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Keywords: DNA methylation; Neuropsychiatry; biomarker; Dosage

EPV1033

Predicting Cardiovascular Disease in Psychiatric Patients: Machine Learning with Electronic Health Records

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Introduction: Cardiovascular disease (CVD) causes staggering losses in quality adjusted life years worldwide.¹ Among patients in the Danish psychiatric hospital setting, heart disease is associated with a decrease in life expectancy of 5.1 years.² The causes underlying this association are likely manifold. For example, severe mental illness is associated with unhealthy lifestyle.³ Furthermore, psychiatrists may focus predominantly on the treatment of mental illness and have less emphasis on detection and prevention of physical illness.⁴ If patients at elevated risk of CVD are pointed out automatically, this may lead to better preventive medicine.

Objectives: To predict which patients develop cardiovascular disease using machine learning.

Methods: We obtained data on all psychiatric hospital contacts in the Central Denmark Region since the initiation of the current EHR system (MidtEPJ). These span from 2011 to 2021 and cover 120,000 patients, of which 3,000 patients developed severe CVD (stroke or coronary event) follow-up. We will train a variety of models (random forests, SVM, deep neural nets) to predict CVD within one year from a planned contact to hospital.

Results: The modelling is currently underway, intermediary results are expected in January.

Conclusions: We explore whether predicting CVD is feasible using state-of-the-art technologies and a uniquely detailed dataset. This may pave the way for machine learning to act as a clinical support decision system, since we're only training on data that is available in a live, clinical context.

References

- 1: Khan 2019
- 2: Erlangsen 2017
- 3: Scott 2011
- 4: Fagiolini 2009

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EPV1034

Precision Medicine & Pharmacogenomics: Personalized Medication in Neuropsychiatric Disorders using AI and telepsychiatry

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Introduction: The term "personalised therapy" refers to the use of genetic data to better treat or determine the predisposition to a

specific genetic disease, with the ultimate goal of improving quality of life. Telepsychiatry and AI are key to support it..

Objectives: Determine benefits of pharmacogenomic analysis (PGx) in CNS diseases regarding: - cost effectiveness - adverse drug reactions - reduced hospitalizations - drug interactions - efficacy - quality of life - "trial and error" approach avoidance

Methods: Questionnaires before and after the treatment provided using PGx tests Telepsychiatry for consultation along face to face sessions were conducted. Artificial intelligence in data analyses

Results: Benefits of pharmacogenomic analysis (PGx) in CNS diseases: - cost effective savings - prediction and prevention of adverse drug reactions - reduced hospitalization due to ineffectiveness of medication - reduced risk of drug interactions - more effective treatments - better quality of life for the patient - with the analysis (PGx) the "trial and error" approach is avoided

Conclusions: In a number of studies in patients with mental disorders, pharmacogenomic analysis (PGx) has led to an increase in both clinical response and remission, better tolerated treatments, fewer side effects, and reduced treatment costs. In conclusion, pharmacogenomic analysis is ideal for patients with CNS diseases: a) Not responding to treatment b) Who in their history have many relapses and hospitalizations c) They show serious side effects d) Who do not comply with the treatment e) Taking many medications and suffering from serious illnesses f) Who are wary of taking psychotropic drugs

Disclosure: No significant relationships.

Keywords: Precision Psychiatry; e-mental health; telepsychiatry; Artificial intelligence

EPV1035

Clinical effects of Cariprazine and their relationship with polymorphisms of dopamine and serotonin receptors: preliminary results from a prospective study on schizophrenia and bipolar disorder

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Introduction: Cariprazine (CAR) is a D2, D3, 5HT1A receptor partial agonist and a 5HT2A, 5HT2B antagonist, used to treat Schizophrenia and Bipolar disorder. Interindividual variability in therapeutic and side effects of antipsychotics is difficult to predict, due to non-genetic and genetic factors. Single nucleotide polymorphisms (SNPs) are the main source of genetic variability, the ones in dopamine and serotonin receptors to which CAR binds are indeed likely to determine response to treatment.

Objectives: The aim of the study is to define a relationship between CAR clinical efficacy and SNPs in dopamine and serotonin receptors genes of patients affected by schizophrenia and bipolar disorder.

Methods: We recruited 16 patients starting a monotherapy with CAR, evaluated at baseline and after 2, 4 and 8 weeks through BPRS rating scale. We selected a panel of SNPs in DR2, DR3, 5HT1A and 5HT2A receptors, with a frequency higher than 10% in Caucasians

and functionally characterized. Cut-off for response to treatment was a 50% reduction of BPRS score. Statistical analysis was performed with one-way ANOVA followed by the test for linear trend between columns.

Results: All subjects achieved response after 8 weeks of treatment, but 6 patients after 4 weeks. Early responders have a genetic profile associated with increased dopamine and serotonin receptor expression and/or binding affinity for their specific ligands. The association don't reach statistical significance, probably due to low number of patients.

Conclusions: Preliminary results suggest that an array of dopamine and serotonin receptors SNPs could predict time to respond to CAR in schizophrenia and bipolar disorder.

Disclosure: The study is funded by Recordati AG, that commercialize the drug under study (Cariprazine) in Switzerland. Funding covers the costs for genetic analysis and other procedures of the study, no financial compensation is planned for investigators/authors.

Keywords: real world setting; Antipsychotics; Precision Medicine; pharmacogenomics

EPV1036

Individual-specific changes in circadian rest-activity rhythm and sleep in symptom-free patients tapering their antidepressant medication

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Introduction: Group-level studies showed cross-sectional and prospective between-person associations between circadian rest-activity rhythms (RAR), physical activity (PA), sleep, and depressive symptoms. However, whether these associations replicate at the within-person level remains unclear. Therefore, it is clinically relevant to investigate these associations within persons and study whether changes in depressive symptoms are related to changes in circadian rhythm and sleep variables.

Objectives: To identify changes in circadian rhythm elements in proximity to a transition in depressive symptoms, whether changes are less frequent in individuals without compared to those with transitions, and whether there are individual differences in the direction of change of circadian rhythm variables.

Methods: Data of remitted individuals tapering antidepressants were used: 12 with and 14 without a transition in depressive symptoms. RAR, PA, and sleep variables were calculated as predictors from four months of actigraphy data. Transitions in depressive symptoms were based on weekly SCL-90 scores and evaluation interviews. Kernel Change Point analyses were used to detect change points (CPs) and CP timing in circadian rhythm variables for each individual separately.

Results: In 67% of individuals with depressive symptoms transitions, CPs were identified in proximity to symptom transitions. CPs were detected less frequently in the no-transition group with 7 CPs in 14 individuals, compared to transition groups with 10 CPs in 12 individuals. For several RAR and sleep variables, consistent changes were detected in expected directions.

Conclusions: Circadian rhythm variables provide potentially clinically relevant information although their patterns around transitions are highly person-specific. Future research is needed to disentangle which variables are predictive for which patients.

Disclosure: No significant relationships.

Keywords: individual models; circadian rhythm; Depression; sleep

EPV1037

Neurodevelopmental continuum and pathogenic CNV detection in adult onset psychiatric disorders: microarray analysis in psychiatric clinical practice.

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Introduction: Structural variations of DNA, such as copy number variations (CNVs), are important contributors to risk for human diseases. Several CNVs have been associated with an increased risk of early-onset neurodevelopmental disorders (NDD), adult-onset psychiatry disorders and physical comorbidities. While in Pediatrics the microarray is the first-line genetic analysis technique in the study of child onset NDD, its use in psychiatry care of young/adult onset NDD has been limited to research purposes.

Objectives: Review of the diagnostic yield of the use of microarrays analysis in psychiatric clinical practice of severe mental disorder care in adults, according to the concept of a neurodevelopmental continuum.

Methods: An exploratory literature review on the topic in PubMed, including the terms: “copy number variants/CNVs” AND “neurodevelopmental delay/disorders, congenital anomalies/malformations, ADHD, autism/ASD, learning disabilities, epilepsy, Tourette, schizophrenia, bipolar, behaviour”.

Results: The prevalence of carriers of pathogenic or likely pathogenic CNVs among the different NDD phenotypes investigated by microarray analysis ranged from 3-22.5%. The majority of studies in adult psychiatric populations examined schizophrenia. Intellectual disability, autism spectrum disorders, dysmorphic features and multiple NDD/psychiatric diagnoses were described as predictors of an increased diagnostic yield of microarray testing.

Conclusions: While CNV testing is frequent in early-onset NDD; microarray analysis has not been established in psychiatric clinical practice despite the evidence of a high prevalence of findings in adult-onset NDD. The potential benefits in the detection of CNV are associated with physical comorbidities detection, understanding of pathogenesis of disease or genetic counseling. High-quality research designs are required before a routine clinical use.

Disclosure: No significant relationships.

Keywords: schizophrenia; CNVs; Neurodevelopmental disorders; microarray analysis