

# Population neuroimaging: How to responsibly handle big data in the age of biobanks

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The UK-Biobank has released over 15,000 neuroimaging datasets that are accompanied with deep phenotyping. The ABCD Study has released over 11,000 neuroimaging data from 9 to 11 year old children. Many researchers have accessed these data and have begun demonstrating that even very small effect sizes can be statistically significant with such a large sample. The full potential of these data can be better realized with additional consideration of effect size, generalizability, bias, and confounding. For example, currently, little attention is given to the effect of confounding bias on associations between neuroimaging data and a given phenotype; at most, a few central covariates are adjusted for in statistical models. Further, generalizability of findings is often poorly described in brain mapping studies. How meaningful are results that may only apply to a highly select subgroup of the population? These crucial epidemiological aspects are lacking in most neuroscience, psychology, and brain mapping training programs, and this education session will ensure more awareness of the common mistakes and misconceptions involved in big data usage.

## Objective

- 1.) Have a concrete understanding and awareness of core epidemiological concepts, including confounding and forms of bias that can render statistically significant results as invalid.
- 2.) Have an improved understanding of p-values, confidence intervals, and effect sizes, three issues that are crucial when interpreting and reporting data from studies with high power.
- 3.) Utilize more accurate terminology and comprehensive reporting when describing study methods and results.

## Target Audience

The target audience of this education session is all scientists utilizing big data/biobanks, which predominately includes young researchers (students, post-docs) without a background in epidemiology.

## Presentations

### The seven plagues of conventional brain imaging studies: Towards Population Neuroscience

Neuroimaging studies are typically small scale and not designed with an epidemiological framework. This can impact internal validity and generalizability. In this talk seven common epidemiological challenges faced by neuroimaging studies are discussed, examples are mostly taken from the child psychiatric developmental imaging literature. These problems include no sampling frame or study base, insufficient control for confounding, no clear design that allows the study of the temporal direction of effect, no life course model to account for critical periods, multiple hypothesis testing with too few hierarchical models, too few studies of co-occurrence of different psychiatric traits and dichotomous modelling, and insufficient sample size for the expected small effects and interactions. Finally, selected ongoing Population Neuroscience approaches are presented that are trying to address these challenges.

#### Presenter

*Henning Tiemeier*, Harvard Boston, MA  
United States

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### Big Data for Precision Neuroscience : Novel approaches for charting resting-state functional connectivity & connectopies

Large clinical and population cohort neuroimaging resources are increasingly coming online, forming a new field of imaging epidemiology. These offer a unified perspective that links brain connectional organization to behaviour and cognition. Currently, however, the full potential of these resources for understanding brain connectivity is not being realized. This is due to a lack of suitable analysis tools that explore relationships between and integrate across modalities, are sensitive to subtle changes in individual connectivity profiles and provide a means to move beyond simple case-control analysis towards understanding inter-individual differences in connectivity. In this talk I will outline novel approaches for charting the organisation of functional connectivity and introduce a 'normative modelling' strategy for utilising big cohort data for generating individualised predictions with application in clinical neuroimaging studies.

#### Presenter

*Christian Beckmann*, Donders Institute Nijmegen, Gelderland  
Netherlands

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## Population neuroimaging meets genetics: important considerations with data, both big and small

If the immense dimensionality of imaging data alone were not enough, adding genomic data into the mix increases the multiple testing problem exponentially. However, different approaches for melding imaging and genomic data are available for different research questions. Voxel-wise GWAS, Candidate gene work, polygenic risk scores, and G-x-E interactions are all actively being used in the brain mapping field. What's especially crucial is that having a large sample size isn't always a requirement. For certain research questions and analysis methods, power is a necessity while for others a modest sample will suffice. Covering these concepts, this talk will utilize existing studies to provide examples and will encourage participant interaction through brief quizzes during the lecture.

### **Presenter**

Anqi Qiu, National University of Singapore Singapore, Singapore  
Singapore

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## Replication in population neuroimaging studies: The what, when, why, and how?

It is no secret that the field of neuroimaging lags behind in terms of replication. With such large biobank-scale sample sizes, do we need to implement replication into our research? This presentation will discuss replication in the era of biobanks. Different approaches and methods for replication, opportunities to embed replication into biobank-scale studies, and publically available replication datasets will be discussed. Audience interaction will take place with short quizzes throughout the talk.

### **Presenter**

Xi-Nian Zuo, Chinese Academy of Science Beijing, Beijing  
China

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## Introduction to population neuroimaging

Population neuroimaging lies at the intersection between epidemiology and neuroscience and the last decade has seen the emergence of a number of large scale population-based neuroimaging cohorts. This primer into the topic of population neuroimaging will discuss what makes a specific study population-based, what are some of the key concepts that should be considered in working with large-scale population-based data, and what can such studies bring to the table of both clinical practice and public health. This talk will provide the transition to the following talks, including potential pitfalls. Audience interaction will take place with short quizzes throughout the talk.

## Presenter

*Tonya White, MD, PhD*, Erasmus University Medical Centre  
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## **Application of epidemiological concepts in neuroimaging**

Methodological thinking in brain mapping has largely drawn from the psychological sciences, neuroscience, medicine, and engineering. Elegantly complementary, epidemiological methods offer a fresh look at how we can conceptualize our neuroimaging studies and analyses. How should confounding bias be approached? What impact does selection bias have on results, and how can missing data be handled? As large population-based cohorts with neuroimaging data become more common, consideration and implementation of such techniques becomes increasingly important. For this lecture, strategies for examining confounding bias and selection bias will be presented. Further, best practices for presenting analyses and results will be discussed. Audience interaction will take place with short quizzes throughout the talk.

## Presenter

*Ryan Muetzel*, Erasmus University Medical Centre Rotterdam, Zuid Holland  
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