This is a registered report on a meta-analysis of structural connectivity and social cognition. The authors propose a series of meta-analyses to: (RA1) examine the relationship between social cognition and structural connectivity; (RA2) identify white matter regions associated with social cognition; and (RA3) investigate potential moderators including socio-cognitive constructs (i.e., subdomains), diffusion metrics, and population/diagnosis-specific effects (RA3). Meta-analysis 1 (MA1) will include correlations between diffusion metrics and social cognitive scores (RA1). MA2 will involve a coordinate-based meta-analysis using seed-based d mapping (SDM) from voxel-based and tract-based studies (RA2). MA3 will include correlations between tract-based diffusion metrics and social cognitive measures (RA2). All MAs will be followed by a meta-regression (sex ratio) and subgroup analyses (socio-cognitive construct, diffusion metric, population/diagnosis, age group, whole brain vs. region of interest) to assess RA3. They will also include tests for publication bias and heterogeneity.

This study proposes a novel meta-analysis and provides good justification for examining structural connectivity and social cognition. They cite a previous systematic review (Wang et al., 2018), which supports the existence of relevant literature for the proposed meta-analysis. The inclusion of potential moderators is important given the breadth of the proposed meta-analyses, which are expected to have high heterogeneity.

## Major comments:

- Has the search strategy been reviewed by an academic librarian? Some terms may be too general and/or capture irrelevant areas of research (e.g., social skills/functioning refer more to outcomes than social cognition). Use of wildcards (e.g., social cogniti\*) would be appropriate. A preliminary search would ensure feasibility and potentially help revise the search strategy, as too many hits could hinder the screening process.
- The introduction should include a deeper elaboration of socio-cognitive constructs based on the literature or justification on those selected. It currently includes some examples, such as emotion recognition, theory of mind, and empathy, but omits other areas, such as social perception, social knowledge, and attributional style). This could help guide the search terms for a more comprehensive investigation of social cognition.
- How will the socio-cognitive measures be categorized into constructs will this be based on the selected papers (if reported) or done separately by the research team? If the latter, the constructs should be categorized by 2+ experts in social cognition based on the measures/scores used and done separately from the data extraction. The coding sheet should therefore include the score used for the social cognitive measure assessed, to ensure that categorization of social cognitive construct is precise.
- The organization of the series of meta-analyses and follow-up meta-regressions/subgroup analyses could be improved. Although there are 3 research aims and 3 meta-analyses, they do not clearly map onto one another. It appears MA1 will address RA1 and RA3 and that MA2 and MA3 will both address RA2 and RA3. How will the findings regarding RA3 be compared across MAs?
- MA2 involves a seed-based d mapping procedure using voxel and tract-based correlations between diffusion metrics and social cognition. Is this typically reported in the literature at such a fine-grained level? A few citations of relevant papers would show feasibility here.

- MA2 also includes mention of downsampling the voxel-based data to TBSS templates; how will this be done without the raw data? Will this reduce MA2 to a tract-based analysis rather than whole brain and, if so, what is the additional value of MA3?
- It was difficult to get a sense of how many total meta-analyses would be performed, but it appears as though there may be many. The authors should consider correcting for multiple comparisons given a potentially large number of primary and subgroup analyses.

## Minor comments:

- How will articles that use complex statistical techniques be treated, especially ones that involve correlations between brain and behavioural measures (e.g., partial least squares)?
- How will articles that include high-risk groups be treated (e.g., relatives of patients, subclinical treatment-seeking individuals)?
- Articles will be excluded if they fail to report "relevant details on the defined moderators". Is this on any or all of the moderators?
- What is the justification for the age groups selected (<20, 20-55, >55)?
- Given the objective to identify "diagnosis-specific effects", the coding sheet should include the diagnostic category of the sample, in addition to the healthy/patient comparison.
- To guide future research, I would strongly recommend distinguishing between regions/tracts that are non-significant from those that were not assessed when reporting findings. An example can be found in our similar meta-analysis on neurocognition and brain structure (Figure 3): <a href="https://doi.org/10.1016/j.neubiorev.2021.11.034">https://doi.org/10.1016/j.neubiorev.2021.11.034</a>
- Pre-registration plan should be detailed (PROSPERO? OSF?).

Signed,

## Katie Lavigne, Ph.D.

Assistant Professor, Department of Psychiatry, McGill University, Montreal, Quebec, Canada

Researcher, Douglas Research Centre, Montreal, Quebec, Canada

Lead, Douglas Open Science Program