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Evaluation of Orthostatic Reactions in Real-World Environments Using Wearable Sensors

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***Abstract*— As global life expectancy is constantly rising, the early detection of age-related, neurodegenerative diseases, such as Parkinson's disease, is becoming increasingly important. Patients suffering from Parkinson's disease often show autonomic nervous system dysfunction which is why its examination is an important diagnostic tool. Measuring the response of the heart rate (variability) to postural transitions and thereby assessing the orthostatic reaction is a common indicator of autonomic nervous system functioning. However, since these measurements are commonly performed in a clinical environment, results can be impaired by the white coat effect. To reduce this influence as well as inter- and intra-day variations, our work aims to investigate the assessment of orthostatic reactions in free-living environments. We collected IMU and ECG data of seven healthy participants over four days and evaluated differences in orthostatic reactions between standardized tests at lab, at home, as well as unsupervised recordings during real-world conditions. Except for the first lab recording, we detected significant changes in heart rate due to postural transitions in all recording settings, with the strongest response occurring during standardized tests at home. Our findings show that real-world assessment of orthostatic reactions is possible and provides comparable results to supervised assessments in lab settings. Additionally, our results indicate high inter- and intra-day variability which motivates the continuous orthostatic reaction measurement over the span of multiple days. We are convinced that our presented approach provides a first step towards unobtrusive assessment of orthostatic reactions in real-world environments, which might enable a more reliable early detection of disorders of the autonomic nervous system.**

I. Introduction

Early detection of age-related diseases, such as neurodegenerative disorders, is becoming increasingly important as the average age of the world's population is continuously rising [1]. One of the most prominent examples of such neurodegenerative disorders is Parkinson's disease (PD). PD manifests itself through cardinal motor symptoms, such as tremor, rigor and bradykinesia, as well as through non-motor symptoms, such as a dysfunction of the autonomic nervous system (ANS) [2]. Among other functions, the ANS is responsible for adapting the cardiovascular system to increased physical activity or postural transitions (PT), e.g., the transition from a sitting to a standing position (also referred to as orthostatic reaction (OR)), which cause a drop in blood pressure. In order to counteract this and, thus, to maintain the blood supply to the brain, veins and arteries in the legs constrict and the heart rate (HR) increases [3]. Failure of OR leads to orthostatic dysfunction (OD) which is indicated by a considerable drop in blood pressure and missing HR response after transitioning from a sitting to a standing position. OD has a high prevalence among patients suffering from PD (about 47%) [4] and can predict the onset of PD years before motor symptoms become visible [5]. Moreover, in combination with other non-motor symptoms, OD can affect the patient's quality of life, as it often leads to restrictions in everyday activities [6]. Therefore, the examination of OD and heart rate (variability) (HR(V)) is a very promising method for the early detection of ANS disorders which may lead to an early treatment to slow disease progression.

OD is typically assessed during clinical procedures, such as by using the tilt table test and the Schellong test [7]. While these procedures allow a standardized measurement of the cardiovascular reaction to PTs, the validity is often reduced by the white coat syndrome, which is the presence of elevated blood pressure in a clinical setting due to anxiety [8]. In previous work, we presented an approach to assess ORs using smartphone sensors and a wearable ECG patch [9]. We were able to classify healthy participants from PD patients based on the acquired data. However, we evaluated our solution in clinical environments and using single recordings only. These snapshot measurements, though, do not account for the intra- and inter-day fluctuations of cardiovascular reactivity. They additionally increase the risk of missing HRV irregularities, which occur only infrequently [10]. Therefore, collecting HR(V) responses to PTs outside of the clinical environment and over the span of multiple days might help to obtain more representative evidence of an orthostatic dysfunction.

Previous studies have evaluated HRV to classify OD [10], [11]. Although these results are very promising, the authors only collected HRV data during sleep to reduce the influence of movement artifacts. Hence, they did not assess the ANS reactivity to sudden changes of cardiovascular load, as induced by PTs. However, analyzing these direct HR(V) responses can provide additional valuable information for the evaluation of OD. Therefore, we aim to investigate the feasibility of assessing ORs in free-living environments by using a light-weight wearable sensor that combines the collection of cardiovascular data, measured via the electrocardiogram (ECG), with PT information, measured via an inertial measurement unit (IMU). To the best of our knowledge, our study is the first to investigate the direct cardiovascular response

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to PTs in an unsupervised real-world setting and provides a first step towards the unobtrusive assessment of orthostatic dysfunction in free-living environments.

II. Methods

A. Data Acquisition

For evaluating ORs in free-living environments we collected data of 7 healthy participants (3 male, 4 female, aged 22.8 ± 1.8 years). Data were recorded by a wearable sensor node (Portabiles GmbH, Erlangen, Germany) including an IMU (3-axis accelerometer, 3-axis gyroscope) and an ECG unit (1-channel ECG according to Lead I of Einthoven's Triangle) attached on a chest strap. All sensor data were logged onto the internal storage of the sensor node with a sampling frequency of 256 Hz. After data collection, raw data were transmitted to a computer as binary files for subsequent data processing. The study protocol was approved by the Ethics Committee of the Friedrich-Alexander-Universität Erlangen-Nürnberg (number 106_13B).

Our study protocol was divided into three parts:

1) Lab Recording I (Lab I): The study started at the laboratory between 9 a.m. and 10 a.m. All participants provided written informed consent before testing. Moreover, participants were asked to fill out a demographic questionnaire and the Physical Activity Readiness Questionnaire (PAR-Q) [12] to exclude participants with insufficient physical condition. In addition to the sensor, participants received a smartwatch with an event logging application for the free-living section. The procedure at the lab was comprised of two repetitions of the Schellong test [7]. One repetition consists of five minutes of sitting to allow the cardiovascular system to adapt to the sitting position, followed by standing up and remaining in a standing position for two minutes while ECG data were continuously acquired.

2) Home Recording (Home-Free/Home-Tests): After finishing the *Lab I* session, participants immediately started the collection of free-living data. Data were recorded for four days in the participants' everyday life. To improve comparability between the data collected at home and those during the lab sessions, participants performed the same procedure of standardized tests (two repetitions of the Schellong test) at home three times a day: between 7 a.m. and 9 a.m., between 11 a.m. and 1 p.m. and between 5 p.m. and 7 p.m. Participants were instructed to label the beginning of each standardized test procedure at home using the logging application on the smartwatch. Home data collected during free-living activities are denoted as *Home-Free*, whereas data collected during standardized tests are denoted as *Home-Tests*.

3) Lab Recording II (Lab II): At the end of the study participants repeated the lab procedure once again between 12 p.m. and 2 p.m.

B. Data Processing

The ECG was used to calculate HR and HRV. RR intervals were computed based on the R peaks extracted from the ECG signal after filtering and applying the QRS detection algorithm by Hamilton [13] provided by the *Neurokit2* library [14]. As final step, artifacts in RR intervals were reduced by removing RR intervals corresponding to an HR lower than 45 bpm or higher than 200 bpm, as well as by applying statistical outlier removal methods, i.e, RR intervals based on a z-score ≥ 1.96. Removed RR intervals were replaced by linear interpolation. For computing HRV, R-peaks locations were corrected using an algorithm presented by Lipponen et al. [15].

Acceleration data were processed to detect PTs from free-living data. Whenever a PT was detected, we assessed the OR. We used an algorithm proposed by Adamowicz et al. for PT detection [16]. Even though the algorithm was originally designed for sensors placed at the lower back, a pre-study also proved its applicability to reliably detect PTs from acceleration data acquired by a chest-worn sensor.

III. Evaluation

A. ECG Measures

For quantifying ORs and computing relevant measures, we extracted the signal intervals one minute before and after each PT detected by the algorithm. We additionally selected and computed HRV measures according to guidelines by the HRV Task Force [17], as well as the change of these measures during a PT. Due to the fast cardiac recovery after a PT, only a short ECG interval is of interest to assess the OR. Therefore, we used the time-domain HRV measures *RMSSD* (root mean square of successive differences) and *pNN20* (percentage of successive RR intervals ≥ 20 ms).

B. Statistics

Pairwise t-tests were used to determine significant changes in HR(V) before and after PTs over all participants. Repeated-measures ANOVA was used to determine differences in the magnitude of OR between the different recording settings. As post-hoc tests, pairwise t-tests were used to identify individual group differences. The significance level was set at $\alpha = 0.05$. Effect sizes of ANOVA are reported as η_p^2 and of pairwise t-tests as Cohen's d. All methods for statistical analysis were performed in Python using the *Pingouin* library [18]. In all Figures and Tables we used following notation to indicate statistical significance: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

IV. Results

Due to problems during data acquisition, the data of one participant had to be completely and the data of three participants had to be partially removed. In total, 152 hours of recording, corresponding to 189 PTs detected by the algorithm (*Lab I*: 10, *Lab II*: 12, *Home-Tests*: 81, *Home-Free*: 86), were analyzed for ORs. On average, PTs induced HR increases throughout all recording settings. Significant increases were observed for *Lab II*, *Home-Tests*, *Home-Free*, but not for *Lab I* (Table I). The absolute change in HR caused by PTs was highest during *Home-Tests* (Figure 1, left). HRV parameters showed significant decreases in both *Home* settings except for *RMSSD* in *Home-Free*, whereas a significant change at the laboratory was only found for

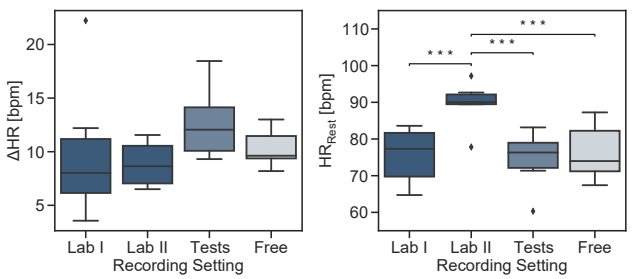

Fig. 1. Absolute change in HR before and after PTs (*left*) and HR_{Rest} before PTs (*right*) for all participants and the different recording settings, respectively. *Home-Tests* are denoted as *Tests*; *Home-Free* are denoted as *Free*.

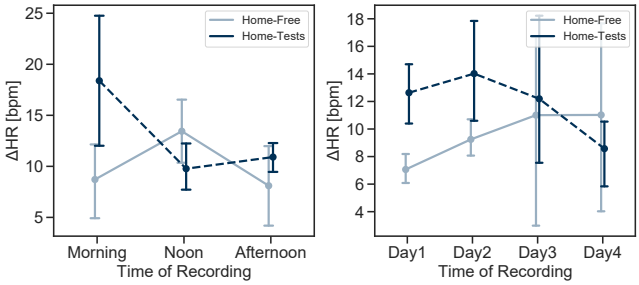

Fig. 2. Absolute change in HR during PTs within the day (*left*) and over the study procedure (*right*). Data were averaged per participant and *Time of Recording*, respectively. Values are depicted as mean and standard error over all participants.

RMSSD at *Lab I* (Table I). HR_{Rest} was highest for *Lab II* (89.5 ± 7.1 bpm) and lower for *Home-Tests* (74.4 ± 8.0 bpm), *Home-Free* (76.3 ± 7.9 bpm) and *Lab I* (75.5 ± 7.8 bpm). On average, participants showed lower HR_{Rest} during *Home-Tests* and *Home-Free* than at the laboratory (Figure 1, right).

TABLE I
PAIRWISE T-TESTING OF HR(V) BEFORE AND AFTER POSTURAL TRANSITIONS.

Measure	Setting	DoF	t	p	Cohen's d
HR	*Lab I*	3	-2.691	0.074	-1.277
	Lab II	4	-6.334	0.003 **	-1.523
	Home-Tests	5	-9.110	< 0.001 ***	-1.614
	Home-Free	5	-13.385	< 0.001 ***	-1.302
pNN20	*Lab I*	3	2.814	0.067	1.597
	Lab II	4	0.221	0.836	0.038
	Home-Tests	5	10.281	< 0.001 ***	0.989
	Home-Free	5	3.612	0.015 *	0.574
RMSSD	*Lab I*	3	-3.242	0.047 *	-1.918
	Lab II	4	1.306	0.261	0.405
	Home-Tests	5	-2.966	0.031 *	-0.579
	Home-Free	5	0.562	0.598	0.184

ANOVA revealed significant differences of HR_{Rest} between the different recording settings ($F(3,15) = 37.64, p < 0.001, \eta_p^2 = 0.882$). However, no significant difference was found for OR-induced changes in HR between the different recording settings ($F(3,15) = 1.05, p = 0.399, \eta_p^2 = 0.174$). As the data of *Lab II* for one participant had to be removed, Missing values were replaced by the population mean of this recording setting. For all days, except for Day 4, the change in HR during *Home-Tests* was higher than the change in HR in *Home-Free*. Furthermore, high fluctuations of the data between the recording days, within one day and between participants are noticeable (Figure 2).

V. DISCUSSION

The main objective of our study was to investigate the feasibility of assessing HR(V) in response to PTs in real-world settings and to evaluate the potential of complementing clinical snapshot measurements for detecting orthostatic dysregulations by home monitoring data. Results indicate a significant increase in HR after PTs in both *Home-Tests* and *Home-Free* data and, therefore, correlate with results of prior investigations in laboratory environments [19]. Analogously, HRV measurements show the tendency to decrease. The increase in HR and decrease in HRV measures reflect increased sympathetic activity, confirming our goal to apply unobtrusive HR(V) assessment at home for examining cardiovascular reactivity in response to PTs.

Comparing the HR increase between the different recording settings revealed a considerably higher increase in HR during *Home-Tests* than during *Lab* recordings, which might be attributed to the "white coat syndrome" due to the unknown lab environment. This can also be observed when examining HR_{Rest} between the different recording settings. On average, participants showed a higher HR_{Rest} at the *Lab II* than during both *Home* settings. However, the average HR_{Rest} in *Home-Tests* was comparable to the average HR_{Rest} during *Lab I*. Moreover, there was an unexpected difference between the HR_{Rest} of *Lab I* and *Lab II*. This may be attributed to the participants' leisure activities, such as intense physical activity before a PT or the consumption of alcohol the night before, as both directly affect HR_{Rest} [20], [21].

The high intra- and inter-day variations, as depicted in Figure 2, can be caused by many different factors, such as stress and negative emotions, both decreasing HRV [22]. Because the human body is exposed to many different social and environmental situations, large intra- and inter-day HR(V) fluctuations are common. Since HR(V) is such a sensitive measure, recordings should always be performed for several days, preferably at the same time of day, in order to reduce such variations. In future studies, a diary should be kept, including physical activity, sleep time and alcohol consumption, to provide more information about the source of intra- and inter-day fluctuations. The high inter-participant variances might be caused by different physical conditions of the participants and different HR_{Rest}. Therefore, longer lasting studies with more participants are required to further increase the confidence in the described findings.

Furthermore, standardized tests at home showed a more pronounced OR than measurements in a real-world environment, except for Day 4 (Figure 2). Therefore, for unobtrusive HRV assessment at home, it might not be necessary to

actually perform a continuous free-living data acquisition throughout the whole day. Based on our findings, it might be sufficient to conduct standardized tests at home at defined times, potentially complemented by unsupervised assessments during the morning hours.

Since this study was solely conducted with young healthy adults in good physical condition, the results need to be validated with cohorts of patients suffering from autonomic nervous disorders and age-matched controls. However, the aim of this first pilot study was to investigate whether it is generally possible to achieve comparable results at home as in the clinic.

Study results also showed some PT events with negative HR changes. As the study was conducted with healthy participants, HR decreases were not expected. A more detailed investigation of these events revealed that negative HR changes were either the result of incorrect PTs (e.g. false positives or delays in detection) or due to vigorous physical activity before a PT. Even though we solely considered PTs which were preceded by five minutes of sitting, following the guidelines for clinical examinations, for our analysis, the HR can continuously decrease within 30 min after exercise until reaching rest values [21]. Hence, this cooling-down effect might overlay the PT-induced HR increase. Future work should therefore include activity detection into the analysis pipeline and only consider PTs if no moderate or vigorous physical activity occurred during at least 30 min before the event.

VI. Conclusion and Outlook

In this work we demonstrated that free-living HR(V)-based assessment of ORs is possible, providing comparable results to supervised assessments in clinical environments. Given further validation with patients, our approach might be promising for improving the early diagnosis of OD and neurodegenerative diseases. Study results further indicate that continuous free-living monitoring of HRV parameters might not be necessary, but performing standardized tests at predefined times is sufficient for reliable OR assessment.

In future work we plan to conduct a study using a similar study protocol with patients suffering from dysfunctions of the ANS such as PD. In order to provide more information about inter- and intra-day fluctuations, confounding variables such as exercise, medication and daily living activities should be recorded in a diary. In the context of this work, we only considered changes in HR(V) for the classification of OD, as unobtrusive continuous blood pressure measurement is challenging due to motion artifacts. However, continuous measurement of pulse transit time to estimate PT-induced blood pressure changes might be a valuable additional data source to provide a more reliable assessment of OR and should be included in future studies.

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