Topic: Objective Assessment of Prodromal Hyperkinetic Movements Using Wearable Sensors and Machine Learning in Huntington´s Disease

Huntington´s disease (HD) is a rare autosomal-dominant, neurodegenerative disease with various symptoms, including movement impairment, cognitive and psychiatric disturbances [1]. The predominant movement impairment is chorea, which manifests as involuntary, hyperkinetic body movements. While genetic testing allows the identification of a gene carrier, manifest HD is diagnosed clinically, based on the presence of typical symptoms, usually appearing around the age of 30-50 years [2]. Before this clinically defined disease onset, patients are referred to as prodromal. In clinical routine, motor impairment is measured by the Unified Huntington´s Disease Rating Scale (UHDRS) Total Motor Score (TMS), but subtle prodromal motor symptoms might be missed during routine examinations [3]. So far, there is no cure for HD available [4], but medications treating symptoms are available [5], which are usually administered with the clinical onset. Also, a variety of disease modifying trials are on the horizon [6]. Hence, an early detection of disease onset is crucial for the management of HD and may be of uttermost importance in regard of putatively available disease-modifying strategies.

Wearable motion sensors gained increasing interest in the objective assessment of motor symptoms in HD in the past decade [7]. Existing studies proposed instrumented gait analysis using body-worn inertial sensors to classify HD patients at different disease stages and healthy controls or correlate the TMS to changes in spatio-temporal gait parameters [8, 9]. Also, functional tests like the money box test were instrumented by a combination of wrist and chest-worn accelerometers to classify HD patients and healthy controls [10]. Furthermore, first attempts to transfer wearable sensor-based systems from clinical to home assessments for HD have been made [11, 12, 13].

Although first evidence of the use of wearable sensors for an objective assessment of HD motor symptoms exists in the literature, sensitive digital endpoints are still missing. Specifically, an objective assessment of chorea is rarely addressed. In combination with recent advancements in machine learning (ML) and artificial intelligence (AI), wearable sensor-based systems have the potential to generate sensitive clinical endpoints detecting early motor symptoms prior to clinical diagnosis.

Therefore, the Huntington’s Disease Outpatient Center of the Department of Molecular Neurology of the University Hospital Erlangen (PD Dr. med. F. Marxreiter) and the Machine Learning and Data Analytics Lab of the FAU-Erlangen (Prof. Dr. B. Eskofier) initiated a study in 2019 to evaluate the applicability of wearable inertial sensors for the detection of prodromal hyperkinetic movements in HD. The study protocol includes simple tasks, mostly requiring the participants to sit in a chair simulating some everyday life scenarios. During the study, participants wear a body sensor network of five synchronized IMUs (3D accelerometer + 3D gyroscope) attached to the lower back, ankles, and wrists to be able to measure full-body movements. For reference, the participants are additionally filmed. Based on the video recordings, a clinical expert

will provide annotations of choreatic events, together with UHDRS and TMS ratings performed prior to the sensor recordings.

The goal of this thesis is the development and evaluation of data-driven ML or AI models to transfer abstract wearable sensor data into meaningful clinical endpoint measures for HD. Today, recordings of 8 symptomatic and 8 prodromal HD patients and 11 age, matched healthy controls are available, and recordings are ongoing. To assess the progression of symptom severity, additional one-year follow-up measurements are available for 10 study participants. Some first promising insights into the dataset were conducted during a student thesis in 2020. Still, the limited number of available datasets at this point did not yet allow for sophisticated ML or AI models.
With now more data available, new models need to be developed that are also transferable into the home-monitoring domain to test the system's feasibility in real-world environments and to detect prodromal choreatic events in HD patients' everyday lives without the need to visit the hospital.

The proposed work consists of the following parts:

- Literature and patent research of relevant work resulting in a comprehensive list of existing studies about sensor-based approaches measuring movement impairment of HD patients
- Support of the data collection at the UK-Erlangen over the course of the thesis
- Development of different ML or AI models to classify choreatic events and/or UHDRS -TMS and/or novel clinical endpoints from time series wearable sensor data
- Evaluation of the implemented models regarding their accuracy on the collected data
- Evaluation of the feasibility of transferring the developed system into a real-world scenario (if possible, collect some first real-world HD-patient datasets in cooperation with the UK-Erlangen)
- (If anticipated, try to publish the results at an international conference or journal)

The thesis must contain a detailed description of all developed and used algorithms, as well as a profound result evaluation and discussion. The implemented code has to be documented and provided. An extended research on literature, existing patents, and related work in the corresponding areas has to be performed.

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