

psychotropic drugs are available (PGx drugs), but PGx testing is used only limitedly in psychiatric clinical practice.

Objectives: The aim of this study is to pinpoint different aspects of PGx drug use in the population, to support clinical uptake of PGx.

Methods: This drug utilization study investigated prescription PGx drug use in 56,065 young individuals with different severe mental disorders (SMD) in the Danish iPSYCH sample (born 1981-2005). We investigated the number of PGx drug users (incidence, prevalence), age (at first PGx drug use), sex, multiple PGx drugs per user (in light of panel-based PGx testing) and concomitant use of PGx drugs (in light of combinatorial PGx testing).

Results: We identified substantial PGx drug use in terms of incidence rates (e.g. 333 per 10,000 person years for the anticonvulsant lamotrigine) and prevalence (e.g. 15,260 users for the antidepressant citalopram) in patients with SMD. The age of first time PGx drug use ranged from 11.6-20 years, depending on SMD and sex. On average, more than one PGx drug was used by a single person (range 1.6-5.6 drugs, depending on SMD) or even used concomitantly (41-69%) affecting mostly two different PGx genes (84-92% of concomitant PGx drug users).

Conclusions: PGx drugs were frequently used in young individuals with SMD, often subsequently and concomitantly, arguing for panel-based/combinatorial PGx testing over single-gene testing. PGx testing could be applied already at a very young age.

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Keywords: Pharmacogenetics; Drug Utilization; severe mental disorders

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Pharmacogenetics and adhd treatment outcomes in the danish population-based IPSYCH sample

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Introduction: Pharmacogenetics (PGx) studies genetic variance and related differences in drug outcomes. The aim of PGx testing is to increase therapy efficacy and safety, by applying e.g. dose adjustments in patients with a specific geno- or phenotype. PGx guidelines for psychotropic drugs are available (PGx drugs), including atomoxetine used in the treatment of attention deficit hyperactivity disorder (ADHD). In Denmark, broad implementation of PGx is currently still low, possibly due to the lack of population-based studies investigating the real-world impact of PGx variability.

Objectives: The aim of this study is to investigate the association of PGx variability (patients' genotype/phenotype) in users of

atomoxetine and different treatment outcomes in a large population-based sample of individuals with ADHD.

Methods: This study will use data of the large Danish population-based iPSYCH case-cohort study sample including information on genetic variants, prescription drug use and outcome data, e.g. psychiatric and somatic hospitalizations and death. The study population comprises all individuals diagnosed with ADHD born 1981-2005 with at least one prescription for atomoxetine between 1995 and 2016. All individuals will be categorized according to their CYP2D6 phenotypes. We will perform Cox regression analysis to estimate the hazard ratios comparing the rates of the different outcomes in people with different phenotypes adjusted for a number of confounding factors.

Results: We have identified approximately 20,000 individuals with ADHD, of whom an estimated 10-20% have filled at least one prescription of atomoxetine.

Conclusions: We expect results in the beginning of 2021.

Disclosure: We thank the iPSYCH consortium, in specific the iPSYCH PI's (Merete Nordentoft, Anders Børglum, Preben B. Mortensen, Ole Mors, Thomas Werge and David M. Hougaard). The iPSYCH project is funded by the Lundbeck Foundation Denmark and the universities and un

Keywords: Pharmacogenetics; ADHD; atomoxetine

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Pharmacogenetic profiles of young danish individuals with and without severe mental disorders

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Introduction: Pharmacogenetics (PGx) studies genetic variance and related differences in drug outcomes. PGx guidelines for psychotropic drugs are available (PGx drugs). By executing PGx testing in a prospective or pre-emptive setting, dose adjustments or even change of treatment type can be applied prior to start of therapy to patients who carry a specific geno- or phenotype (i.e. actionable geno- or phenotypes). By doing so, increased efficacy of therapy or reduced risk of adverse events of treatment can be accomplished. In Denmark, broad implementation of PGx is currently still low.

Objectives: The aim of this study is to classify the PGx profiles of Danish individuals with and without severe mental disorders (SMD), to be used in follow-up studies investigating PGx and drug outcomes.

Methods: This study made use of imputed genotyping data of the Danish iPSYCH sample, which includes 77,639 young individuals born between 1981-2005, with or without a diagnosis of one or more of five selected SMD (i.e. depression, attention-deficit/hyperactivity disorder, autism, bipolar disorder and schizophrenia). We investigated a panel of 48 genetic variants with known PGx

applications (part of the U-PGx consortium, a Horizon2020 funded project on clinical relevant PGx in the EU).

Results: Imputed data contains over 11 million SNPs of 77,639 individuals.

Conclusions: We expect results in the end of 2020.

Disclosure: We thank the iPSYCH consortium, in specific the iPSYCH PTs (Merete Nordentoft, Anders Borglum, Preben B. Mortensen, Ole Mors, Thomas Werge and David M. Hougaard). The iPSYCH project is funded by the Lundbeck Foundation Denmark and the universities and un

Keywords: genotype; phenotype; Pharmacogenetics

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Identification of robust and interpretable brain signatures of autism and clinical symptom severity using a dynamic time-series deep neural network

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Introduction: Autism spectrum disorder (ASD) is among the most common and pervasive neurodevelopmental disorders. Yet, despite decades of research, the neurobiology of ASD is still poorly understood, as inconsistent findings preclude the identification of robust and interpretable neurobiological markers and predictors of clinical symptoms.

Objectives: Identify robust and interpretable dynamic brain markers that distinguish children with ASD from typically-developing (TD) children and predict clinical symptom severity.

Methods: We leverage multiple functional brain imaging cohorts (ABIDE, Stanford; N = 1004) and exciting recent advances in explainable artificial intelligence (xAI), to develop a novel multivariate time series deep neural network model that extracts informative brain dynamics features that accurately distinguish between ASD and TD children, and predict clinical symptom severity.

Results: Our model achieved consistently high classification accuracies in cross-validation analysis of data from the ABIDE cohort. Crucially, despite the differences in symptom profiles, age, and data acquisition protocols, our model also accurately classified data from an independent Stanford cohort without additional training. xAI analyses revealed that brain features associated with the default mode network, and the human voice/face processing and communication systems, most clearly distinguished ASD from TD children in both cohorts. Furthermore, the posterior cingulate cortex emerged as robust predictor of the severity of social and communication deficits in ASD in both cohorts.

Conclusions: Our findings, replicated across two independent cohorts, reveal robust and neurobiologically interpretable brain features that detect ASD and predict core phenotypic features of ASD, and have the potential to transform our understanding of the etiology and treatment of the disorder.

Disclosure: No significant relationships.

Keywords: autism; biomarkers; brain dynamics; fMRI

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One treatment fits all: Effectiveness of a multicomponent cognitive behavioral therapy program in data-driven subtypes of perinatal depression

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Introduction: It has been well established that depressive disorders including perinatal depression are very heterogeneous, which partly explain the ineffectiveness of available treatments for many patients. Recent innovations in data science can help elucidate the nature of perinatal depression especially the heterogeneity in its presentation.

Objectives: The present study aims to elucidate heterogeneous subtypes of PND and assess the effectiveness of a multicomponent cognitive behavioral therapy (CBT) across heterogeneous subtypes of PND.

Methods: This study was conducted in 2005 in two rural areas of Rawalpindi, Pakistan. Out of a total of 3,898 women, 903 pregnant women were identified with PND (using DSM-IV) and randomly assigned to intervention and control group. Baseline assessments included interviewer administered Hamilton Depression Scale (HDS) and social risk factors. Follow-up assessments were conducted at 6 months and 12 months post-intervention. Principle component analysis was run to reduce dimensionality of the HDS. Two step cluster analysis was then run to elucidate subtypes of PND using the dimensional scores. Thereafter, effectiveness of CBT was compared across these subtypes of PND using multilevel modelling.

Results: Principle component analysis revealed a four component solution for the Hamilton depression rating scale. Using these dimensional scores, cluster analysis (average silhouette= 0.5) revealed a parsimonious four cluster solution of participants with mild PND symptoms (n=326); predominant sleep problems (n=311) c) predominant atypical symptoms (n=80) and d) comorbid depressive and anxiety symptoms (n=186). CBT yielded moderate effect sizes across all these subtypes of PND (Cohen's d > 0.8).

Conclusions: Multicomponent CBT is effective across heterogeneous presentations of PND.

Disclosure: No significant relationships.

Keywords: cluster analysis; Postpartum depression; phenotypic subtypes; heterogeneity

Prevention of mental disorders

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Home environment as a factor in maintaining the mental health of the individual in the family

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