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TREMOR12: An Open-Source Mobile App for Tremor Quantification

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Tremor · App · Measurement · Smartphone · Accelerometer

Abstract
Background: Evaluating the effect of treatment of tremor is mostly performed with clinical rating scales. Mobile applications facilitate a more rapid, objective, and quantitative evaluation of treatment effect. Existing mobile apps do not offer raw data access, which limits algorithm development. ***Objective:*** To develop a novel open-source mobile app for tremor quantification. ***Methods:*** TREMOR12 is an open-source mobile app that samples acceleration, rotation, rotation speed, and gravity, each in 3 axes and time-stamped in a frequency up to 100 Hz. The raw measurement data can be exported as a comma-separated value file for further analysis in the TREMOR12P data processing module. The app was evaluated with 3 patients suffering from essential tremor, who were between 55 and 71 years of age. ***Results:*** This proof-of-concept study shows that the TREMOR12 app is able to detect and register tremor characteristics such as acceleration, rotation, rotation speed, and gravity in a simple and nonburdensome way. The app is compatible with current regulatory oversight by the European Union (MEDDEV regulations) and the Food and Drug Administration (FDA) guidance on mobile medical applications. ***Conclusion:*** TREMOR12 offers low-cost tremor quantification for research purposes and algorithm development, and may help to improve treatment evaluation.

Introduction

Essential tremor or tremor related to Parkinson's disease can be treated with medication or surgery (in particular deep brain stimulation). To measure treatment effect, most studies rely on clinical rating scales such as the Essential Tremor Rating Scale (ETRS) or the Bain and Findley Rating Scale in case of essential tremor, or the MDS-UPDRS in case of Parkinson's disease [1, 2]. Tremor quantification can be done with electromyography, but this approach limits patients' mobility and is not suited for measurements in daily living. Modern portable technology could provide cost-effective tools for tremor quantification, but need further development. Quantitative features can be extracted from the motion sensors on the device and used to develop mathematical models for predicting rating scores from kinematic data [3]. Accelerometers integrated in smartphones or wrist-worn devices can also be used for this purpose [4], which lowers the threshold for tremor quantification during activities of daily living.

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A few mobile apps are available for tremor measurement, but none of them offer the option to export all raw measurement data for offline analysis. This is a serious drawback in advancing tremor quantification as this limits the opportunities to develop new algorithms that correlate tremor measurements with clinical rating scales and patient outcome. We describe a new mobile app for tremor measurement that fills this gap.

Methods

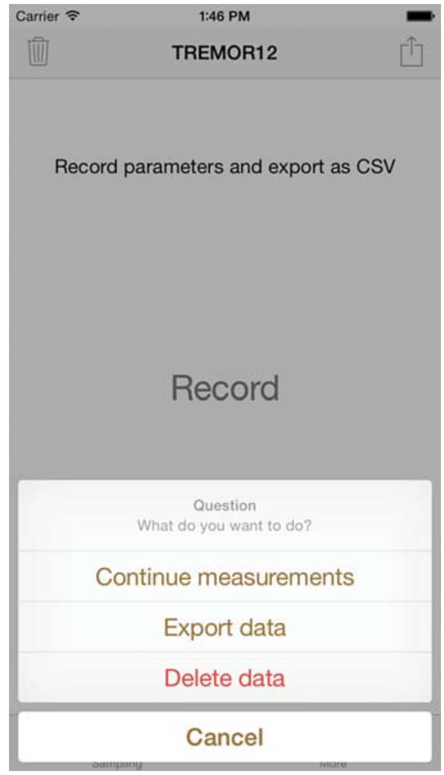
The first author (P.L.K.), who is a neurosurgeon and experienced app developer, developed the TREMOR12 app and the accompanying TREMOR12P data processing module. The app was evaluated with 3 patients suffering from essential tremor (between 55 and 71 years of age).

TREMOR12
TREMOR12 was developed in Xcode 7 (Apple Inc., Mountain View, Calif., USA) using the Swift programming language version 2.0. It implements the CMDeviceMotion class to extract 4 parameters, each in 3 axes (x, y, and z). These parameters are: acceleration (in *g*), rotation (in radians), rotation speed (in radians per second), and gravity (in *g*). The first three parameters offer tremor quantification parameters, the fourth can be used to calculate a standardized 3D space to facilitate between-measurements comparisons. Sampling can be performed up to 100 Hz (tested on iPhone 6) and all samples are time stamped. Samples can be exported as a comma-separated value file for further analysis. TREMOR12 runs on iPhone and iPod Touch and requires iOS8 or a newer version, and can be downloaded free of charge from the App Store. The source code is available from GitHub [5].

TREMOR12P
TREMOR12P is the accompanying data processing module for TREMOR12. It was developed in Python 3.4, using the Anaconda IPython distribution (Continuum Analytics Inc., Austin, Tex., USA) and the Jupyter Notebook format [6]. It implements the modules NumPy [7], pandas [8], and matplotlib [9]. TREMOR12P generates a table with descriptive statistics and graphical representations for all tremor parameters. Graphs can be saved as 300-dpi images, which can be used for scientific publications. The source code is available from GitHub [10].

Results

TREMOR12
Figure 1 displays a screenshot of the app, including automated support of data export. When working memory is low, a warning is triggered on the device, which also triggers this data export dialog to prevent data loss. No patient identification parameters are needed for measurements, and during export (using e-mail or various online file storage providers) a coded identity can be used. For measurement, the device can be strapped to the wrist using regular straps, which are available from fitness stores. These can also be cleaned or replaced for optimal patient hygiene.



Color version available online

Fig. 1. A screenshot of TREMOR12, including automated support of data export.

TREMOR12P
Table 1 displays an example of descriptive statistics of a 1-min tremor registration sample. Figure 2 demonstrates the graphical representations of the same data set, with acceleration, rotation, rotation speed, and gravity along the x, y, and z axes displayed in separate figures. Due to its open-source nature, the Jupyter Notebook is easily expandable for more advanced analysis. If preferred, the comma-separated value data set can also be analyzed using other software packages, e.g. Microsoft Excel, SPSS, R, or MATLAB, instead of the IPython environment.

Discussion

This proof-of-concept study shows that the TREMOR12 app is able to detect and register characteristics associated with severity of tremor, such as acceleration, ro-

Table 1. Example of descriptive statistics from tremor samples, generated by TREMOR12P

	Roll	Pitch	Yaw	rotX	rotY	rotZ	accX	accY	accZ	gravX	gravY	gravZ
Count	5,118	5,118	5,118	5,118	5,118	5,118	5,118	5,118	5,118	5,118	5,118	5,118
Mean	0.238496	1.941351	0.041704	–0.032966	0.021286	0.027093	0.070704	0.018804	0.020109	0.231555	–0.040610	–0.956016
SD	0.101082	0.272076	0.146855	1.007162	1.103074	0.793427	0.203841	0.096156	0.117541	0.093034	0.141694	0.045171
Min.	0.030151	–0.148439	–0.297604	–4.077140	–3.610956	–4.686596	–0.665783	–0.592198	–0.904086	0.029524	–0.744670	–0.996675
25%	0.158735	1.869798	–0.053646	–0.520178	–0.623812	–0.254967	–0.067122	–0.037234	–0.049955	0.156735	–0.144994	–0.977606
50%	0.224884	1.959899	0.041614	–0.017855	0.024481	0.024261	0.033525	0.019520	0.019381	0.222349	–0.041602	–0.967394
75%	0.309339	2.025479	0.145506	0.537265	0.719671	0.352662	0.208951	0.079540	0.098045	0.302081	0.053620	–0.946841
Max.	0.633858	2.330922	0.840041	3.143363	3.777648	3.595384	0.834990	0.663146	0.562611	0.480032	0.293231	–0.538920

rot = Rotation speed (radians/second); acc = acceleration (*g*); grav = gravity (*g*). Roll, pitch and yaw are rotation parameters (in radians).

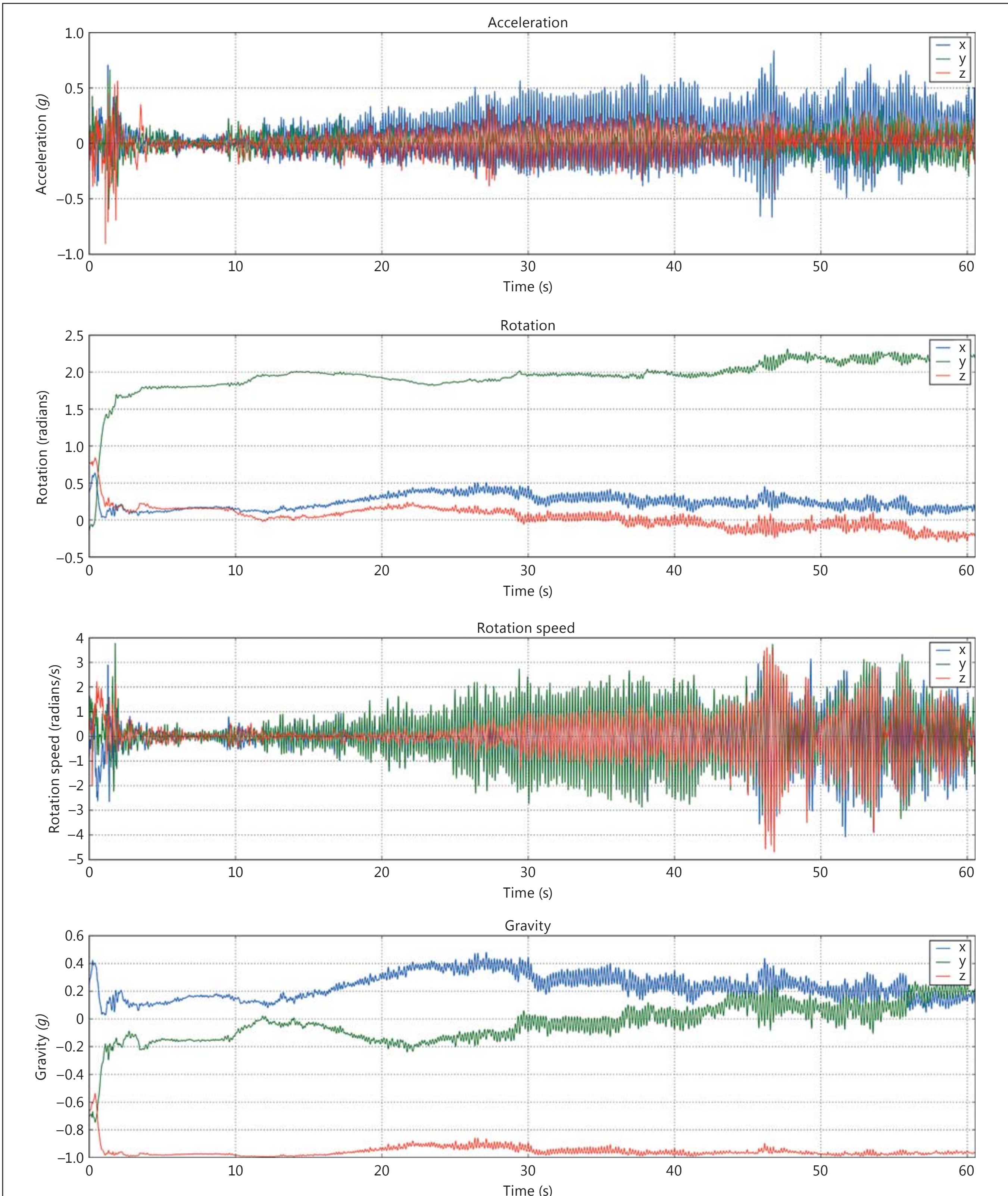
tation, rotation speed, and gravity in a simple and nonburdensome way.

Tremor quantification can help to improve outcome measurements of treatment of essential tremor or tremor-dominant Parkinson's disease. Electromyography is not portable enough to support measurements during daily living. Mobile devices can help to achieve this goal, and mobile apps may offer high cost-effectiveness. Currently available apps are limited in their possibilities to share measurement data. Lift Pulse merely calculates tremor frequency and magnitude on the device [11]. Although easy to use, the app's functionality is limited to just these two parameters and has no possibility for expansion. mPower has been introduced by Apple as one of the five starting apps that support ResearchKit [12]. Unfortunately, the app can only be downloaded from the USA App Store and data cannot be exported directly. It is also not clear from the website which tremor parameters are exactly recorded. The Georgia Tech Research Institute developed iTrem, but regulatory issues by the Food and Drug Administration (FDA) prevent the release of the app [13]. Senova et al. [4] reported on Itremor, which also does not provide researchers with the raw data, but instead with a few calculated statistics (like acceleration, frequency, and magnitude). The app is only available from Ad Hoc distribution, not from the App Store. Parra et al. [14] described an Android-based tremor tracking app which reports a few parameters and allows export of these parameters (not the raw data). They did not report the name of this application and it is not available for download from Google Play. Galán-Mercant et al. [15] compared the accelerometer from the iPhone 4 with an InertiaCube3 sensor and concluded that the inertial sensor mounted in the iPhone 4 is sufficiently reliable and accurate to evaluate and identify the kinematic patterns in an Extended Timed Get and Go test. In addition to these smartphone applications, there are commercially available solutions like LeapMotion [16], Kinesia360 [17], and the Parkinson's KinetiGraph [18]. In all cases, the researcher does not get the raw measurement data; with the commercially available products, the researcher also does not get the underlying algorithms.

The diversity in apps that neither offer access to the raw data nor access to their source code limit the opportunities for clinical researchers to develop effective algorithms that can correlate quantitative tremor parameters with clinical outcome. Furthermore, additional information may be extracted from the raw data that we are currently not aware of, and we stay unaware as long as we remain satisfied with simple descriptives like tremor frequency and magnitude. TREMOR12 can fill this gap by offering an open-source application for iPhone and iPod Touch, available from the App Store and allowing full access to the raw data while simultaneously offering extensive data processing capacities using the TREMOR12P module.

Regulatory Oversight

For European countries, the MEDDEV legislation describes when software has to be considered as a medical device. Summarizing a white paper supported by the Dutch Centre of Expertise for Standardisation and eHealth (NICTIZ), a mobile medical application requires CE (Conformité Européenne) marking if it performs data manipulation or if it has been developed for diagnostic or therapeutic purposes in individual patient care [19]. Using the accelerometer data to calculate tremor frequency and magnitude should be considered as data manipulation, as the information which is displayed to the user is a result of calculations that are performed on the raw data. Using the device sensors to measure data and using them for clinical purposes would also require CE marking, although in both cases this would be a class I registration (low risk), which is relatively straightforward.



Color version available online

Fig. 2. Graphical representations of tremor parameters, generated by TREMOR12P. Modalities visualized in top-down order are: acceleration, rotation, rotation speed, and gravity.

In the USA, the FDA offers a guidance on mobile medical applications which to date still contains nonbinding recommendations [20, 21]. The FDA intends to exercise enforcement discretion on mobile medical apps that help to organize and track patients' health information. The FDA reports two interesting exceptions in which someone is not to be considered as a mobile medical app manufacturer: (1) licensed practitioners, including physicians, dentists, and optometrists, who manufacture a mobile medical app or alter a mobile medical app solely for use in their professional practice and do not label or promote their mobile medical apps to be generally used by other licensed practitioners or other individuals, and (2) persons who manufacture mobile medical apps solely for use in research, teaching, or analysis and do not introduce such devices into commercial distribution. We note that while persons conducting research using mobile medical apps involving human subjects are exempt from registration and listing, they may instead be subject to investigational device exemption regulations.

TREMOR12 has been developed with regulatory oversight in mind. It does not perform on-device calculations or any other form of data manipulation. Further, there is a clear message in the startup screen that the app is solely meant for research purposes and not for direct patient care. The app is also not marketed this way. Any research protocol using TREMOR12 that has been approved by an institutional research board effectively has an investigational device exemption [22]. Furthermore, the source code is available for anyone who wishes to alter the app and use it under the first FDA exception mentioned above. Therefore, the research tool TREMOR12 should not be considered as a mobile medical device, which facilitates uptake in the research community.

Further Developments

TREMOR12 has been evaluated in 3 patients as a proof-of-concept study, which was successful. We are currently preparing clinical validation and encourage other research groups to participate. Further, TREMOR12 can be extended to the Apple Watch, allowing even more mobility during measurements and long-term recordings. In its current form, 1 min of data samples (sampling at ~100 Hz) requires 1 megabyte of data storage: this high temporal resolution is useful to develop algorithms, but is impracticable during long-term recordings. A solution can be to use such algorithms to calculate some summary parameters at regular time intervals and use these for long-term recordings. Obviously this requires a new evaluation regarding the mobile medical device status. Also, the device's pedometer can be implemented to measure bradykinesia in Parkinson patients, which is not available in the current version of TREMOR12.

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