THESIS

THE ASSOCIATION BETWEEN OCCUPATIONAL COMPLEXITY AND WHITE MATTER HEALTH IN THE BRAIN

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ABSTRACT

THE ASSOCIATION BETWEEN OCCUPATIONAL COMPLEXITY AND WHITE MATTER HEALTH IN THE BRAIN

Occupational complexity (OCC) refers to experiences that increase one's environmental stimulation in a job and provide greater opportunities for skill development. Understanding the association between OCC and brain white matter is critical in aging research as it can elucidate the potential protective effects of stimulating environments on brain health and shed light on strategies for preserving microstructural integrity as individuals age. The current study examines whether working a complex job is associated with white matter integrity, determined by fractional anisotropy (FA). Participants included 58 healthy adults aged 18-85 (M = 49.2, SD =21.7) who completed diffusion-weighted imaging scans and a subcategory of a validated work survey to assess OCC. A principal component analysis reduced the survey items to four meaningful constructs. Higher age was consistently associated with lower FA. Information processing was significantly associated with FA in the inferior longitudinal fasciculus. Additionally, a significant interaction between information processing and age in the forceps major suggests the effect of OCC on FA is dependent on age. These findings highlight that while OCC is associated with FA, its effects may vary by regions and age, pointing to a more nuanced relationship between work characteristics and brain health.

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The Association Between Occupational Complexity and White Matter in the Brain

Within the aging population in the U.S., an array of challenges exists that encompasses not only cognitive changes typical of aging but also more severe neurodegenerative conditions like Alzheimer's disease and related dementias. Promoting brain health throughout the lifespan may help alleviate the concerns that arise during aging. There is a growing interest in identifying protective factors that may delay the onset of cognitive decline and neuropathology. In this thesis, I aim to examine whether working a complex job supports brain health.

White Matter and Aging

Biological aging is associated with structural changes in the brain's white matter, including variations in myelin degeneration (Salat et al., 2005; Bennett et al., 2010; Coelho et al., 2021). These changes can be measured using diffusion-weighted imaging (DWI). DWI is a non-invasive imaging method that uses magnetic resonance imaging (MRI) technology to measure water movements within the microarchitecture of brain tissue, such as white matter (Raja et al., 2019). Diffusion tensor imaging (DTI) is a specific model used with DWI data to estimate the magnitude and direction of water molecule diffusion within white matter (Soares et al., 2013). Measures derived from the DTI model, like fractional anisotropy (FA), are related to the microstructural properties of white matter. Water diffuses in specific directions due to axonal fiber structures. FA quantifies the degree of anisotropy of water diffusion within a voxel of brain tissue. Higher FA values are associated with intact, well-organized tracts, whereas lower FA values indicate abnormalities in white matter (Soares et al., 2013).

Age-related changes in white matter may be attributed to myelin and axon degeneration independent of disease (Madden et al., 2012). Patterns of white matter changes have also been identified in the literature such as lateralized patterns of damage identified in neuropathology (Liu et al., 2018). These patterns may also be region-specific. Regions that are late to mature have been hypothesized to be more vulnerable to change (Raz et al., 2005; Madden et al., 2012; Yoon et al., 2008; Burzynska et al., 2010). Larger age-associated differences in FA in frontal white matter are consistent with an anterior-posterior gradient of changes. Age-related changes in the corpus callosum have shown that the genu and anterior portions decrease in volume with increasing age, whereas posterior areas of the callosum comparatively remain the same (Janowsky et al., 1996; Salat et al., 2005). Together, these findings suggest regional diversity in white matter changes occur over time.

Reserve

Previous research has explored the variations in cognitive decline observed in healthy aging to understand why some individuals undergo more pronounced decline than others (Stern et al., 2003; Gunstad et al., 2006; Rentz et al., 2009; Singh-Manoux et al., 2011). Terms such as maintenance, compensation, resilience, and reserve have often been used to describe these individual differences (Barulli & Stern, 2013; Cabeza et al., 2018; Stern et al., 2019). A consensus framework has been developed to provide researchers standardized nomenclature that sets clear and precise operational definitions to facilitate research on these concepts (Stern et al., 2023). Resilience is an all-encompassing term that considers any concept related to the brain's capacity to maintain cognition and function with aging and disease. Reserve and maintenance are thought to be the underlying mechanisms supporting resilience. In general, reserve describes the brain's ability to protect cognitive performance. Maintenance refers to the brain's capability to sustain structural and functional integrity over time despite aging-related changes. Compensation involves recruiting alternative neural networks or cognitive strategies to mitigate the impact of age-related declines. Based on the current study's aim to investigate how life experiences, such as occupational complexity, are associated with brain health, the concept of reserve will be focused on.

Previous authors have used specific terms such as cognitive reserve and brain reserve to explain the processes attenuating cognitive decline in aging. Cognitive reserve refers to the adaptability of cognitive processes in the presence of brain changes due to aging or pathology (Stern et al., 2020). Engaging in stimulating physical or mental activities has been shown to help maintain cognitive functioning in healthy aging and delay the onset of age-related cognitive decline (Bialystok et al., 2012). However, because cognitive reserve cannot be directly measured, several proxy measures, such as education and occupation, have been used to summarize the experiences that affect reserve (Stern et al., 1999). Stern et al. (2023) posit that research of cognitive reserve should include: 1) factors related to life-course changes believed to affect cognitive outcomes, 2) a measure of cognitive changes related to these factors, and 3) a moderating variable that is associated with 1 and 2. For example, research has indicated that individuals with higher IQ, education attainment, occupational attainment, or participation in leisure activities exhibit less severe clinical or cognitive changes in the presence of age-related decline or Alzheimer's disease pathology (Tucker & Stern, 2011) In this example, age-related cognitive decline and Alzheimer's disease are element one, and the cognitive outcomes related to IQ, education and occupation attainment, and leisure activities are element two. Cognitive reserve is the variable influencing the relationship between elements one and two.

Brain reserve is a concept used to relate the neurobiological status of the brain at a given time and does not involve adapting functional cognitive processes in the presence of injury (Stern et al., 2023). It has been associated with individual differences in level of cognition given a specific amount of brain change, injury or disease (Valenzuela & Sachdev, 2006). According to Stern et al. (2023), research investigating brain reserve should include: 1) measures of brain features, and 2) related measures of cognition. For example, one study where intracranial volume was used a proxy of brain reserve, researchers found a positive effect of brain reserve and cognition in the presence of Alzheimer's disease pathology (Groot et al., 2018). In this example, intracranial volume is the measure of brain features (element 1), and the study's use of a standardized neuropsychological test battery was the related measure of cognition (element 2). It is possible that measures of reserve can reflect both the effect of pathologies and the impact of protective factors throughout the lifespan, making the brain and cognitive reserve concepts complementary to one another. Thus, specifying cognitive reserve and brain reserve may not be necessary in the context of the current study.

Occupational Complexity

Considering the characteristics of one's occupation is crucial in evaluating reserve. Occupational complexity (OCC) has been defined in previous literature (Finkel et al., 2009) as work related to data, people, and things; the greater presence of these elements the more complex a job is considered. Cognitive demands in a job are consistent with the reserve hypothesis in that a cognitively stimulating environment may increase neuronal performance by helping the brain counteract neural damage that could manifest as disease (Jefferson et al., 2011). OCC has been identified as a significant contributor to reserve, with studies demonstrating its association with brain structure, cognitive health, and the pace of cognitive decline in aging individuals (Evans et al., 2018; Fujishiro et al., 2019; Huh et al., 2024; Rydström et al., 2022). These findings underscore the importance of considering OCC as a factor in promoting brain health in aging populations.

To the best of my knowledge, only one other study has investigated the relationship between OCC and white matter health (Kaup et al., 2018). Kaup and colleagues used data from 669 individuals who participated in the Coronary Artery Risk Development in Young Adults (CARDIA) study to investigate associations between occupational cognitive complexity during early to mid-adulthood and gray matter volume, white matter integrity, and cognitive function. The researchers derived occupational cognitive requirement scores (OCRS) from participants' occupational data at Years 10 and 15. OCRS were calculated using the O*NET database, which contains survey data from U.S. workers rating the cognitive activity levels in their occupation on a scale from 0 to 7, with 7 being the highest rating (Peterson et al., 1999). A maximum OCRS was calculated for each participant across Years 10 and 15 to represent the complexity of their most demanding occupation, which served as the measure for OCC in analyses. Mean FA values were calculated across the whole brain and by lobe. Linear mixed models were used to test the relationship between OCC, gray matter volume, white matter FA, and cognitive performance. The results found differences in FA values associated with OCC, specifically that occupational cognitive complexity during early to mid-adulthood is associated with higher white matter integrity in older age (Kaup et al., 2018). However, the association between OCC and FA by lobe may be too simplistic to depict the region-specific changes in white matter previously described (Raz et al., 2005; Burzynska et al., 2010; Coelho et al., 2021).

The current study will replicate and extend these findings by operationalizing OCC with the Work Design Questionnaire (WDQ, Morgeson & Humphrey, 2006). While assigning scores to job titles may be an objective measure of OCC, it may not capture individual variability within the same role. The WDQ addresses this limitation by including items that cover multiple dimensions of work and related constructs.

This study aimed to explore whether workers' perceptions of engaging in a complex occupation promotes white matter structural integrity. I hypothesized that working a complex job would predict higher FA after controlling for age. Second, I hypothesized that working a complex job would mediate the effects of education on FA after controlling for age.

Methods

Participants

Participants were adults ages 18-85 (M = 50.9, SD = 21.5) recruited from Northern Colorado between June 2019 and December 2022. The eligibility criteria were: 1) aged 18 to 85; 2) reported no major psychiatric or neurological illness; 3) demonstrated normal or corrected-to-normal vision; 4) were free from MRI contraindications; 5) had no history of major head injury; 6) were cognitively normal based on a Montreal Cognitive Assessment (MoCA) score greater than or equal to 26 (Nasreddine et al., 2005); 7) did not have uncontrolled hypertension; and 8) were fluent English speakers. Of the eligible participants, 58 completed the occupation measure survey, and 46 had valid DTI data. The study sample comprised 37 females (63.8%), mean education years completed was 16 (SD = 1.93), all identified as white race, and 3 (8.1%) as Hispanic or Latino ethnicity. Participant demographic characteristics are reported in Table 1.

This study was approved by Colorado State University's Institutional Review Board. Written and informed consent was obtained from all participants. Participants were recruited through a flyer campaign throughout the northern Colorado region.

MRI Acquisition

Participants were scanned using a Siemens MAGNETOM Skyra 3Tesla MR system (model #145672) with a 64-channel Head/Neck coil (HC1-7:NC1). All scans were acquired during a single 60-minute scan session at the Translational Medicine Institute at Colorado State University.

An anatomical 3D high-resolution T1-weighted magnetized-prepared rapid gradient echo (MPRAGE) sequence with the Generalized Autocalibrating Partially Parallel Acquisition

(GRAPPA) was acquired (TR = 2400ms; TI = 1000ms; TE = 2.32ms; flip angle = 8°; FOV = 230mm x 230mm; matrix size = 255 x 255; in-plane resolution = 0.9mm; slice thickness = 0.9mm; slices = 192; slice spacing = 0; acceleration factor = 2; acquisition orientation = sagittal). Whole-brain diffusion tensor imaging (DTI) data were acquired using echo-planar imaging sequence (RT = 3500 ms, TE = 74 ms, FOV = 245 mm, matrix 128 x 128, voxel size = 1.9 x 1.9x 2.0 mm, slice = 58, slice thickness = 2.0 mm, slice spacing =0, acceleration factor = 2, acquisition orientation = transversal) in the A-P and P-A phase encoding direction. Diffusion gradients were applied in 64 directions with b= 1000 s/mm^2 , and b =0 s/mm^2 interleaved.

Processing of DTI data

DTI data were processed using the FSL 4.1 Diffusion Toolbox (FDT: http://www.fmrib.ox.ac.uk/fsl/) in a multistep procedure that includes: 1) motion and eddy current correction, 2) removing skull and non-brain tissue using the Brain Extraction Tool (Smith, 2002), and 3) voxel-by-voxel calculation of the diffusion tensors. Using the diffusion tensor information, FA maps were computed using DTIFit within the FDT tool.

TBSS analysis

FSL Software (Smith et al., 2004) was used to perform voxel-wise statistical analysis of white matter using Tract Based Spatial Statistics (TBSS, Smith et al., 2006) and included: 1) aligning each participant's FA volume to standard Montreal Neurological Institute (MNI152) space via the FMRIB58_FA template using the FMRIB's Nonlinear Registration Tool (FNIRT, Andersson et al., 2019), 2) calculating the mean of all aligned FA images, 3) creating a skeleton image to represent the common tracts among all subjects by perpendicular non-maximum-suppression of the mean FA image and setting the FA threshold to 0.2, and 4) perpendicular projection of the highest FA value onto the skeleton was conducted for each subject.

Regions of Interest

White matter FA was calculated for the following regions of interest: 1) Fornix, 2) External capsule, 3) Cingulum bundle, 4) Forceps Major, 5) Forceps Minor, 6) Longitudinal Fasciculus (Inferior), 7) Anterior limb of Internal Capsule, and 8) Posterior limb of Internal Capsule. The ROIs were defined using the probabilistic Johns Hopkins University ROI atlas (Mori et al., 2008). To create the ROIs, the "fslmeants" command on the FA skeletonized data was applied, ensuring that the mean FA values within each ROI were accurately extracted. Additionally, a threshold was applied to the ROIs at 2500 intensity value. The selected association and commissural fibers were chosen based on their specific connections and functional associations with regional patterns of white matter changes and their unique vulnerability to aging and neurodegeneration (Bullock et al., 2022; Schilling et al., 2022).

Quantifying Occupational Complexity

The Work Design Questionnaire (Morgeson & Humphrey, 2016) was used to quantify OCC. The WDQ is a validated measure for assessing job design and the nature of work. This measure encompasses various dimensions of work, allowing for a holistic assessment of job roles and tasks. Participants answered the knowledge characteristics section of the WDQ which measures dimensions such as job complexity, information processing, problem solving, skill variety and specialization. Participants answered this section twice. The first time they answered, they were asked to refer to their current or most recent occupation. The second time they answered, they were asked to refer to other major occupations since the age of 30 (or earlier if employment continued well into their 30s). However, answering these items a second time was optional. Therefore, not all eligible participants completed this section. Participants' responses for their most recent job were used in the analyses to account for the wide range of ages in the study. Younger participants may have only held one job, making this approach more inclusive, while older participants are likely to provide more accurate responses by recalling their most recent position, given the potential challenges of remembering details from jobs held earlier in life. All items used a 7-point “strongly disagree” to “strongly agree” scale, with greater levels of agreement indicating a higher presence of the work characteristic, except for the “job complexity” items which are reverse coded.

Cognitive Assessment Battery

The National Institute of Health Toolbox- Cognition Battery (NIHTB-CB, (Gershon et al., 2014) is a computer-administered protocol that offers a comprehensive and standardized approach to assessing cognitive function across different age groups and populations. It is designed to test multiple cognitive domains, including 1) attention, 2) executive function, 3) language, 4) memory, and 5) processing speed. Composite scores of fluid cognition, crystallized cognition, and their combined average are calculated, where higher scores reflect higher levels of cognitive functioning. Scores from NIHTB-CB can be used to screen for subjects that may be experiencing early decline. Therefore, an exploratory analysis of the effects of cognitive scores on FA was also performed. No significant associations were found so the cognitive battery scores were not considered as covariates in subsequent analyses.

Statistical Analysis Plan

Linear regression models were performed to test whether the main effect of each occupation component, age, and their interaction predicted FA in the selected ROIs (Hypothesis 1). The dependent variable was FA values of each ROI. The independent variables were the occupation component scores and age. These variables were scaled (mean-centered) before forming the interaction term to account for the individual effects of occupational complexity and age, and their combined influence on FA. These models were tested using the “stats” package in base R software (Bates et al., 2015). Analyses also examined whether education mediates the relationship between occupational complexity and FA (Hypothesis 2). Education was defined as the years of education completed (doctoral degree = 20 years, master’s or professional degree = 18 years, bachelor’s degree = 16 years, high school diploma or equivalent = 12 years). Age was included in the model as a covariate to control for its confounding effect on education and FA.

Results

Principal Components Analysis

To reduce dimensionality and to identify core composites within the WDQ items, a principal component analysis (PCA) using oblique (oblimin) rotation was performed using the parallel analysis method from the "psych" package in R (Revelle, 2023). Four components were identified. The eigenvalues for each component were greater than one and a scree plot confirmed that four components should be retained (Figure 1). While the subscales of the WDQ are assumed to measure five dimensions of occupational characteristics, the loading matrix of the PCA suggests four distinct constructs: problem solving, specialization, information processing, and job complexity. Problem solving and skill variety variables loaded highly onto Component 1 and explained 24% of the variance. The items that loaded onto this component emphasized problem-solving and applying a range of skills to deal with novel and ambiguous situations. Specialization items loaded onto Component 2 and explained 18% of the variance. The items that loaded highly onto the specialization component reflected job demands and expertise. Information processing items loaded strongly to Component 3 and explained 18% of the total variance. Variables that loaded highly to this component concerned synthesizing information necessary for job performance. Job complexity items primarily loaded on Component 4 and explained 17% of the total variance. Items that loaded highly to this component were associated with the complexity of tasks. Overall, the model showed good fit with a Root Mean Square Residual (RMSR) of 0.06 and an off-diagonal value of 0.98. Loadings for the four components are reported in Table 2. Component correlations are reported in Table 3. The "predict" function in base R was used to assign the new component scores from the PCA to each study observation based on their responses.

Hypothesis 1: Job complexity predicts FA

Fornix

Linear regression models examined the relationships between FA in the fornix and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 4. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effects of all four component scores were not significant. Specifically, an increase in specialization and job complexity were associated with a nonsignificant increase in FA, while problem solving, and information processing were associated with a nonsignificant decrease in FA (*p*s > .1). Additionally, the interaction terms between age and each component did not significantly predict FA in the fornix (*p*s > .1), suggesting that the relationship between the occupation component and FA does not vary by age.

External capsule

Linear regression models examined the relationships between FA in the external capsule and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 5. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effects of all four component scores were not significant (*p*s > .1); however, the main effect of job complexity on FA was significant on a trend level (*p* = .078). Specifically, higher job complexity was associated with marginally lower FA in this region. The main effects of problem solving, and specialization were associated with nonsignificant increases in FA, while the main effect of information processing was associated with a nonsignificant decrease in FA. Additionally, the interaction term between age and information processing was marginally significant (*p* = .052) indicating a trend where the relationship between information processing and FA in the external capsule is stronger in older individuals. The interaction terms between age, problem solving, specialization, and job complexity did not significantly predict FA (*p*s > .1), suggesting that the relationship between these components and FA does not vary by age.

Cingulum bundle

Linear regression models examined the relationships between FA in the cingulum bundle and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 6. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effects of all four component scores were not significant (*p*s > .1); however, the main effect of information processing was significant on a trend level (*p* = .08). Specifically, higher information processing was marginally associated with lower FA. The main effects of all other components were associated with nonsignificant decreases in FA. Additionally, the interaction terms between age and each component did not significantly predict FA in the cingulum bundle (*p*s > .1), suggesting that the relationship between the occupation components and FA does not vary by age.

Forceps Major

Linear regression models examined the relationships between FA in the forceps major and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 7. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effects of all four component scores were not significant (*p*s > .1). Specifically, the main effects of problem solving, and specialization were associated with a nonsignificant increase in FA, while information processing and job complexity were associated with a nonsignificant decrease in FA. Additionally, the interaction term between age and information processing was significant (*p* = .011), showing that the relationship between information processing and FA in the forceps major becomes stronger with increasing age. The interaction terms between age, problem solving, specialization, and job complexity did not significantly predict FA, suggesting that the relationship between these components and FA does not vary by age.

Forceps Minor

Linear regression models examined the relationships between FA in the forceps minor and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 8. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effects of all four component scores were not significant (*p*s > .1); however, the main effect of information processing was significant on a trend level (*p* = .094). Specifically, higher information processing was marginally associated with lower FA. The main effects of all other occupation components were associated with nonsignificant decreases in FA. Additionally, the interaction terms between age and each component did not significantly predict FA in the forceps minor (*p*s > .1), suggesting that the relationship between the occupation components and FA does not vary by age.

Inferior Longitudinal Fasciculus

Linear regression models examined the relationships between FA in the inferior longitudinal fasciculus (ILF) and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 9. Across all models, the effect of age on FA was significant, with higher age associated with lower FA (*p*s < .001). The main effect of information processing on FA was significant (*p* = .033), such that higher information processing was associated with lower FA. The main effects of all other components on FA were not significant (*p*s > .1). Specifically, an increase in problem solving and specialization was associated with a nonsignificant increase in FA, while job complexity was associated with a nonsignificant decrease in FA. Additionally, the interaction term between specialization and age on FA was marginally significant (*p* = .064) indicating a trend where the relationship between specialization and FA is stronger in older individuals. The interaction terms between age and problem solving, information processing, and job complexity did not significantly predict FA (*p*s > .1), suggesting that the relationship between these components and FA does not vary by age.

Anterior Internal Capsule

Linear regression models examined the relationships between FA in the anterior limb of the internal capsule (ALIC) and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 10. The main effect of age on FA was significant for specialization (*p* = .039) and information processing (*p* = .044) with higher age associated with lower FA. The main effect of age on FA for problem solving was significant at a trend level (*p* = .053) with higher age marginally associated with lower FA. The main effects of all four component scores on FA were not significant (*p*s > .1). Specifically, an increase in problem solving, specialization, and information processing was associated with a nonsignificant increase in FA, while an increase in job complexity was associated with a nonsignificant decrease in FA. Additionally, the interaction terms between age and each component did not significantly predict FA (*p*s > .1), suggesting that the relationship between these components and FA does not vary by age.

Posterior Internal Capsule

Linear regression models examined the relationships between FA in the posterior limb of the internal capsule (PLIC) and the four occupation component scores from the PCA results with age included as both a predictor and an interaction term (i.e., the age-by-component effect). Parameter estimates are reported in Table 11. The main effect of age on FA was significant for problem solving (*p* = .047) and information processing (*p* = .042), with higher age associated with lower FA. The main effect of age on FA was significant at a trend level for information processing (*p* = .067), suggesting higher information processing was marginally associated with lower FA. The main effects of all four component scores on FA were not significant (*p*s > .1). Specifically, an increase in problem solving and information processing was associated with a nonsignificant increase in FA, while an increase in specialization and job complexity was associated with a nonsignificant decrease in FA. Additionally, the interaction terms between age and each component did not significantly predict FA (*p*s > .1), suggesting that the relationship between these components and FA does not vary by age.

Hypothesis 2: Education mediates the effects of job complexity on FA

Linear regression models examined the direct effect of education on the four occupation constructs from the PCA results. Parameter estimates are reported in Table 12. Across all models, these effects were not significant (*p*s > .1). Due to the non-significant effect of education on the occupation components, the mediation analysis was not completed since the lack of a significant relationship impedes the possibility for occupational complexity to mediate the effects of education on FA.

Discussion

The current study explored the relationship between workers' perceptions of occupational complexity and FA in aging. Previous research has shown age-related changes in white matter with varying degrees of vulnerability based on specific brain regions (Burzynska et al., 2010; Dvorak et al., 2021; Medina et al., 2021; Salat et al., 2005). By examining how perceived cognitive demands of a person's job contribute to cognitive and brain reserve theories, this study aimed to offer insight into potential protective measures against neurological decline in aging.

Contrary to the first hypothesis, working a complex job did not predict higher FA in all the observed brain regions. The effects are shown in Figures 2-9. A significant main effect of age on FA was seen in 28 of 32 models tested. This is consistent with previous literature showing that higher age is associated with lower FA (Bennett et al., 2010; Burzynska et al., 2010; Coelho et al., 2021; Mendez Colmenares et al., 2023; Salat et al., 2005).

The main effects of the occupation components on FA were significant or trending on a significant level in 3 of the 32 models. A significant main effect of information processing was seen in the inferior longitudinal fasciculus (ILF). Specifically, higher information processing was associated with lower FA. The main effects of other occupation components were not significant; however, higher job complexity was marginally associated with lower FA in the external capsule, and information processing was marginally associated with lower FA in the cingulum bundle and forceps minor. Although not all the models produced significant results, the descriptive main effects of information processing and job complexity suggest that higher levels of these components may only be beneficial in older age.

Significant or trending interactions were seen in 3 out of 32 models. A significant interaction of information processing on FA was detected in the forceps major, indicating that a higher level of information processing is strongly associated with FA in this region as people get older. Interactions between information processing and FA in the external capsule and specialization and FA in the ILF were marginally significant. The interaction between information processing on FA in the external capsule hints that this relationship may strengthen with age. However, the interaction between specialization and FA in the ILF implies that this relationship may become weaker as people age. Further research is necessary to understand why components of occupational complexity differ in their abilities to withstand white matter integrity loss.

The second hypothesis that occupational complexity mediates the effects of education while controlling for age was also not supported. An illustrative figure of the indirect relationship between occupational complexity, education, and FA is shown in Figure 10. Namely, education was not a significant predictor of any occupation component (A path). Without a significant A path, a mediation cannot be meaningfully tested (Gunzler et al., 2013). Consequently, the nonsignificant results precluded further testing of the relationship between OCC and FA (B path), and the indirect relationship of education, OCC, and FA (c' path). These null findings raise questions about the role of education in shaping occupational experiences that contribute to brain health. Lövdén et al. (2020) found that the impact of education on cognitive reserve depends on how education is translated into more complex, cognitively demanding environments. Their study reported that the protective effects of education on brain health diminished when controlling for occupational complexity, suggesting that education's benefits rely on exposure to stimulating job demands. However, the current study's inability to replicate this effect may be due to an insufficient sample size to detect a similar pattern, rather than a definitive lack of association.

Applying an occupational health lens to brain health outcomes provides additional insights to healthy aging trajectories. For example, the Brain aging: Occupational Stimulation and Stress (BOSS) model, suggests that occupational characteristics can influence brain health either by promoting protective or risk factors (Burzynska, 2021). A notable finding from Burzynska et al. associated perceived physical stress at work to smaller hippocampal volumes and poorer memory performance. One can infer that subjective perceptions of job demand have an independent impact on brain health. As people age, their capacity to adapt to and handle complex cognitive demands at work may change. This potentially amplifies the effects of perceived occupational complexity on brain health outcomes suggesting that age might intensify the experience of these demands.

A correlation matrix in Table 13 provides additional insights into the relationships between the occupation components and demographic factors. Here, cognitive ability, particularly fluid and crystallized cognition, is positively associated with job complexity and education attainment, while age also plays a role in cognitive performance and job complexity. These results underscore the importance of considering both cognitive and demographic factors when assessing occupational complexity. Older individuals may have had more opportunities to take on more cognitively demanding roles due to accumulated experience and knowledge.

The current findings differ from Kaup et al. (2018), who reported a positive association between occupational complexity and FA. The discrepancy in the results could be due to methodological differences. Kaup et al. used measures based on job titles from the O*NET database, which classifies occupations based on standardized criteria. In contrast, this study utilized individuals' evaluations of the complexity of their work. Workers' perception of occupational complexity may not have a strong enough effect to offset the age-related changes in brain structure.

The results of this study should be interpreted considering several limitations. First, the sample includes younger subjects who have not worked an occupationally complex job as long as older participants. While age is related to microstructural changes in white matter, differences in FA as a function of OCC may still be observed even in young adults (Stern, 2005). This assumption then leads to the possibility that if older participants express FA values similar to young subjects, the relationship between white matter integrity and OCC can be present in both groups. While a subgroup analysis within the existing dataset could be conducted to focus specifically on the older adult population, this would be redundant with the interaction models used; that is, our analysis approach explicitly tested whether the associations between OCC and FA differed by age group. Second, the homogeneity of the sample limits the ability to generalize the findings. Third, the cross-sectional design constrains our ability to make causal inferences. Primarily, the data only provides a snapshot of OCC and does not capture how time spent working a complex job influences structural integrity over time. Fourth, the prevalence of null findings raises concerns about the validity of the few significant effects that were detected, prompting one to question whether these findings reflect genuine relationships or if they are the result of Type 1 error, particularly given the increased risk of family-wise error when multiple comparisons are made. Future research should address these limitations by increasing the sample size with a more diverse population and incorporating explicit items to measure one's occupational history, such as duration and changes in complexity across different points in a career.

Occupational complexity is a broad, multifaceted concept that encompasses various dimensions of work such as problem solving, specialization, information processing, and job complexity. Because of this, it is important to disentangle these components to gain a comprehensive understanding of how occupation characteristics support reserve. By identifying the most influential aspects of occupational complexity, researchers can inform evidence-based strategies to design interventions and implement workplace policies aimed at promoting healthy aging.

Table 1
Participant demographic characteristics

	Female	Male	Overall
	(N=37)	(N=21)	(N=58)
Age			
Mean (SD)	48.9 (21.7)	49.6 (22.2)	49.2 (21.7)
Median [Min, Max]	62.0 [19.0, 85.0]	62.0 [18.0, 77.0]	62.0 [18.0, 85.0]
Race			
White	37 (100%)	21 (100%)	58 (100%)
Ethnicity			
Hispanic	1 (2.7%)	0 (0%)	1 (1.7%)
Hispanic or Latino	2 (5.4%)	0 (0%)	2 (3.4%)
Not Hispanic	34 (91.9%)	21 (100%)	55 (94.8%)
Educations (Years)			
Mean (SD)	15.9 (1.77)	16.3 (2.20)	16.0 (1.93)
Median [Min, Max]	16.0 [12.0, 22.0]	16.0 [12.0, 21.0]	16.0 [12.0, 22.0]
Total MoCA Score			
Mean (SD)	28.1 (1.51)	28.4 (1.33)	28.2 (1.44)
Median [Min, Max]	28.0 [26.0, 30.0]	29.0 [26.0, 30.0]	29.0 [26.0, 30.0]
Imaging			
DTI	26 (70.3%)	20 (95.2%)	46 (79.3%)

Table 2

Loading scores of the PCA showing the transformed components of the oblique rotation

	Transformed Components			
	TC1	TC2	TC3	TC4
Job Complexity 1	0.19	-0.45	**0.59**	0.14
Job Complexity 2	0.05	0.01	0.15	**0.84**
Job Complexity 3	0.13	0.17	0.02	**0.84**
Job Complexity 4	0.05	0.18	0.02	**0.87**
Information Processing 1	-0.06	0.27	0.87	0.02
Information Processing 2	0.06	0.21	**0.63**	0.38
Information Processing 3	-0.02	-0.23	**0.97**	-0.06
Information Processing 4	0.17	0.11	**0.64**	0.27
Problem Solving 1	**0.79**	-0.07	0.08	0.05
Problem Solving 2	**0.84**	-0.08	0.04	0.08
Problem Solving 3	**0.79**	-0.17	0.02	0.30
Problem Solving 4	**0.93**	-0.03	-0.21	0.14
Skill Variety 1	**0.56**	0.40	0.33	-0.36
Skill Variety 2	**0.69**	0.35	0.20	-0.28
Skill Variety 3	0.39	0.38	0.24	0.22
Skill Variety 4	**0.59**	0.33	0.20	-0.18
Specialization 1	-0.19	**0.83**	0.16	0.13
Specialization 2	0.08	**0.74**	-0.22	0.32
Specialization 3	0.19	**0.74**	-0.03	0.23
Specialization 4	0.10	**0.73**	0.02	0.07

Note. PCA= Principal component analysis, TC= Transformed component. Values in bold denote loadings strongly correlated to the respective component.

Table 3

Component correlations of the PCA results

	TC1	TC2	TC3	TC4
TC1	1.00	0.32	0.35	0.27
TC2	0.32	1.00	0.21	0.28
TC3	0.35	0.21	1.00	0.08
TC4	0.27	0.28	0.08	1.00

Note. PCA= Principal component analysis, TC= Transformed component

Table 4

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the fornix

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Fornix	Intercept	0.03	0.10	0.244	.809
	Problem Solving	-0.05	0.12	-0.426	.673
	Age	**-0.73**	**0.10**	**-7.171**	**<.001**
	Problem Solving:Age	0.01	0.11	0.113	.910
	Intercept	0.06	0.11	0.507	.616
	Specialization	0.03	0.13	0.234	.817
	Age	**-0.77**	**0.11**	**-7.018**	**<.001**
	Specialization:Age	-0.10	0.13	-0.777	.442
	Intercept	0.04	0.10	0.384	.703
	Information Processing	-0.18	0.12	-1.534	.134
	Age	**-0.76**	**0.10**	**-7.745**	**<.001**
	Information Processing:Age	0.10	0.12	0.772	.445
	Intercept	-0.02	0.12	-0.143	.887
	Job Complexity	0.01	0.12	0.102	.919
	Age	**-0.74**	**0.11**	**-6.462**	**<.001**
	Job Complexity:Age	0.09	0.11	0.803	.427

Note. Bold items denote statistical significance based on an alpha level of .05.

Table 5

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the external capsule

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
External Capsule	Intercept	-0.09	0.13	-0.679	.501
	Problem Solving	0.09	0.15	0.578	.567
	Age	**-0.62**	**0.13**	**-4.913**	**<.001**
	Problem Solving:Age	0.14	0.14	0.990	.329
	Intercept	-0.10	0.14	-0.720	.476
	Specialization	0.11	0.17	0.631	.532
	Age	**-0.64**	**0.14**	**-4.580**	**<.001**
	Specialization:Age	0.07	0.17	0.423	.675
	Intercept	-0.05	0.12	-0.433	.668
	Information Processing	-0.12	0.15	-0.793	.433
	Age	**-0.67**	**0.12**	**-5.590**	**<.001**
	Information Processing:Age	0.31	0.15	2.010	.052*
	Intercept	-0.04	0.14	-0.274	.785
	Job Complexity	-0.26	0.14	-1.814	.078*
	Age	**-0.51**	**0.14**	**-3.649**	**.001**
	Job Complexity:Age	-0.05	0.13	-0.386	.702

Note. Bold items denote statistical significance based on an alpha level of .05; *p*-values with * denote values trending towards statistical significance.

Table 6

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the cingulum bundle

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Cingulum Bundle	Intercept	-0.01	0.11	-0.108	.915
	Problem Solving	-0.08	0.13	-0.625	.536
	Age	**-0.77**	**0.11**	**-6.991**	**<.001**
	Problem Solving:Age	0.01	0.12	0.072	.943
	Intercept	0.05	0.12	0.385	.703
	Specialization	-0.06	0.15	-0.428	.671
	Age	**-0.81**	**0.12**	**-6.841**	**<.001**
	Specialization:Age	-0.20	0.14	-1.357	.183
	Intercept	0.01	0.10	0.061	.951
	Information Processing	-0.23	0.13	-1.803	.080*
	Age	**-0.82**	**0.10**	**-7.932**	**<.001**
	Information Processing:Age	0.17	0.13	1.309	.199
	Intercept	-0.05	0.12	-0.440	.662
	Job Complexity	-0.13	0.12	-1.018	.315
	Age	**-0.72**	**0.12**	**-5.925**	**<.001**
	Job Complexity:Age	0.10	0.12	0.903	.372

Note. Bolded items denote statistical significance based on an alpha level of .05.

Table 7

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the forceps major

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Forceps Major	Intercept	0.001	0.11	0.008	.993
	Problem Solving	0.004	0.13	0.033	.974
	Age	**-0.73**	**0.11**	**-6.608**	**<.001**
	Problem Solving:Age	0.17	0.12	1.382	.176
	Intercept	0.06	0.12	0.497	.622
	Specialization	0.03	0.15	0.169	.867
	Age	**-0.79**	**0.12**	**-6.460**	**<.001**
	Specialization:Age	-0.17	0.15	-1.140	.262
	Intercept	0.04	0.10	0.368	.715
	Information Processing	-0.10	0.13	-0.814	.421
	Age	**-0.79**	**0.10**	**-7.692**	**<.001**
	Information Processing:Age	**0.35**	**0.13**	**2.673**	**.011**
	Intercept	0.01	0.13	0.092	.927
	Job Complexity	-0.16	0.13	-1.241	.223
	Age	-0.66	0.13	-5.249	**<.001**
	Job Complexity:Age	0.02	0.12	0.146	.885

Note. Bolded items denote statistical significance based on an alpha level of .05.

Table 8

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the forceps minor

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Forceps Minor	Intercept	-0.04	0.09	-0.406	.687
	Problem Solving	-0.08	0.11	-0.750	.458
	Age	**-0.89**	**0.09**	**-9.774**	**<.001**
	Problem Solving:Age	-0.02	0.10	-0.195	.847
	Intercept	0.01	0.10	0.113	.911
	Specialization	-0.12	0.12	-1.040	.305
	Age	**-0.90**	**0.10**	**-9.280**	**<.001**
	Specialization:Age	-0.17	0.12	-1.428	.162
	Intercept	-0.03	0.09	-0.347	.730
	Information Processing	-0.18	0.11	-1.721	.094*
	Age	**-0.91**	**0.09**	**-10.360**	**<.001**
	Information Processing:Age	0.05	0.11	0.415	.681
	Intercept	-0.06	0.10	-0.568	.574
	Job Complexity	-0.16	0.10	-1.629	.112
	Age	**-0.82**	**0.10**	**-8.338**	**<.001**
	Job Complexity:Age	0.06	0.09	0.602	.551

Note. Bolded items denote statistical significance based on an alpha level of .05.

Table 9

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the inferior longitudinal fasciculus

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Longitudinal Fasciculus	Intercept	-0.02	0.13	-0.180	.858
	Problem Solving	0.00	0.15	0.008	.994
	Age	**-0.69**	**0.13**	**-5.456**	**<.001**
	Problem Solving:Age	0.12	0.14	0.886	.381
	Intercept	0.08	0.13	0.576	.568
	Specialization	0.01	0.16	0.052	.959
	Age	**-0.77**	**0.13**	**-5.892**	**<.001**
	Specialization:Age	-0.31	0.16	-1.913	.064*
	Intercept	0.01	0.12	0.045	.964
	Information Processing	**-0.31**	**0.14**	**-2.214**	**.033**
	Age	**-0.73**	**0.12**	**-6.281**	**<.001**
	Information Processing:Age	0.15	0.15	1.018	.315
	Intercept	-0.01	0.14	-0.093	.927
	Job Complexity	-0.09	0.15	-0.632	.531
	Age	**-0.65**	**0.14**	**-4.527**	**<.001**
	Job Complexity:Age	0.01	0.14	0.040	.968

Note. Bolded items denote statistical significance based on an alpha level of .05; *p*-values with * denote values trending towards statistical significance.

Table 10

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the anterior limb of the internal capsule (ALIC)

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
ALIC	Intercept	-0.05	0.17	-0.290	.774
	Problem Solving	0.23	0.20	1.139	.262
	Age	**-0.33**	**0.16**	**-2.002**	**.053**
	Problem Solving:Age	0.10	0.18	0.575	.569
	Intercept	-0.02	0.18	-0.104	.918
	Specialization	0.15	0.22	0.697	.490
	Age	**-0.38**	**0.18**	**-2.141**	**.039**
	Specialization:Age	-0.06	0.22	-0.289	.774
	Intercept	-0.02	0.17	-0.135	.893
	Information Processing	0.11	0.20	0.563	.577
	Age	**-0.34**	**0.17**	**-2.084**	**.044**
	Information Processing:Age	0.26	0.21	1.256	.217
	Intercept	-0.10	0.18	-0.547	.588
	Job Complexity	-0.20	0.18	-1.110	.274
	Age	-0.22	0.18	-1.226	.228
	Job Complexity:Age	0.16	0.17	0.958	.344

Note. Bolded items denote statistical significance based on an alpha level of .05.

Table 11

Results of linear regression analyses testing the effect of occupation components, age, and their interaction on FA in the posterior limb of the internal capsule (PLIC)

Region	Predictor	Estimate	Std. Error	*t*-value	*p*-value
PLIC	Intercept	-0.09	0.17	-0.539	.594
	Problem Solving	0.11	0.20	0.551	.585
	Age	**-0.33**	**0.16**	**-2.052**	**.047**
	Problem Solving:Age	0.02	0.18	0.125	.901
	Intercept	-0.02	0.18	-0.120	.905
	Specialization	-0.06	0.21	-0.276	.784
	Age	**-0.36**	**0.17**	**-2.079**	**.045**
	Specialization:Age	-0.21	0.21	-0.982	.333
	Intercept	-0.09	0.17	-0.566	.575
	Information Processing	0.06	0.20	0.301	.765
	Age	-0.31	0.16	-1.888	.067*
	Information Processing:Age	-0.09	0.21	-0.435	.666
	Intercept	-0.15	0.18	-0.811	.423
	Job Complexity	-0.13	0.18	-0.726	.473
	Age	-0.26	0.18	-1.476	.149
	Job Complexity:Age	0.15	0.17	0.897	.375

Note. Bolded items denote statistical significance based on an alpha level of .05; *p*-values with * denote values trending towards statistical significance.

Table 12

Results of linear regression analyses testing the effect of education on occupation components

Component	Predictor	Estimate	Std. Error	*t*-value	*p*-value
Problem Solving	Education (Years)	0.18	0.20	0.916	.365
Specialization	Education (Years)	-0.03	0.19	-0.144	.886
Information Processing	Education (Years)	-0.09	0.20	-0.458	.649
Job Complexity	Education (Years)	0.23	0.18	1.304	.199

Table 13

Means, standard deviations, and correlations with confidence intervals

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9	10
1. Problem Solving	0	0.96										
2. Specialization	0	0.9	.33* [.04, .56]									
3. Info Processing	0	0.98	.36* [.08, .59]	0.19 [-.11, .46]								
4. Job Complexity	0	0.94	.30* [.01, .54]	0.05 [-.24, .34]	.33* [.05, .57]							
5. Age	49.16	21.7	0.02 [-.27, .31]	-0.06 [-.34, .24]	.40** [.12, .62]	.47** [.21, .67]						
6. Education Years	16.03	1.93	0.15 [-.15, .42]	-0.1 [-.38, .19]	0.17 [-.13, .44]	.36* [.08, .59]	.43** [.19, .62]					
7. Sex	0.64	0.48	-0.08 [-.36, .22]	-0.26 [-.51, .04]	0.03 [-.26, .32]	0.09 [-.21, .37]	-0.01 [-.27, .24]	-0.12 [-.36, .14]				
8. MoCA	28.22	1.44	-0.03 [-.31, .27]	-0.15 [-.42, .15]	0.1 [-.19, .38]	0.12 [-.18, .39]	0.13 [-.13, .38]	.26* [.00, .49]	-0.11 [-.36, .15]			
9. NIH Fluid Cognition	108.4	14.1	0.05 [-.25, .35]	-0.18 [-.45, .13]	-0.01 [-.31, .30]	0.07 [-.23, .37]	0.21 [-.07, .45]	0.03 [-.24, .30]	.28* [.00, .51]	0.25 [-.03, .49]		

10. NIH Crystal Cognition	118.1	12.3	0.02	-0.23	0.01	-0.08	0.06	.32*	0.16	.29*	.35*	
			[-.28, .32]	[-.50, .07]	[-.29, .31]	[-.37, .22]	[-.22, .32]	[.05, .55]	[-.12, .41]	[.02, .52]	[.08, .57]	
11. NIH Total Cognition	115.5	12.4	0.04	-0.24	0.01	0	0.17	0.2	.28*	.35*	.85**	.78**
			[-.26, .34]	[-.50, .07]	[-.30, .31]	[-.30, .30]	[-.11, .42]	[-.08, .45]	[.00, .51]	[.09, .57]	[.75, .91]	[.65, .87]

Note. M and *SD* are used to represent mean and standard deviation, respectively. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$.

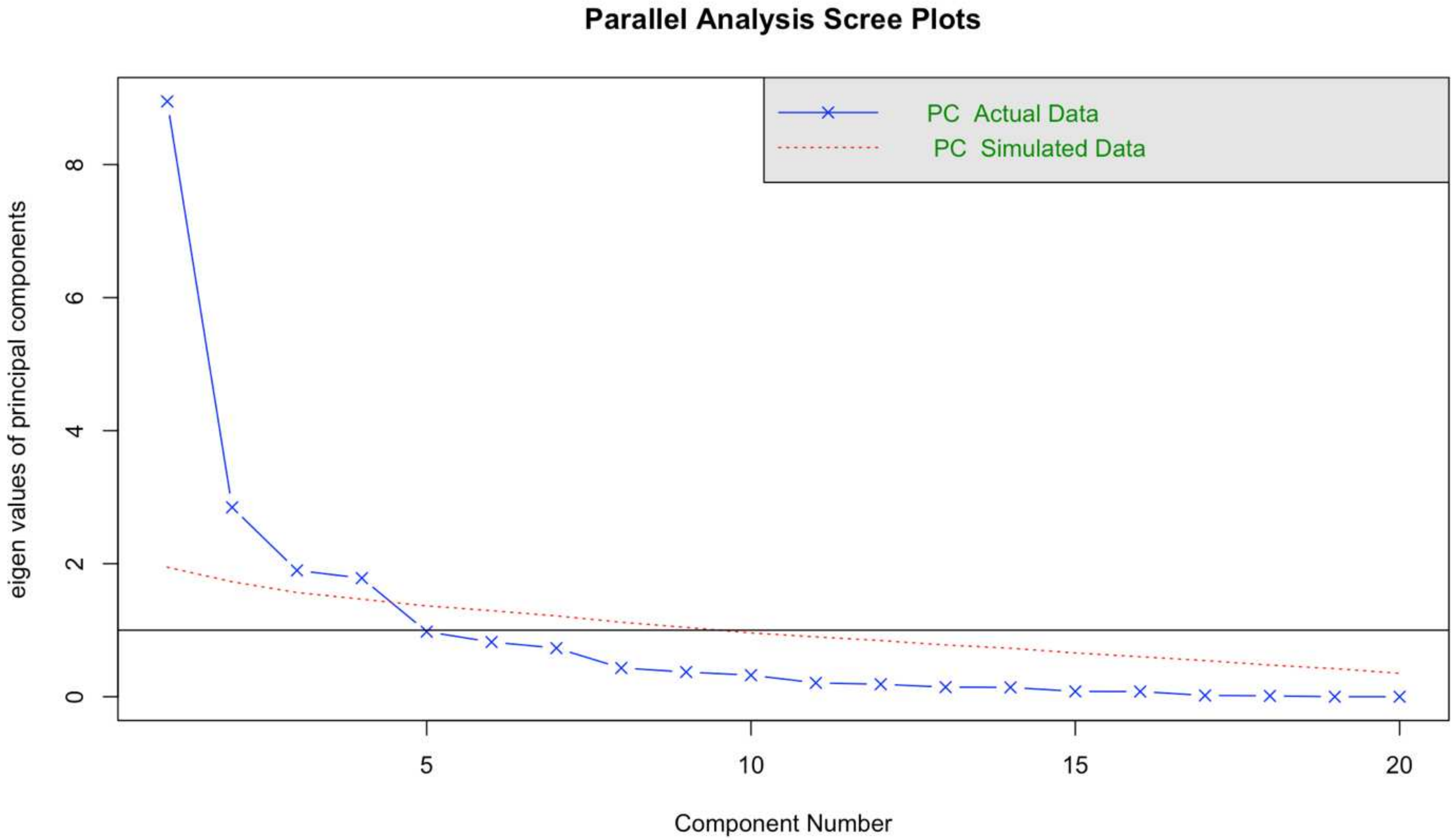


Figure 1: Scree plot confirming PCA results that four components should be retained. Note. PCA= Principal component analysis

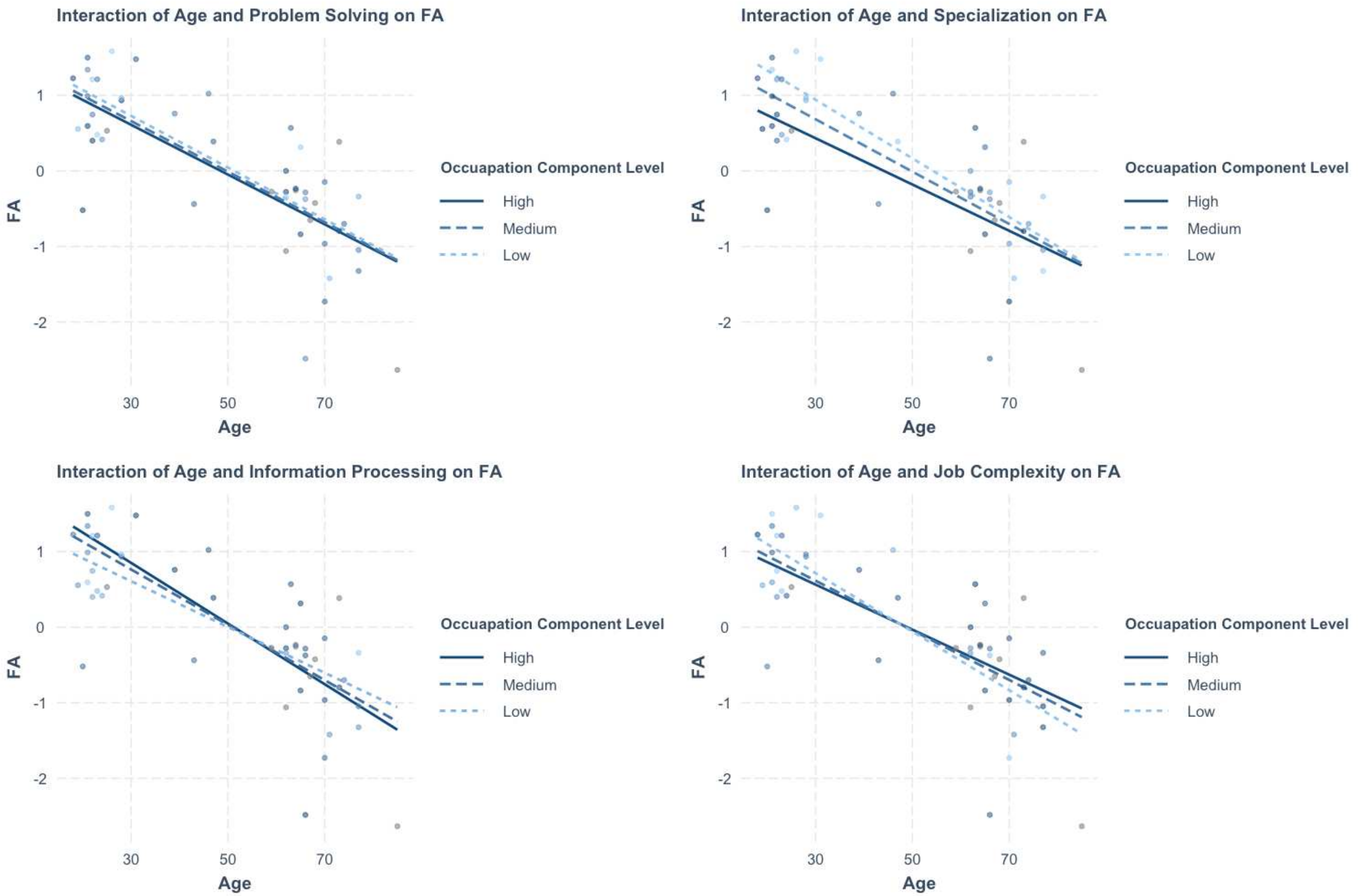


Figure 2: Simple slope plots showing relationship between FA in the fornix and age by occupation component. Note. Variables are scaled (mean-centered).

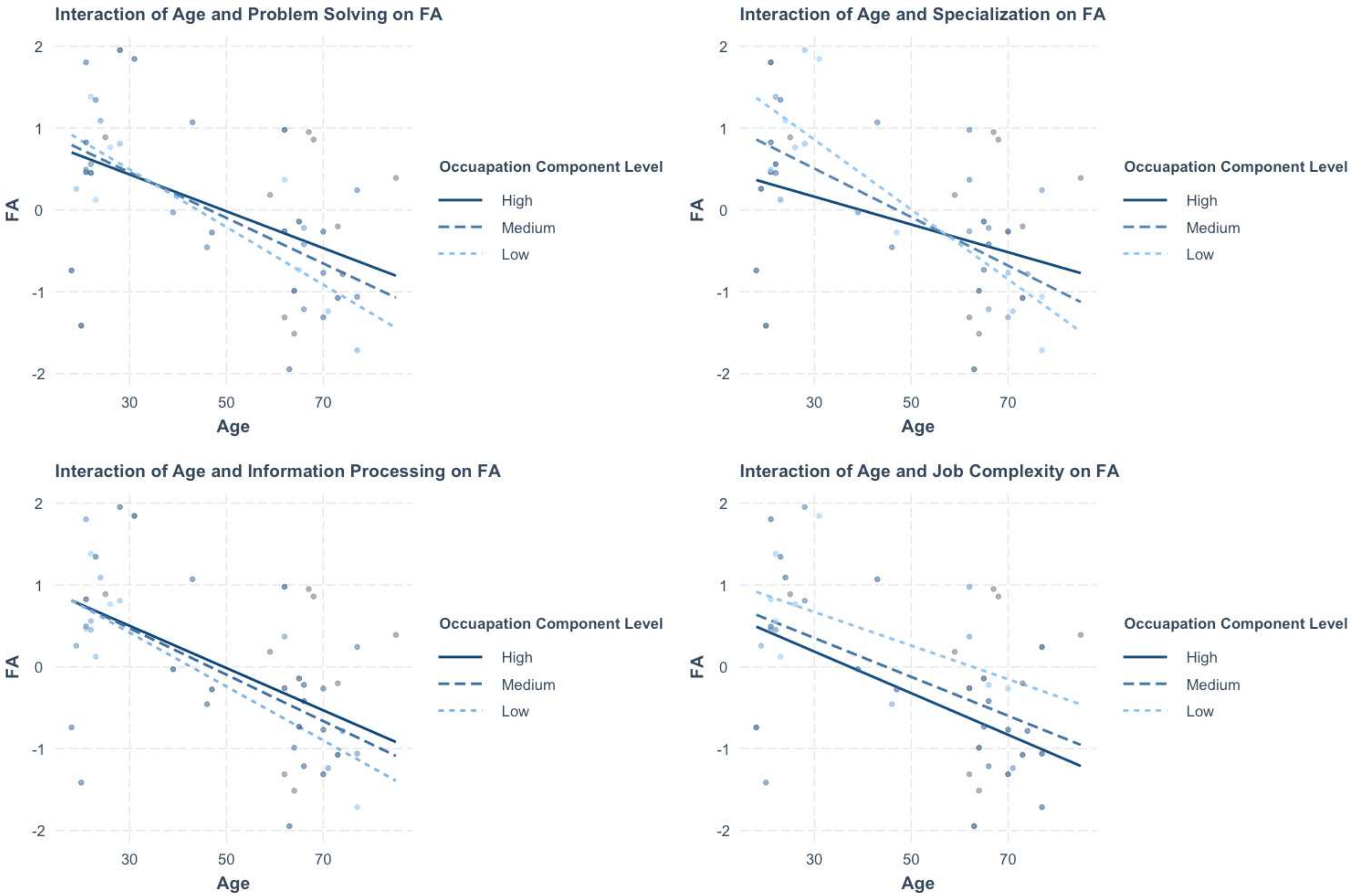


Figure 3: Simple slope plots showing relationship between FA in the external capsule and age by occupation component. Note. Variables are scaled (mean-centered).

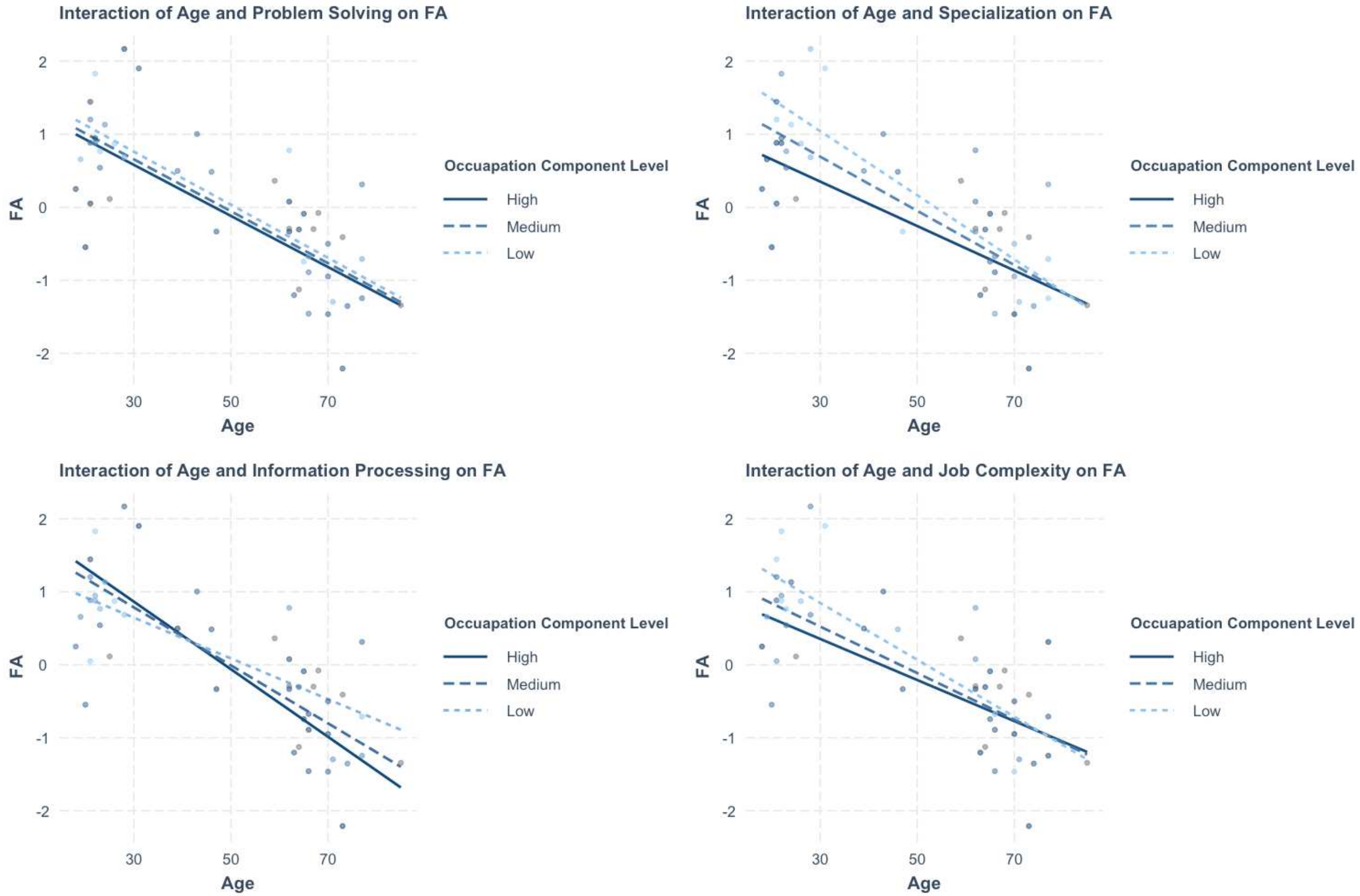
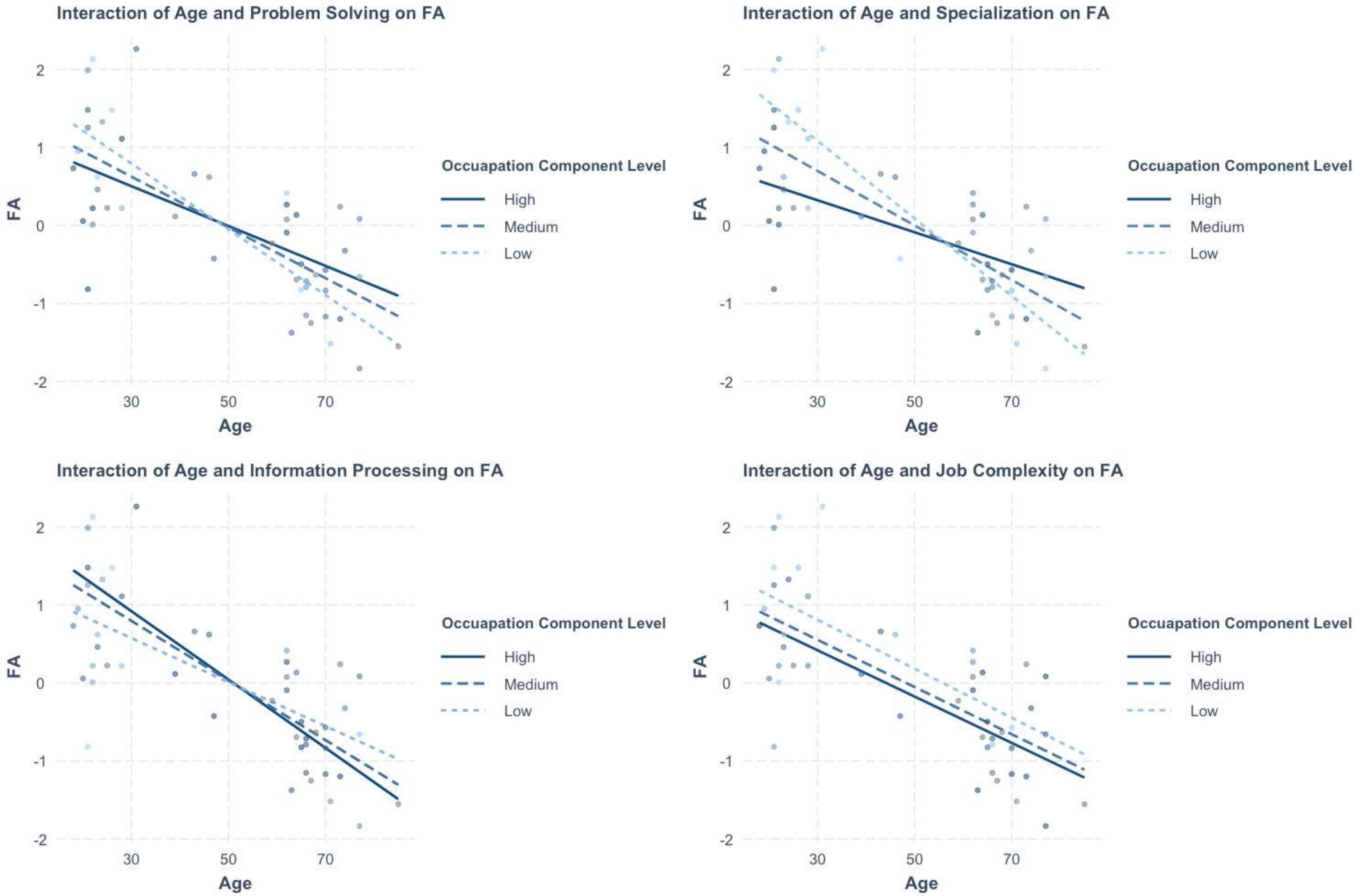


Figure 4: Simple slope plots showing relationship between FA in the cingulum bundle and age by occupation component. Note. Variables are scaled (mean-centered).



Interaction of Age and Problem Solving on FA

Interaction of Age and Specialization on FA

Interaction of Age and Information Processing on FA

Interaction of Age and Job Complexity on FA

Figure 5: Simple slope plots showing relationship between FA in the forceps major and age by occupation component. Note. Variables are scaled (mean-centered).

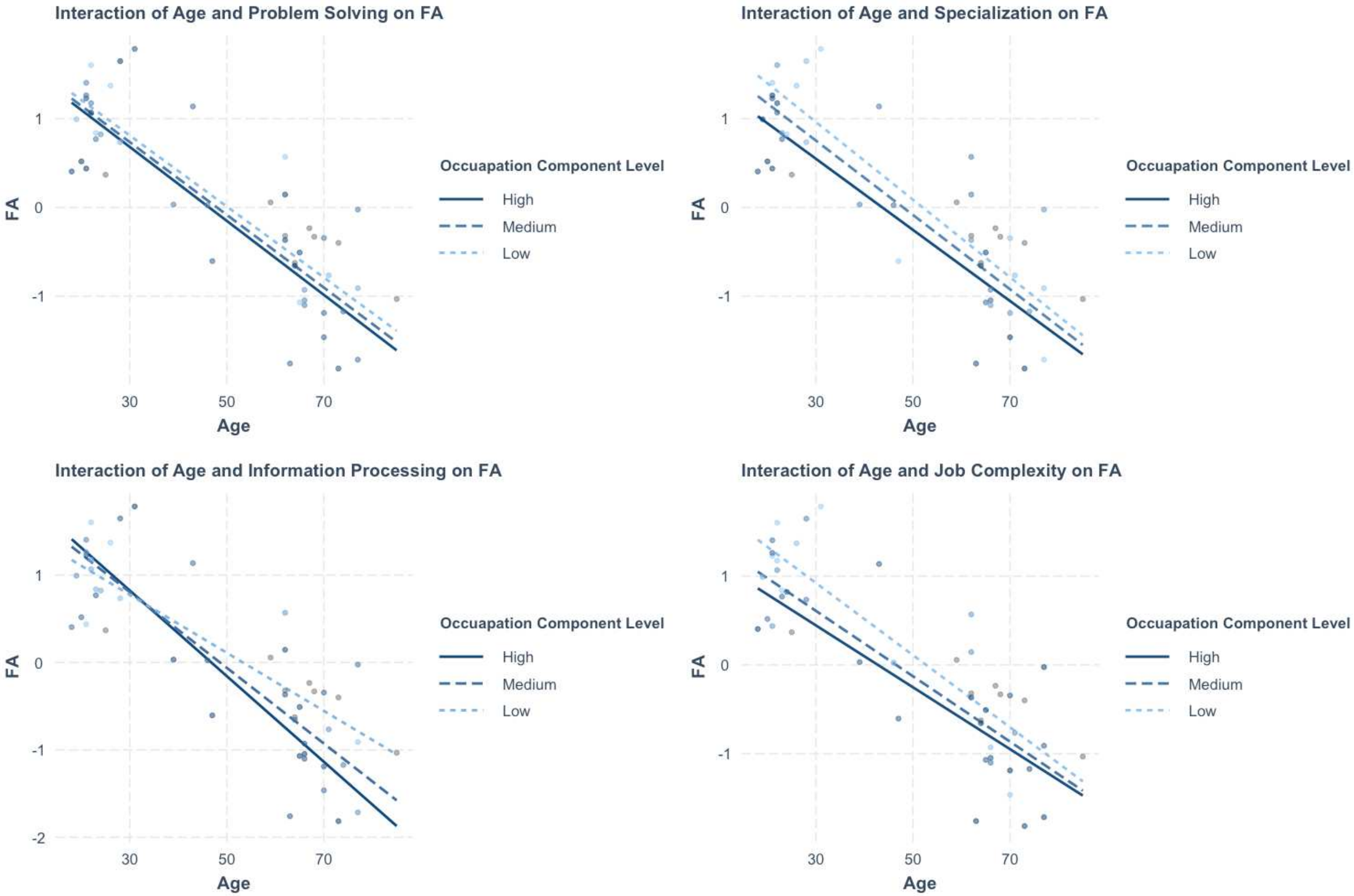


Figure 6: Simple slope plots showing relationship between FA in the forceps minor and age by occupation component. Note. Variables are scaled (mean-centered).

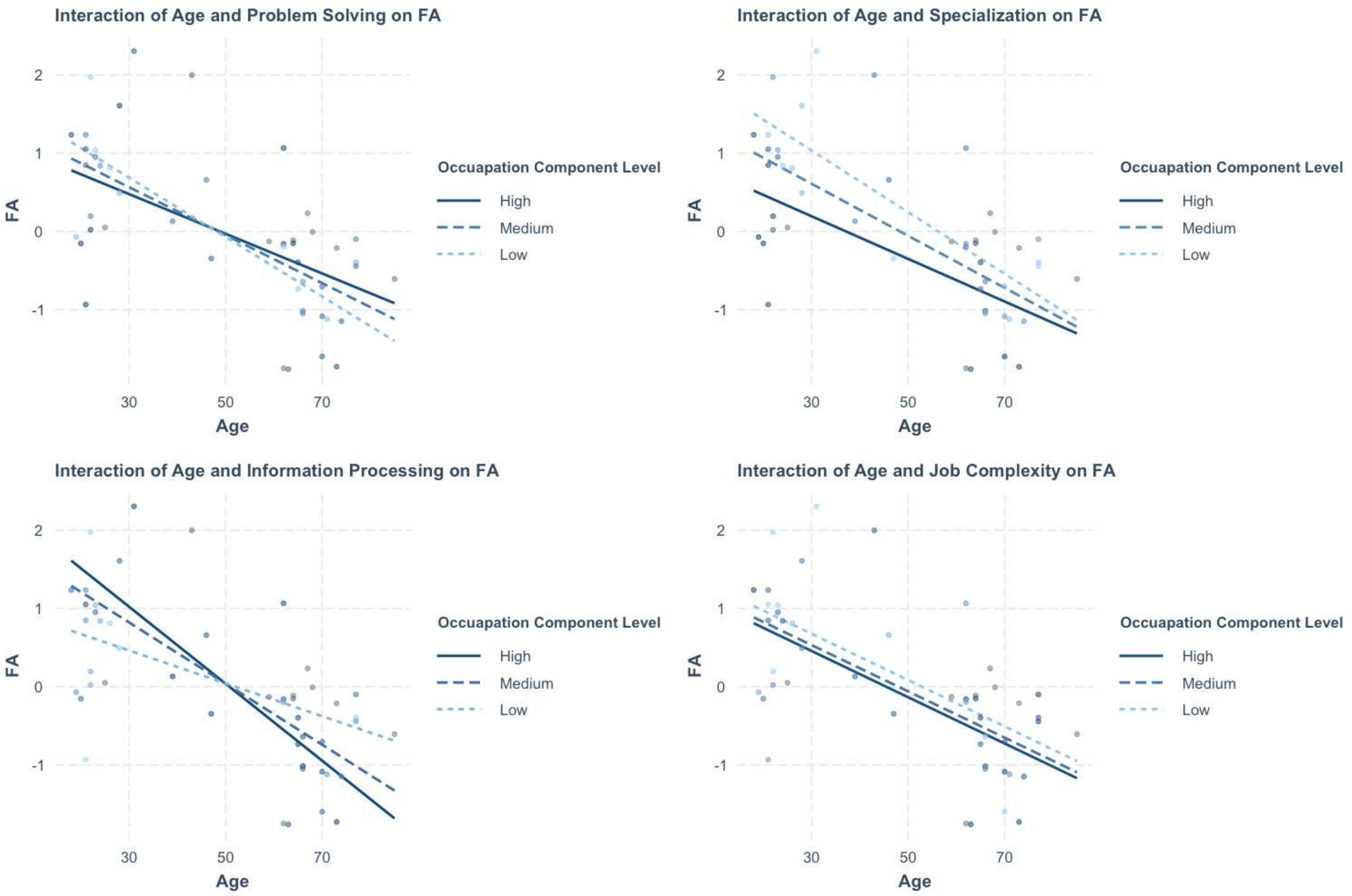
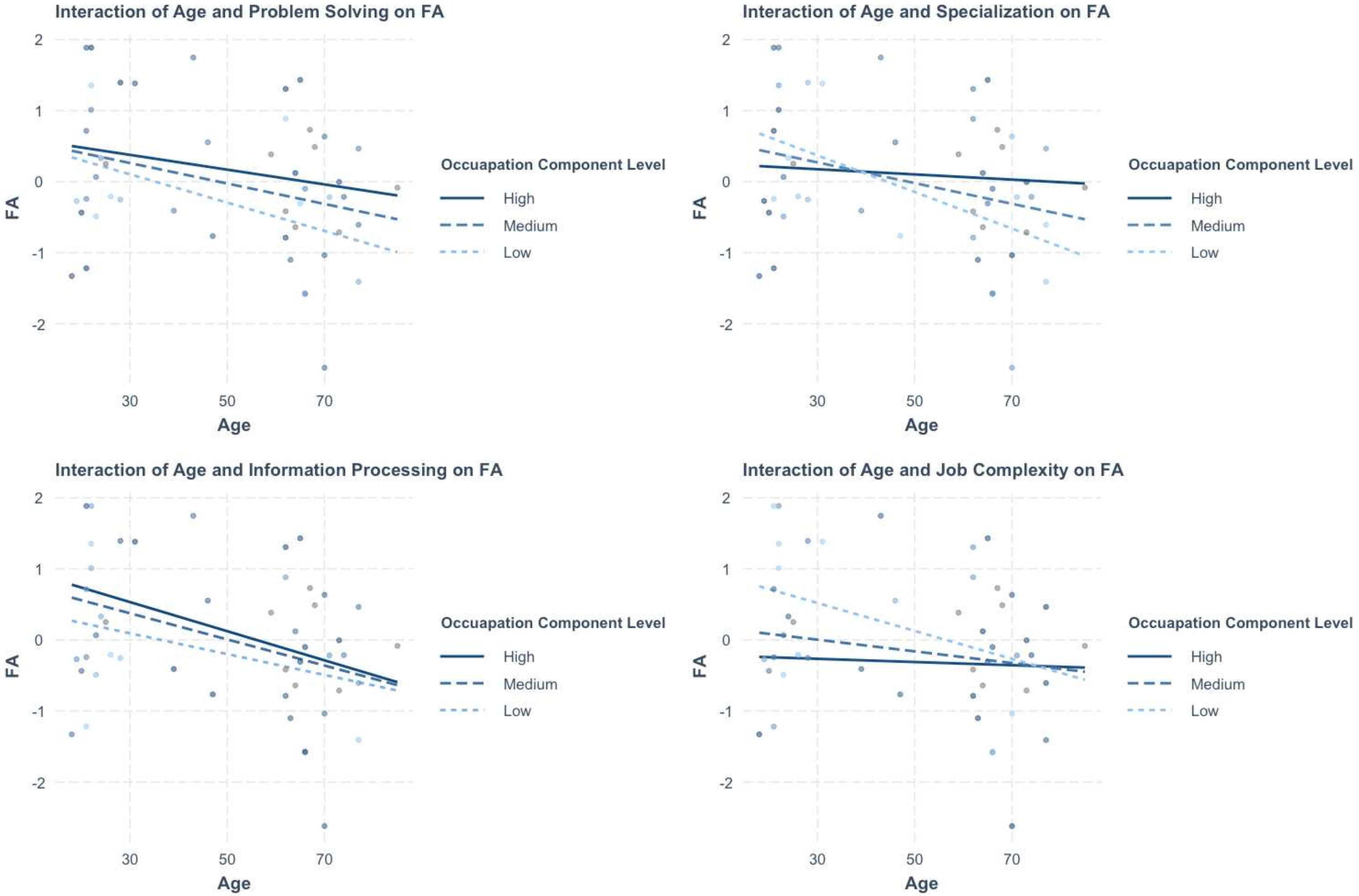


Figure 7: Simple slope plots showing relationship between FA in inferior longitudinal fasciculus (ILF) and age by occupation component. Note. Variables are scaled (mean-centered).



Interaction of Age and Problem Solving on FA

Interaction of Age and Specialization on FA

Interaction of Age and Information Processing on FA

Interaction of Age and Job Complexity on FA

Figure 8: Simple slope plots showing relationship between FA in the anterior limb of the internal capsule (ALIC) and age by occupation component**.** Note. Variables are scaled (mean-centered).

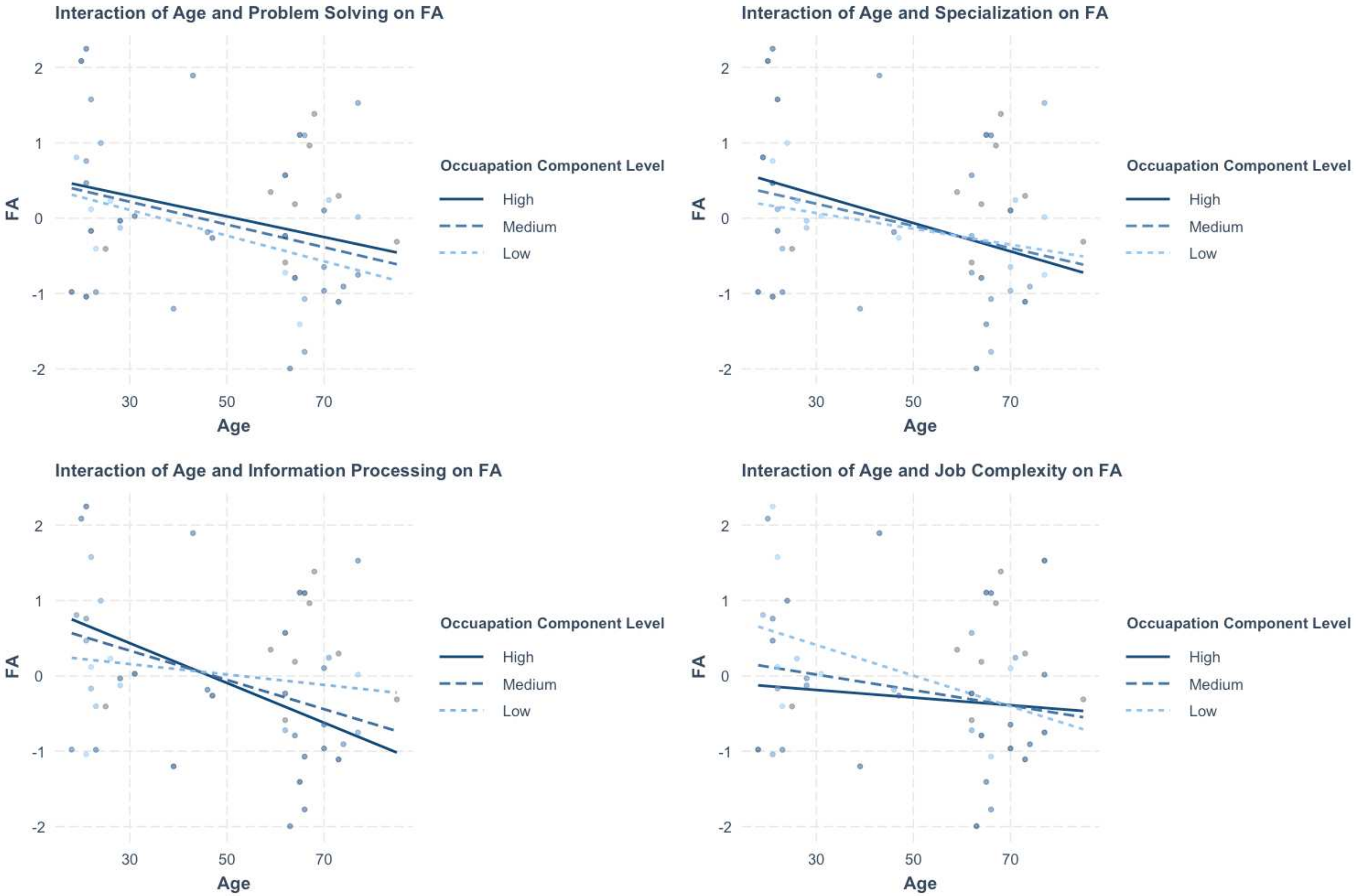


Figure 9: Simple slope plots showing relationship between FA in the posterior limb of the internal capsule (PLIC) and age by occupation component. Note. Variables are scaled (mean-centered).

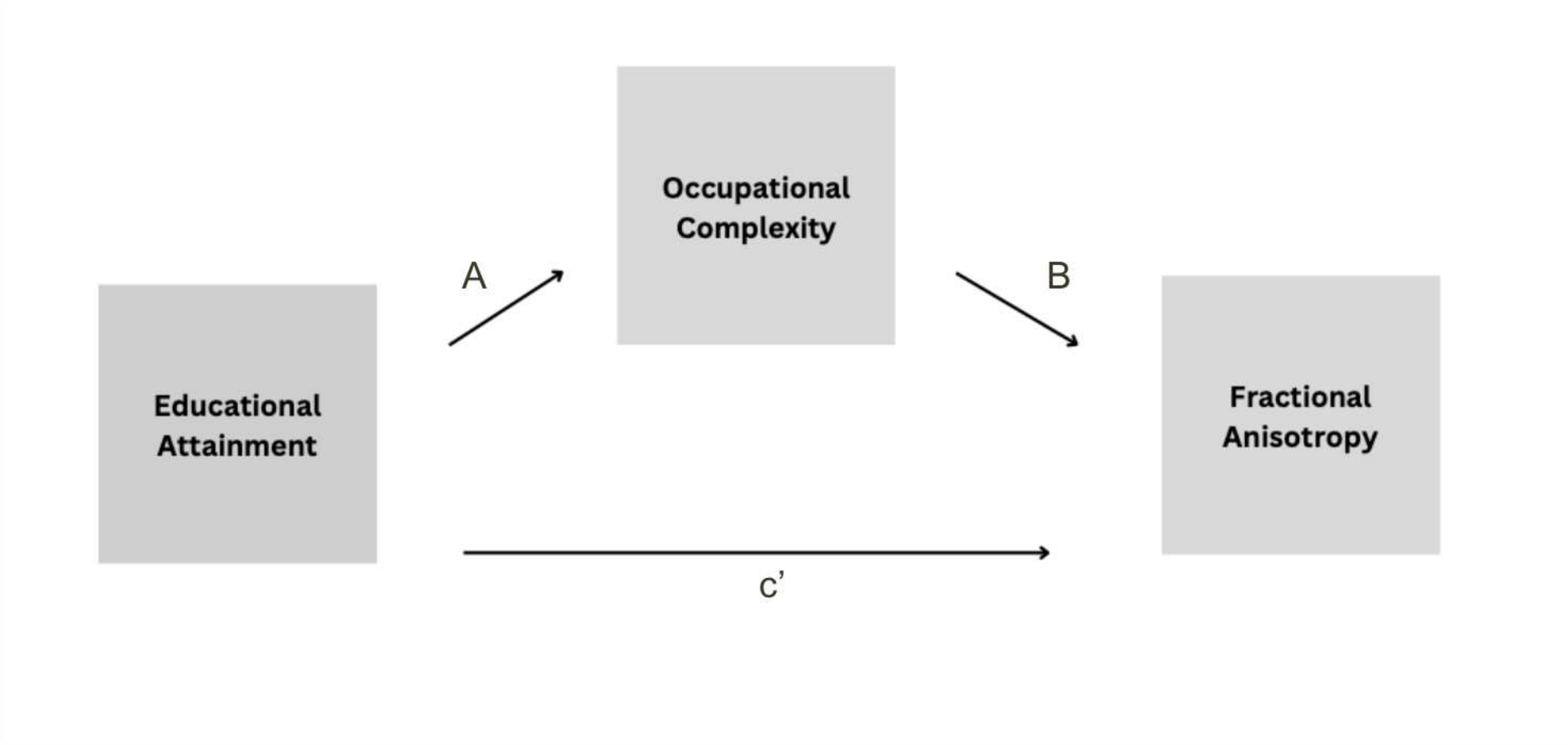


Figure 10: Diagram illustrating the relationship between education and fractional anisotropy, with occupational complexity as a mediation

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