The central executive network in Alzheimer's Disease: A meta-analysis of structural and functional MRI

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Introduction

- Executive functions (EF) provide clinical utility as transdiagnostic predictors of neurocognitive functioning.
- The central executive network (CEN) consists of the prefrontal cortex and posterior parietal cortex and plays a role in attention, working memory, and other processes.
- A moderate relationship between prefrontal cortex (PFC) and EF task performance in healthy controls, including increased cortical thickness and volume associated with EF, has been shown through meta-analyses (Yuan & Raz, 2014).
- There is literature about EF as a predictor of neurocognitive functioning, accordance with structural and functional architecture, and the relation with neuropsychological EF assessments.
- The CEN has been identified as a site of significant pathology in Alzheimer's disease (AD) (Chang et al., 2019), and more information is crucial for developing knowledge of this relation within both the structural and functional modalities.

Questions

- Is there a positive association between increased functional blood oxygen level dependent (BOLD) activity and better performance on EF tasks?
- Is there a positive association between increased cortical volume and thickness and better performance on EF tasks?
- Is there concordance between the functional and structural MRI measures of EF in individuals with AD?

Method: Literature Search, Article Inclusion, & Protocol

Literature Search

Two separate literature searches of PubMed and EBSCO (including PsycINFO and PsycARTICLES) conducted in May 2019 included the following terms:

- **Structural**: (dorsolateral OR dorsal lateral OR BA9 OR BA46 OR BA8 OR BA10 OR posterior parietal OR parietal lobule OR BA5 OR BA7 OR BA49 OR BA30) AND (volume* OR atrophy OR cortical thickness OR cortical thinning OR morphometry) AND (executive OR card sort* OR color word OR Stroop OR trail* OR verbal fluency OR working memory) AND (alzheimer* OR alzheimer* disease OR AD OR dementia)
- **Functional**: (central executive OR frontal executive OR frontal parietal) AND (functional MRI OR fMRI OR functional connectivity OR BOLD) AND (executive OR card sort* OR color word OR Stroop OR trail* OR verbal fluency OR working Memory) AND (alzheimer* OR alzheimer* disease OR AD OR dementia)

Exclusion Criteria

- Case studies
- Research of non-human subjects
- Human participants under 18 years of age

Inclusion Criteria

- 1+ structural neuroimaging measure of grey matter volume, thickness, or morphometry in regions of interest OR functional neuroimaging of either task or resting state BOLD fluctuations
- 1+ measure of EF
- Statistics delineating the relation between EF and imaging

Protocol Registration

- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in the creation of the protocol for this study (Moher, Liberati, Tetzlaf, Altman, The PRISMA Group, 2009)
- The protocol for this study is registered under the National Institute for Health Research (NIHR) PROSPERO International prospective register of systematic reviews (ID: CRD42020141544)

Method: Data Extraction

- Trained graduate research assistants extracted the following variables:
  - Year published, sample size, mean age, age range, standard deviation of age, percentage female, percentage left-handed, country of origin, EF task, statistic coefficient between EF performance and brain imaging, and brain region(s).
- EF tasks were coded as one of the following: Stroop/Color Word (CWI), Verbal Fluency (VF), Working Memory (WM), Trails (TMT), Wisconsin Card Sort (WCST), or an EF Composite score (EFC).
- Studies with multiple cognitive tasks or multiple brain regions were collapsed under a single effect size by averaging Fischer's Z-scores for initial analyses.

Method: Effect Size Calculations & Modeling

Effect Size Calculations

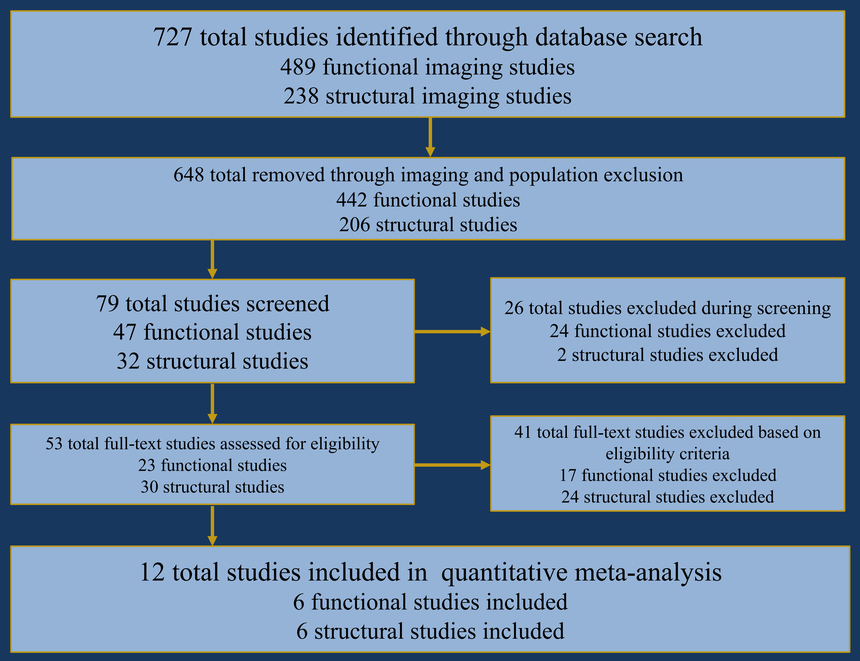
- Meta-Essentials workbook for partial correlation (Suurmond, van Rhee, & Hak, 2017; Van Rhee, Suurmond, & Hak, 2015) data was utilized to conduct random effects modeling in this study.
- Fisher's *Zr* transformation was used for each correlation coefficient to determine the effect size for each sample.

Statistical Modeling

- Between-study variance and subject-sampling variance estimate was used to compute new weights for random-effects analyses.
- Mean effect sizes were computed for groups by weighting each effect size by its sample size.
- 95% confidence intervals (CI) were calculated using standard errors for each group of studies.
- Mean effect sizes for each group were generated from random effects modelling.
- Significance of between groups differences were compared using analysis of variance statistical analysis and determining if CIs overlapped.

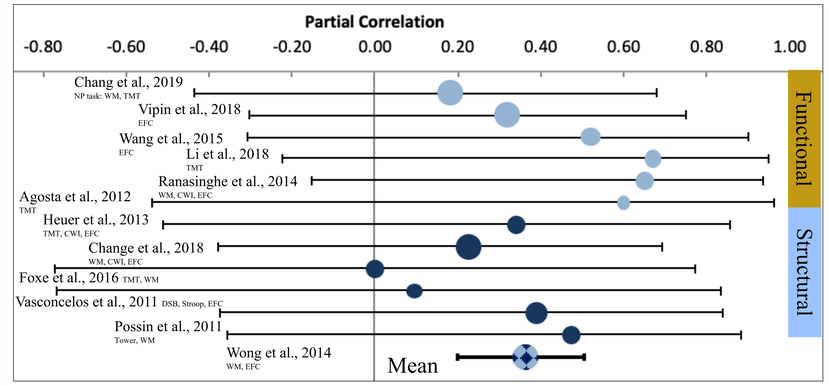
Study Eligibility Flow Diagram

Flow diagram adapted from Moher et al., 2009

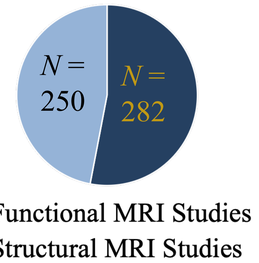


Results

Functional and Structural Imaging Sample Effect Size and 95% CIs



Sample Demographics



	Age (*M* years)	Female (%)
Functional MRI Studies	69.55	51.4%
Structural MRI Studies	66.97	47.4%

- The strength of the brain-behavior relationship pooled across both modalities was medium ($pr = 0.36$).
- Subgroup analyses of effect sizes showed no significant difference in the strength of brain-behavior association ($p = .431$) between structural ($pr = 0.28$) and functional ($pr = 0.44$) modalities, suggesting concordance. Neither mean age ($\beta = -0.39$, $p = .458$) nor percentage of female participants ($\beta = 0.53$, $p = .316$) significantly impacted concordance between findings.
- Larger structural volume is associated with better performance on EF measures ($r = .28$, 95% CI = .05-.47), and greater BOLD activation is associated with better performance on EF measures ($r = .44$, 95% CI = .13-.67).

Discussion

- Results show concordance between structural and functional measures: larger size (structural) and greater BOLD activation (functional) are both associated with better performance on EF measures.
- EF-CEN relationships can be found in both HCs and pathological populations.
- Strength of brain-behavior relationship across both modalities is comparatively stronger than in a previous meta-analysis in healthy adults, ranging from .08 - .23 (Yuan & Raz, 2014) due to a less restricted data range.
- Findings from this study contribute to understanding of the relationship between structure and function in the brain and help to contextualize previous AD research.

References

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