EPP0106

Vocal markers of schizophrenia: assessing the generalizability of machine learning models and their clinical applicability

A. Parola[1]*, A. Rybner[1], E. T. Jessen[1], M. Damsgaard Mortensen[1], S. Nyhus Larsen[1], A. Simonsen[1], Y. Zhou[2], K. Koelkebeck[3], V. Bliksted[1] and R. Fusaroli[1]

[1]Aarhus University, Aarhus, Denmark; [2]Chinese Academy of Sciences, Beijing, China and [3]Hospital and Institute of the University of Duisburg-Essen, Essen, Germany
*Corresponding author.
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Introduction: Machine learning (ML) approaches are a promising venue for identifying vocal markers of neuropsychiatric disorders, such as schizophrenia. While recent studies have shown that voice-based ML models can reliably predict diagnosis and clinical symptoms of schizophrenia, it is unclear to what extent such ML markers generalize to new speech samples collected using a different task or in a different language: the assessment of generalization performance is however crucial for testing their clinical applicability.
Objectives: In this research, we systematically assessed the generalizability of ML models across contexts and languages relying on a large cross-linguistic dataset of audio recordings of patients with schizophrenia and controls.
Methods: We trained ML models of vocal markers of schizophrenia on a large cross-linguistic dataset of audio recordings of 231 patients with schizophrenia and 238 matched controls (>4.000 recordings in Danish, German, Mandarin and Japanese). We developed a rigorous pipeline to minimize overfitting, including cross-validated training set and Mixture of Experts (MoE) models. We tested the generalizability of the ML models on: (i) different participants, speaking the same language (hold-out test set); (ii) different participants, speaking a different language. Finally, we compared the predictive performance of: (i) models trained on a single language (e.g., Danish) (ii) MoE models, i.e., ensemble of models (experts) trained on a single language whose predictions are combined using a weighted sum (iii) multi-language models trained on multiple languages (e.g., Danish and German).
Results: Model performance was comparable to state-of-the art findings (F1: 70%-80%) when trained and tested on participants speaking the same language (out-of-sample performance). Crucially, however, the ML models did not generalize well - showing a substantial decrease of performance (close to chance) - when trained in a language and tested on new languages (e.g., trained on Danish and tested on German). MoE and multi-language models showed a better increase of performance (F1: 55%-60%), but still far from those requested for achieving clinical applicability.
Conclusions: Our results show that the cross-linguistic generalizability of ML models of vocal markers of schizophrenia is very limited. This is an issue if our first goal is to translate these vocal markers into effective clinical applications. We argue that more emphasis needs to be placed on collecting large open datasets to test the generalizability of voice-based ML models, for example, across different speech tasks or across the heterogeneous clinical profiles that characterize schizophrenia spectrum disorder.

Disclosure of Interest: None Declared

EPP0107

Thyroid Stimulating Hormone circadian variations in paranoid schizophrenic psychosis between acute and stable phases. A comparative study.

A. Marcos-Rodrigo[1]*, A. L. Morera-Fumero[2], P. Abreu-Gonzalez[3], E. Diaz-Mesa[4], L. Fernandez-Lopez[2] and J. J. Tascon-Cervera[5]

[1]Servicio de Psiquiatria, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife; [2]Departamento de Medicina Interna, Dermatología y Psiquiatría, Facultad de Ciencias de la Salud; [3]Ciencias Medicas Basicas: Unidad de Fisiologia, Facultad de Ciencias de la Salud; [4]Servicio de Psiquiatria. Hospital Universitario de Canarias. Departamento de Medicina Interna, Dermatologia y Psiquiatria, Universidad de La Laguna and [5]Servicio de Psiquiatria, Hospital Universitario de Canarias, San Cristobal de La Laguna, Spain
*Corresponding author.
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Introduction: Day-night changes in several molecules are studied as biomarkers of circadian rhytms (Morera-Fumero, A. L. *et al.* Progress in Neuro-Psychopharmacology and Biological Psychiatry 2017; 75 207-212). Circadian rhythmicity of the pituitary-thyroid axis has been proven in healthy individuals, with a Thyroid Stimulating Hormone (TSH) peak in serum around midnight and peaks during day hours (Bellastella, G. *et al.* Life 2021; 11(5), 426). A recent meta-analysis has reported differences in serum TSH levels between first-episode psychosis and multiple-episode schizophrenia (Misiak, B. *et al.* Progress in Neuro-Psychopharmacology and Biological Psychiatry 2021; 111, 110402). However, studies assessing quantitative circadian variations on TSH serum in schizophrenic patients are scant.
Objectives: Comparing serum TSH levels at two different times of the day (12:00 and 24:00 hours) and the differences between the acute (hospital admission) and recovered phase (hospital discharge) of the disease.
Methods: Fourteen male patients (age 26,8±9,3 years) with the diagnosis of paranoid schizophrenia psychosis according to the DSM-IV partake in the study. Patients were admitted to the University Hospital of the Canary Islands psychiatric room because of acute relapse. Blood samples were taken in the first 24 h of admission and at 24 h. before discharge. All patients gave written consent to participate in the research study. Serum TSH was determined by ELISA methods. Paired sample t-tests were performed between TSH serum levels at admission and discharge at 12:00 and 24:00 hours. Statistical analyses were performed using IBM® SPSS® Statistics 25 software for MAC (IBM Corporation 1989, 2017).
Results: There were statistical differences between the 12:00 h and the 24:00 h of the TSH serum levels at admission (12:00: 145,856±156,961vs. 00:00: 192,006± 122,757, $p = 0.04$); TSH discharge, (12:00: 134,483±72,882vs 00:00: 244,214±148,697, $p = 0.002$). There were no statistical differences between the 12:00 TSH levels at admission and discharge (145,856±156,961 vs. 134,483± 72,882, $p = 0.66$). The 24:00 h comparison of TSH levels neither elicited significant results (admission: 192,006±122,757 vs. discharge: 244,214± 148,697, $p = 0.15$).
Conclusions: Schizophrenic patients undergo TSH serum changes in a circadian pattern during the acute and stable phases of the disease; nevertheless, they experience smaller deviations during the acute phase. Higher levels of TSH were observed around midnight, as it happens in healthy individuals, with higher peaks during the stable phase compared to the acute one.

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