**Social cognition as a matter of structural brain connections? A systematic review and diffusion weighted imaging meta-analysis**

Rita Hansl[1], Lara Maliske[1], Sofie Valk[2,3,4], Philipp Kanske[1]

[1] Clinical Psychology and Behavioral Neuroscience, Faculty of Psychology, TUD Dresden Technical University, Dresden, Germany

[2] Max Planck Institute for Human Cognitive and Brain Sciences, Stephanstr. 1a, 04103, Leipzig, Germany

[3] Institute of Neuroscience and Medicine, Brain & Behaviour (INM-7), Research Centre Jülich, Jülich, Germany

[4] Institute of Systems Neuroscience, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

**Corresponding author**

Rita Hansl, TUD Dresden Technical University, rita.hansl@tu-dresden.de

Word: abstract – [230], manuscript – [3543]

**Author bios**

Rita Hansl is a PhD candidate in the Department of Clinical Psychology and Behavioral Neuroscience, Faculty of Psychology at the TUD Dresden Technical University. While her background is in pediatric neuropsychology, her PhD project focuses on the role of structural connectivity in social cognition. She aims to apply novel modeling and analysis techniques including Bayesian statistics and Machine learning analysis and to adhere to state-of-the-art open science practices.
Lara Maliske is a post-doctoral researcher in the Department of Clinical Psychology and Behavioral Neuroscience, Faculty of Psychology at the TUD Dresden Technical University investigating how socio-affective and -cognitive processes are represented in the brain at the network level, and in which contexts these networks interact. In her research, she uses functional magnetic resonance imaging and computational approaches to study interaction between brain regions and networks.
Sofie Valk is Lise Meitner research group leader at the Max Planck Institute for Human Cognition and Brain Sciences in Leipzig as well as at INM-7 Juelich, Germany. Together with her research group she aims to understand how human neurobiology and the social world we live in are connected. To do so, she aims to understand the principles of our biosocial minds and develop tools that help answer her questions.
Philipp Kanske is professor for Clinical Psychology and Behavioral Neuroscience at TUD Dresden Technical University. He explores the emotional and cognitive processes that enable social behavior and their alterations in psychopathology. He is the principle investigator and recipient of the ERC consolidator grant for his “INTERACT” project (GA 101088582), investigating the brain networks underlying social interaction.

**Qualifications/Training of researchers in terms of meta-analyses:**

Lara Maliske and Philipp Kanske have sufficient experience performing meta-analyses of neuroimaging data having performed a number of studies using cutting edge techniques.

**Declaration of conflict of interest**

The authors declare no potential conflicts of interest concerning the authorship and/or publication of this article.

**Financial disclosure/funding**

Funded by the European Union. Views and opinions expressed are however those of the authors only and do not necessarily reflect those of the European Union or the European Research Council Executive Agency. Neither the European Union nor the granting authority can be held responsible for them.

This work is supported by the ERC consolidator grant received by Philipp Kanske (INTERACT, GA 101088582, doi: 10.3030/101088582).

**Author's contribution**

| Role | Rita Hansl | Lara Maliske | Sofie Valk | Philipp Kanske |
|---|---|---|---|---|
| Conceptualization | X | X | X | X |
| Pre-testing | X | | | |
| Pre-registration | X | X | X | X |
| Data curation | X | X | | |
| Formal analysis | X | X | | |
| Funding acquisition | | X | | X |
| Investigation | X | | | |
| Pre-registration peer review / verification | X | X | | |
| Literature search | X | | | |
| Datafile study/effect coding | X | | | |
| Reproducible code | X | | | |
| Contacting authors | X | | | |
| Data analysis peer review /verification | X | X | | |
| Methodology | X | X | | |
| Project administration | X | | | X |
| Resources | | | | X |
| Software | X | X | | |
| Supervision | | X | X | X |
| Validation | X | X | | |
| Visualization | X | | | |
| Writing-original draft | X | | | |
| Writing-review and editing | X | X | X | X |

**Rights:**

Social cognition and white matter integrity: Systematic review and meta-analysis

**Full details of all authors**


| First name | Last name | ORCID-ID | OSF profile | Institutional email |
|---|---|---|---|---|
| Rita | Hansl | 0009-0002-8199-6307 | osf.io/tmhdk | rita.hansl@tu-dresden.de |
| Lara | Maliske | 0000-0003-2906-7471 | osf.io/8hb4n/ | lara.maliske@tu-dresden.de |
| Sofie | Valk | 0000-0003-2998-6849 | osf.io/jzfvd | valk@cbs.mpg.de |
| Philipp | Kanske | 0000-0003-2027-8782 | osf.io/rjkvp/ | philipp.kanske@tu-dresden.de |


**Links to project files**

| Content | Link |
|---|---|
| Open access Cloud folder and/or links for coding sheet, datasets, subfolder with password-protected identified papers and final analysis code | https://osf.io/3z4bf/?view_only=ca95cb2546604b6ab7da562fbee68d39 |

Social cognition and white matter integrity: Systematic review and meta-analysis


## Abstract

Social cognition encompasses several cognitive and affective processes essential for successful social interaction and communication (e.g. empathy, mentalizing, compassion). The interplay of the various processes necessary for understanding the thoughts and feelings of others is incredibly complex, requiring smooth interaction through efficient connections between various brain areas. Previous work has evidenced bidirectional associations between social cognitive deficits and deficient structural connectivity, suggesting that structural connectivity and white matter (WM) integrity might be an essential foundation for social cognitive abilities.

The proposed systematic review and meta-analyses aims to integrate the growing body of literature on correlations between WM integrity and metric measures of social cognitive abilities across cohorts. Quantitative meta-analysis of diffusion weighted whole-brain imaging data is aimed to reveal the WM tracts most strongly associated with the investigated social cognitive construct. Meta-analyses of ROI-based studies will grant insights into the relevance of frequently investigated WM tracts. ~~Moderator analysis via m~~Meta-regression and subgroup analysis will differentiate between investigated *socio-cognitive constructs*, *DTI metrics*, *clinical diagnoses*, and *age groups* to investigate potential category-specific effects.

The study has the potential to reveal associations between global WM integrity and social cognitive abilities. Moreover, the location specific findings would lay the basis for future ROI-based investigations while *socio-cognitive construct-*, *diffusion-metric-*, and *diagnosis-specific* effects would allow for insights into the potentially diverging relevance of different tracts and WM properties for distinct social cognitive concepts and in different populations.



***Keywords***: social cognitive neuroscience, social cognition, social affect, structural connectivity, white matter, meta-analysis, diffusion tensor imaging

**Social cognition as a matter of structural brain connections? A systematic review and diffusion weighted imaging meta-analysis**

The ease and pace with which social interactions can be performed continuously in everyday life often mask the incredible intricacy of the tasks at hand. The complexity and fragility of verbal and non-verbal communication becomes especially clear when minor nuances in the tone of voice, the emotional state or differences in personal background as well as various developmental conditions lead to major misunderstandings and failure in information transfer (Happé & Frith, 2014; Kennedy & Adolphs, 2012).

The field of social neuroscience has emerged to investigate the neural underpinnings of the distinct processes necessary to perform successful social interaction which can be united under the term *social cognition* (Alcalá-López et al., 2018; Renfrew et al., 2008). The ~~more~~ distinct automatic and voluntary socio-cognitive processes range from more basic ~~*facial*~~ *emotion recognition* and *social perception* to higher-order processes like *Theory of Mind (ToM)* or ~~*trust*~~ *social motivation* (Alcalá-López et al., 2018; Beer & Ochsner, 2006; Happé et al., 2017). Although some authors have worked on dividing the various constructs into a workable nomenclature (Happé et al., 2017), no comprehensive consensus-based factor-structure has been established to date. Regardless of the precise conceptualizations, ~~and have~~ the existing constructs been robustly subdivided into *affective* (e.g. *empathy*, *compassion*) and *cognitive processes* (e.g. *ToM*, *mentalizing*, *mind-reading*) (Kanske, 2018; Schurz et al., 2021). Various clinical conditions are negatively associated with social functioning, collectively showing the detrimental effects unsuccessful social interaction can have on a person's social and emotional health and well-being (Happé & Frith, 2014; Kennedy & Adolphs, 2012). In a society afflicted by loneliness (World Health Organization, 2023b), social conflict (World Health Organization, 2021) and increasing depression rates associated with social isolation (Santomauro et al., 2021; World Health Organization, 2023a), it has become all the more important to better understand the mechanisms underlying social cognition to allow for targeted intervention and early, effective therapy.

### 1.1. Neuroscience of social cognition

The complexity of socio-cognitive processes requires the smooth integration of tasks like perceptual input, emotion, memory, prediction and executive functions. This has led social neuroscientific research to proposed brain networks rather than confined brain structures to underlie social processes (Alcalá-López et al., 2018; Krendl & Betzel, 2022; Schurz et al., 2021). Integrating the results of 26 neuroimaging meta-analyses of segregated, task-based findings into one "social brain atlas", Alcalá-López et al. (2018) highlight 36 key brain regions previously associated with socio-cognitive processing. These brain areas encompass regions traditionally associated with higher socio-cognitive processes (e.g. right temporo-parietal junction (Alcalá-López et al., 2018; Krall et al., 2015; Schurz et al., 2014)), as well as regions more commonly known for sensory perception (e.g. temporal pole), memory (e.g. hippocampus), and language processing (e.g. precuneus). Hierarchical clustering based on task-based and task-free (resting state) functional connectivity profiles furthermore led to the definition of four activation clusters associated with increasingly complex cognitive functions ( visual-sensory – limbic – intermediate- higher-level) (Alcalá-López et al., 2018).

In a recent meta-analysis of functional magnetic resonance (fMRI) studies on higher-order social cognition (i.e. *empathy* and *ToM*), Schurz et al. (2021) grouped different socio-cognitive tasks based on neural activation patterns. The authors replicated the two priory proposed clusters underlying the more *cognitive* (i.e. *mentalizing*, *ToM*) (e.g. *medial prefrontal cortex* (mPFC), *anterior cingulate cortex* (ACC), *temporoparietal junction* (TPJ)) and *affective* social processes (i.e. *empathy*) (e.g. *inferior frontal gyrus* (IFG), *somatosensory cortex*, *motor cortex*, *temporal pole*, *insula*, *supramarginal gyrus*). In line with previous findings (e.g. Amodio & Frith, 2006; Schurz et al., 2021; Van Overwalle, 2009), brain areas involved in more cognitive social processes cluster along the cortical midline, thereby partially overlapping with *default mode network* (DMN; mPFC, TPJ) (Schurz et al., 2021). The authors further propose a third cluster active during more naturalistic tasks where both cognitive and affective social processes are required (Maliske et al., 2023; Schurz et al., 2021). Taken together, the complexity of social interaction seems to be reflected in the high number of different brain areas, subsumed into functionally specific networks and clusters, which need to work in concert to successfully perform social processes.

### 1.2. Structural connectivity

The dominant method for quantifying brain network organization is functional connectivity, typically operationalized as the co-variation of signaling activity (e.g. in fMRI) of two spatially separate brain regions. ~~Given that neither~~ However, co-varying activity neither ~~does not necessarily~~ impl~~y~~ies direct neural connection nor interaction.~~,~~ Therefore, researchers such as have highlighted the value of structural connectivity as a measure of functional brain organization (e.g. Forkel et al., 2022). The predominant assessment of structural connectivity is *diffusion weighted imaging (DWI)* data, an MRI method that provides information about the movement direction of water molecules ("*diffusion tensor*"). Various different metrics are used to evaluate the integrity of nerve fibers (*microstructure*), the orientation and shape/volume of WM tracts (*mesostructure*) and structural connectivity strength (*macrostructure*) (Van Hecke et al., 2015). The most common microstructural measures are *fractional anisotropy* (FA), the relative restriction of water movement in one direction, interpreted as a measure of overall WM integrity, and *mean diffusivity* (MD), the inverse of membrane density and a marker for vessel ruptures (Tromp, 2016; Van Hecke et al., 2016).

One approach for meaningful quantification of structural connectivity, is the comparison of microstructural WM properties in predefined anatomical locations using standardized brain maps (e.g. standard space, brain atlas) (i.e. *voxel-based analysis* (VBA)).

The second dominating approach is to reconstruct WM tracts based on the FA values *tract-based spatial statistics* (TBSS), often using information about the ROIs that are connected via the resulting *streamlines* (connectome-based approach) (Zhang et al., 2022). Connectome-based methods can be used i) to define tracts of interest for microstructural investigation, ii) investigate the shape of tracts or iii) provide macrostructural information on the *number of streamlines* connecting two regions of interest. While structural connectivity analysis has become a valuable tool for evaluating brain structure and organization, it is important to note that there are considerable limitations to the interpretability of each single metric (Jones & Cercignani, 2010). Therefore,~~ which is why more~~ recent research highlights the importance of combining multiple measures (Meisler et al., 2024; Radua, Borgwardt, et al., 2012; Radua, Grau, et al., 2014) and the benefit of novel, more fine-grained analysis techniques such as fixel-based analysis, bundle analytics, or advanced "multidimensional" diffusion MRI acquisitions (e.g. Chandio et al., 2020; Dhollander et al., 2021; O'Donnell et al., 2019).

### 1.3. Structural connectivity in social cognition

Although functional correlates of social cognitive performance dominate the field, scientific interest in associations between structural connectivity and social cognition has been increasing, as described in a systematic review by Wang et al. (2018). In this context, three types of associations have been established. Firstly, alterations in structural connectivity have been proposed as markers of and candidates for neurobiological mechanisms underlying socio-cognitive symptoms in clinical conditions (e.g. autism, schizophrenia) (Saito et al., 2018; Yamasaki et al., 2017). Most studies on these topics compare WM properties between clinical populations and healthy controls which has led to findings of increased WM volume in the right arcuate fasciculus and left inferior fronto-occipital and uncinate fasciculi in autistic subjects compared to controls (Radua et al., 2011).

In first efforts to investigate possible relations between schizophrenia and WM, a meta-analysis found significantly reduced WM integrity (FA) in the left frontal and temporal deep WM (Ellison-Wright & Bullmore, 2009). A more recent review highlights the relevance of microscale pathologies (neuroinflammation, demyelination, etc.), potentially disrupting local neural circuits in brain areas necessary for social cognition (Adraoui et al., 2023). Secondly, conditions associated with significant WM disruptions (e.g. fronto-temporal dementia, pediatric traumatic brain injury (TBI), brain tumors) are also associated with considerable socio-cognitive deficits. In this context, physical WM disruptions in the uncinate fasciculus (UF) after ischemic stroke or surgical tumor resection have been associated with lower *empathy* while TBI or tumor resection in the cingulum or arcuate fasciculus (AF) have been related to *mentalizing*/*ToM* deficits (Herbet, Lafargue, Moritz-Gasser, Menjot de Champfleur, et al., 2015; Oishi et al., 2015; Wang et al., 2018). Finally, *direct electrical stimulation* (DES) has been used to experimentally test causal effects of WM lesions on social cognition in vivo. Herbet, Lafargue, Moritz-Gasser, Bonnetblanc, et al. (2015) used this technique during awake surgery to create a “virtual lesion” in the axonal connections of the right inferior frontal cortex which resulted in significant deficits in *mentalizing*. In sum, the two-way association between socio-cognitive deficits and structural connectivity supports the idea that effective and unscathed WM connections might be an essential requisite for social cognition.

While an increasing number of single studies in various populations investigate associations of social cognition with structural connectivity and WM integrity, no quantitative transdiagnostic integration of the existing evidence has been provided. The only systematic review on the topic was published by Wang et al. in 2018 who condensed preceding literature regarding three networks of interest: face processing, mirroring/empathy, and mentalizing. According to the authors’ summary, empathy-related tasks were associated with the *inferior longitudinal fasciculus* (ILF), *inferior frontal occipital fasciculus* (IFOF) as well as the *anterior* *thalamic radiations* (ATR), *uncinate fasciculus* (UF) and *fornix* in the limbic system. *Mentalizing* was related to tracts connecting the amygdala including the *IFOF*, *ILF*, and *UF*. Regarding the study properties and the research landscape, the authors highlight the considerable heterogeneity of the identified results, evaluated diffusion metrics, WM tracts/ROIs and the study populations investigated by the 51 reviewed studies which poses major challenges to the integrability of the different results (Wang & Olson, 2018). An updated systematic review and meta-analytic integration of existing evidence has the potential to provide a comprehensive overview of the potential transdiagnostic associations between social cognition and structural connectivity as well as the most important WM tracts related to distinct socio-cognitive functions.

### 1.4. Research aims and hypotheses

This systematic review and meta-analysis (MA), aims to: (**RA1**) examine the overall relationship between continuous measures of social cognition and structural connectivity, (**RA2**) identify specific WM structures and locations associated with socio-cognitive processing, and (**RA3**) investigate important moderators including *socio-cognitive constructs*, *DTI metrics*, and *population/diagnosis-specific* effects. The research hypothesis (H) aimed to test with the performed analysis are as follows:

H1: Overall, diffusion tensor imaging derived metrics are correlated with continuous measures for socio-cognitive functions underlying social interaction.

H2: Associations between structural connectivity and socio-cognitive functions can are localized in specific brain regions.

H3: Specific white-matter structures are associated with distinct socio-cognitive functions.

H4: Associations are significantly moderated by the evaluated DTI-metric, the assessed socio-cognitive construct as well as population characteristics such as age and diagnosis.

### 1.5. Moderators

The following moderators for the relationships between social cognition and structural connectivity are assessed:

(1) measure for social cognition,
   a. socio-cognitive construct (grouped measurement tools)
(2) DTI analysis
   a. whole brain vs ROI analysis
      i. ROI/ WM tract of interest
   b. DTI metric
(3) population
   a. age group (<20, 20-55, >55) (e.g. Bethlehem et al., 2022; Sherin & Bartzokis, 2011)
   b. diagnosis (including the category ~~or~~ *healthy*)
   c. sex-ratio

## 2. Methods

### 2.1. Open science disclosures

This study is planned as a registered report, meaning the theoretical reasoning, hypotheses and study design are peer-reviewed via the PCI platform (peercommunityin.org). Data collection and analysis only start after reviewers agree to the rationale and methods. All procedures, materials, datasets, and analysis code are shared via an OSF repository [https://osf.io/3z4bf/?view_only=ca95cb2546604b6ab7da562fbee68d39].

### 2.2. Design

Firstly, relevant scientific databases are searched systematically with the primary effect size of interest being the correlation between *socio-cognitive measure* and *DTI metrics* (**RA1**). Consequently, design-related characteristics and outcomes of included studies are reviewed systematically to describe the research landscape, its frequently investigated *socio-cognitive constructs*, *DTI metrics*, and *populations*, and common methodologies. Additionally, variables relevant for study quality are reported including sample, imaging, and analysis specific characteristics. Moreover, risk of bias in primary studies is assessed using the RoBANS 2 scales (Seo et al., 2023) as well as a rating scheme of relevant study characteristics proposed by Khalil et al. (2022).

Subsequently, three levels of meta-analyses are preformed (for details see section 2.7):

**MA1)** To examine the overall relationship between metric measures of social cognition and structural connectivity (**RA1**) correlations in all identified studies are meta-analyzed. Thereby, ~~–across~~studies investigating different *socio-cognitive constructs*, *DTI-metrics*, *populations/diagnoses* and *methodologies* are integrated and the study variability is accounted for using sub-group analysis and meta-regression.~~.~~

**MA2)** To identify WM locations with the strongest associations with socio-cognitive measures (**RA2**), a neuroimaging meta-analysis of whole brain studies is performed.

**MA3)** To meta-analyze tract-specific results (**RA2**), ROI studies of specific white matter tracts are integrated in separate effect-size meta-analyses to assess tract-specific associations.

Additionally, meta-regression and subgroup analysis is performed in each meta-analysis to investigate important *construct*-, *DTI metric* and *population-related* moderators (**RA3**).

### 2.3. Search strategy

The electronical databases PubMed, Scopus and Web of Science are ~~used to~~ searched for literature containing at least one of the keywords for social cognition (following the concepts proposed by ~~(~~Happé et al.~~,~~ (2017)) ~~-~~and one for structural connectivity in the title, abstract or keywords. Where possible, the results are filtered for only human studies and empirical research articles in English, German or Spanish language. Based on previous research in the field (Schurz et al., 2021; Wang et al., 2018), the search string is set as follows:

("social cogniti*~~on~~" OR "social skills" OR "social funct*~~ioning~~" OR "social process*~~ing~~" OR "socio-cognitive process*~~ing~~" OR “social knowledge” OR “social motivat*” OR “social learning” OR "emotion recognition" OR "affect recognition" OR “social percept*” OR

"social affect" OR "empath*~~y~~" OR "socio-affective process*~~ing~~" OR "affect sharing" OR "emotion sharing" OR "compassion" OR
"theory of mind" ~~OR "ToM"~~ OR "mind reading" OR "mind-reading" OR "perspective taking" OR "mentaliz*~~ing~~" OR "mentalis*~~ing~~" OR "cognitive affect" OR "affective cogniti*~~on~~" OR "social decision-making")
AND
("structural connect*~~ivity~~" OR "white matter" ~~OR "structural connectome" OR "diffusion weighted"~~ OR "diffusivity~~on~~" OR "tensor" OR "DTI" OR ~~"diffusivity" OR~~ "anisotropy" OR "tractography" OR "tractometry" OR "tract-based spatial statistics" OR "TBSS" ~~OR "tracts"~~ OR "fasciculus" OR "nerve fibers" OR "axons")

Variations regarding the spelling and grammatical form of the original keywords are included. ~~Moreover~~Additionally, the reference list of included articles will be searched and articles citing included articles (forward-search) will be screened. Finally, for the neuroimaging meta-analysis, authors of included studies will be inquired about potential additional statistical maps of correlations between structural connectivity metrics and socio-cognitive measures that are not available within the encountered publications.

### 2.4. Inclusion and exclusion criteria

All empirical neuroimaging studies on humans that report correlations of a metric measure of social cognition with a DTI derived metric of structural connectivity will be eligible for inclusion in the meta-analysis. Since the construct of interest is social cognition in humans, studies will be excluded if:

(1) Not reporting a metric measure of social cognition

(2) Using purely emotion- or perception-related measures without a social component (e.g., stimulus materials that do not explicitly feature other people, such as car accidents, or viewing pictures of neutral facial expressions)

(3) not performing correlations between metric measures of structural connectivity and social cognition

(4) exclusively performing group comparisons

(5) manipulating target variables (social cognition, structural connectivity) before the assessment

(6) investigated species are not humans

For methodological reasons, studies are excluded if:

(7) failing to report relevant details on the defined moderators unless they can be obtained from authors

(8) the assessment of structural connectivity is not DTI-based

(9) not written in English, German, or Spanish unless all necessary information is provided in English or can be obtained from authors

(10) not having undergone peer-review (except for ~~primary data~~additional statistical maps by authors of included studies)

A list of excluded studies along with the corresponding reason for exclusion is provided in the supplementary material.

## 2.5. Screening procedure

The results from the different databases are compiled and deduplicated using evaluated tools (e.g ASySD) (Hair et al., 2023). Following the PRISMA guidelines (Page et al., 2021), the resulting articles are first screened for suitability based on title and abstract, whereby all articles not fulfilling the predefined criteria are excluded. In any case, the reason for exclusion is recorded. For all remaining articles, the full text is screened to assess eligibility and to evaluate study characteristics. *Figure 1* is used to document the search procedure. All steps of the screening procedure are conducted by the first author as well as a second researcher. Inter-rater coherence is evaluated by calculating Cohen's Kappa.

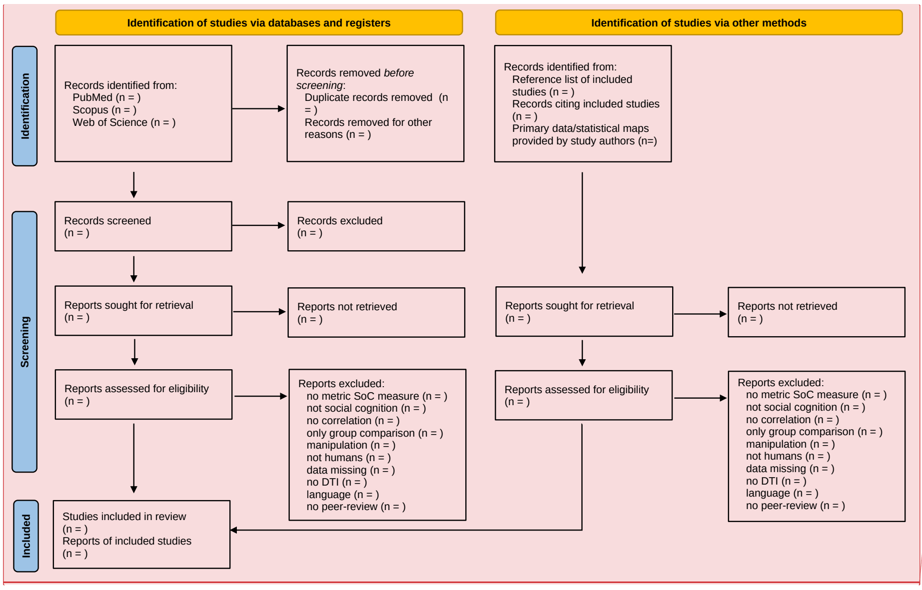
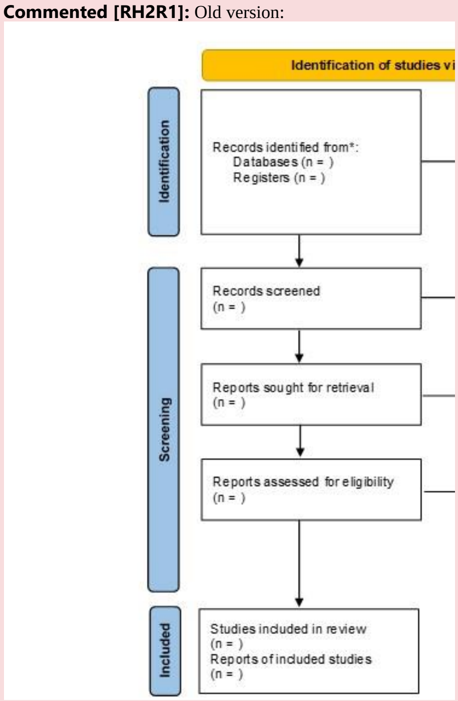



*Figure 1*. Meta-analysis flow diagram in accordance with the PRISMA guidelines (Page et al., 2021)

*Note.* This figure is provided by the PRISMA website (https://www.prisma-statement.org/prisma-2020-flow-diagram)

**Commented [RH1]:** Updated version of figure 1f

**Commented [RH2R1]:** Old version:




## 2.6. **Coding**

For all included articles, information on the announced moderators is recorded following the structure of "coding_sheet_template", which is available in the OSF project folder [https://osf.io/gec34]. The recorded variables include information on sample demographics (*age group*, *sex-ratio*, *language*, *population/diagnosis*, *sample size*), imaging acquisition (*scanner*, *b-value*, *DWI resolution*, etc.), analysis procedure (*VBA vs. TBSS*, *WB vs. ROI*, *threshold*, *standard space*, *brain atlas*), the investigated socio-cognitive construct (*psychological assessment*, *mean* and *sd* for measure, *category of construct*), and study outcomes (*effect size for correlation*, *p-value*, *activation intensity*). Thereby, psychological measures derived from different assessment tools are grouped by the socio-cognitive constructs/processes they aim to assess (Happé et al., 2017). The grouping is performed by the research team which includes neuroscientific and clinical psychological experts on social cognition. For studies investigating multiple samples (e.g. patients vs. healthy controls), samples with differing diagnoses will be coded separately. If multiple groups are reported for one diagnosis, the values are combined to receive only one *mean* and *sd* per population. If multiple studies report on the same sample, the larger sampled study is used for the analysis. If one study calculates multiple correlations on different tracts or with various metrics, these are coded separately, and the dependencies are accounted for via study IDs. All available measures for the variables of interest are recorded, however, the prioritized measure of interest is FA, the *mean* and *sd* of which are requested from the authors in case they are not reported.

### 2.7. **Analysis**

Due to the anticipated methodological heterogeneity of preceding literature, a series of meta-analyses (**MA1-3**) is conducted. Figure 2 is a flow chart, depicting the meta-analytic procedure. The minimum number of studies for the performance of a subgroup MA is $n$=5. The specifics for each level of analysis are described in detail below.

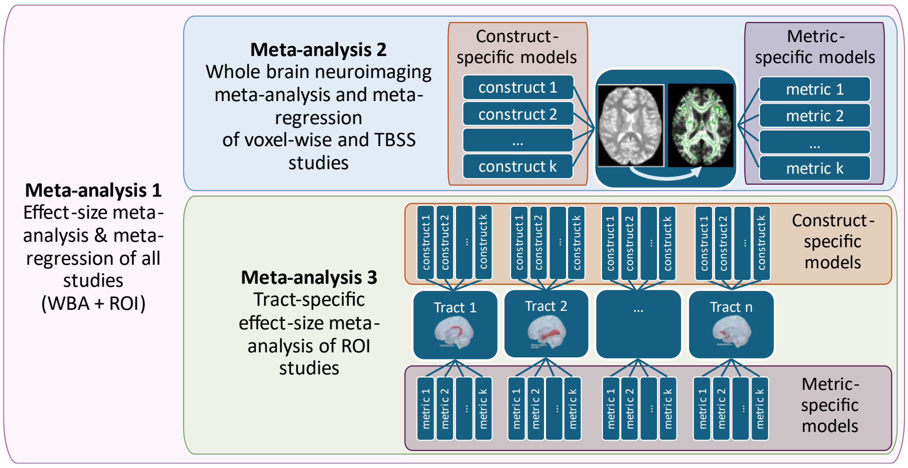



*Figure 2*. Flow chart for sequence of meta-analyses.

*Note*. Three types of meta-analyses are performed, each including distinct subsets of the retrieved data. MA1 focuses on effect-sizes and will include WB as well as ROI studies, MA2 is a neuroimaging study, including only whole-brain data. MA3 is a again a effect size study, meta-analyzing studies with equal tracts of interest. For MA2 and MA3, additional meta-analyses are calculated for *socio-cognitive constructs* and *DTI metrics* analyzed by a minimum of 5 studies to get more thorough insights into interactions and moderation.

### *2.7.1. MA1: Global correlation between social cognition and structural connectivity*

For **research aim 1** (**RA1**), an effect size meta-analysis for the correlation of measures for social cognition and structural connectivity across all studies is calculated. The effect-size of interest is the correlation between socio-cognitive performance and a WM metric, which is standardized to Cohen’s d.

The Robust Bayesian Meta-analysis (RoBMA) method proposed by Maier et al. (2023) is applied, which uses model-averaging to incorporate various prior assumptions and publication bias into the analysis. Benefits of this approach include the aptness for small sample sizes, consideration of various assumptions and, as a Bayesian method, the ability to provide evidence both for and against the null- and alternative hypothesis (Bartoš et al., 2022). The analysis is conducted in R using the RoBMA-package provided by Bartós (2023). Following the authors' recommendations, effect-sizes are converted to Cohen's d and standard normal priors (Normal (0,1)) ~~with a mean of 0~~ are used for effect size. Inverse-gamma distribution is used for between-study heterogeneity $\tau$ (InvGamma(shape = 1, scale = 0,15))(Maier et al., 2023).~~.~~ In case of ~~significant~~ evidence for study heterogeneity and moderation by a specific factor and if more than 5 studies are available, separate analyses for different diffusion metrics and socio-cognitive constructs are performed. Regarding diffusion metrics, the preferred measure, which is attempted to be retrieved from all studies and will be prioritized over other metrics is FA. In these smaller models, comparability of results is prioritized over inclusivity and power.

#### 2.7.2. *Meta-regression and sub-group analysis*

To investigate the impact of the various defined moderators (*socio-cognitive construct, diffusion metric, population/diagnosis, age group, sex-ratio, WB vs. ROI*) on the correlation effect, ~~a~~ meta-regression and sub-group analysis ~~is~~ are performed. To this end, the meta-regression function of the RoBMA method by (Bartoš et al., 2023) is used, which calculates Bayes Factors (BF) indicating evidence for or against moderation effects. To perform this analysis, all continuous moderators are mean-centered and scaled. Scaled orthonormal contrasts are used to calculate the difference from the grand mean for each level of categorical variables. For the sub-group analysis, Savage Dickey density ratios are used to calculate Bayes factors for each level of the categorical moderators incorporated in the model (*socio-cognitive constructs, DTI-metrics, population/diagnosis, age groups, WB vs. ROI*) (Bartoš et al., 2023). Following the authors' recommendations, normal priors with *mean*=0 and *sd*=0.25 are used for the mean difference contrast in case of categorical moderators and for the standardized meta-regression coefficients in case of continuous moderators. Sensitivity analysis testing different priors will be performed post hoc using ~~(~~Höfler~~, (~~(2021) shiny app for Bayesian Regions of Evidence analysis (*Bayesian Regions of Evidence*, n.d.). Study-IDs are used to account for the dependencies between multiple correlations calculated between different measures within one study (FBartos, 2023). Patient and control groups are handled as separate samples and assumed to be independent.

~~*2.7.2.1.*~~ ~~Sub-group analysis~~

~~Consequently, sub-group analysis is performed for categorical moderators (*socio-cognitive constructs, DTI-metrics, population/diagnosis, age groups, WB vs. ROI*) to investigate category-specific correlations effects. Again, the RoBMA method is applied, which uses Savage-Dickey density ratios to calculate Bayes factors for each moderator level incorporated in the model (Bartoš et al., 2023).~~

Formatted: Normal

### 2.7.3. *MA2: White matter locations most strongly associated with social cognition*

To identify brain locations at which structural connectivity is most strongly associated with social cognition (**RA2**), studies using whole-brain (WB) analysis are integrated in a coordinate-based neuroimaging meta-analysis. The effect-size of interest is the location-specific correlation between social cognition and structural connectivity measures.

As analysis software, seed-based *d* mapping (SDM) software is used, which can integrate whole brain (WB) maps from VBA with peak values reported in standard space (Radua, Rubia, et al., 2014). While TBSS overcomes many disadvantages of brain map standardization by creating subject and sample specific tract-templates, this comes with reduced comparability and integrability of result. To still be able to integrate all WB (VBA and TBSS) data, VBA have to be down-sampled to TBSS templates as proposed by Peters et al., (2012). Additionally, if more than 5 studies are available for any other diffusion metric, those are analyzed separately. The preferred measure, which is attempted to be retrieved from all studies, is FA and a separate analysis will be run with only studies investigating correlations between FA and social cognition. In this approach, comparability is prioritized over inclusivity. Jack-knife sensitivity analysis is used to control for the robustness of the model. Following the developers' recommendations, an uncorrected main threshold of $p = 0.005$ is used to optimally balance sensitivity and specificity to the corrected p-value = 0.05 (0.025) in original studies (Radua, Mataix-Cols, et al., 2012). Where possible, family-wise error (FEW) correction is performed using a significance threshold of $p = 0.05$. The minimum cluster size is of 10 voxels. Results are reported in MNI space (Albajes-Eizagirre et al., 2019).

#### *2.7.3.1. Meta-regression and sub-group analysis*

The continuous moderator sex-ratio is introduced into the model to control for sex-specific effects. The categorical moderators *diffusion metric, socio-cognitive construct, age group* and *population/diagnosis* are integrated in the model and analyzed using linear contrasts. For category-levels with at least 5 datasets, subgroup-specific models are calculated to investigate population-, construct and analysis-specific effects and their interactions (**RA3**).

### *2.7.4. MA3: Tract-specific correlations of structural connectivity and social cognition*

For **RA2,** studies focusing on single WM structures or brain regions rather than performing WB analyses are grouped per tract. Like in the first meta-analysis (**MA1**), a correlational effect-size meta-analysis using RoBMA is performed for locations investigated by at least 5 studies. First, lateralized and bilateral analysis are pooled into one analysis per tract. Following the same pipeline as **MA1**, meta-regression and sub-grouping is performed to investigate metric-, population-, and construct-specific effects (**RA3**). In addition to the moderators in **MA1**, effects of *laterality* (right, left, bi-lateral) are included as an additional moderator.

### *2.7.5. Publication Bias*

For all meta-analyses, funnel plots are created for visual examination of publication bias. Moreover, Eggers test is used with a significance threshold of .05 (Egger et al., 1997). For **MA1** and **MA3**, publication bias is addressed via model averaging including PET and PEESE models. BFs for between-study heterogeneity are reported (Maier et al., 2023).

| Question | Hypothesis | Sampling plan | Analysis Plan | Interpretation given different outcomes | Theory that could be shown wrong by the outcomes |
|---|---|---|---|---|---|
| Are diffusion metrics for structural connectivity and white matter associated with socio-cognitive functions? | Overall, diffusion tensor imaging derived metrics are correlated with continuous measures for socio-cognitive functions underlying social interaction. | A systematic literature review is conducted to identify studies assessing correlations between continuous diffusion-based metrics for structural connectivity and socio-cognitive abilities in humans. Based on a preceding review (Wang et al., 2018) a minimum sample of n=50 studies are expected. | Due to its suitability for smaller sample sizes and the inclusion of multiple moderators, the Robust Bayesian Meta-analysis (RoBMA) method is applied (Maier et al., 2023), which uses model-averaging to account for various prior assumptions as well as publication bias. Following the authors' recommendations, effect-sizes are converted to Cohen's d and standard normal (prior: Normal(0, 1))~~priors with a mean of 0 are used for the effect size~~. Normal priors with *mean* 0 and *sd* of 0.25 are used for the moderators and inverse-gamma distribution for between-study heterogeneity (τ: InvGamma(shape = 1, scale = 0,15) (Maier et al., 2023). | Based on the recommendations by Lee and Wagenmakers (2014, p.105) Bayes Factors of 0-3 or 1/3 are interpreted as anecdotal, 3-10 or 1/3-1/10 as moderate and >10 or <1/10 as strong evidence for/against the hypothesized effects. | Strong evidence ~~against the H1~~in favor of the null-hypothesis would indicate a lack of the hypothesized correlation between structural connectivity and socio-cognitive abilities. A lack of strong effects could arise from inadequacy of the chosen metrics, deficient power or excessive heterogeneity among the analyzed studies. |

| | | | | | |
|---|---|---|---|---|---|
| | | | Additionally, the meta-regression function of the RoBMA method by (Bartoš et al., 2023) is used to investigate the potential difference of the association depending on the defined moderators: *socio-cognitive construct*, *diffusion metric*, *WB vs. ROI*, *population*, *age group*, *sex-ratio*. In case of ~~significant~~ evidence for moderation, separate models are calculated for constructs and *DTI metric*s analyzed by a minimum of 5 studies. For the subgroup MAs, the same pipeline as in the main MA is used, only omitting the grouping moderator (*DTI metric*/*construct*). | | |
| Where in the brain does structural connectivity/white matter integrity show the strongest associations with | Associations between structural connectivity and socio-cognitive functions can are localized in specific brain | See H1. For this neuro-imaging meta-analysis, only studies providing voxel- and TBSS-based whole brain | Seed-based *d* mapping (SDM) software is used, which can integrate whole brain (WB) maps from VBA and TBSS outcomes with peak values reported in | Following the developers' recommendations, an uncorrected main threshold of $p = 0.005$ is used to optimally balance sensitivity and specificity | If no locations of white matter connectivity show relevant correlations with socio-cognitive functions, this indicates the lack of |

| | | | | | |
|---|---|---|---|---|---|
| socio-cognitive functions? | regions.~~Prior evidence can be integrated into brain maps identifying the areas where diffusion metrics most strongly correlate with socio-cognitive functions.~~ | data can be included. | standard space (Radua, Rubia, et al., 2014). If more than 5 studies are available for any *diffusion metric* (e.g. FA, MD, etc.) or *socio-cognitive construct*, additional separate analyses are performed. Jack-knife sensitivity analysis is used to account for the robustness of the model. The moderators *socio-cognitive construct*, *diffusion metric*, *population*, *age group*, *and sex-ratio* are integrated as linear contrasts or continuous moderators in the model to investigate *construct-*, *DTI metric-*, *and population-specific* effects. | to the corrected p-value = 0.05 (0.025) in original studies (Radua, Mataix-Cols, et al., 2012). Where possible, family-wise error (FEW) correction is performed using a significance threshold of $p = 0.05$. The minimum cluster size is of 10 voxels. Results are reported in MNI space (Albajes-Eizagirre et al., 2019). Correlations above Cohen's $d = 0.1$ are considered meaningful. | converging evidence for a clear association between investigated diffusion metrics and the assessed socio-cognitive measure. Lacking evidence could also be caused by deficient power, high heterogeneity and coarseness of diffusion metrics. |
| Are different white matter structures differentially associated with socio-cognitive functions? | Specific white-matter structures are associated with distinct socio-cognitive functions. | See hypothesis 1 | In addition to the sub-group analyses and meta-regression results in the prior investigations, separate effect-size meta-analyses are conducted for all white matter tracts | See hypothesis 1 | ~~Strong e~~Evidence ~~against the H1~~ in favor of the null-hypothesis would indicate a lack of the hypothesized correlation between |

| | | | | | |
|---|---|---|---|---|---|
| | | | investigated by a minimum of 5 studies. The same RobMA method as in study 1 is applied with the additional moderator of *laterality* since studies examining tracts bi- and uni-laterally are pooled. | | specific white matter tracts and distinct socio-cognitive constructs. Given MA1 results indicate a global association, insignificant results in ROI studies would point toward a less localized association. In contrast, evidence for association in specific structures without evidence for global associations would support the idea of only certain white matter structures being relevant for social cognition. A lack of strong effects could arise from inadequacy of the chosen metrics, deficient power or excessive heterogeneity among the analyzed studies. |

| | | | | | |
|---|---|---|---|---|---|
| Which study parameters are to be considered important moderators for potential associations between structural connectivity and social cognition? | Associations between structural connectivity and socio-cognitive functions are localized in specific brain regions. | See hypothesis 1 | Meta-regression and subgroup analysis is performed in each of the analyses described above. Moreover, separate tract, metric and construct specific meta-analyses are performed wherever a minimum of 5 studies is available to assess moderation and interaction effects in more homogenous samples. | See hypothesis 1 and 2 | Evidence in favor of the null-hypothesis (no moderation) would indicate that the association between DTI-metrics and social cognition does not depend on the specific metric used, the SoC construct assessed or the analyzed tract, nor that the association differs between distinct populations. |

## References

Adraoui, F. W., Douw, L., Martens, G. J. M., & Maas, D. A. (2023). Connecting Neurobiological Features with Interregional Dysconnectivity in Social-Cognitive Impairments of Schizophrenia. In *International Journal of Molecular Sciences* (Vol. 24, Issue 9). https://doi.org/10.3390/ijms24097680

Albajes-Eizagirre, A., Solanes, A., Fullana, M. A., Ioannidis, J. P. A., Fusar-Poli, P., Torrent, C., Sol&#233, B., Bonn&#237, C. M., n, Vieta, E., Mataix-Cols, D., & Radua, J. (2019). Meta-analysis of Voxel-Based Neuroimaging Studies using Seed-based d Mapping with Permutation of Subject Images (SDM-PSI). *JoVE (Journal of Visualized Experiments)*, *153*, e59841. https://doi.org/10.3791/59841

Alcalá-López, D., Smallwood, J., Jefferies, E., Van Overwalle, F., Vogeley, K., Mars, R. B., Turetsky, B. I., Laird, A. R., Fox, P. T., Eickhoff, S. B., & Bzdok, D. (2018). Computing the Social Brain Connectome Across Systems and States. *Cerebral Cortex*, *28*(7), 2207–2232. https://doi.org/10.1093/cercor/bhx121

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews Neuroscience*, *7*(4), 268–277. https://doi.org/10.1038/nrn1884

Bartós, F. (2023). *RoBMA: Robust Bayesian Meta-Analysis*. https://fbartos.github.io/RoBMA/

Bartoš, F., Maier, M., Quintana, D. S., & Wagenmakers, E.-J. (2022). Adjusting for Publication Bias in JASP and R: Selection Models, PET-PEESE, and Robust Bayesian Meta-Analysis. *Advances in Methods and Practices in Psychological Science*, *5*(3), 25152459221109259. https://doi.org/10.1177/25152459221109259

Bartoš, F., Maier, M., Stanley, T. D., & Wagenmakers, E.-J. (2023). *Robust Bayesian Meta-Regression—Model-Averaged Moderation Analysis in the Presence of Publication Bias*. OSF. https://doi.org/10.31234/osf.io/98xb5

*Bayesian Regions of Evidence*. (n.d.). Retrieved December 20, 2024, from https://htaor.shinyapps.io/shinyroe/

Beer, J. S., & Ochsner, K. N. (2006). Social cognition: A multi level analysis. *Brain Research*, *1079*(1), 98–105. https://doi.org/10.1016/j.brainres.2006.01.002

Bethlehem, R. a. I., Seidlitz, J., White, S. R., Vogel, J. W., Anderson, K. M., Adamson, C., Adler, S., Alexopoulos, G. S., Anagnostou, E., Areces-Gonzalez, A., Astle, D. E., Auyeung, B., Ayub, M., Bae, J., Ball, G., Baron-Cohen, S., Beare, R., Bedford, S. A., Benegal, V., … Alexander-Bloch, A. F. (2022). Brain charts for the human lifespan. *Nature*, *604*(7906), 525–533. https://doi.org/10.1038/s41586-022-04554-y

Chandio, B. Q., Risacher, S. L., Pestilli, F., Bullock, D., Yeh, F.-C., Koudoro, S., Rokem, A., Harezlak, J., & Garyfallidis, E. (2020). Bundle analytics, a computational framework for investigating the shapes and profiles of brain pathways across populations. *Scientific Reports*, *10*(1), 17149. https://doi.org/10.1038/s41598-020-74054-4

Dhollander, T., Clemente, A., Singh, M., Boonstra, F., Civier, O., Duque, J. D., Egorova, N., Enticott, P., Fuelscher, I., Gajamange, S., Genc, S., Gottlieb, E., Hyde, C., Imms, P., Kelly, C., Kirkovski, M., Kolbe, S., Liang, X., Malhotra, A., … Caeyenberghs, K. (2021). Fixel-based Analysis of Diffusion MRI: Methods, Applications, Challenges and Opportunities. *NeuroImage*, *241*, 118417. https://doi.org/10.1016/j.neuroimage.2021.118417

Egger, M., Smith, G. D., & Phillips, A. N. (1997). Meta-analysis: Principles and procedures. *BMJ*, *315*(7121), 1533–1537. https://doi.org/10.1136/bmj.315.7121.1533

Ellison-Wright, I., & Bullmore, E. (2009). Meta-analysis of diffusion tensor imaging studies in schizophrenia. *Schizophrenia Research*, *108*(1–3), 3–10. https://doi.org/10.1016/j.schres.2008.11.021

FBartos. (2023). *RoBMA: An R Package for Risk of Bias Assessment in Meta-Analysis*. https://rdrr.io/github/FBartos/RoBMA/

Forkel, S. J., Friedrich, P., Thiebaut de Schotten, M., & Howells, H. (2022). White matter variability, cognition, and disorders: A systematic review. *Brain Structure & Function*, *227*(2), 529–544. https://doi.org/10.1007/s00429-021-02382-w

Hair, K., Bahor, Z., Macleod, M., Liao, J., & Sena, E. S. (2023). The Automated Systematic Search Deduplicator (ASySD): A rapid, open-source, interoperable tool to remove duplicate citations in biomedical systematic reviews. *BMC Biology*, *21*(1), 189. https://doi.org/10.1186/s12915-023-01686-z

Happé, F., Cook, J. L., & Bird, G. (2017). The Structure of Social Cognition: In(ter)dependence of Sociocognitive Processes. *Annual Review of Psychology*, *68*(Volume 68, 2017), 243–267. https://doi.org/10.1146/annurev-psych-010416-044046

Happé, F., & Frith, U. (2014). Annual Research Review: Towards a developmental neuroscience of atypical social cognition. *Journal of Child Psychology and Psychiatry*, *55*(6), 553–577. https://doi.org/10.1111/jcpp.12162

Herbet, G., Lafargue, G., Moritz-Gasser, S., Bonnetblanc, F., & Duffau, H. (2015). Interfering with the neural activity of mirror-related frontal areas impairs mentalistic inferences. *Brain Structure and Function*, *220*(4), 2159–2169. https://doi.org/10.1007/s00429-014-0777-x

Herbet, G., Lafargue, G., Moritz-Gasser, S., Menjot de Champfleur, N., Costi, E., Bonnetblanc, F., & Duffau, H. (2015). A disconnection account of subjective empathy impairments in diffuse low-grade glioma patients. *Neuropsychologia*, *70*, 165–176. https://doi.org/10.1016/j.neuropsychologia.2015.02.015

Höfler, M. (2021). *Bayesian regions of evidence (for normal distributions)*. OSF. https://doi.org/10.31234/osf.io/mg23h

Jones, D. K., & Cercignani, M. (2010). Twenty-five pitfalls in the analysis of diffusion MRI data. *NMR in Biomedicine*, *23*(7), 803–820. https://doi.org/10.1002/nbm.1543

Kanske, P. (2018). The social mind: Disentangling affective and cognitive routes to understanding others. *Interdisciplinary Science Reviews*, *43*(2), 115–124. https://doi.org/10.1080/03080188.2018.1453243

Kennedy, D. P., & Adolphs, R. (2012). The social brain in psychiatric and neurological disorders. *Trends in Cognitive Sciences*, *16*(11), 559–572. https://doi.org/10.1016/j.tics.2012.09.006

Khalil, M., Hollander, P., Raucher-Chéné, D., Lepage, M., & Lavigne, K. M. (2022). Structural brain correlates of cognitive function in schizophrenia: A meta-analysis. *Neuroscience & Biobehavioral Reviews*, *132*, 37–49. https://doi.org/10.1016/j.neubiorev.2021.11.034

Krall, S. C., Rottschy, C., Oberwelland, E., Bzdok, D., Fox, P. T., Eickhoff, S. B., Fink, G. R., & Konrad, K. (2015). The role of the right temporoparietal junction in attention and social interaction as revealed by ALE meta-analysis. *Brain Structure & Function*, *220*(2), 587–604. https://doi.org/10.1007/s00429-014-0803-z

Krendl, A. C., & Betzel, R. F. (2022). Social cognitive network neuroscience. *Social Cognitive and Affective Neuroscience*, *17*(5), 510–529. https://doi.org/10.1093/scan/nsac020

Lee, M. D., & Wagenmakers, E.-J. (2014). *Bayesian Cognitive Modeling: A Practical Course*. Cambridge University Press. https://doi.org/10.1017/CBO9781139087759

Maier, M., Bartoš, F., & Wagenmakers, E.-J. (2023). Robust Bayesian meta-analysis: Addressing publication bias with model-averaging. *Psychological Methods*, *28*(1), 107–122. https://doi.org/10.1037/met0000405

Maliske, L. Z., Schurz, M., & Kanske, P. (2023). Interactions within the social brain: Co-activation and connectivity among networks enabling empathy and Theory of Mind. *Neuroscience and Biobehavioral Reviews*, *147*(September 2022), 105080. https://doi.org/10.1016/j.neubiorev.2023.105080

Meisler, S. L., Kubota, E., Grotheer, M., Gabrieli, J. D. E., & Grill-Spector, K. (2024). A practical guide for combining functional regions of interest and white matter bundles. *Frontiers in Neuroscience*, *18*. https://doi.org/10.3389/fnins.2024.1385847

O'Donnell, L. J., Daducci, A., Wassermann, D., & Lenglet, C. (2019). Advances in Computational and Statistical Diffusion MRI. *NMR in Biomedicine*, *32*(4), e3805. https://doi.org/10.1002/nbm.3805

Oishi, K., Faria, A. V., Hsu, J., Tippett, D., Mori, S., & Hillis, A. E. (2015). Critical role of the right uncinate fasciculus in emotional empathy. *Annals of Neurology*, *77*(1), 68–74. https://doi.org/10.1002/ana.24300

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *The BMJ*, *372*, n71. https://doi.org/10.1136/bmj.n71

Peters, B. D., Szeszko, P. R., Radua, J., Ikuta, T., Gruner, P., DeRosse, P., Zhang, J.-P., Giorgio, A., Qiu, D., Tapert, S. F., Brauer, J., Asato, M. R., Khong, P. L., James, A. C., Gallego, J. A., & Malhotra, A. K. (2012). White Matter Development in Adolescence:

Diffusion Tensor Imaging and Meta-Analytic Results. *Schizophrenia Bulletin*, *38*(6), 1308–1317. https://doi.org/10.1093/schbul/sbs054

Radua, J., Borgwardt, S., Crescini, A., Mataix-Cols, D., Meyer-Lindenberg, A., McGuire, P. K., & Fusar-Poli, P. (2012). Multimodal meta-analysis of structural and functional brain changes in first episode psychosis and the effects of antipsychotic medication. *Neuroscience & Biobehavioral Reviews*, *36*(10), 2325–2333. https://doi.org/10.1016/j.neubiorev.2012.07.012

Radua, J., Grau, M., van den Heuvel, O. A., Thiebaut de Schotten, M., Stein, D. J., Canales-Rodríguez, E. J., Catani, M., & Mataix-Cols, D. (2014). Multimodal Voxel-Based Meta-Analysis of White Matter Abnormalities in Obsessive–Compulsive Disorder. *Neuropsychopharmacology*, *39*(7), 1547–1557. https://doi.org/10.1038/npp.2014.5

Radua, J., Mataix-Cols, D., Phillips, M. L., El-Hage, W., Kronhaus, D. M., Cardoner, N., & Surguladze, S. (2012). A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *European Psychiatry*, *27*(8), 605–611. https://doi.org/10.1016/j.eurpsy.2011.04.001

Radua, J., Rubia, K., Canales-Rodríguez, E. J., Pomarol-Clotet, E., Fusar-Poli, P., & Mataix-Cols, D. (2014). Anisotropic Kernels for Coordinate-Based Meta-Analyses of Neuroimaging Studies. *Frontiers in Psychiatry*, *5*, 13. https://doi.org/10.3389/fpsyt.2014.00013

Radua, J., Via, E., Catani, M., & Mataix-Cols, D. (2011). Voxel-based meta-analysis of regional white-matter volume differences in autism spectrum disorder versus healthy controls. *PSYCHOLOGICAL MEDICINE*, *41*(7), 1539–1550. https://doi.org/10.1017/S0033291710002187

Renfrew, C., Frith, C., Malafouris, L., & Frith, C. D. (2008). Social cognition. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1499), 2033–2039. https://doi.org/10.1098/rstb.2008.0005

Saito, Y., Kubicki, M., Koerte, I., Otsuka, T., Rathi, Y., Pasternak, O., Bouix, S., Eckbo, R., Kikinis, Z., von Hohenberg, C. C., Roppongi, T., Del Re, E., Asami, T., Lee, S.-H., Karmacharya, S., Mesholam-Gately, R. I., Seidman, L. J., Levitt, J., McCarley, R. W., … Niznikiewicz, M. A. (2018). Impaired white matter connectivity between regions containing mirror neurons, and relationship to negative symptoms and social cognition, in patients with first-episode schizophrenia. *BRAIN IMAGING AND BEHAVIOR*, *12*(1), 229–237. https://doi.org/10.1007/s11682-017-9685-z

Santomauro, D. F., Herrera, A. M. M., Shadid, J., Zheng, P., Ashbaugh, C., Pigott, D. M., Abbafati, C., Adolph, C., Amlag, J. O., Aravkin, A. Y., Bang-Jensen, B. L., Bertolacci, G. J., Bloom, S. S., Castellano, R., Castro, E., Chakrabarti, S., Chattopadhyay, J., Cogen, R. M., Collins, J. K., … Ferrari, A. J. (2021). Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *The Lancet*, *398*(10312), 1700–1712. https://doi.org/10.1016/S0140-6736(21)02143-7

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: A meta-analysis of functional brain imaging studies. *Neuroscience & Biobehavioral Reviews*, *42*, 9–34. https://doi.org/10.1016/j.neubiorev.2014.01.009

Schurz, M., Radua, J., Tholen, M. G., Maliske, L., Margulies, D. S., Mars, R. B., Sallet, J., & Kanske, P. (2021). Toward a hierarchical model of social cognition: A neuroimaging meta-analysis and integrative review of empathy and theory of mind. *Psychological Bulletin*, *147*(3), 293–327. https://doi.org/10.1037/bul0000303

Seo, H.-J., Kim, S. Y., Lee, Y. J., & Park, J.-E. (2023). RoBANS 2: A Revised Risk of Bias Assessment Tool for Nonrandomized Studies of Interventions. *Korean Journal of Family Medicine*, *44*(5), 249–260. https://doi.org/10.4082/kjfm.23.0034

Sherin, J. E., & Bartzokis, G. (2011). Human Brain Myelination Trajectories Across the Life Span: Implications for CNS Function and Dysfunction. In E. J. Masoro & S. N. Austad (Eds.), *Handbook of the Biology of Aging (Seventh Edition)* (pp. 333–346). Academic Press. https://doi.org/10.1016/B978-0-12-378638-8.00015-4

Tromp, D. (2016). DTI Scalars (FA, MD, AD, RD)—How do they relate to brain structure? *The Winnower*, *3*. https://doi.org/10.15200/winn.146119.94778

Van Hecke, W., Emsell, L., & Sunaert, S. (2015). Diffusion Tensor Imaging: A Practical Handbook. In *Diffusion Tensor Imaging: A Practical Handbook*. https://doi.org/10.1007/978-1-4939-3118-7

Van Hecke, W., Leemans, A., & Emsell, L. (2016). DTI Analysis Methods: Voxel-Based Analysis. In W. Van Hecke, L. Emsell, & S. Sunaert (Eds.), *Diffusion Tensor Imaging: A Practical Handbook* (pp. 183–203). Springer. https://doi.org/10.1007/978-1-4939-3118-7_10

Van Overwalle, F. (2009). Social cognition and the brain: A meta-analysis. *Human Brain Mapping*, *30*(3), 829–858. https://doi.org/10.1002/hbm.20547

Wang, Y., Metoki, A., Alm, K. H., & Olson, I. R. (2018). White matter pathways and social cognition. *NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS*, *90*, 350–370. https://doi.org/10.1016/j.neubiorev.2018.04.015

Wang, Y., & Olson, I. R. (2018). The Original Social Network: White Matter and Social Cognition. *TRENDS IN COGNITIVE SCIENCES*, *22*(6), 504–516. https://doi.org/10.1016/j.tics.2018.03.005

World Health Organization. (2021). *Mental health conditions in conflict situations are much more widespread than we thought*. https://www.who.int/news-room/commentaries/detail/mental-health-conditions-in-conflict-situations-are-much-more-widespread-than-we-thought

World Health Organization. (2023a, March 31). *Depressive disorder (depression)*. World Health Organization (WHO). News Room. https://www.who.int/news-room/fact-sheets/detail/depression

World Health Organization. (2023b, November). *WHO launches commission to foster social connection*. https://www.who.int/news/item/15-11-2023-who-launches-commission-to-foster-social-connection

Yamasaki, T., Maekawa, T., Fujita, T., & Tobimatsu, S. (2017). Connectopathy in Autism Spectrum Disorders: A Review of Evidence from Visual Evoked Potentials and Diffusion Magnetic Resonance Imaging. *FRONTIERS IN NEUROSCIENCE*, *11*. https://doi.org/10.3389/fnins.2017.00627

Zhang, F., Daducci, A., He, Y., Schiavi, S., Seguin, C., Smith, R. E., Yeh, C.-H., Zhao, T., & O'Donnell, L. J. (2022). Quantitative mapping of the brain's structural connectivity using diffusion MRI tractography: A review. *NeuroImage*, *249*, 118870. https://doi.org/10.1016/j.neuroimage.2021.118870