International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY202460005

doi: 10.37766/inplasy2024.6.0005

Received: 03 June 2024

Published: 03 June 2024

Human brain white matter development across the lifespan in diffusion tensor imaging studies: A protocol for a systematic review, meta-analysis and mega analysis of associations between age, fractional anisotropy and mean diffusivity

Tuulari, JJ; Audah, HK; Barron, A; Mariani Wigley, ILC; Rosberg, A; Jolly, A; Vartiainen, E; Suuronen, I; Hashempour, N; Li, R; Luotonen, S; Bano, W; Merisaari, H; Karlsson, H; Karlsson, L; Seidlitz, J; Bethlehem, RAI; Pulli, EP.

Corresponding author:
Elmo Pulli

elmo.p.pulli@utu.fi

Author Affiliation:
Department of Clinical Medicine, FinnBrain Birth Cohort Study, University of Turku, Turku, Finland.

ADMINISTRATIVE INFORMATION

Support - Financial Support | Jetro J. Tuulari: Finnish Medical Foundation, Emil Aaltonen Foundation, Sigrid Juselius Foundation, Signe and Ane Gyllenberg Foundation, Hospital District of Southwest Finland State Research Grants | Elmo P. Pulli: Finnish Cultural Foundation, Turku University Foundation.

Review Stage at time of this submission - Formal screening of search results.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460005

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 June 2024 and was last updated on 03 June 2024.

INTRODUCTION

Review question / Objective Primary question: What is the association of chronological age to diffusion tensors (fractional anisotropy [FA] / mean diffusivity [MD] values) across the postnatal human lifespan across the whole brain?
Secondary question: What is the coverage of regions of interest in the white matter and can we extend the primary question to region of interest (ROI) level if we identified sufficient overlap in the ROI's?
Exploratory analyses will probe, to what extend methodological variation explains the associations.

Rationale Current studies and reviews tend to focus on specific age ranges when investigating the developmental trajectories of brain structures such as white matter, leaving a critical gap in our understanding of how diffusion tensor imaging (DTI) metrics, which are key indicators of white matter integrity, change across the human lifespan. This gap limits our ability to fully comprehend the developmental and ageing processes of white matter and their implications for cognitive and mental health. Conducting a systematic review to map associations between age and brain white matter integrity across healthy populations will address this gap by providing a comprehensive overview of existing research, identifying inconsistencies, and highlighting areas where evidence is lacking. By doing so, it will not only advance our understanding of how white matter integrity evolves throughout life but will also direct future research towards areas where there is a lack of data.

Condition being studied Here, we conceptualize age from birth as the exposure and brain white

matter ‘integrity’ as the outcome and map associations across non-clinical populations. One of the key milestones in neuroscience was achieved in 2022 when human brain growth charts were developed and released for the first time (Bethlehem et al., 2022). These brain charts for human lifespan were based on brain volume and entailed the cortical grey matter, white matter and subcortical grey matter volumes (https://www.cam.ac.uk/stories/BrainCharts). White matter development is of special interest as its volumetric growth peaks in young adulthood at age 28.7 years and is the last of the brain tissue compartments to accomplish maturation. Focusing on the white matter organization via measures of tissue integrity is key to advance (developmental) cognitive neuroscience and the field of psychiatry as it holds significant potential for mapping out trajectories that predispose individuals to developmental and mental disorders (Solmi et al., 2022; Paus, Keshavan, & Giedd, 2008). Currently, the available studies and reviews focus on specific age ranges. Thus, we lack information on how the diffusion tensor values change across the entire human lifespan.

METHODS

Search strategy The screening and assessment for eligibility for this systematic review is conducted by 11 people (authors AB, AJ, AR, EV, HKA, ILCMW, IS, NH, RL, SL, WB). In the screening phase, each article is assessed by 2 people, who then discuss possible disagreements, and in unclear cases the final decision is made by author EPP.

The goal of this literature search was to cover all diffusion tensor imaging (DTI) research in typically developing humans. The search phrase was made with the help from a librarian from the University of Turku.

The search phrase for PubMed is:

(brain* OR "brain"[MeSH Terms] OR "white matter*") AND (age[tw] OR aging* OR ageing* OR "aging"[MeSH Terms] OR grow* OR developmen* OR "growth and development"[Mesh] OR trajector*) AND (DTI OR dMRI OR DWI OR diffus* OR anisotrop* OR "Diffusion Magnetic Resonance Imaging"[Mesh]) NOT (cancer* OR "neoplasms"[MeSH Terms] OR epileps* OR "epilepsy"[MeSH Terms] OR "multiple sclerosis"[MeSH Terms] OR "multiple sclerosis*" OR preterm* OR ALS OR bipolar* OR schizophrenia* OR "schizophrenia"[MeSH Terms] OR Parkinson* OR "parkinson disease"[MeSH Terms] OR "parkinsonian disorders"[MeSH Terms] OR Alzheimer* OR "alzheimer disease"[MeSH Terms] OR gambl* OR "gambling"[MeSH Terms] OR deficienc* OR ADHD OR "attention deficit disorder with hyperactivity"[MeSH Terms] OR "attention deficit disorder with hyperactivit*" OR impairment* OR hemodialys* OR "renal dialysis"[MeSH Terms] OR "renal dialys*" OR Wilson*[tw] OR phenylketonuria* OR "phenylketonurias"[MeSH Terms] OR amputation* OR "amputation, surgical"[MeSH Terms] OR migraine* OR "migraine disorders"[MeSH Terms] OR "sleep apn*" OR "sleep apnea syndromes"[MeSH Terms] OR disease* OR autism* OR "autistic disorder"[MeSH Terms] OR neuralgia* OR "neuralgia"[MeSH Terms] OR ischaemic* OR ischemic* OR alcohol* OR "brain injur*" OR "brain injuries"[MeSH Terms])

The search phrase for Embase is:

(brain* OR 'brain'/exp OR 'white matter*') AND (age OR aging* OR ageing* OR grow* OR developmen* OR 'growth and development' OR trajector* OR 'growth, development and aging'/exp) AND (dti OR dmri OR dwi OR diffus* OR anisotrop* OR 'diffusion magnetic resonance imaging' OR 'diffusion tensor imaging'/exp OR 'diffusion weighted imaging'/exp) NOT (cancer* OR 'neoplasm*' OR 'neoplasm'/exp OR epileps* OR 'epilepsy'/exp OR 'multiple sclerosis*' OR 'multiple sclerosis'/exp OR preterm* OR 'premature labor'/exp OR als OR 'amyotrophic lateral sclerosis'/exp OR bipolar* OR 'bipolar disorder'/exp OR schizophrenia* OR 'schizophrenia'/exp OR “parkinson disease*” OR 'parkinson disease'/exp OR “alzheimer disease*” OR 'alzheimer disease'/exp OR gambl* OR 'gambling'/exp OR 'pathological gambling'/exp OR deficienc* OR adhd OR 'attention deficit hyperactivity disorder'/exp OR 'attention deficit disorder with hyperactivit*' OR impairment* OR hemodialys* OR 'renal dialysis' OR 'renal dialys*' OR 'dialysis'/exp OR 'wilson disease*' OR 'wilson disease'/exp OR phenylketonuria* OR 'phenylketonuria'/exp OR amputation* OR 'amputation'/exp OR migraine* OR 'migraine'/exp OR 'sleep apn*' OR 'sleep apnea syndromes'/exp OR disease* OR autism* OR 'autistic disorder*' OR 'autism'/exp OR neuralgia* OR 'neuralgia'/exp OR ischaemic* OR ischemic* OR alcohol* OR 'brain injur*' OR 'brain injury'/exp)

The formatting of the search phrase is slightly modified depending on the database. The only filter used in the search is to only include English publications. Literature search from all covered databases will be updated before publication and

will be reported according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021).

Participant or population The participants of the systematic review are healthy term-born individuals. Since the scope of the systematic review is to cover the lifespan, we do not have an upper age limit, we include the data from infants to elderly population. Individuals with a disorder that is expected to affect neurodevelopment (including cancer, epilepsy, multiple sclerosis, amyotrophic lateral sclerosis, bipolar disorder, schizophrenia, depression, anxiety disorders, Parkinson's disease, Alzheimer's disease, vitamin/similar deficiency, attention deficit hyperactivity disorder, dialysis, Wilson's disease, phenylketonuria, any surgical amputation, cognitive or physical impairment, migraine, sleep apnea, autism, neuralgia, brain injury ischemic brain even in medical history, or addiction to alcohol, drugs, or gambling), or an increased risk for any of the aforementioned disorders are ineligible.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included We include cross sectional and longitudinal studies that pass the inclusion criteria.

Eligibility criteria Screening

Screening is done based on title and abstract only. If the article meets one or more of the exclusion criteria, it is excluded. The exclusion criteria are:

1. The article is not in English.

2. The article is a review, meta-analysis, mega-analysis, or case report.

3. Any non-human animals or only post-mortem samples are studied.

4. The article concerns any treatment, disorder or syndrome (including substance use and behavioral addictions), brain anomaly (anything that would usually be considered an "incidental finding" in a brain image), neurotoxin exposure, any high-risk gene/allele, or any type of head trauma of the participant.

5. The article concerns a chemical or pathogen exposure in utero (e.g., maternal medications, drugs of abuse, environmental toxins, human immunodeficiency virus).

6. Article studies the effects of preterm birth / low birth weight or states that it uses a sample of preterm born / low birth weight individuals. Mean and/or median gestation < 37 weeks or birthweight < 2,500g. Even one participant with gestation < 32 week or birthweight < 1,500g.

7. There is no indication that magnetic resonance imaging was done.

Seeking reports for retrieval and assessment for eligibility

We will search for full-text articles of the abstracts that passed screening. Preprints are included, but in cases where both preprint and journal article are available, only the final published version of the study is included.

Assessment for eligibility is done using the following exclusion criteria. If one or more of the criteria are met, the article is excluded.

1. All the same criteria as in the screening phase.

2. No diffusion tensor scalars – fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD) or axial diffusivity (AD) – values for any white matter region were reported either as a scatterplot or numerically in either the manuscript or any available supplementary materials.

3. The population includes any participants with a disorder that is expected to affect neurodevelopment (including cancer, epilepsy, multiple sclerosis, amyotrophic lateral sclerosis, bipolar disorder, schizophrenia, depression, anxiety disorders, Parkinson's disease, Alzheimer's disease, vitamin/similar deficiency, attention deficit hyperactivity disorder, dialysis, Wilson's disease, phenylketonuria, any surgical amputation, cognitive or physical impairment, migraine, sleep apnea, autism, neuralgia, brain injury ischemic brain even in medical history, or addiction to alcohol, drugs, or gambling), or the population was selected based on an increased risk for any of the aforementioned disorders.

During assessment for eligibility, the data is extracted from included articles. In cases in which the article does not meet any exclusion criteria, but the data is not available in a format that we could directly extract, we will contact the corresponding author and ask them to provide the required information (preferably scatter plots).

Information sources The covered databases include MEDLINE (PubMed), Web of Science, Scopus, and Embase.

Main outcome(s) The main focus is the global white matter integrity measured with fractional anisotropy (FA) and mean diffusivity values (MD). Therefore, our first outcome is how global white matter integrity changes in association with age across the postnatal human lifespan.

Additional outcome(s) The secondary outcome is to be able to investigate the same association between age and white matter integrity regionally if the overlap in the regions of interest suffices.

Data management Data extraction will be performed manually and automatically. We expect the statistical tests and corresponding effect size estimates to vary considerably across studies (Pearson / Spearman correlations, as well as partial correlations and regression models with variable covariates). Thus, we intend to use the information available in scatter plots to extract the brain metrics with tools such as MetaLab (Mikolajewicz & Komarova, 2019; https://github.com/NMikolajewicz/MetaLab).

Quality assessment / Risk of bias analysis This study is not assessing the evidence for an intervention, and we are excluding all articles in which subjects have a diagnosis which may affect brain development, which may also be prone to sampling bias. The design of individual studies is therefore not anticipated to affect the data that we extract from them (e.g., age, FA, and MD). Furthermore, most common risk of bias tools, such as the Cochrane risk of bias tool (Higgins et al., 2011), are intended for reporting of randomized trial and are not applicable to our review. For this reason, we will evaluate only the methodological quality of the studies based on DTI parameters reported in the articles (considering the effects of variables such as b values, Tesla of MRI scanner, voxel size, etc.).

Strategy of data synthesis We will apply linear/quadratic regressions and non-linear generalized additive models (GAM) on data form all individual participants in mega analysis, site mean/SD, site median/percentiles and report outcome variables including coefficients, R-squared, and p-values.

Subgroup analysis The study will not perform a large number of subgroup analyses, and these will depend on data availability from the included studies. The one variable planned for subgroup analysis is biological sex – to determine whether whole-brain mean FA and MD vary with age differently in males and females.

Sensitivity analysis Sensitivity analyses may probe whether our models are robust by removing random individual sites, re-running the models, and assessing any differences.

Language restriction Only articles published in English will be considered for inclusion.

Country(ies) involved Finland, Italy, the United States of America, and the United Kingdom.

Other relevant information
Second co-authors
Hilyatushalihah K. Audah, these authors contributed equally to this work.
Aaron Barron, these authors contributed equally to this work.
Isabella L. C. Mariani Wigley, these authors contributed equally to this work.
Aylin Rosberg, these authors contributed equally to this work.

Keywords Diffusion tensor imaging; meta-analysis; white matter; brain development; lifespan.

Dissemination plans We intend to publish a preprint once the manuscript is finished and then submit the article to a scientific journal. Publication has not been discussed with any specific journal at this stage. Following publication, we will employ standard measures of communication including through press releases, publication on websites and blog posts.

Contributions of each author
Author 1 - Jetro Tuulari - Conceiving and designing the review, planning the protocol, interpretation of data, and writing – original draft.
Email: jjttul@utu.fi
Author 2 - Hilyatushalihah Audah - Screening and assessing the eligibility of studies, data collection, data management, data analysis, writing – preregistration and writing – original draft.
Email: hkauda@utu.fi
Author 3 - Aaron Barron - Screening and assessing the eligibility of studies, data collection, data management, data analysis, writing – preregistration and writing – original draft.
Email: aaron.barron@utu.fi
Author 4 - Isabella Mariani Wigley - Screening and assessing the eligibility of studies, data collection, data management, data analysis, writing – preregistration and writing – original draft.
Email: ilmawi@utu.fi

Author 5 - Aylin Rosberg - Screening and assessing the eligibility of studies, data collection, data management, writing – preregistration and writing – original draft.
Email: aylin.a.rosberg@utu.fi
Author 6 - Ashmeet Jolly - Screening and assessing the eligibility of studies, data collection.
Email: ashmeet.a.jolly@utu.fi
Author 7 - Elena Vartiainen - Screening and assessing the eligibility of studies, data collection.
Email: elena.t.vartiainen@utu.fi
Author 8 - Ilkka Suuronen - Screening and assessing the eligibility of studies, data collection.
Email: ilksuu@utu.fi
Author 9 - Niloofar Hashempour - Screening and assessing the eligibility of studies, data collection.
Email: nilhas@utu.fi
Author 10 - Ru Li - Screening and assessing the eligibility of studies, data collection.
Email: ru.li@utu.fi
Author 11 - Silja Luotonen - Screening and assessing the eligibility of studies, data collection.
Email: sisolu@utu.fi
Author 12 - Wajiha Bano - Screening and assessing the eligibility of studies, data collection.
Email: wajiha.bano@utu.fi
Author 13 - Harri Merisaari - Software and writing – review and editing.
Email: haanme@utu.fi
Author 14 - Hasse Karlsson - Established the FinnBrain Birth Cohort and built the infrastructure for carrying out the study, writing – review and editing.
Email: hasse.karlsson@utu.fi
Author 15 - Linnea Karlsson - Established the FinnBrain Birth Cohort and built the infrastructure for carrying out the study, writing – review and editing.
Email: linnea.karlsson@utu.fi
Author 16 - Jakob Seidlitz - Writing – review and editing.
Email: jakob.seidlitz@pennmedicine.upenn.edu
Author 17 - Richard Bethlehem - Writing – review and editing.
Email: rb643@cam.ac.uk
Author 18 - Elmo Pulli - Designing the review, planning the protocol, coordinating the review, writing – original draft.