Title: Age-related differences in structural and functional prefrontal networks during a logical reasoning task

Abbreviated title: Aging, belief, and logical reasoning

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Abstract

In logical reasoning, difficulties in inhibition of currently-held beliefs may lead to unwarranted conclusions, known as belief bias. Aging is associated with difficulties in inhibitory control, which may lead to deficits in inhibition of currently-held beliefs. But, no study, to date, has investigated the underlying neural substrates of age-related differences in logical reasoning and the impact of belief loads. The aim of the present study was to delineate age differences in brain activity during a syllogistic logical reasoning task while the believability load of the logical inferences was manipulated. Twenty-nine, healthy, younger and thirty, healthy, older adults (males and females) completed a functional magnetic resonance imaging experiment in which they were asked to determine the logical validity of conclusions. Unlike younger adults, older adults engaged a large-scale network including anterior cingulate cortex (ACC) and inferior frontal gyrus (IFG) during conclusion stage. Our functional connectivity results suggest that while older adults engaged the ACC network to overcome their intuitive responses for believable inferences, the IFG network contributed to higher control over responses during both believable and unbelievable conditions. This result was further supported by mediation analysis indicating the role of Uncinate Fasciculus tract as a mediator for a relationship between age and rejection of believable statements. These novel findings lend evidence for age-related differences in belief bias, with potentially important implications for socially-relevant decision making where currently-held beliefs and given assumptions are in conflict.

Keywords: Inhibitory control; Logical reasoning; Anterior Cingulate Cortex (ACC); Inferior Frontal Gyrus (IFG); Uncinate Fasciculus (UF); White Matter (WM).

Introduction

Logical reasoning requires drawing a necessary conclusion from given assumptions. Beliefs and prior knowledge, however, may overshadow these assumptions and lead to unwarranted conclusions; a phenomenon known as belief bias (De Neys, 2012; Tsujii et al., 2010). A number of factors influence belief bias including time constraints (Evans & Curtis-Holmes, 2005; Trippas et al., 2013), emotional content of the reasoning statements (Goel & Vartanian, 2011), and higher cognitive ability (Sá et al., 1999; Trippas et al., 2015). Besides, the ability to inhibit current beliefs (De Neys, 2012; Houde & Borst, 2015; Houde et al., 2000) is critical for adaptive behaviors (Houde et al., 2000) and arriving at a logical conclusion (Houde & Borst, 2015). Considering the critical role of logical reasoning in personal, complex political, and societal decisions, a reduced ability in inhibition of beliefs may indicate underlying neural changes, which could have consequences for daily decision-making.

Inhibitory control – a foundation of many cognitive functions such as attention and memory (Paxton et al., 2008) – shows age-related changes; improves from childhood to early adulthood but declines in later life. Age-related decline in inhibitory control may lead to difficulties in the inhibition of currently-held beliefs and, consequently, result in reduced logically correct decisions. Further, evidence suggests that normal aging is associated with a reduction of gray matter volume in frontal regions (Mann et al., 2011) and reduction of structural white matter tracts between frontal and other parts of the brain (Hasan et al., 2009; Treit et al., 2014; Wolf et al., 2014). Thus, understanding the age-related differences in structural and functional networks involved in inhibitory control provides further insights to reasoning and decision-making in late adulthood.

To our knowledge, only two studies have investigated the age-related differences in logical reasoning so far. De Neys and Van Gelder (2009) examined the relation between deductive reasoning performance and cognitive control ability behaviorally. They found that reasoning performance decreases among older adults when beliefs and logic are in conflict. No difference in performance was found when logic and beliefs agreed; belief inhibition was not required. In another study, Tsujii and colleagues (2010) examined the role of the inferior frontal gyrus (IFG) – a critical region in reasoning and inhibitory control – in the inhibition of current beliefs during a logical reasoning task using near-infrared spectroscopy. Unlike younger adults, older adults recruited the bilateral inferior frontal gyrus – when belief and logic were in conflict – suggesting a possible mechanism to compensate for the age-related decline in inhibitory control. Although Tsujii et al's (2010) finding was critical in highlighting the role of IFG in logical reasoning in aging, no study to date has investigated the underlying neural networks involved in logical reasoning and the impact of belief in late adulthood.

In this study, we aimed to identify age-related differences in both structural and functional substrates of logical reasoning when the belief load of inferences and currently-held beliefs are either in conflict or agreement. Younger and older adults completed a syllogistic reasoning task in which they identified if a conclusion logically followed given assumptions. The believability content of the inferences was either congruent (believable; all parrots are birds) or incongruent (unbelievable; all lizards are mammals) with currently-held beliefs. In this study, in order to measure cognitive control, we define *performance* as correctly accepted unbelievable or correctly rejected

believable statements. Given that more cognitive control is required to suppress currently-held beliefs, we anticipated that cognitive control areas, such as anterior cingulate cortex (ACC) and inferior frontal gyrus, would contribute to higher performance (correctly rejecting believable and correctly accepting unbelievable statements). Converging evidence highlights the importance of the IFG region in the resolution of belief-logic conflict and logical reasoning (Prado et al., 2011; Reverberi et al., 2012; Reverberi et al., 2010; Stollstorff et al., 2012), and inhibitory control (Brass et al., 2005), supporting the choice of IFG as a seed for functional connectivity analyses. Furthermore, mounting evidence supports the critical role of ACC in self-regulation functions such as monitoring of conflict (Botvinick et al., 2001; Botvinick et al., 2004), regulating emotions (Buhle et al., 2014; Bush et al., 2000; Ziaei et al., 2017), conflict monitoring (Vassena et al., 2017), and responding to errors (Holroyd & Coles, 2002) - all of which are required to inhibit currently-held beliefs during logical reasoning. The role of ACC was also highlighted in deductive reasoning in the absence of any visual input (Knauff et al., 2002).

Using functional connectivity analysis, we investigated functional networks of the ACC and IFG during a logical reasoning task. Existing theories argue that unbelievable inferences encourage a more thorough reasoning because of the conflict between belief load and logic. According to the mental model theory, individuals construct mental models from syllogisms. If the belief load of the syllogisms is in conflict with the mental model, it initiates a search for an alternative model of the premises (Johnson-Laird, 2001; Johnson-Laird, 2010; Johnson-Laird et al., 2015). Therefore, correctly *accepting* unbelievable statements and *rejecting* believable ones prompts conflict and thus demands higher cognitive control. Given the well-documented inhibitory control deficits in late adulthood (Gazzaley & D'Esposito, 2007; Hasher & Zacks, 1988), we hypothesized that older adults would show difficulties to accept an unbelievable statement or reject a believable one correctly, both of which requires higher cognitive control ability.

Given the existing evidence on the relationship between the lower white matter integrity and age-related cognitive decline (Madden et al., 2009), we examined whether the structural strength of pathways connecting frontal and other brain areas contribute to logically correct reasoning and if this relationship would differ between younger and older adults. We have selected the Cingulum bundle and Uncinate Fasciculus tracts that are mainly involved in inhibitory control (Catani, 2010; Grieve et al., 2007; Li et al., 2018), executive functioning (Grieve et al., 2007), and belief updating (Moutsiana et al., 2015). In line with our functional connectivity predictions, we anticipated rejecting believable and accepting unbelievable statements correctly require higher cognitive control, possibly relying on the white matter integrity. Furthermore, it is expected that the integrity of white matter tracts underlies the relationship between age and logical reasoning performance. That is, older adults with greater white matter integrity would be more capable in correctly rejecting believable statements and correctly accepting unbelievable ones.

Material and Methods

Participants

Thirty-two, healthy, older and thirty-one, healthy, younger adults participated in this study. Two older and two younger adults were excluded from the analysis due to brain signal loss and extensive movement, leaving 30

older adults (aged 61-78 years; $M = 70.34$, $SD = 4.27$; 15 females) and 29 younger adults (aged 18-26 years; $M = 21.13$, $SD = 2.72$; 15 females). All younger adults were undergraduate students at the University of Queensland who were reimbursed either with course credits or \$15 AUD per hour. Older adults were volunteers from the community recruited through advertising in public notice boards of different clubs, libraries, churches, and the University of Queensland's Aging Mind Initiative. Older adults were reimbursed \$20 AUD per hour. Before taking part in this study, all participants were screened for MRI compatibility as well as claustrophobia, mood disorder such as depression and anxiety, neurological and psychiatric medication including cardiovascular and epilepsy. All participants were right-handed, English speakers who had normal or corrected-to-normal vision using MRI compatible glasses with no history of psychiatric illnesses, cardiovascular disease, head or heart surgery, and neurological impairment. Both age groups were similar in education years and gender. Older adults underwent screening to rule out cognitive decline on a widely used dementia screen, the Mini Mental State Examination (Folstein et al., 1975). All older adults scored above the recommended cut-off of 27 ($M = 29.34$, $SD = 0.82$). Participants took part in two separate sessions of testing, the first involving fMRI scanning and the second involving behavioral/neuropsychological assessment. Informed consent was obtained from all individual participants included in the study and were debriefed upon the completion of the second session. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the independent Bellberry Human Research Ethics Committee.

Task materials

A logical *statement* in this study follows a generic form of *<quantifier, subject, copula, predicate>*, e.g., All parrots are birds, where "All" is a quantifier, "parrots" is a subject, "are" is a copula, and "birds" is a predicate. There are three choices for the quantifier that are "All", "No", and "Some", and two choices for the copula that are "are" and "are not". Four propositions are generated by combining a quantifier and a copula: Proposition type *A* that is a combination of "All" and "are"; Proposition type *E* that is a combination of "No" and "are"; Proposition type *I* that is a combination of "Some" and "are"; Proposition type *O* that is a combination of "Some" and "are not". Other combinations (e.g., "All" and "are not") are not used in this study.

A logical argument in this study included three statements, two premises and one conclusion, in the form of a standard syllogism (Table 1). In a premise, the subject and the predicate are arbitrary sets (e.g., dogs, mammals, furniture). Exactly one set is *shared* between two premises that may appear in either the subject or the predicate in either of the premises (Set_2 in Table 1). Hence, an argument with two premises involves exactly three sets (Set_1, Set_2, and Set_3), two uniquely used in each premise and one used in both. The conclusion of a syllogism is a statement about the sets that appear uniquely in premises (Set_1 and Set_3). A conclusion "follows" from the premises if the premises provide conclusive evidence to support it. Otherwise, the conclusion "does not follow" from the premises. This includes the conclusion that is wrong, given the premises, or is not completely supported by the premises.

Conclusions and premises can be believable or unbelievable statements. For example, "all birds are mammals" is an unbelievable statement while "all parrots are birds" is a believable statement. In addition, premises may provide a neutral context, for example, "all parrots are nickhomes", where "nickhomes" is a meaningless pseudo-word. This type of statement was only used in the premises in such a way that the pseudo-word was always the shared set between the premises. Hence, the premises were either believable, unbelievable, or neutral while the conclusion was either believable or unbelievable. The phrases "believable", "neutral", and "unbelievable" mean that the first premise was always a believable statement while the second was either believable, neutral, or unbelievable, respectively. The following are two examples of syllogisms with a believable premise/unbelievable conclusion and an unbelievable premise/believable conclusion, respectively:

All sparrows are birds; All birds are animals; Therefore, no animals are sparrows: believable premise/unbelievable conclusion

All oranges are citrus; No citrus are fruits; Therefore, some fruits are not oranges: unbelievable premise/believable conclusion

[Insert Table 1 about here]

We used propositions *A* (All, are) and/or *E* (No, are) in both of premises (counter balanced across all runs). We avoided the use of proposition *E* in both premises of the same argument as it simplifies the reasoning task; making the premises AA, AE, and EA. For the conclusions, however, we used the propositions required to ensure that the conclusions that followed the premises and those that did not follow the premises were balanced.

We also balanced the way the sets in the subject and predicate of the premises were ordered. In this experiment, we used two types of ordering: i) the shared set belonged to the subject of premise 1 and the subject of premise 2, and ii) the shared set belonged to the predicate of premise 1 and the subject of premise 2. The conclusion takes the unique sets from each premise, combines them through a proposition, and the logical reasoning task is to decide if the generated statement follows from the premises or not. Whether the subject of the conclusion was drawn from the first or second premise was also counterbalanced.

An algorithm was developed that creates all of the syllogisms based on criteria specified in Table 1. A total of 96 syllogisms was generated, within six conditions: 1. believable premise/believable conclusion, 2. believable premise/unbelievable conclusion, 3. unbelievable premise/believable conclusion, 4. unbelievable premise/unbelievable conclusion, 5. neutral premise/believable conclusion, 6. neutral premise/unbelievable conclusion (see Supplementary Material for access to all of the syllogisms used in the study and more details on the structure of the syllogisms used in this experiment).

Experimental design

During the logical reasoning task, participants ascertained if the conclusion statement logically followed from the premises. They responded with two keys on an MRI-compatible response box. The first premise was presented for 2 seconds followed by a second premise for 4 seconds. After the second premise, the conclusion statement was presented for 12 seconds (Figure 1). To minimize the working memory load, all statements remained

on the screen until the end of the presentation of the conclusion. A fixation cross was presented after the conclusion, which was randomly jittered using four-time intervals: 0.5 seconds (16 trials), 1 second (16 trials), 1.5 seconds (16 trials), and 2 seconds (16 trails). The task consisted of 6 runs, each run lasting for 5.16 minutes. Three runs of the task were presented before and three after the structural scans.

[Insert Figure 1 about here]

Procedure

The experiment consisted of two sessions; scanning session and behavioral/neuropsychological assessment session. Each participant's scanning session lasted 45 minutes and included two components: structural MRI and the logical reasoning task with functional MRI. Prior to the scan, participants were verbally instructed about the task and a practice run was continued until they were familiar with the timing and instruction of the task. Three runs of the task were presented before and three after the structural scans. Following completion of the scanning session, participants were asked to complete number of background measures.

Background measures

During the behavioral/neuropsychological assessment session, all participants completed a number of tasks to assess executive functioning measured by Stroop task and Trail Making Test (Reitan & Wolfson, 1986); emotional well-being measured by Depression, Anxiety, Stress Scale (DASS-21, Lovibond & Lovibond, 1995); and intelligence measured by the National Adult Reading Test (Nelson, 1982). Descriptive and inferential statistics of background measures are reported in Table 2.

[Insert Table 2 about here]

fMRI image acquisition

Functional images were acquired at the Centre for Advanced Imaging using a 3T Siemens scanner with a 32-channel head coil. The functional images were obtained using a whole-head T2*-weighted multiband sequence (473 interleaved slices, repetition time (TR) = 655ms, echo time (TE) = 30ms, voxel size = 2.5mm^3, field of view (FOV) = 190mm, flip angle = 60º, multi-band acceleration factor = 4). High-resolution T1-weighted images were acquired with an MP2RAGE sequence (176 slices with 1mm thickness, TR = 4000ms, TE = 2.89ms, TI = 700ms, voxel size = 1mm^3, FOV = 256mm). To minimize the noise and head movement, participants were provided with cushions and earplugs around their head inside the head coil. Participants observed the tasks on a computer screen through a mirror mounted on top of the head coil.

Preprocessing

For functional analysis, T2*-weighted images were preprocessed with Statistical Parametric Mapping Software (SPM12; http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 2015b (Mathworks Inc., MA). Following realignment to a mean image for head-motion correction, images were segmented into gray and white matter. Then, images were spatially normalized into a standard stereotaxic space with a voxel size of 2 mm^3, using

the Montreal Neurological Institute (MNI) template, and then spatially smoothed with a 6 mm^3 Gaussian Kernel. None of the participants had head movement in the scanner, which exceeded than 1mm.

fMRI analyses

The imaging data were analyzed using a model-free, multivariate analytical technique, Partial Least Squares (PLS; McIntosh et al., 1996; McIntosh et al., 2004). For a detailed tutorial and review of PLS, see Krishnan et al. (2011), as implemented in PLS software running on MATLAB 2012b (The MathWorks Inc., MA). In brief, PLS analysis uses singular value decomposition (SVD) of a single matrix that contains all data from all participants to find a set of orthogonal latent variables, which represent linear combinations of the original variables. Rather than making assumptions about conditions or imposing contrasts for each pattern, PLS decomposes all images into a set of patterns that capture the greatest amount of covariance in the data. Therefore, PLS enables differentiation of the contribution of brain regions associated with task demands, functional seed activity, and behavioral or anatomical covariates. Usually, the first latent variable accounts for the largest covariance of the data, with a progressively smaller amount of covariance for subsequent latent variables. Each latent variable delineates cohesive patterns of brain activity related to experimental conditions. The brain score reflects how strongly each participant contributes to the pattern expressed in each latent variable. Brain scores are calculated as the dot product of a participant's image volume of each latent variable. Therefore, each latent variable consists of a singular image of voxel saliences (*i.e.*, a spatiotemporal pattern of brain activity), a singular profile of task saliences (*i.e.*, a set of weights that indicate how brain activity in the singular image is related to the experimental conditions, functional seeds, or behavioral/anatomical covariates), and a singular value (*i.e.*, the amount of covariance accounted for by the latent variable).

PLS offers multiple advantages compared to other traditional methods and thus, has been used as a primary method of analyzing fMRI data in this experiment. PLS is constrained to examine the covariance between brain activity and task design. In this regard, we are capable of examining robust patterns of activity only associated with the experimental conditions. Along these same lines, PLS is capable of analyzing multiple conditions simultaneously to examine covariance of response across conditions. Thus, by using PLS, limitations associated with age-related differences in BOLD and Hemodynamic Response Function modelling would not impact the results (Fynes-Clinton et al., 2019).

In this study, we use the onsets of conclusion statements for the decision-making stage using an event-related design analysis. The statistical significance of each latent variable was assessed using a permutation test, which determines the probability of a singular value from 500 random reordering and resampling (McIntosh et al., 1996). Additionally, to determine the reliability of the saliences for each brain voxel, a standard error of each voxel's salience on each latent variable was estimated by 100 bootstrap resampling steps (Efron & Tibshirani, 1985). Peak voxels with a bootstrap ratio (*i.e.,* salience/standard error) > 2.5 were considered to be reliable, as this approximates $p < 0.01$ (Sampson et al., 1989). In the current study, we used task PLS and brain-behavior PLS to examine the whole-brain activity pattern for conclusions as a function of believability load and to assess the link between performance in the logical reasoning task and connectivity pattern from seeds. Because PLS is a

multivariate approach and considers all voxels simultaneously, it does not require correction for multiple comparisons (McIntosh et al., 2004), which remains a fraught issue for the GLM framework (Eklund et al., 2016).

DTI data acquisition

High-angular resolution DWIs were acquired using High Angular Resolution Diffusion Imaging (HARDI) sequence; 60 slices, TR = 8600 ms, TE = 109 ms, Diffusion direction = 64, b value = 3000 s/mm2, size = 2.3mm^3) and processed using FSL software (Fischl, 2012).

DTI data processing

The DWI images were first corrected for the eddy current distortion and head motion using the FMRIB's Diffusion Toolbox (FDT) (Andersson & Sotiropoulos, 2016). Non-brain tissues were removed from the corrected images using the Brain Extraction Tool (Smith, 2002). We then used the FDT to locally fit the diffusion tensor model at each voxel and prepare the map of Fractional Anisotropy (FA) values throughout the brain of each subject. FA is a general marker of white matter integrity that reflects the coherence within a voxel and fiber density (Alexander et al., 2007; Beaulieu, 2002). In the absence of other diffusivity measures, FA is accepted as a nonspecific marker of microstructural change (Alexander et al., 2007). The FA map of each subject was then realigned to match the standard brain template, MNI 152 T1 1mm space, using the FMRIB's Linear Image Registration Tool (FLIRT) (Greve & Fischl, 2009; Jenkinson et al., 2002; Jenkinson & Smith, 2001), with 12 degrees of freedom and trilinear interpolation. This provides an affine transformation that ensures the transformed FA maps are in the same 3D coordinate system as of one another. We then generated the desired white matter mask for the tract of interest using the ICBM-DTI-81 white-matter atlas (Hua et al., 2008; Oishi et al., 2010; Wakana et al., 2007); We generated the masks for inferior Longitudinal Fasciculus, Cingulum, and Uncinate Fasciculus tracts that have been shown to play a role in executive functioning, inhibitory control, and in aging (Hasan et al., 2009; Li et al., 2018). The average of FA values in the tract of interest for each subject were then calculated and used in structure-behavior analysis

Whole-brain task-related functional activity

We examined how belief loads of the conclusions influenced the logical reasoning in the whole-brain analyses (task PLS). This analysis focused on the time that participants had to decide about the logical validity of the conclusions, hence, named as decision-making stage. Onsets from the beginning of the *conclusions* for all six experimental conditions were included in this analysis aiming to identify the brain activation related to the conclusions' belief loads. However, to ensure that brain activities reported are related to the reasoning and are not confounded with other processes that are involved during reasoning (visual and language processes, for instance), brain activities from the 3rd to 9th TRs (correspond to 1.96 - 5.89 seconds after presentation of the conclusion statement) are reported here. This period of conclusion precedes the period where the maximum probability of responses occurred during these three TRs. Only trials with correct responses, i.e. correct rejecting of a believable or correct accepting an unbelievable inference, were included in the analyses. Due to the low number of incorrect trials, this analysis is not reported here.

Brain-behavior connectivity analyses

The aim of brain-behavior connectivity analysis was to examine whether the functional connectivity of the frontal regions differs between younger and older adults during the correct rejection of believable and correct acceptance of unbelievable inferences. Furthermore, we investigated whether there is any association between the task-related brain functional networks of frontal regions with behavioral performance. Given that the whole-brain activation pattern during conclusion was stronger for older than younger adults, in order to reduce the biases toward one age group, we have chosen two seed regions from the Meta analyses reported in Neurosynth (Yarkoni et al., 2011) and therefore, included both age groups in the brain-behavior connectivity analyses. For functional connectivity, inferior frontal gyrus (IFG: Right: [48 22 8]; Left: [-48 22 16]) and anterior cingulate cortex (ACC: [0 32 22]) were chosen. The selection of these two seeds was primarily based on previous studies highlighting the importance of these regions in deductive reasoning (Prado et al., 2011; Reverberi et al., 2012; Reverberi et al., 2010; Stollstorff et al., 2012) as well as other underlying cognitive processes that are crucial for inhibiting beliefs such as monitoring conflicts and regulating emotions.

To delineate the task-related functional brain networks from these seeds, the signal intensity values from the peak voxels of the seed regions were extracted and then correlated with values in the rest of the brain across participants and with behavioral performance. These correlations were then combined into a matrix and decomposed with singular value decomposition and formed the functional connectivity results. The functional connectivity analyses resulted in a set of latent variables that characterize the brain regions in which activity correlated with that of the seed regions and with behavioral performance during the experimental conditions. Permutation and bootstrap sampling were used to determine the significance and reliability of the seed-behavior functional analyses following the whole brain task-related analysis. Given that rejection rates evaluate the ability of the participants to ignore their currently-held belief and make decisions based on the given assumptions, only rejection rates were used in our functional connectivity analyses.

Structure-behavior analysis

To investigate the role of structural integrity underlying logical reasoning, we chose three tracts: inferior Longitudinal Fasciculus, Cingulum, and Uncinate Fasciculus. These tracts include several critical frontal areas such as the anterior cingulate and orbitofrontal cortex, regions that were consistently found in our whole-brain task-related functional findings during the conclusion stage (Table 3) and temporal areas. For instance, the altered integrity of the Uncinate Fasciculus tract due to age (Meltzer-Baddeley et al. 2011) may reduce control on regions associated with processing semantic knowledge. We also need to note that inferior Longitudinal Fasciculus tract was chosen as a control to demonstrate the specificity of the effect to the regions such as cingulate and temporal lobe rather than general white matter integrity. Therefore, we performed a nonparametric bootstrapping mediation analyses to test the mediation model of FA values in white matter tracts as mediators of the relationship between age (independent variable) and rejection rates (dependent variable). Mediation is significant if the 95% confidence intervals for the indirect effect do not include zero (Preacher & Hayes, 2004; Preacher et al., 2007). Results were

calculated based on the 10,000 bootstrapped samples for both left and right sides of white matter tracts, independently.

Statistical analysis for behavioral data

It has to be noted that a high performance in this task is defined by a high ratio of correctly rejecting believable or correctly accepting unbelievable statements. Given that rejecting a believable or accepting an unbelievable statement requires higher control over currently-hold beliefs, these two measures are reflecting higher cognitive control abilities. In other words, participants who can inhibit their currently-held beliefs when necessary, are able to reject a believable or accept an unbelievable statement, correctly. Without loss of generality, we only considered correct rejection for our analyses as this value is the complement of correct endorsement when only correct responses are included. Hence, a high performance refers to a high rejection rate in believable statements and a low rejection rate in unbelievable statements. The rejection rate was the number of times each participant correctly rejected a given syllogism divided by the total number of statements that should have been correctly rejected. Repeated measures ANOVA were performed on dependent variables such as RT, and rejection rates for syllogisms with believable and unbelievable loads from conclusion stage. Although the task was not fast-paced and participants were told to prioritize performance over speed, we have analyzed reaction times as well to examine if there were any differences in speed of responding to believable versus unbelievable statements.

Results

Behavioral results

Reaction Times

A 2 (conclusion belief loads: believable or unbelievable) by 2 (age group: younger and older adults) repeated measure ANOVA on reaction times showed a significant main effect of conclusion ($F(1,57) = 15.73$, $p = .000$, $\eta_p^2 = .21$), suggesting that participants responded slower to believable ($M =5.86$, $SD =1.53$) conclusions relative to unbelievable ($M =5.60$ sec, $SD =1.49$) ones. Main effect of group was significant ($F(1,57) = 31.83$, $p = .000$, $\eta_p^2 = .35$), with older adults ($M =6.6$ sec, $SD =1.19$) responding slower than younger adults ($M =4.8$ sec, $SD =1.22$; Table 2). Interaction between age group and conclusion belief loads was not significant ($F(1,57) = 2.43$, $p = .12$, $\eta_p^2 = .04$).

Rejection rate

A 2 (conclusion belief loads: believable or unbelievable) by 2 (age group: younger and older adults) repeated measure ANOVA revealed a significant main effect of conclusion belief load ($F(1,57) = 10.35$, $p = .002$, $\eta_p^2 = .15$), participants had higher rejection rate for unbelievable ($M =.92$, $SD = .13$) conclusions relative to believable ($M =.84$, $SD =.22$) conclusions ($t(58) = 3.07$, $p = .003$, $d = .80$). A main effect of age group reached a significant level ($F(1,57) = 16.91$, $p = .000$, $\eta_p^2 = .22$), suggesting that older adults had lower performance relative to younger counterparts. An interaction between age group and conclusion conditions was also significant ($F(1,57) = 8.32$, $p = .006$, $\eta_p^2 = .12$), suggesting that older adults significantly rejected unbelievable statements more than

believable ones ($t(29) = 3.61$, $p = .001$, $d = 1.34$. The difference between believable and unbelievable rejection rate, however, was not significant among younger adults ($t(28) = .31$, $p = .75$, $d = .11$)

Imaging results

Whole-brain results

Our analyses during decision-making stage showed one significant latent variable which accounted for 49% of the variance of the data ($p < .001$) only among older adults. This latent variable consisted of sets of brain regions such as right ACC, bilateral IFG, bilateral superior temporal gyrus, left temporal pole, left superior parietal lobe, and right hippocampus (Table 3) and these regions were more activated for all conditions relative to younger adults. Figure 2 shows brain activities based on different TRs from 3rd to 9th TRs. Our whole-brain task-related functional analyses during conclusion stage revealed that older adults engaged a large-scale network including regions implicated in cognitive control for all conditions more than their younger counterparts.

[Insert Figure 2 & Table 3 about here]

Brain-behavior results

ACC and rejection rate

Our brain-behavior analyses on ACC and rejection rates revealed one significant latent variable accounted for 15% of covariance of the data ($p = .001$). This network comprised of regions such as right medial cingulate cortex, left paracentral lobule, right inferior frontal gyrus, bilateral superior temporal gyrus, left middle temporal gyrus, bilateral middle frontal gyrus, right lingual gyrus, bilateral thalamus, and right hippocampus (Table 4). This network was engaged for believable inferences (believable premise/believable conclusion (BB)) and contributed to more rejection rates. In other words, individuals who recruited this network more, rejected the believable syllogisms to a greater extent (Figure 3). However, during the unbelievable inferences, this network was not engaged among older adults and was not reliably activated for younger adults (CIs crossing zero).

[Insert Figure 3 about here]

IFG and Rejection rates

The brain-behavior analysis with IFG and rejection rates revealed one significant latent variable which accounted for 20% of the covariance of the data ($p = .001$). This network included bilateral IFG, right anterior cingulate cortex, left middle temporal gyrus, left temporal pole, right inferior parietal lobule, middle occipital gyrus, and bilateral hippocampus (Table 4). This network was connected to bilateral IFG and contributed to more rejection rates for believable inferences (believable premise/believable conclusion (BB)) and lower rejection rates for unbelievable inferences (unbelievable premise/unbelievable conclusion (UU); Figure 4). This network was not engaged by younger adults, nor contributed to the performance among younger adults (CIs crossing zero).

[Insert Figure 4 & Table 4 about here]

In sum, the results from the functional connectivity analyses yield that the IFG network contributed to the rejection rates for both believable and unbelievable inferences, whereas the ACC network was involved in rejection of believable inferences only.

Structure-behavior analyses

Next, we examined whether the relation between age group and the rejection rates is mediated by the integrity of the fractional anisotropy (FA) values obtained from these tracts. The results indicated that the relationship between age group and rejection rates was mediated by the integrity of the left Uncinate Fasciculus tract during believable conclusion, but not unbelievable ones. The total effect of age group on rejection rates was significant (total effect = -.0041, standard error =.0012, $p<.001$, Figure 5A, pathway c), and the direct effect was also significant (direct effect = -.0039, standard error =.001, $p<.001$). The standardized indirect effect using bootstrapped procedure found to be significant (indirect effect lower 95% CI= -.005, upper 95% CI=-.0001, pathway c'). Older adults' participants showed lower integrity in the left Uncinate Fasciculus (Figure 5A, pathway a) and that lower integrity of the left Uncinate Fasciculus predicted less rejecting of the believable conclusions after controlling for age (Figure 5A, pathway b). This result suggests that the relationship between age and logical reasoning performance during believable statement was mediated by the left Uncinate Fasciculus integrity. None of the other effects for Cingulum or Inferior Longitudinal Fasciculus were significant in mediation analyses.

[Insert Figure 5 about here]

Discussion

The present study provides evidence to explain the age-related differences in logical reasoning and the impact of currently-held beliefs using a syllogism task, supporting inhibitory deficit hypothesis (Hasher & Zacks, 1988) . First, the whole-brain task-related functional results showed that older adults engaged a large-scale brain pattern, including anterior cingulate cortex (ACC) and inferior frontal gyrus (IFG), for all conditions more than their younger counterparts during the decision-making stage (conclusion statement). Third, our functional connectivity results suggest that older adults who engaged the ACC network to a larger extent showed better control over their intuitive responses to reject the believable statements (higher rejection rates for believable inferences). Among older adults, the IFG network was comparably engaged across all conditions during decision-making stage and contributed to higher and lower rejection rates to believable and unbelievable inferences, respectively. Finally, structure-behavior mediation analyses showed that the integrity of the left Uncinate Fasciculus tract contributed to rejection rate for believable inferences, so that older adults who have better preserved integrity in this tract rejected the believable inferences more.

The role of ACC

During the decision-making stage, older adults engaged a large-scale brain pattern including bilateral IFG and ACC for all conditions. We observed sustained engagement of the ACC during the conclusion stage, from early TRs until the end of the decision-making stage (Figure 4), among older adults. The ACC – a central region of the executive attention network – has been linked to a variety of self-regulation functions such as monitoring of conflict

(Botvinick et al., 2001; Botvinick et al., 2004), regulating emotions (Buhle et al., 2014; Bush et al., 2000; Ziaei et al., 2017), responding to errors (Holroyd & Coles, 2002), and responses-outcome association (Alexander & Brown, 2010), to name a few. In aging, studies have reported a link between ACC activity and performance in a number of tasks such as Stroop (Milham et al., 2002), memory encoding of negative stimuli (Ziaei et al., 2017), and theory of mind (Ziaei et al., 2016). In the context of our findings, engagement of the ACC from the beginning of the conclusion stage emphasizes the importance of early engagement of inhibitory control and response monitoring during logical reasoning in late adulthood. Our functional connectivity results further support this claim and highlight the role of fronto-parietal network functionally connected to the ACC during the syllogistic reasoning task. Critically, the fronto-parietal network contributes to correctly rejecting believable inferences. That is, the more the fronto-parietal network is engaged, older adults are more able to correctly reject believable statements. This is a challenging task as a believable inference is in line with currently-held beliefs and rejecting this statement requires more cognitive effort. To our knowledge, this study is the first to investigate age-related changes in functional networks of the ACC during a reasoning task. The engagement of fronto-parietal network in deductive reasoning is in line with previous findings (Monti et al., 2009; Reverberi et al., 2007) and our results take the previous finding further and suggest that the logical reasoning task was cognitively demanding for older individuals, evidenced by behavioral and neuroimaging fidnings, which resulted in engagement of the fronto-parietal network relative to their younger counterparts.

The role of IFG

The importance of the IFG has been highlighted for reasoning in previous studies using functional MRI (Prado et al., 2011; Reverberi et al., 2012; Reverberi et al., 2010) as well as repetitive transcranial magnetic stimulation (Tsujii et al., 2011). For instance, Tsujii and colleagues (2011) examined the role of the superior parietal lobe and the IFG during a logical reasoning task in which the believability load of the inferences was manipulated. They found that stimulation of bilateral parietal lobe disrupted performance on incongruent – unbelievable – inferences whereas stimulation of the left IFG impaired performance during congruent – believable – inferences and facilitated incongruent – unbelievable – reasoning performance. Findings from our functional connectivity results yield a link between the bilateral IFG network, higher rejection of believable, and lower rejection of unbelievable inferences. The increased activity in the network connected to the IFG as seen among older adults might also suggest the cognitive effort exerted during the task. The IFG network is primarily involved in attentional effort during the task and the coupling between ACC and parietal lobe with the IFG suggest the cognitive effort needed to perform the task (Berry et al., 2017).While IFG is critical in inhibitory control (Aron et al., 2014), previous studies have also shown that the IFG might be involved in detecting cues regardless of whether the inhibitory control is required (Hampshire et al., 2010). In line with our findings, it might be that during a logical reasoning task, believability load of the statements might have triggered orientation of attention toward cues necessary to initiate inhibitory control over currently-held beliefs.

While most studies agree on the role of IFG in reasoning, nonetheless there are still inconsistencies between findings about the importance of IFG laterality in various logical reasoning tasks. It seems that a belief-based heuristic system activates the left IFG (Ragni et al., 2016) and inhibition of the default heuristic system (or

enabling the logical system) engages the right IFG (Reverberi et al., 2010; Tsujii et al., 2010; Tsujii et al., 2011). The bilateral engagement of the IFG in this study, however, can be related to the multivariate method used in this study, PLS. As previously mentioned, the PLS is more sensitive than traditional GLM and can examine robust patterns of activity associated with multiple experimental conditions simultaneously. Given that most previous studies have used univariate method to examine neural correlates of logical reasoning, the bilateral engagement of the IFG in this study takes prior research one step further and demonstrates the advantage of multivariate methods for examining higher-order cognitive tasks such as logical reasoning.

Altogether, our functional connectivity results reveal that sub-regions of the prefrontal cortex, the ACC and IFG, might have slightly different roles for the inhibition of currently-held beliefs. The IFG and its network contributed to the higher rejection of believable and lower rejection of unbelievable statements. On the other hand, the ACC and its network contributed to currently rejecting believable statements more than other conditions. More work is needed to explore the role of other frontal and subcortical brain areas during a reasoning task and the inhibitory control that is required to outperform such a task.

The role of Uncinate Fasciculus

Another important finding was the relation between Uncinate Fasciculus and the rejection rates for believable inferences. The Uncinate Fasciculus has been implicated in a number of functions, such as language, memory, and social-emotional processing (Von Der Heide et al., 2013). This tract is usually associated with the limbic system and connects the prefrontal cortex, including Broadman area 10, 9, to the temporal lobes through bidirectional pathways (Hasan et al., 2009). This tract is often associated with the limbic structure and is involved in emotion and memory (Olson et al., 2015; Von Der Heide et al., 2013), emotional empathy (Oishi et al., 2015), and in diseases with the hallmark of temporal lobe functional deficiency such as depression (Zhang et al., 2012) and epilepsy (Von Der Heide et al., 2013) and mild cognitive impairment and Alzheimer diseases (Fouquet et al., 2009; Rémy et al., 2015; Villain et al., 2010). The lower integrity of the left Uncinate Fasciculus contributed to the lower rejection of believable statements. This finding is in line with previous results on updating beliefs that have reported activation of frontal lobes and subcortical areas such as hippocampus and amygdala (Li et al.; Moutsiana et al., 2015). It is not surprising that the limbic area would be engaged during a logical reasoning performance; specifically, the hippocampus, in semantic retrieval of currently-held assumptions, and the amygdala, in emotional response toward belief load. Thus, the better integrity of the Uncinate Fasciculus tract indicates better ability to retrieve previously stored information and better control over emotional responses, which could result in inhibition of beliefs and better logical reasoning performance overall. In aging, however, the deficit in cognitive control ability and lower integrity in white matter structures, such as Uncinate Fasciculus, among older adults resulted in lower logical reasoning performance. In other words, older adults with preserved integrity in this tract, were able to control their intuitive response and to reject the believable statements more.

Conclusion

The primary aim of this study was to examine the age-related differences in functional networks of ACC and IFG during a logical reasoning task and to investigate if these networks are modulated by the believability load

of the inferences among two age groups. Our whole-brain task-related and functional connectivity results support the critical role of inhibitory control and response inhibition – reflected in the functional networks from ACC and IFG – during logical reasoning among older adults. Interestingly, through analysis of the relationship between Uncinate Fasciculus and behavioral performance, our results further support that the structural integrity of these tracts and their connections are underlying the logical reasoning performance. In summary, our behavioral, functional, and structural data suggest that older adults might have more difficulties in inhibition of their current beliefs that is reflected in the engagement of wide-spread frontal and parietal networks during the syllogistic reasoning task. Furthermore, our results provide a possible explanation suggesting that the white matter integrity might be an underlying factor contributing to the age-related changes in engagement of these functional networks.

Difficulties in reasoning and drawing conclusions from assumptions might have serious consequences in many instances, ranging from simple and personal instances to complex and political ones. Incongruency of the given assumptions with currently-held personal beliefs in different circumstances adds to the complexity and the importance of this topic. It seems that our ability to inhibit currently-held beliefs, required for a well-construed conclusion, changes with age. This difficulty might result in age-related deficits in evaluating a social situation and hinder the ability to respond to social norms and cues appropriately.

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Compliance with ethical standards

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Conflict of interest

Authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in this study.

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Tables

Table 1. Form of syllogisms, quantifiers, subjects, copula, and predicate used in the experimental design

	Quantifier	Subject	Copula	Predicate
Premise 1	All	Set_1	is	Set_2
Premise 2	No	Set_2	is	Set_3
Conclusion	Some	Set_3	is not	Set_1

Table 2. Descriptive and inferential statistics of performance on background measures and logical reasoning task

Measurements	Younger adults Mean (SD)	Older adults Mean (SD)	Inferential statistics t
Age	21.13 (2.72)	70.66 (4.21)	5.79**
Gender	15 females	15 females	-
Education (yrs)	15.28 (1.97)	16.50 (4.07)	1.40
NART FSIQ	112.02 (4.77)	119.47 (4.99)	5.51**
Trail Making Test (sec)			
Trail A	18.14 (5.24)	27.43 (5.86)	6.40**
Trail B	40.05 (12.55)	53.04 (13.44)	3.83**
B-A index	21.90 (10.34)	25.61 (13.00)	1.20
DASS – 21			
Stress	6.06 (5.19)	5.06 (4.83)	0.76
Anxiety	2.68 (3.55)	1.60 (2.54)	1.35
Depression	3.31 (4.60)	1.66 (2.92)	1.64

Stroop test (sec)

Congruent		0.72 (0.12)	1.24 (0.23)	10.69[**]
Incongruent		0.82 (0.16)	1.46 (0.36)	8.68[**]
Neutral		0.70 (0.10)	1.13 (0.19)	10.50[**]
Stroop effect		0.16 (0.12)	0.29 (0.21)	2.88[*]

Conclusion

RT (sec)	Unbelievable	4.57 (1.00)	5.60 (1.49)	6.17[**]
	Believable	4.88 (1.04)	5.86 (1.53)	4.95[**]
Rejection	Unbelievable	0.96 (0.07)	0.88 (0.16)	2.47[*]
	Believable	0.95 (0.14)	0.74 (0.23)	4.27[**]

*$p < 0.05$, **$p < 0.005$. NART FSIQ = National Adult Reading Test Full-Scale Intelligence Quotient; Stroop effect = (Incongruent – neutral/neutral); DASS-21 = Depression, Anxiety, Strees Scale; sec = second; SD = standard deviation; M = mean; t = two-sample t test.

Table 3. Whole-brain task-related results showing regions for all conditions among older adults during the decision-making stage

Regions	Hem	MNI coordinates XYZ	BSR
Anterior cingulate cortex	R	2 54 10	7.9374
Anterior cingulate cortex	R	0 46 -4	8.3378
Inferior frontal gyrus (p. Triangularis	L	-52 32 10	6.3213
Middle frontal gyrus	L	-26 32 46	7.208
Precentral gyrus	R	38 -20 52	8.443
Superior temporal gyrus	L	-58 -12 -4	7.3709
Superior temporal gyrus	R	64 -18 -6	7.0866
Temporal pole	L	-40 18 -18	4.4267
Superior parietal lobe	L	-6 -36 48	8.6503
Postcentral gyrus	L	-58 -6 28	5.0609
Lingual gyrus	L	-14 -74 -8	5.5967
Fusiform gyrus	R	26 -30 -18	5.7254
Superior occipital gyrus	L	-20 -86 36	6.0812
Superior occipital gyrus	R	16 -86 34	4.8526
Middle occipital gyrus	L	-50 -74 6	6.0241
Inferior occipital gyrus	R	42 -78 -10	5.2606
Occipital gyrus	R	42 -70 6	7.4544
Occipital lobe	L	-30 -84 2	5.7525

Hippocampus	R	22 -14 -14	5.124

Hem = hemisphere; BSR = bootstrap ratio; MNI = Montreal Neurological Institute.

Table 4. Functional brain networks of IFG and ACC for all conditions among older adults during the decision-making stage.

Regions	Hem	MNI coordinates XYZ	BSR
Anterior cingulate cortex network			
Anterior cingulate cortex	R	-10 36 18	-4.61
Anterior cingulate cortex	L	8 40 4	-4.84
Medial cingulate cortex	R	4 -16 38	-5.83
Paracentral lobule	L	-6 -36 60	-6.91
Inferior frontal gyrus (p. Orbitalis)	R	46 18 -12	-5.90
Inferior frontal gyrus (p. Triangularis)	R	56 16 22	-4.68
Superior temporal gyrus	R	54 -24 4	-5.54
Superior temporal gyrus	L	-56 -8 0	-5.15
Middle temporal gyrus	L	-44 -74 20	-4.98
Middle frontal gyrus	R	42 34 18	-5.10
Middle frontal gyrus	L	40 18 56	-4.53
Superior frontal gyrus	R	20 16 60	-4.95
Lingual gyrus	R	22 -44 -2	-4.83
Superior medial gyrus	L	-8 48 24	-4.82
Thalamus	R	26 -20 -2	-6.18
Thalamus	L	-10 -32 6	-3.54

	Hem	MNI	BSR
Cerebellum	R	8 -74 -14	-3.97
Cuneus	L	-12 -58 24	-3.41
Hippocampus	R	36 -18 -16	-3.84

Inferior frontal gyrus network

	Hem	MNI	BSR
Inferior frontal gyrus (p. Triangularis)	R	46 2 8	-16.14
Inferior frontal gyrus (p. Triangularis)	L	-50 20 16	-14.26
Anterior cingulate cortex	R	18 42 4	-4.71
Middle occipital gyrus	R	38 -84 0	-5.48
Middle temporal gyrus	L	-56 6 -22	-5.95
Temporal pole	L	-46 8 -22	-6.80
Inferior parietal lobule	R	-50 -50 38	-5.54
Hippocampus	R	38 -24 -14	-5.04
Hippocampus	L	-31 -8 -17	4.76
Cerebellum	L	-20 -50 -16	-5.32
Precuneus	R	2 -62 62	-5.15

Hem = hemisphere; BSR = bootstrap ratio; MNI = Montreal Neurological Institute.

Figures' Legends

Figure 1. The timing and example of the experimental design. In this experiment, participants were presented with the first premise for two seconds followed by the second premise that was shown for 4 seconds. During the conclusion presentation, 12 seconds, participants were asked to choose if the conclusion follows the two premises or not, using the MRI compatible response box. Onsets from the second premise were used to assess the brain activity during premise integration and onsets from the conclusion stage were used to measure brain activity related to the decision-making stage.

Figure 2. Whole-brain task-related results during decision-making. Onsets of the conclusion stage for all six experimental conditions were used for this analysis and results reported in multiple TRs, from 3rd TR (around 1.96 sec) to 9th TR (around 5.89 sec). Older adults recruited these areas more than their younger counterparts for all conditions. All reported regions have bootstrap ratio $\geq$ 3.5 and cluster size $\geq$ 50 voxels. Abbreviations: L = left hemisphere, R = right hemisphere.

Figure 3. Anterior cingulate cortex functional connectivity results among older adults. Onsets of conclusion stage were used for this analysis. *Panel A*, Brain regions shown in yellow were positively correlated with the anterior cingulate and contributed to more rejection for believable inferences (believable premise/believable conclusion; BB) among older adults (Panel C), but none of the effect is significant among younger adults (Panel B). *Panel B,* A correlation between the brain activity pattern in panel A and behvioral performance among younger adults. *Panel C*, A correlation between brain activity pattern in panel A and behavioral performance among older adults. All experimental conditions were included in this analysis but for the simplicity of representation, only significant conditions are shown. Peak coordinate used for ACC = [0 32 22]. All reported regions have bootstrap ratio $\geq$ 3 and cluster size $\geq$ 50 voxels. Abbreviations: ACC = anterior cingulate cortex, L = left hemisphere, R = right hemisphere.

Figure 4. Inferior frontal gyrus functional connectivity results among older adults. Onsets of the conclusion stage were used for this analysis. *Panel A*, Brain regions shown in yellow were positively correlated with the inferior frontal gyrus and contributed to more rejection for believable inferences (Believable premise/believable conclusion; BB) and less rejection of unbelievable inferences (Unbelievalbe premise/unbelievable conclusion; UU) among older adults (Panel C), but none of the effect is significant among younger adults (Panel B). *Panel B*, A correlation between the brain activity pattern in panel A and behvioral performance among younger adults. *Panel C*, A correlation between the brain activity pattern in panel A and behvioral performance among older adults. All experimental conditions were included in this analysis but for the simplicity of representation, only significant conditions are shown. Peak coordinate used for IFG = [48 22 8] and [-48 22 16]. All reported regions have bootstrap ratio $\geq$ 2.5 and cluster size $\geq$ 50 voxels. Abbreviations: IFG = inferior frontal gyrus, L = left hemisphere, R = right hemisphere, UU = unbelievable premise/unbelievable conclusion, BB = believable premise/believable conclusion.

Figure 5. Mediation of the effect of age on inhibition of belief via integrity of Uncinate Fasciculus fractional anisotropy (FA). *Panel A,* mediation analysis on rejection rates of believable inferences. The numbers

along the paths represent standardized regression coefficients. The coefficient below the path from age group to believable inference represents the indirect effect (c') when left or right Uncinate Fasciculus FA value was included as a mediator and coefficient above the path represents the direct effect with no mediator in the model. ***Panel B,*** mediation analysis on rejection rates of unbelievable inferences. The numbers along the paths represent standardized regression coefficients. The coefficient below the path from age group to believable inference represents the indirect effect (c') when left or right Uncinate Fasciculus FA value was included as a mediator and coefficient above the path represents the direct effect with no mediator in the model.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5