DOI : 10.31363/2313-7053-2019-4-1-53-54

The PsyCourse Infrastructure as an Example for Longitudinal Research in Biological Psychiatry

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Summary. Both genetic and environmental factors play a major role in the etiology of mental illnesses. Longitudinal studies collecting many phenotypes and biomaterials help to elucidate this complex interplay. PsyCourse is an observational longitudinal multi-center (19 centers) study of severe mental disorders conducted in Germany and Austria, that, to date, collected data from more than 1,500 patients and control individuals. Here, we give an overview of the key properties and, specifically, the infrastructure of the PsyCourse study. Beside the study protocol, we provide information on IT tools, data management, data protection, quality control, data analysis, and data sharing with collaborators. We also highlight the need for fundamental preparation.

Keywords: longitudinal study, schizophrenia, bipolar, psychosis, depression, data protection, data management.

Инфраструктура PsyCourse как пример лонгитудинального исследования в биологической психиатрии

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Резюме. Генетические факторы и факторы окружающей среды играют важную роль в этиологии психических заболеваний. Лонгитудинальные исследования со сбором большого количества фенотипов и биоматериала помогают понять это сложное взаимодействие. PsyCourse — обсервационное продольное многоцентровое (19 центров) исследование тяжелых психических расстройств, проводимое в Германии и Австрии, которое на сегодняшний день включает данные более чем 1500 пациентов и контрольных лиц. В данной статье мы даем обзор ключевых свойств исследования PsyCourse и, в частности, его инфраструктуры. Помимо протокола исследования, мы предоставляем информацию об инструментах IT, управлении данными, защите данных, контроле качества, анализе данных и обмене данными с сотрудниками. Мы также подчеркиваем необходимость фундаментальной подготовки.

Ключевые слова: продольное исследование, шизофрения, биполярное расстройство, психоз, депрессия, защита данных, управление данными.

Background: To better understand and treat mental disorders, cross-sectional research is no longer enough. Consideration of both genetic and environmental factors in the disease course are crucial for the future of psychiatric research.

Properties of the PsyCourse study: Founded originally under the name "Klinische Forschergruppe 241" in 2011, PsyCourse is an observational longitudinal multi-center (19 centers) study conducted in Germany and Austria (Budde et al., 2019). For the PsyCourse study, both clinical (patients) and nonclinical (controls) participants are recruited. The interviewers are trained raters, the vast majority of whom were psychologists and psychiatrists. They are provided with instructions in written form for all instruments and each new interviewer is extensively trained in administering the phenotyping battery by an experienced interviewer.

Key Inclusion Criteria:

Clinical participants: Patients can be included in the study, if they meet both of the following criteria:

Adult (≥18 years)

ICD 10 life-time diagnosis of schizophrenia (F20.x), brief psychotic disorder (F23.x), schizo-affective disorder (SZA; F25.x), bipolar disorder (F31.x), manic episode (F30.x), or recurrent major depression (reMDD; F33.x)

Corresponding DSM-IV diagnoses were confirmed after conducting the SCID Interview, which is part of the first study visit: schizophrenia (295.1/.2/.3/.6/.9), schizophreniform disorder (295.4), brief psychotic disorder (298.8), schizoaffective disorder (295.7), bipolar disorder (296.X [bipolar disorders incl. manic episode]) or recurrent major depression (296.3).

Nonclinical participants: Controls must meet all of the following inclusion criteria to be eligible for enrollment into the trial:

Adult (≥18 years)

Key Exclusion Criteria:

Clinical participants: Subjects must be excluded from the study if one of the following criteria applies:

Patient not able to give written informed consent

Patient without legal capacity who is unable to understand the nature, scope, significance and consequences of the clinical trial (cognitive dysfunction)

The DSM-IV diagnosis ascertained through SCID interview differed from the aforementioned DSM-IV diagnostic categories

Patient is not proficient in the German language

Nonclinical participants: Control participants must be excluded from the study if:

They have ever been treated as inpatient for one of the investigated ICD-10 diagnoses

They are not proficient in the German language

Trial Procedures: Study participants are assessed at four points in time, in intervals of 6 months, hereafter referred to as study visits 1 (baseline), 2 (+6 months), 3 (+12 months), and 4 (+18 months). At each study visit, venous blood samples are collected, permitting extraction of biomaterials such as DNA, RNA, plasma and serum.

Measurements: Participants were phenotyped using a comprehensive battery including data on sociodemographics, psychopathology, cognition, and functioning assessed at each of four visits.

Data Protection and Data Management: Due to collection of sensitive phenotypic data and biomaterials, a data protection concept was developed (http://www.kfo241.de/materials/20120718_datenschutzkonzept.pdf). It includes an array of organizational measures such as pseudonymization to minimize the risk of participant identification and unauthorized transmission of personal data to third parties. Four different IT components have been established by the Department of Medical Informatics at the University Medical Center, Göttingen, Germany (Demiroglu et al., 2012):

The identity tool, responsible for storing the identifying data and for generating two different pseudonyms.

The administrative tool, for managing study organization, informed consent, and communication with the study participants (linked to the identity tool).

The phenotype database, containing information collected using rating scales, questionnaires, and cognitive tests. Data capturing is web-based, and can be carried out by each clinical center.

The biomaterial database for administering the collected biological samples, which are stored in freezers at a few locations.

The query tool, linking the phenotype database and the biomaterial database.

Quality Control: Quality management is carried out on several levels:

- Data collection:
- Phenotypic data: SOPs for recruitment, documentation and specific tests and rating scales
- Biomaterials: SOP for laboratory procedueres
- Data entry:
- SOP for entering data into the phenotypic database
- Quality management: permanent monitoring of study centers, e.g. missing diagnosis, giving feedback on SCID interviews
- Database maintenance:
- Assessing the contents of databases: How many samples/individuals? How many individual diagnoses or biomaterial types? Are there cases without information?
- Data analysis:
- Versioned analysis dataset
- Codebook describing all variables in detail
- State-of-the-art analysis platform in a protected clinical IT environment

Open Science:

PsyCourse is open to collaboration with research scientists all over the world. If scientists are interested in PsyCourse data and want to perform data analysis, they must submit a proposal provided on the PsyCourse website, which is then evaluated by a PsyCourse scientists.

Preparation: Conducting a longitudinal study requires fundamental preparation. Relevant steps for successful implementation of the study are:

- Pilot Study
- Clear responsibilities
- Leading study center
- Study offices: coordination of appointments, documentation etc.
- Trained interviewers and their regular participation in rater trainings conducted by the leading study center
- Trained lab staff
- SOPs for each trial workflow
- Professional biobank for sample storage
- IT-system support, also in clinical centers

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