environMENTAL Seminar 3

May 23th, 2022

Validation of putative biomarkers in clinical cohorts

Tobias Banaschewski, Henrik Walter & Emanuel Schwarz

Goals and Objectives

Goals

- Improved prevention and therapy in a health-economically meaningful way
- Translation of the risk/resilience signatures derived from population cohorts into clinical practice

Objectives

- Validation of environmental risk and resilience signatures / biomarker profiles for symptoms of depression, anxiety, stress, and substance misuse identified in epidemiological cohorts in clinical populations
  - examine whether these explain the severity of symptoms and predict onset and courses of mental disorders across the lifetime
- Determine their clinical utility as risk profiles
  - whether they support clinical decision-making (severity of symptomatology, functioning and impairment) across the life span

Cohort overview

SampleName	Diagnosis	Size (approx)	f(MRI)	Age (years)	Genotypes	Geospatial	WP integration
Population samples, registries							
Norwegian Biobanks		400.000	N=500	18-70	+	+	1,4,12
COVIDMENT		450.000	-	18-70	+	+	1,3,4,12
National cohorts							
UK Biobank	SCZ, MDD, bipolar	500.000	N=42.000	38-73	+	+	1,3,4,12
NAKO		200.000	N=30.000	20-69	+	+	1,3,4,12
Deep phenotyped population samples							
IMAGEN		2.000	N=2.000	14-23	+	+	1,3,4,5,12
MARS		384	N=172	3mo.-34	+	+	1,3,4,5,12
PEZ		700	N=500	18-31	+	+	1,3,4,5,12
Fudan HC		5.000	N=3.000	18-20	+	+	1,3,4,5,12
Deep phenotyped clinical samples							
Stratify/ESTRA	Alcohol, MDD, anxiety	800	N=800	19-25	+	+	3,4,5,6,12
AUD cohort	Alcohol	401	N=348	20-67	+	+	3,4,6,12
NIMH CAT-D	MDD	284	N=200	18-40	-	+	4,6,12
Fudan depression	First-episode depression	1.000	N=900	18-65	+	+	3,4,6,12
SUPER	MDD	80	N=75	>18	+	+	3,4,6,12
MooDS/Integrament	MDD, bipolar, SCZ	400	N=300	20-50	+	+	3,4,6,12
INDICATE	MDD, SCZ	100	N=80	20-50	+	+	3,4,6,12
Fudan SCZ	SCZ	2.000	N=1.800	16-40	+	+	3,4,6,12
ESPRIT	SCZ	200	N=150	20-50	+	+	3,4,6,12
NeuroIMAGE	ADHD	600	N=591	5-30	+	+	3,4,6,12
EU AIMS	ASD	737	N=639	6-30	+	+	3,4,6,12
Fudan ASD	ASD/high ASD risk	1.500	N=1.300	3-18	+	+	3,4,6,12
International consortia							
ENIGMA		50.000	N=50.000		+	-	1,4,12

We will capitalize on deeply-phenotyped longitudinal clinical cohorts (total n > 2000; age range: 6-65 y)

Tasks

Task 1: Data harmonization of clinical cohorts and recalibration of the population-derived normative models predicting psychopathological symptoms (of depression, anxiety, stress and substance abuse) **based on ERRS in clinical cohorts**

- Create a harmonised data structure; cohorts into a common format for recalibration
- Apply the population based normative models to clinical cohorts and generate multivariate environmental risk and resilience signatures (adjustment for specific clinical populations)
- Quantify alterations in clinical cohorts and evaluate their ability to explain variance in the clinical datasets using machine learning models (cross-validation and cross-cohort prediction of onset, severity and progression of psychopathological symptomatology)

Tasks

Task 2 Analyses of ERRS scores within and across disorders longitudinally

- quantify and parse within-disorder heterogeneity; analyse disorder-specific associations (construct validity)
- determine associations with polygenic risk scores, multidimensional – omics signatures, and brain activity and structure
- analyse severity and courses of transdiagnostic symptoms, functional impairment and neurocognitive deficits are predicted by ERRS in clinical populations (prognostic validity)

Task 3 Cross-validation in independent cohorts

- validate the specificity and generalizability of our findings across other mental disorder (e.g., schizophrenia, ADHD autism) and populations using independent large international clinical cohorts from the Zhangjiang International Biobank in China and the ENIGMA consortium

Cohort overview

SampleName	Diagnosis	Size (approx)	f(MRI)	Age (years)	Genotypes	Geospatial	WP integration
Population samples, registries							
Norwegian Biobanks		400.000	N=500	18-70	+	+	1,4,12
COVIDMENT		450.000	-	18-70	+	+	1,3,4,12
National cohorts							
UK Biobank	SCZ, MDD, bipolar	500.000	N=42.000	38-73	+	+	1,3,4,12
NAKO		200.000	N=30.000	20-69	+	+	1,3,4,12
Deep phenotyped population samples							
IMAGEN		2.000	N=2.000	14-23	+	+	1,3,4,5,12
MARS		384	N=172	3mo.-34	+	+	1,3,4,5,12
PEZ		700	N=500	18-31	+	+	1,3,4,5,12
Fudan HC		5.000	N=3.000	18-20	+	+	1,3,4,5,12
Deep phenotyped clinical samples							
Stratify/ESTRA	Alcohol, MDD, anxiety	800	N=800	19-25	+	+	3,4,5,6,12
AUD cohort	Alcohol	401	N=348	20-67	+	+	3,4,6,12
NIMH CAT-D	MDD	284	N=200	18-40	-	+	4,6,12
Fudan depression	First-episode depression	1.000	N=900	18-65	+	+	3,4,6,12
SUPER	MDD	80	N=75	>18	+	+	3,4,6,12
MooDS/Integrament	MDD, bipolar, SCZ	400	N=300	20-50	+	+	3,4,6,12
INDICATE	MDD, SCZ	100	N=80	20-50	+	+	3,4,6,12
Fudan SCZ	SCZ	2.000	N=1.800	16-40	+	+	3,4,6,12
ESPRIT	SCZ	200	N=150	20-50	+	+	3,4,6,12
NeuroIMAGE	ADHD	600	N=591	5-30	+	+	3,4,6,12
EU AIMS	ASD	737	N=639	6-30	+	+	3,4,6,12
Fudan ASD	ASD/high ASD risk	1.500	N=1.300	3-18	+	+	3,4,6,12
International consortia							
ENIGMA		50.000	N=50.000		+	-	1,4,12