UMEÅ UNIVERSITET

# Methods for Longitudinal Brain Imaging Studies with Dropout

**Tetiana Gorbach**

## Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie doktorsexamen framläggs till offentligt försvar i Hörsal 1031, Norra Beteendevetarhuset,
fredagen den 22 februari, kl. 10:15.
Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor, Martin A. Lindquist,
Department of Biostatistics at the Johns Hopkins Bloomberg School of Public Health at Johns Hopkins University, Baltimore, USA.

**Department of Statistics, USBE**

**Organization**
Umeå University
Department of Statistics
Umeå School of Business,
Economics and Statistics

**Document type**
Doctoral thesis

**Date of publication**
1 February 2019

**Author**
Tetiana Gorbach

## Title
Methods for Longitudinal Brain Imaging Studies with Dropout

## Abstract
One of the challenges in aging research is to understand the brain mechanisms that underlie cognitive development in older adults. Such aging processes are investigated in longitudinal studies, where the within-individual changes over time are observed. However, several methodological issues exist in longitudinal analyses. One of them is loss of participants to follow-up, which occurs when individuals drop out from the study. Such dropout should be taken into account for valid conclusions from longitudinal investigations, and this is the focus of this thesis. The developed methods are used to explore brain aging and its relation to cognition within the Betula longitudinal study of aging.

Papers I and II consider the association between changes in brain structure and cognition. In the first paper, regression analysis is used to establish the statistical significance of brain-cognition associations while accounting for dropout. Paper II develops interval estimators directly for an association as measured by partial correlation, when some data are missing. The estimators of Paper II may be used in longitudinal as well as cross-sectional studies and are not limited to brain imaging.

Papers III and IV study functional brain connectivity, which is the statistical dependency between the functions of distinct brain regions. Typically, only brain regions with associations stronger than a predefined threshold are considered connected. However, the threshold is often arbitrarily set and does not reflect the individual differences in the overall connectivity patterns. Paper III proposes a mixture model for brain connectivity without explicit thresholding of associations and suggests an alternative connectivity measure. Paper IV extends the mixture modeling of Paper III to a longitudinal setting with dropout and investigates the impact of ignoring the dropout mechanism on the quality of the inferences made on longitudinal connectivity changes.

## Keywords
Missing data, nonignorable dropout, sensitivity analysis, uncertainty intervals, pattern-mixture models, aging, cognition, MRI, brain structure, resting-state functional connectivity

**Language**
English

**ISBN**
978-91-7855-011-1

**ISSN**
1100-8989

**Number of pages**
20 + 4 papers