynomial fit (1st order) of the peak-to-peak intervals in the defined period.
	Intercept P2P [s]		X		Intercept term of a polynomial fit (1st order) of the peak-to-peak intervals in the defined period.
	RMSE P2P [s]		X		Root means square error of a polynomial fit (1st order) of the peak to peak intervals in the defined period.

TABLE 3 Average age and standard deviation (SD) of age and BMI per age group of healthy volunteers and the patient group.

	Age in years (+/- SD)	BMI in kg/m² (+/- SD)
Healthy volunteers group 1	22.6 (+/-2.0)	23.6 (+/- 2.8)
Healthy volunteers group 2	48.5 (+/-5.3)	25.1 (+/- 3.7)
Healthy volunteers group 3	71.9 (+/- 4.0)	25.6 (+/- 2.7)
Patients	64.7 (+/- 9.4)	Not recorded

TABLE 4 Calculated mean values, intraclass correlation coefficients (ICC), minimal detectable effect (MDE), and p-value for the effect of trial, for parameters from tasks 1, 5, and 6. Only parameters which had an ICC value of 0.5 or larger were included in this table. with a value of 0.5 or larger for task 1, 5 and 6.

Parameter	Mean	ICC	MDE	p-value	F (NUMDF, DENDF)
TASK 1					
Total Grip	176.60 [kg*s]	0.70	146.20 [kg*s]	=.074	2.36 (3, 140.2)
Maximum Grip	7.53 [kg]	0.66	3.41 [kg]	=.060	1.21 (3, 140.6)
Hold Time	38.35 [s]	0.59	20.59 [s]	=.011	3.82 (3, 153.9)
TASK 5					
Frequency Dominance Grip	0.32 [a.u.]	0.55	0.09 [a.u.]	= .006	4.33 (3, 165.5)
Frequency Power Grip	3.55 [kg²]	0.59	2.26 [kg²]	=.083	2.27 (3, 165.4)
Correlation Grip and Angle	0.51 [a.u.]	0.64	0.23 [a.u.]	< .001	6.81 (3, 165.2)
Number of Openings	24.25 [#]	0.79	11.04 [#]	< .001	18.57 (3, 175.1)
Ratio Successful Openings	71.45 [a.u.]	0.67	21.41 [a.u.]	= .016	3.56 (3, 175.1)
Dominant Frequency Angle	1.29 [Hz]	0.79	0.53 [Hz]	< .001	19.34 (3, 175.1)
Frequency Dominance Angle	0.38 [a.u.]	0.51	0.08 [a.u.]	< .001	9.50 (3, 175.2)
TASK 6					
Maximum Grip	19.75 [kg]	0.87	5.57 [kg]	< .001	6.30 (3, 168.3)
Total Grip	4218.71 [kg*s]	0.71	3181.58 [kg*s]	< .001	6.01 (3, 168.6)

TABLE 5 Effect of age-group on parameter value. Contrasts (estimate of difference (95% CI)) and p-value between groups with at least one significant difference between groups (p<.05).

Parameter	Age-group		
	(20-40) vs (41-60)	(20-40) vs (61-80)	(41-60) vs (61-80)
TASK 1			
Total Grip [kg*s]	-109.45 (-214.03, -4.86) p=.041	-76.58 (-186.21, 33.06) p=.168	32.87 (-75.76, 141.50) p=.548
Slope Grip [kg/s]	0.05 (-0.05, 0.15) p=.316	-0.08 (-0.18, 0.03) p=.144	-0.13 (-0.23, -0.02) p=.017
Maximum Grip [kg]	-1.69 (-3.94, 0.57) p=.139	-4.00 (-6.37, -1.63) p=.001	-2.31 (-4.66, 0.04) p=.054
TASK 5			
Dominant Frequency Grip [Hz]	-0.29(-0.57, -0.02) p=.039	-0.20 (-0.47, 0.07) p=.142	0.09 (-0.18, 0.36) p=.517
Frequency Dominance Grip [a.u.]	-0.05 (-0.10, 0.01) p=.084	-0.10 (-0.15, -0.05) p<.001	-0.05 (-0.10, 0.00) p=.054
Frequency Power Grip [kg²]	-0.83 (-2.22, 0.56) p=.239	-2.77 (-4.13, -1.40) p<.001	-1.94 (-3.32, -0.56) p=.007
Correlation Grip and Angle [a.u.]	-0.17 (-0.33, -0.01) p=.039	-0.13 (-0.29, 0.03) p=.110	0.04 (-0.12, 0.20) p=.605
NOO [#]	7.55 (0.58, 14.51) p=.034	17.53 (10.56, 24.49) p<.001	9.98 (3.01, 16.94) p=.006
Ratio Successful Openings [a.u.]	-4.85 (-19.43, 9.73) p=.508	12.70 (-1.88, 27.29) p=.087	17.55 (2.97, 32.13) p=.019
Dominant Frequency Angle [Hz]	0.46 (0.11, 0.80) p=.011	0.74 (0.39, 1.09) p<.001	0.28 (-0.06, 0.63) p=.108
Frequency Dominance Angle [a.u.]	-0.03 (-0.08, 0.02) p=.172	-0.05 (-0.10, 0.00) p=.037	-0.02 (-0.07, 0.03) p=.452
Intercept Peak to Peak [s]	-0.41 (-0.77, -0.04) p=.031	-0.55 (-0.92, -0.19) p=.004	-0.15 (-0.52, 0.22) p=.424

SUPPLEMENTS

SUPPLEMENTARY TABLE S1 ICC values for task 1 for the highest resistive torque for healthy participants.

Parameter	Mean	ICC	MDE	p-value	F (NUMDF, DENDF)
Total Grip	177.93 [kg*s]	0.71	146.33 [kg*s]	=.074	2.36 (3, 140.2)
Slope Grip	0.12 [kg/s]	0.34	0.17 [kg/s]	=.060	2.53 (3, 143.6)
Maximum Grip	7.53 [kg]	0.66	3.41 [kg]	=.069	1.21 (3, 140.6)
RMSE Grip	0.56 [kg]	0.27	0.33 [kg]	=.309	2.41 (3, 144.4)
Hold Time	38.60 [s]	0.60	20.57 [s]	=.011	3.82 (3, 153.9)
Slope Angle	-0.33 [deg/s]	0.37	0.62 [deg/s]	=.031	3.05 (3, 155.1)
RMSE Angle	1.77 [deg]	0.21	0.92 [deg]	=.534	0.73 (3, 156.2)

SUPPLEMENTARY TABLE S2 ICC values for task 5 for the highest resistive torque for healthy participants.

Parameter	Mean	ICC	MDE	p-value	F (NUMDF, DENDF)
Dominant Frequency Grip	0.61 [Hz]	0.33	0.48 [Hz]	=.694	0.48 (3, 166.2)
Frequency Dominance Grip	0.32 [a.u.]	0.55	0.09 [a.u.]	=.006	4.33 (3, 165.5)
Frequency Power Grip	3.55 [kg²]	0.59	2.26 [kg²]	=.083	2.27 (3, 165.4)
Correlation Grip and Angle	0.51 [a.u.]	0.64	0.23 [a.u.]	<.001	6.81 (3, 165.2)
NOO	24.25 [#]	0.79	11.04 [#]	<.001	18.57 (3, 175.1)
Ratio Successful Openings	71.45 [a.u.]	0.67	21.41 [a.u.]	=.016	3.56 (3, 175.1)
Quadratic Term Angle	0.00 [deg/s²]	0.07	0.05 [deg/s²]	=.516	0.76 (3, 175.7)
Slope Angle	-0.22 [deg/s]	0.19	1.21 [deg/s]	=.640	0.56 (3, 175.5)
Dominant Frequency Angle	1.29 [Hz]	0.79	0.53 [Hz]	<.001	19.34 (3, 175.1)
Frequency Dominance Angle	0.38 [a.u.]	0.51	0.08 [a.u.]	<.001	9.50 (3, 175.2)
Frequency Power Angle	44.76 [deg²]	0.37	14.03 [deg²]	=.109	2.05 (3, 175.3)
Slope Peak to Peak	-0.01 [s/#]	0.00	0.05 [s/#]	=.016	3.53 (3, 175.3)
Intercept Peak to Peak	1.17 [s]	0.46	0.62 [s]	<.001	13.67 (3, 174.4)
RMSE Peak to Peak	0.26 [s]	0.38	0.21 [s]	=.488	0.81 (3, 174.5)

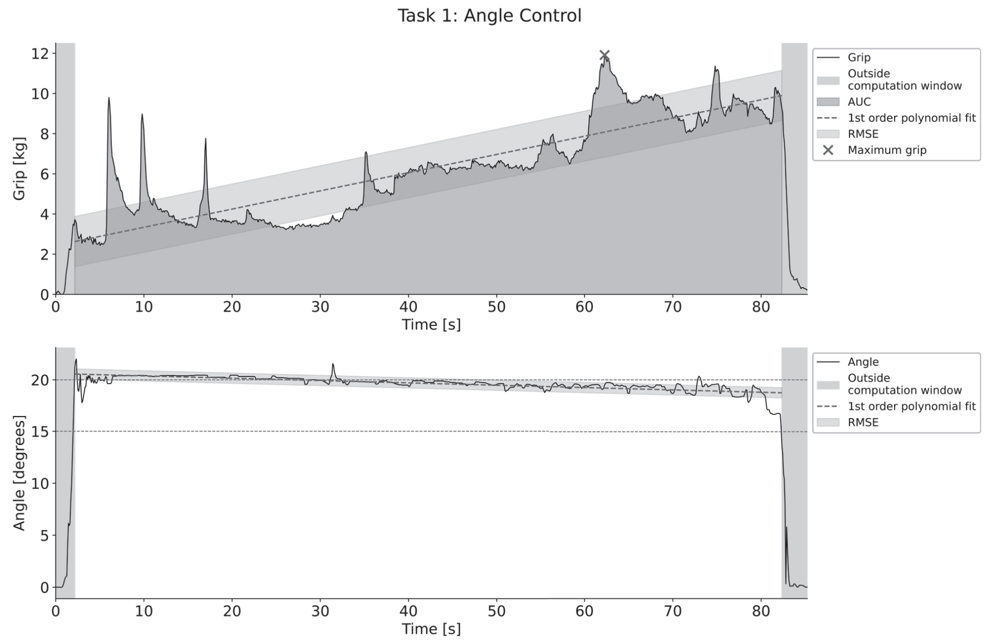
SUPPLEMENTARY TABLE S3 ICC values for task 6.

Parameter	Mean	ICC	MDE	p-value	F (NUMDF, DENDF)
Hold Time	31.03 [s]	0.48	16.68 [s]	=.335	1.14 (3, 169.3)
Maximum Grip	19.75 [kg]	0.87	5.57 [kg]	<.001	6.30 (3, 168.3)
Total Grip	4218.71 [kg*s]	0.71	3181.58 [kg*s]	=.001	6.01 (3, 168.6)
Slope Grip	-0.27 [kg/s]	0.25	0.30 [kg/s]	=.229	1.45 (3, 170.2)

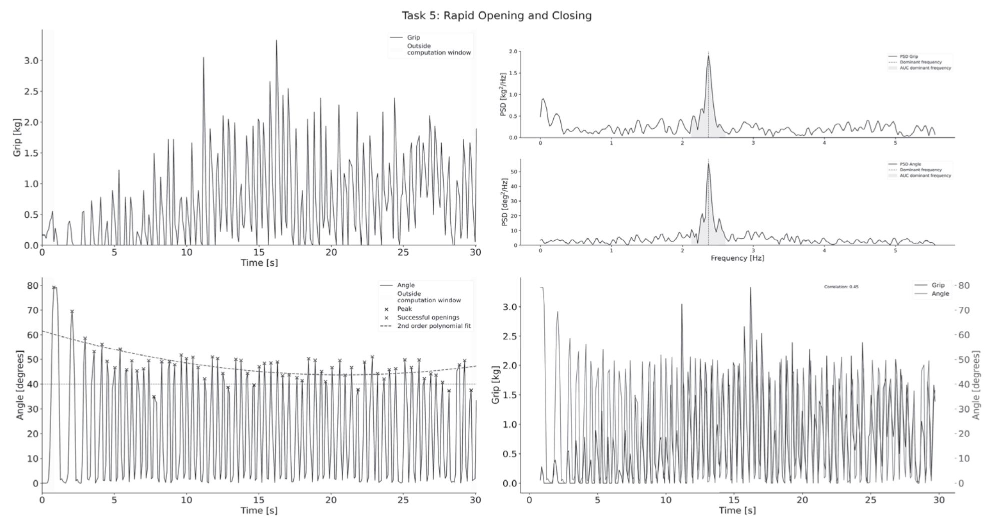
SUPPLEMENTARY TABLE S4 Effect of age-group on parameter value. Contrasts (95% CI) and p-value between groups. Parameters indicated with an asterisk are exp-transformed.

Parameter	Age Group		
	(20-40) vs (41-60)	(20-40) vs (61-80)	(41-60) vs (61-80)
Total Grip [kg*s]	-109.45 (-214.03, -4.86) p=.041	-76.58 (-186.21, 33.06) p=.168	32.87 (-75.76, 141.50) p=.548
Slope Grip [kg/s]	0.05 (-0.05, 0.15) p=.316	-0.08 (-0.18, 0.03) p=.144	-0.13 (-0.23, -0.02) p=.017
RMSE Grip [kg]	-0.02 (-0.21, 0.16) p=.803	-0.05 (-0.25, 0.15) p=.647	-0.02 (-0.22, 0.18) p=.824
Maximum Grip [kg]	-1.69 (-3.94, 0.57) p=.141	-4.00 (-6.37, -1.63) p=.001	-2.31 (-4.66, 0.04) p=.054
Hold Time [s]	-5.27 (-19.26, 8.72) p=.455	6.62 (-8.12, 21.36) p=.373	11.89 (-2.86, 26.64) p=.113
Slope Angle e^[deg/s] *	0.05 (-0.07, 0.17) p=.385	0.06 (-0.08, 0.17) p=.489	-0.01 (-0.14, 0.12) p=.895
RMSE Angle [deg/s]	-0.23 (-0.72, 0.26) p=.347	-0.15 (-0.67, 0.37) p=.569	0.08 (-0.44, 0.61) p=.751
TASK 5			
Dominant Frequency Grip [Hz]	-0.29(-0.57, -0.02) p=.039	-0.20 (-0.47, 0.07) p=.142	0.09 (-0.18, 0.36) p=.517
Frequency Dominance Grip [a.u.]	-0.05 (-0.10, 0.01) p=.084	-0.10 (-0.15, -0.05) p<.001	-0.05 (-0.10, 0.00) p=.054
Frequency Power Grip [kg^2]	-0.83 (-2.22, 0.56) p=.239	-2.77 (-4.13, -1.40) p<.001	-1.94 (-3.32, -0.56) p=.007
Correlation Grip and Angle [a.u.]	-0.17 (-0.33, -0.01) p=.039	-0.13 (-0.29, 0.03) p=.110	0.04 (-0.12, 0.20) p=.605
Number of Openings [#]	7.55 (0.58, 14.51) p=.034	17.53 (10.56, 24.49) p<.001	9.98 (3.01, 16.94) p=.006
Ratio Successful Openings [a.u.]	-4.85 (-19.43, 9.73) p=.508	12.70 (-1.88, 27.29) p=.087	17.55 (2.97, 32.13) p=.019
Quadratic Term Angle e^ [deg/s^2] *	0.00 (-0.02, 0.02) p=.974	0.01 (-0.01, 0.03) p=.217	0.01 (-0.01, 0.03) p=.228
Slope Angle [deg/s]	0.11 (-0.51, 0.73) p=.722	-0.29 (-0.91, 0.32) p=.343	-0.41 (-1.02, 0.21) p=.194
Dominant Frequency Angle [Hz]	0.46 (0.11, 0.80) p=.011	0.74 (0.39, 1.09) p<.001	0.28 (-0.06, 0.63) p=.108
Frequency Dominance Angle [a.u.]	-0.03 (-0.08, 0.02) p=.172	-0.05 (-0.10, 0.00) p=.037	-0.02 (-0.07, 0.03) p=.452
Frequency Power Angle [deg^2]	-6.60 (-14.84, 1.65) p=.115	-2.31 (-10.56, 5.95) p=.579	4.29 (-3.96, 12.54) p=.303
Slope Peak to Peak [s/#]	(-0.01, 0.03) p=.208	0.02 (0.00, 0.04) p=.135	0.00 (-0.02, 0.02) p=.801
Intercept Peak to Peak [s]	-0.41 (-0.77, -0.04) p=.031	-0.55 (-0.92, -0.19) p=.004	-0.15 (-0.52, 0.22) p=.424
RMSE Peak to Peak [s]	-0.03 (-0.16, 0.09) p=.579	-0.11 (-0.23, 0.01) p=.071	-0.08 (-0.20, 0.04) p=.203

SUPPLEMENTARY FIGURE S1 Example of the data collected during Task 1.



SUPPLEMENTARY FIGURE S2 Example of the data collected during Task 5.



SUPPLEMENTARY FIGURE S3 Example of the data collected during Task 6.