1 **Cross-sectional white matter microstructure differences in aging and**

2 **trait mindfulness**

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Abstract

The process of aging can be characterized by a decline in cognitive performance, which may be accompanied by deterioration in specific structural properties of the brain. In this study we sought to investigate to what extent mindfulness changes over the aging process, and which alterations in brain structure can be associated to aging and concomitant changes in mindfulness. We collected Mindful Attention Awareness Scale questionnaire data to assess trait mindfulness and acquired diffusion-weighted imaging data fitted to the diffusion tensor model in a group of 97 middle-aged to elderly participants. Our results showed that trait mindfulness increased with age. In terms of white matter structure our results suggested that there was a general increase of omnidirectional diffusion, which favored radial over axial diffusivity, leading to a decrease in fractional anisotropy (FA) in older participants. We further showed that trait mindfulness mediated the FA-age effect in a localized area consisting of the internal and external capsule, as well as the corona radiata. The implication of this mediation analysis is that trait mindfulness may deter age-associated neurocognitive decline, perhaps by preventing age-associated microlesions specifically in cortico-subcortical white matter tracts. This study can be considered a pioneer of using DTI studies to investigate the relationship between age and trait mindfulness.

Introduction

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39   Healthy aging has become an important research topic, due to increasingly

40   effective healthcare keeping our elders alive longer. Life expectancy has been

41   increasing since the industrial revolution and is approaching an average of 70 years

42   worldwide [1]. Birthrates have gone down in many countries, especially in those with

43   low child mortality rates [1]. In the forthcoming years, wealthy countries will see

44   larger cohorts of elderly people as compared to younger individuals. This shift in the

45   population's age distribution increases the importance of neuropsychological research

46   aimed at finding efficient ways of maintaining mental health in aging.

47   Cognitive decline is generally accepted as a "normal" part of aging. Yet, not all

48   cognitive processes will decline with age. So far, research has shown that some

49   cognitive processes (e.g., vocabulary, world knowledge) are less impaired while other

50   cognitive processes such as speed of processing, working memory, and reasoning

51   show large decrements with increasing age [2]. In particular, many studies have

52   provided evidence showing that older adults have deteriorated cognitive control

53   functions, such as less working memory capacity [3,4,5], a deficit in inhibitory

54   processing[6, 7], and a lack of cognitive flexibility [8,9]. One possible fundamental

55   deficit that triggers these cognitive problems with increasing age is a general decrease

56   in the *control* over task-relevant mental processes. That is, it becomes increasingly

57   more difficult for older adults to apply new rules, to coordinate multiple rules, and to

58   maintain relevant information in the context of interfering information.

59   More practically, age-related declines in cognitive functions have been shown to

60   be associated with severe deficits in the elders' everyday life activities. For example,

61   some researchers have found performance on cognitive assessments to be associated

62   with instrumental activities of daily living (IADL), such as paying bills, shopping for

63   groceries [10,11]. There are findings showing that updating working memory and

64   task-switching have the strongest relationships with IADL (three domains: home

65   management, financial management, and health and safety). There is also evidence

66   cognitive function influences self-care capacity. For example, learning proper

67   inhaler-use technique has been found to be associated with higher scores on the

68   Executive Interview among older adults [12]. In addition, older adults who exhibited

69   poor performance on tests measuring cognitive flexibility have been found to have

70   increased difficulty in everyday problem solving.

71   Cognitive function and flexibility have been found to be intimately linked with

72   mindfulness [13,14]. It is important to investigate whether mindfulness plays a role in

73   the aging process. Mindfulness can be divided into two broad categories: state and

74   trait mindfulness [15]. State mindfulness refers to how mindful an individual is in the

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75   present moment, hence reflecting a more transient, moment-to-moment experience of

76   mindfulness [16]; whereas trait mindfulness refers to an individual's natural or innate

77   mindfulness tendency, which has been perceived as a stable, permanent characteristic

78   [17]. Research reporting the relationship between mindfulness and aging has focused

79   more on the manipulation of state mindfulness rather than trait mindfulness. For

80   example, accumulating evidence has suggested that mindfulness-based interventions[1]

81   (MBI; [18,19,20]) may provide a way to deter the detrimental effects of aging, by

82   promoting body, cognitive, and emotional health [21,22,13,23,24,25].

83   Mindfulness-based interventions may work because they provide a more holistic

84   attentional training, in the sense that they allow training of general attentional

85   mechanisms, the improvement of which benefits many cognitive tasks. However,

86   neurocognitive research on mindfulness is scarce, and the effect of mindfulness on

87   brain structure has not been elucidated yet. Studies report neural benefits of

88   mindfulness such as increases of overall brain f*ractional anisotropy* (FA) [26] and

89   altered concentrations of important brain metabolites [27] (see Fox et al., 2014 and

90   2016 [28,29] for reviews on the neurocognitive underpinnings of mindfulness

91   meditation). These findings are interesting, yet there is not enough evidence to allow

92   us to draw general conclusions.

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[1] Please note, in this study, we defined mindfulness-based intervention as a broad term, including a variety of mindfulness-related practices, such as various forms of attention-based and active-based meditations.

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93   Although research into state mindfulness has important clinical applications, trait

94   mindfulness may provide more insight to infer how individual differences in

95   mindfulness may interact with aging processes [17]. Based on the current literature, it

96   still remains unclear to what extent individual differences in trait mindfulness may

97   interact with the aging process, and whether these interactions are reflected in

98   individual differences in brain structure and plasticity. Prior research discovering

99   differences in the cognitive trajectories of healthy older adults [30] suggests that

100   cognitive decline may not be a necessary consequence of aging, but may result from a

101   range of risk factors that become more prevalent with increasing age. Understanding

102   the mechanisms that contribute to different trajectories of cognitive decline in

103   clinically intact older adults is a significant target for the prevention or reduction in

104   progression of cognitive decline and dementia in old age.

105   In this study, we investigate whether trait mindfulness shows an association with

106   age and whether brain structural differences (in terms of white matter tract) can

107   inform us about age and mindfulness. In order to answer these questions, we recruited

108   a group of healthy participants from middle-age to elderly and acquired their

109   diffusion-weighted imaging (DWI) data that were further fitted to a diffusion tensor

110   model (i.e., diffusion tensor imaging; DTI) to detect water diffusion directionality, which

111   in turn shows the microstructural architecture of tissue. A questionnaire survey containing

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112   the Mindful Attention Awareness Scale (MAAS; [31]) was used to measure trait

113   mindfulness.

Methods

115   All procedures performed in studies involving human participants were in

116   accordance with the ethical standards of the institutional research ethical committee at

117   National Cheng Kung University, and with the 1964 Helsinki declaration and its later

118   amendments or comparable ethical standards.

Participants

120   A total of 97 participants who were part of a larger lifespan data set collected at

121   National Cheng Kung University were recruited for the present study. All participants

122   were right-handed (Edinburgh Handedness Inventory; [32]), in good general health,

123   without major neurological and psychological disorders, and had normal or

124   corrected-to-normal vision. Demographic information about these 97 participants is

125   presented in Table 1 All participants signed the informed consent form before participating

126   in the experiments. All subjects were paid 1,500 NTD (around $50 USD) after

127   completion of the experiment.

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129 **Table 1. Demographics information of pariticipants**

	Mean	**Range**	**SE**
Age	57.26	40-77	0.95
Education	13.72	4-18	0.30
MoCA	26.80	22-30	0.19
BDI-II	5.12	0-13	0.42
PSQI	6.16	1-14	0.35
MAAS	61.48	41-90	1.15

130 *Note.* SE: standard error; MoCA: Montreal Cognitive Assessment; BDI-II: Beck

131 Depression Inventory II; PSQI: Pittsburgh Sleep Quality Index; MAAS: Mindful

132 Attention Awareness Scale.

Questionnaires

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134   A set of neuropsychological questionnaires was implemented: (1) The Montreal

135 Cognitive Assessment (MoCA) to screen participants for probable dementia [33]. (2)

136 The Beck Depression Inventory (BDI-II) to screen depression [34]. (3) A Chinese

137 version of the Pittsburgh Sleep Quality Index-PSQI to measure the quality and

138 patterns of sleep [35]. (4) The 15-item Mindful Attention Awareness Scale (MAAS)

139 to measure trait mindfulness [36]. It took between 5 and 10 minutes to complete all

140 questionnaires.

Imaging Protocols

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142   Magnetic resonance images (MRI) were acquired using a GE MR750 3T scanner

143   (GE Healthcare, Waukesha, WI, USA) in the Mind Research Imaging (MRI) center of

144   National Cheng Kung University. High resolution structural images were acquired

145   using fast-SPGR, consisting 166 axial slices (TR/TE/flip angle, 7.6 ms/3.3 ms/12°;

146   field of view (FOV), 22.4 × 22.4 cm2; matrices, 224 × 224; slice thickness, 1 mm),

147   and the entire process lasted for 218 s. Diffusion weighted imaging (DWI) were

148   obtained with a spin-echo-echo planar sequence (TR/TE = 5500 ms/minimum, 50

149   directions with b= 1000 s/mm2, 100 x 100 matrices, slice thickness = 2.5 mm, voxel

150   size = 2.5 x 2.5 x 2.5 mm, number of slices = 50, FOV = 25 cm, NEX = 3). 6

151   non-diffusion-weighted (b = 0 s/mm^2) volumes were acquired, 3 of which were

152   acquired with reversed phase encoding so as to allow correction for susceptibility

153   induced distortions.

DTI processing

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155   All DWI data processing and analyses were carried out using FMRIB's Software

156   Library (FSL, version 5.0.9; www.fmrib.ox.ac.uk/fsl; [37]). Diffusion weighted

157   images were first converted from DICOM to NIFTI format using the MRIcron's

158   dcm2nii tool (https://www.nitrc.org/projects/mricron/). TOPUP [37,38] and EDDY

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159   [39] were used to clean the DWI images of artifacts caused by susceptibility induced

160   distortions, eddy currents, and head motion. A single image without diffusion

161   weighting (b0; b value = 0 s/mm2) was extracted from the concatenated data, and

162   non-brain tissue was removed using FMRIB's brain extraction tool [40] to create a

163   brain mask that was used in subsequent analyses. DTIFIT (diffusion tensor imaging

164   fitting model; [41]Behrens et al., 2003) was applied to fit a tensor model at each voxel

165   of the data to derive f*ractional anisotropy* (FA), mean diffusivity (MD), axial

166   diffusivity (AD), and radial diffusivity (RD) measures for further analyses.

167   In order to perform tract-based investigations into DTI measures we performed

168   tract-based spatial statistics (TBSS; [42]) in FSL, which involves voxel-wise

169   statistical analyses of the DWI data. FA images were slightly eroded and end slices

170   were zeroed in order to remove likely outliers from the diffusion tensor fitting. The

171   images were then nonlinearly aligned to each other and the most representative image

172   was then identified. This target image was subsequently affine transformed to 1mm

173   MNI space. FA images were transformed to 1mm MNI space using a combination of

174   the nonlinear and affine registration. A skeletonization procedure was then performed

175   on the group-mean FA image, the result of which was thresholded at FA > 0.2 to

176   identify areas most likely to belong to white matter tracts of nontrivial size.

Statistical analyses

178   Linear regressions were performed in R (version 3.0.2; R Foundation for

179   Statistical Computing, http://www.R-project.org) to test for (1) a linear association

180   between participant's age and their self-reported MAAS mindfulness score,

181   controlling for gender and MoCA, BDI, and PSQI scores as regressors of no interest;

182   and (2) a linear association between DTI measures (i.e., FA, MD, RD, AD) and age,

183   controlling for gender, and MoCA, BDI, PSQI, and MAAS scores (1 regression per

184   measure). In addition, we performed a mediation analysis predicting age based on FA

185   using MAAS scores as a mediator. For the Bayesian version of these tests we used the

186   BayesFactor (http://bayesfactorpcl.r-forge.r-project.org/) and BayesMed

187   (https://CRAN.R-project.org/package=BayesMed;[43]) toolboxes. For the voxel-wise

188   univariate regressions we used FSL's randomize function on a model mimicking our

189   whole-brain average regressions, testing for a linear association between FA and

190   MAAS scores, controlling for age, gender, and MoCA, BDI, and PSQI scores.

191   For both the behavioral and DTI results we report classical frequentist p-values,

192   as well as Bayes factors, which provide a more conservative evaluation of the

193   correlations. For ease of reading, we provide both BF_{10} (Bayes factor for the presence

194   of a correlation) and BF_{01} (Bayes factor for the absence of a correlation). These are

195   inversely related (i.e., $BF_{10} = 1/BF_{01}$ and $BF_{01} = 1/BF_{10}$). Bayes factors may be

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196   interpreted as proportional evidence for the presence or absence of an effect. For

197   instance BF_{10} of 5 may be interpreted as the data being 5 times more likely to occur

198   under the alternative hypothesis then under the null-hypothesis. In addition, we can

199   interpret the Bayes factor categorically based on a grouping proposed by Jeffreys

200   [44]. Table 2 shows this evidence categorization for the BF_{01}, edited by and taken

201   from Wetzels and Wagenmakers ([45]; Table 1, p. 1060). For a detailed explanation

202   of the Bayesian statistics and the Bayes factor, see [46].

203   **Table 2. Suggested categories for interpreting Bayes factors based on Jeffreys**

204   **[44]**

Bayes factor BF_{01}			Interpretation
	$>$	100	Extreme evidence for H_0
30	–	100	Very Strong evidence for H_0
10	–	30	Strong evidence for H_0
3	–	10	Moderate evidence for H_0
1	–	3	Anecdotal evidence for H_0
	1		No evidence
1/3	–	1	Anecdotal evidence for H_1
1/10	–	1/3	Moderate evidence for H_1
1/30	–	1/10	Strong evidence for H_1
1/100	–	1/30	Very Strong evidence for H_1
	$<$	1/100	Extreme evidence for H_1

Results

Age and MAAS

We performed a linear regression predicting age based on MAAS scores. Gender,

MoCA, BDI, and PSQI scores were added to the GLM as regressors of no interest. A

classical linear regression showed a significant association of MAAS scores ($t =$

3.267, $p = 0.00154$; Fig 1) with age, suggesting that older individuals have higher

mindfulness scores than younger individuals (note our sample's age range: 40 - 77).

In addition, a Bayesian linear regression showed strong evidence of a positive

association between age and MAAS ($BF_{10} = 206.9$).
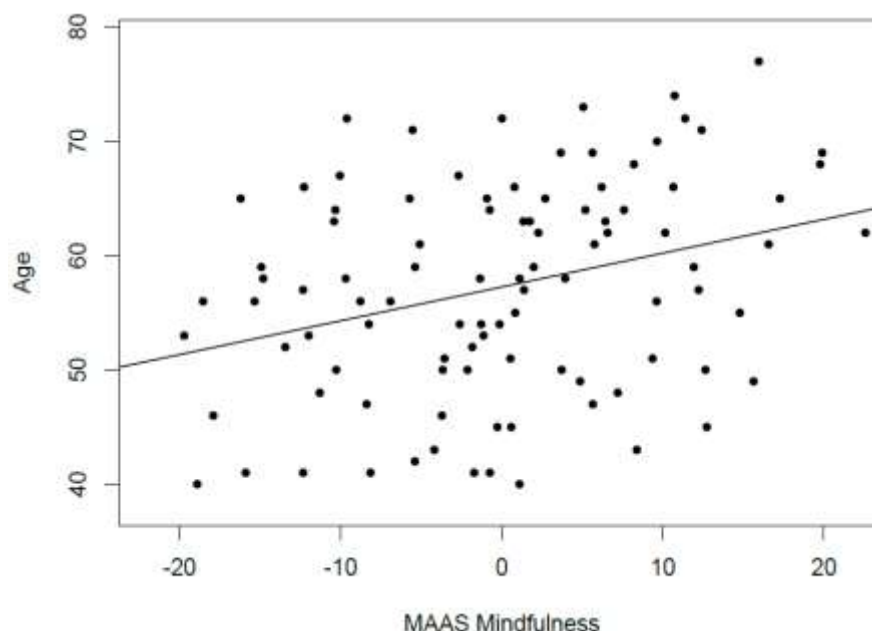
Fig. 1. Positive correlation between age and mindfulness assessed by the Mindful

**Attention Awareness Scale (MAAS). Scatterplot with regression line.**

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DTI and Age

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218   We performed a linear regression predicting whole brain average FA based on

219   age while regressing out variance attributed to gender, and scores on MAAS, MoCA,

220   BDI, and PSQI. We observed a negative correlation between FA and age ($t = -5.497$,

221    $p = 0.000000357$, $BF_{10} = 21379$, Table 3 & Fig 2), suggesting that in older individuals

222   the diffusion tensor is less fractionally anisotropic than in relatively younger

223   individuals. Increases in FA may arise from both a relative decrease in RD, as well as

224   from a relative increase in AD. In addition, MD provides information about the

225   overall omnidirectional diffusion. To elucidate the precise nature of the tensor

226   transformation leading to our observed FA-age relation, we also extracted

227   whole-brain skeleton-averaged RD, AD, and MD, and regressed these against

228   subject's age (again controlling for gender, MAAS, MoCA, BDI, and PSQI). Results

229   can be seen in Table 3 We observed a positive relation between RD and age ($t =$

230   5.033, $p = 0.00000246$, $BF_{10} = 9540$; Fig 3), and non-significant positive relation

231   between AD and age ($t = 1.895$, $p = 0.0613$, $BF_{10} = 1.546$).   For the purpose of

232   understanding the nature of the tensor transformation underlying our observed FA-age

233   effect, it is sufficient to attend to the direction of the correlation, which is positive,

234   indicating an increase in diffusion along the principle diffusion direction (i.e., AD).

235   For the negative FA-age correlation to emerge, the RD has to sufficiently increase as

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236 well, which indeed seems to be the case. In addition, we observe a positive correlation

237 between MD and age (t = 4.286, p = 0.0000455, BF_{10} = 754.7; Fig 4), in accordance

238 with the increase in both AD and RD. As such, we may expect that with age there is a

239 general increase of omnidirectional diffusion, which favors radial over axial

240 diffusivity, leading to a decrease in FA. This cross-sectional effect serves as a

241 hypothesis for longitudinal follow-up phases of this study.

242 **Table 3. Correlation between FA/MD/RD/AD and Age**

	t	p	BF_{10}	BF_{01}
FA	-5.497	0.000000357	21379	0.00004677
MD	4.286	0.0000455	754.7	0.001325
RD	5.033	0.00000246	9540	0.0001047
AD	1.895	0.0613	1.54641	0.6467

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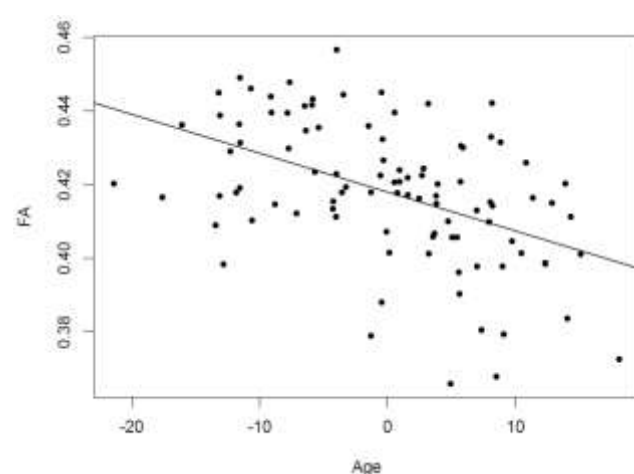
245 **Fig. 2. Negative correlation between FA and age. Scatterplot with regression line.**

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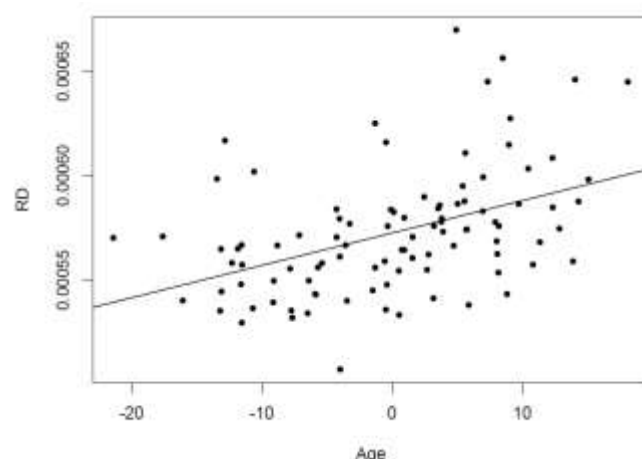
Fig. 3. Positive correlation between RD and age. Scatterplot with regression line.
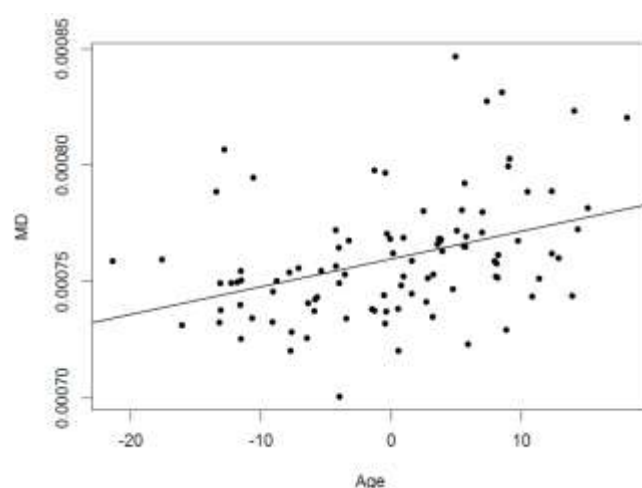
Fig. 4. Positive correlation between MD and age. Scatterplot with regression line.

DTI and MAAS

In addition to cross-sectional age differences, we were interested in

cross-sectional differences in DTI measures relating to MAAS scores. We performed

a linear regression between DTI measures and MAAS, while regressing out age,

gender, and scores on MoCA, BDI, and PSQI. We found no significant relation

between MAAS and FA ($t = 1.095$, $p = 0.2764$, $BF_{10} = 0.2977$). Inverting the Bayes

256　factor here provides substantial evidence in favor of the null-hypothesis (the absence

257　of a relation), $BF_{01} = 3.576$. We subsequently investigated the remaining DTI

258　measures MD, RD, and AD, which were also found not to be associated with MAAS

259　scores (all $BF_{01} > 3$, Table 4).

260　**Table 4. Correlation between FA/MD/RD/AD and MAAS**

	t	**_p_**	**BF_{10}**	**BF_{01}**
FA	1.095	0.2764	0.2977	3.576
MD	0.074	0.9415	0.3126	3.199
RD	-0.311	0.7563	0.3281	3.048
AD	1.026	0.3075	0.2530	3.952

261　　　　We performed an additional mass-univariate regression analysis within the

262　whole-brain white matter skeleton in order to pinpoint spatially localized relations

263　between MAAS and white matter microstructure (i.e., tensor-derived measures). We

264　found a positive relation between FA and MAAS in the left hemisphere, specifically

265　in the internal and external capsule, extending widely from the anterior to the

266　posterior parts of both of these white-matter tracts, and extending dorsally into the

267　corona radiata ($t = 5.482$, $p < 0.05$ corrected for multiple comparisons; Fig 5). As

268　mentioned previously, differences in FA can be driven by differences in RD as well as

269　AD, so we extracted the mask-average AD and RD from the voxels showing a

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270   positive relation between FA and MAAS. We found a positive relation between AD

271   and MAAS scores (t = 3.479, p = 0.000777, BF_{10} = 8.90), and a negative relation

272   between RD and MAAS scores (t = -3.687, p = 0.000387, BF_{10} = 3.02). As such, it

273   seems that in individuals with a higher self-report score on the MAAS mindfulness

274   scale, the diffusion tensor displays a relatively decreased RD, and a relatively

275   increased AD, as compared to low-mindfulness individuals, leading to an overall

276   increase of FA in mindful individuals in the internal and external capsule extending

277   dorsally into the corona radiata.

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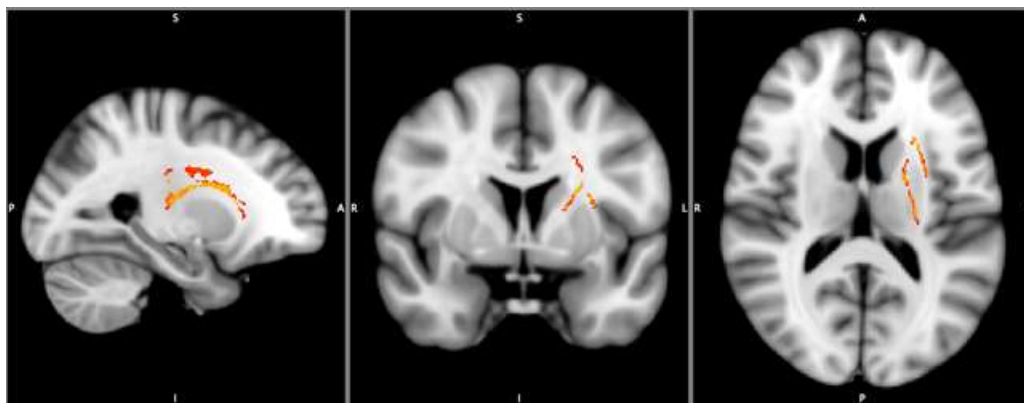
279   **Fig. 5. FA-MAAS correlation at x, y, z coordinates: 115, 128, 86.**

280   # Mediation analysis: Age, MAAS, and FA

281   In light of this finding we were additionally interested in whether MAAS may

282   serve as a mediator between age and FA within the spatially localized area which

283   showed significant MAAS-FA associations. A mediation analysis showed that MAAS

284   was indeed mediating the association between FA and age within this area (BF_{10} =

285   45.39). We interpret this finding to suggest that as individuals age, FA in this region is

286   preserved, especially for individuals who self-report to be more mindful.

Discussion

288   In this study we sought to investigate the relation between characteristics of white

289   matter microstructure, age, and MAAS. To this end we acquired diffusion weighted

290   imaging data in combination with a set of questionnaires (MAAS, MoCA, BDI,

291   PSQI) from a group of elderly participants. We found that age was positively

292   associated with MAAS suggesting that older individuals tend to have higher

293   mindfulness scores. Raes et al. [47] also found a similar age-MAAS effect, as did

294   Mahoney et al. [48], although they used a younger age range and nonlinear aging

295   effects were observed.

296   In terms of DTI metrics and age our results suggested that in older participants

297   there is a general increase of omnidirectional diffusion, which favors radial over axial

298   diffusivity, leading to a decrease in FA. This is consistent with previous findings

299   which also showed a general decline in FA with age [49,50,51,52].

300   Our voxelwise investigation into DTI metrics and MAAS found a localized

301   positive association between FA and MAAS in the left hemisphere corona radiata and

302   the internal and external capsule. This finding is in line with some studies using a

303   MBI approach (a measure of state mindfulness), where FA was shown to increase in

304   the corona radiata after intervention. For example, Tang et al [53,54] found that by

305   training participants using a form of mindfulness meditation, integrative body-mind

306   training (IBMT), FA increased in the corona radiata. Corona radiata is an important

307   white matter tract connecting the anterior cingulate cortex (ACC) to other brain

308   structures, so its communication efficiency plays a role in modulating brain activity in

309   the ACC [55]. In line with the finding that FA increased in the corona radiata due to

310   mindfulness mediation, Grant and colleagues [56] observed that cortical thickness in

311   the dorsal ACC was greater for participants with experience in meditation than those

312   without. Therefore, these findings provide convergent evidence for the important role

313   of radiata corona in relation to state mindfulness.

314   In addition to the corona radiata tract and ACC, some researchers suggest that

315   other brain regions are related to state mindfulness, including insula, temporo-parietal

316   junction, dorsal prefrontal cortex (dPFC), ventro-medial PFC, hippocampus,

317   amygdala, medial PFC, posterior cingulate cortex, insula, and temporo-parietal

318   junction (see [57], Table 2). Based on this neural evidence for an association between

319   brain structures and different facets of mindfulness meditation (e.g., intention,

320   attention, attitude, body awareness, reappraisal, and changes in perspectives on self),

321   Grecucci and colleagues [55] suggest that there are top-down and bottom-up neural

322   circuits involved in the processes of mindful emotion regulation. These circuits

323   include top-down control regions such as the PFC and the ACC and bottom-up

324   emotional regions such as the insula (I) and the amygdala (A). Furthermore, these two

325   neural circuits (PFC-ACC & A-I) may interact with each other via connective neural

326   structures such as the corona radiata. Based on the neuroimaging evidence derived

327   from these MBI studies, the current finding that the FA in the corona radiata tract is

328   positively correlated with MAAS appears to be reconciled with Grecucci et al.'s [55]

329   postulation that the increased FA in the corona radiata tract may facilitate the

330   connection between the two neural circuits (PFC-ACC & A-I), resulting in FA being

331   highly associated with MAAS. Furthermore, our additional mediation analysis

332   showing that MAAS mediated the relationship between age and FA in the radiata

333   corona tract, suggests that as individuals age, FA in the radiata corona is preserved,

334   especially for those individuals with higher trait mindfulness(as reflected by MAAS

335   scores).

336   It is worth noting that the current finding of a FA-MAAS association is

337   characterized by a thinning and elongation of the diffusion tensor, this is both due to

338   AD increasing with respect to MAAS, as well as RD decreasing. As such, it seems the

339   white-matter in this area is more streamlined for individuals who self-report to be

340   more mindful. The tensor model used here cannot directly inform us about the

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341   biological causes of these effects [58], although we could speculate that an overall

342   loss of FA due to white matter lesions occurs with age [51], and that mindfulness in

343   life may prevent some of these lesions. This speculation can be supported by the

344   current mediation analysis showing that MAAS was indeed mediating the association

345   between FA and age within the internal and external capsule, as well as the corona

346   radiata. Future studies could test this hypothesis by employing mindfulness-based

347   interventions longitudinally, since the cross-sectional nature of this study precludes a

348   direct observation of age-related change.

349   Although the current findings using DTI and trait mindfulness approaches appear

350   to be reconciled with those reported by the studies employing the MBI approach

351   [53,54,55,56,57], research into structure-function associations in trait mindfulness is

352   still considered scarce, and the literature is not yet unified regarding the involved

353   brain systems in state mindfulness. For example, Luders et al. [26] found larger FA in

354   different brain structures to be associated with mindfulness training, including a fiber

355   tract constituting the temporal component of the superior longitudinal fasciculus

356   (tSLF) and a fiber tract linked to the hippocampus, i.e., the uncinated fasciculus

357   (UNC). On the other hand, Tang et al. [53] and Hölzel et al. [57] additionally

358   observed larger FA in an entire fiber tract connecting frontal and tempro-parietal

359   regions, the SLF, and in a fiber bundle linked to the hippocampus, the cingulate

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360 cortex hippocampus (CgH), to be associated with active mediation practices.

361 Furthermore, in addition to the aforementioned DTI-based studies, Fox et al. [28]

362 reviewed and used activation likelihood estimation to perform a meta-analysis on the

363 brain structures underpinning mindfulness, in which they observed larger voxel based

364 morphometry in intra- and inter-hemispheric communication (e.g., SLF; corpus

365 callosum) to be associated with meditation. Given these various findings regarding

366 which fiber tracts are related to mindfulness experience, further studies are needed to

367 clarify the involvement of specific brain structures.

368 Conclusion

369   The current results show that with increasing age, an individual's trait

370 mindfulness tends to increase, but in contrast, whole-brain overall FA decreases due

371 to increasing omnidirectional diffusion. On the other hand, FA in a localized area

372 consisting of the internal and external capsule, as well as the corona radiata, showed

373 an increase with trait mindfulness. Interestingly, we subsequently found that trait

374 mindfulness mediates the FA-age effect in this localized area. Therefore, we speculate

375 that trait mindfulness may deter age-associated neurocognitive decline, perhaps by

376 preventing age-associated microlesions specifically in cortico-subcortical white

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377 matter tracts. This study can be considered a pioneer of using DTI studies to

378 investigate the relationship between age and trait mindfulness.

Acknowledgments

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