ACCSCIENCE PUBLISHING

Advanced Neurology

REVIEW ARTICLE

Brief risk rating scale: A preliminary screening and monitoring tool emphasizing individual differences for better prognosis in Alzheimer's disease

Supplymentary File

Table S1. Summary of structural connectivity studies in AD-spectrum patients.

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Saykin *et al.* (2006)[1]	Cross-sectional	T1 MRI	HC: n=40 (71.0 ± 5.1) SCD: n=40 (73.3 ± 6.0) MCI: n=40 (72.9 ± 7.1)	Limbic (MTL) and frontotemporal regions	—	SCD and MCI showed decreased GM volumes in the MTL, frontotemporal, and other neocortical regions. MCI also showed decreased HP volumes.
Jessen *et al.* (2006)[2]	Cross-sectional	T1 MRI	HC: n=14 (66.5 ± 6.4) SCD: n=12 (66.1 ± 7.3) MCI: n=15 (68.2 ± 5.5) AD: n=13 (68.8 ± 9.7)	Limbic region (ERC and HP)	—	SCD showed smaller ERC and left HP compared to HC.
Tepest *et al.* (2008)[3]	Cross-sectional	T1 MRI	HC: n=13 (67.5 ± 5.5) SCD: n=14 (66.4 ± 7.3) MCI: n=15 (68.2 ± 5.4) AD: n=12 (69.2 ± 10.0)	Limbic region (HP)	—	HP surface deformation in the CA1 subfield was most pronounced in AD, less so in MCI, and minimal in SCD.
Striepens *et al.* (2010)[4]	Cross-sectional	T1 MRI	HC: n=48 (66.3 ± 6.2) SCD: n=21 (65 ± 7.2)	Limbic region (HP, ERC, and amygdala)	—	SCD showed reduced volume of bilateral HP, bilateral ERC, and right amygdala.
Nunes *et al.* (2010)[5]	Longitudinal (3.5 years)	T1 MRI	HC: n=11 (69.5 ± 5.5) SCD: n=15 (65.9 ± 7.7) MCI: n=17 (70.8 ± 6.4)	Limbic region (HP and amygdala)	—	SCD and MCI showed reduced volume in HP. MCI also showed reduced volume in amygdala.
Shen *et al.* (2010)[6]	Cross-sectional	T1 MRI	HC: n=38 (70.6 ± 5.2) SCD: n=39 (72.8 ± 6.1) MCI: n=37 (72.7 ± 7.1) AD: n=11 (75.6 ± 6.8)	Limbic region (HP)	—	Only MCI and AD showed reduced volume in HP compared to HC.
Stewart *et al.* (2011)[7]	Longitudinal (4 years)	T1 MRI	SCD: n=1336 (72.0 ± 4.0)	Limbic region (HP)	—	SCD at baseline was associated with subsequent change in HP volume and at follow-up, impairment was associated with previous change in HP and GM volume as well as with subcortical WM lesion increases.
Scheef *et al.* (2012)[8]	Longitudinal (35 months)	T1 MRI	HC: n=48 (66.5 ± 7.2) SCD: n=27 (67.4 ± 6.5)	Limbic region (HP)	—	SCD showed reduced GM volume in the right HP.

(Cont'd...)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Selnes *et al.* (2012)[9]	Cross-sectional	T1 MRI DTI	HC: n=21 (62.0,49 -77) SCD: n=16 (59.2,45 -71) MCI: n=50 (61.2,45 -77)	Parietal and limbic regions (HP)	—	SCD and MCI showed higher RD and MD. MCI also showed higher FA, thinner precuneal and inferior parietal cortices, as well as smaller HP.
Hafkemeijer *et al.* (2013)[10]	Cross-sectional	T1 MRI	HC: n=29 (71.3 ± 3.4) SCD: n=25 (71.4 ± 9.2)	Limbic, frontal, parietal, and occipital regions	—	SCD showed GM volume reductions in HP, ACC, medial prefrontal cortex, cuneus, precuneus, and precentral gyrus.
Kim *et al.* (2013)[11]	Cross-sectional	T1 MRI	HC: n=28 (70.7 ± 5.5) SCD: n=90 (65.8 ± 8.5)	Limbic region (HP and amygdala)	—	SCD showed smaller volumes of HP and amygdala. Less depressive symptoms were associated with smaller HP in SCD.
Peter *et al.* (2014)[12]	Cross-sectional	T1 MRI	HC: n=53 (67.1 ± 6.1) SCD: n=24 (66.0 ± 7.1)	Limbic region (HP)	—	SCD showed greater similarity to an AD in terms of GM pattern compared to HC, which was found associated with episodic memory decline.
Kiuchi *et al.* (2014)[13]	Cross-sectional	T1 MRI DTI	HC: n=41 (75.2 ± 5.34) SCD: n=28 (70.5 ± 7.30) MCI: n=43 (74.6 ± 6.40) AD: n=39 (73.2 ± 7.98)	Limbic region (MTL)	—	SCD showed no significant differences compared to HC. AD and MCI showed the same extent of brain atrophy and diffusion changes.
Perrotin *et al.* (2015)[14]	Cross-sectional	T1 MRI	HC: n=40 (69.4 ± 6.4) SCD: n=17 (69.1 ± 8.5) AD: n=21 (68.3 ± 9.5)	Limbic region (HP)	—	Patients showed diseased HP TIV-normalized volume mainly in the lateral part (CA1).
Meiberth *et al.* (2015)[15]	Cross-sectional	T1 MRI	HC: n=69 (66.1 ± 6.9) SCD: n=41 (68.9 ± 7.2)	Limbic region (ERC)	—	SCD showed cortical thickness reduction in the left ERC.
Cherbuin *et al.* (2015)[16]	Longitudinal (4 years)	T1 MRI	HC: n=218 (62.68 ± 1.32) SCD: n=39 (62.26 ± 1.43)	Limbic region (HP)	—	SCD at follow-up was associated with greater hippocampal atrophy.
Cantero *et al.* (2016)[17]	Cross-sectional	T1 MRI	NC: n=47 (68.1 ± 3.2) SCD: n=48 (69.6 ± 4.3)	Limbic region (HP)	—	SCD showed lower volumes of CA1, CA4, dentate gyrus, and molecular layer.
Verfaillie *et al.* (2016)[18]	Longitudinal (3 years)	T1 MRI	sSCD: n=253 (61 ± 9) pSCD: n=49 (69 ± 6)	Limbic region (HP)	—	HP volumes, thinner cortex, and various AD-signature subcomponents were associated with increased risk of progression.
Hong *et al.* (2016)[19]	Cross-sectional	T1 MRI DTI	Low risk: n=27 (62.1 ± 7.1) High risk: n=19 (67.1 ± 6.5)	Limbic and frontotemporal regions	—	High-risk group showed lower FA in HP, parahippocampal gyrus, supramarginal gyrus, and frontotemporal lobes without more GM atrophy.
Sun *et al.* (2016)[20]	Cross-sectional	T1 MRI	HC: n=61 (64.11 ± 8.59) SCD: n=25 (65.52 ± 6.12)	Limbic region (HP)	—	SCD showed no significant differences in GM volume.

(Cont'd...)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Rogne *et al.* (2016)[21]	Cross-sectional	T1 MRI	HC: n=58 (70.6 ± 6.7) SCD: n=25 (70.0 ± 9.1) MCI: n=115 (74.5 ± 7.5)	Limbic region (HP) and lateral ventricles	—	SCD and MCI showed larger lateral ventricles and smaller HP volumes compared to HC.
Perrotin *et al.* (2017)[22]	Cross-sectional	T1 MRI	HC: n=35 (65.8 ± 8.6) SCD (clinic): n=28 (67.6 ± 7.7) SCD (community): n=35 (70.8 ± 7.5)	Limbic region (HP)	—	Subclinical depression and hippocampal atrophy were associated with medical help seeking.
Ryu *et al.* (2017)[23]	Cross-sectional	T1 MRI DTI	HC: n=27 (70.6 ± 6.1) SCD: n=18 (69.9 ± 6.3)	Limbic region (HP and ERC)	—	SCD showed lower entorhinal volumes and FA with higher MD in the HP body and entorhinal WM.
Tijms *et al.* (2018)[24]	Longitudinal (2.2 years)	T1 MRI	sSCD: n=100 (67 ± 8) pSCD: n=122 (68 ± 8)	Temporal and frontal regions	—	Lower network parameter values were associated with increased risk of progression.
Verfaillie *et al.* (2018)[25]	Cross-sectional	T1 MRI	SCD: n=231 (62.95 ± 9.22)	Frontal, temporal, and occipital regions	—	SCD with a more randomly organized GM network showed steeper decline in language and global cognition.
Verfaillie *et al.* (2018)[26]	Cross-sectional	T1 MRI	SCD: n=233 (63 ± 9)	Frontal, temporal, and occipital regions	—	SCD showed a faster rate of memory loss, which was found associated with thinner frontal, temporal, and occipital cortex.
Sanchez-Benavides *et al.* (2018)[27]	Cross-sectional	T1 MRI	HC: n=2098 (55.4 ± 6.6) SCD-: n=319 (55.6 ± 6.2) SCD+: n=253 (59.1 ± 7.1)	Limbic region	—	SCD+ showed lower GM volumes compared to SCD-.
Fan *et al.* (2018)[28]	Cross-sectional	T1 MRI DTI	HC: n=34 (67.8 ± 7.4) SCD: n=43 (66.1 ± 7.0) aMCI: n=44 (73.9 ± 8.0)	Limbic region (HP and ERC)	—	SCD showed significant cortical atrophy in bilateral parahippocampus, perirhinal, and left ERC as well as decreased mean FA in bilateral uncinate fasciculi.
Yue *et al.* (2018)[29]	Cross-sectional	T1 MRI	HC: n=67 (67.7 ± 6.6) SCD: n=111 (69.8 ± 7.6) MCI: n=30 (75.5 ± 7.6)	Limbic region (HP and amygdala)	—	SCD and MCI showed decreased right HP and amygdala volumes and different levels of asymmetry in HP and amygdala.
Niemantsverdriet *et al.* (2018)[30]	Cross-sectional	T1 MRI	NC: n=93 (67.3 ± 8.5) SCD: n=102 (68.6 ± 9.8) MCI: n=379 (74.6 ± 8.0) AD: n=313 (77.5 ± 8.0)	Whole brain	—	Baseline atrophy of whole-brain, GM, and cortical GM predicted cognitive impairment.
Zhao *et al.* (2019)[31]	Cross-sectional	T1 MRI	HC: n=42 (64.2 ± 6.2) SCD: n=35 (64.5 ± 7.3) aMCI: n=43 (67.5 ± 10.0) AD: n=41 (68.9 ± 7.9)	Limbic region (HP)	—	AD spectrum showed the trend of volume reduction in CA1, subiculum, presubiculum, molecular layer, and fimbria.
Scheef *et al.* (2019)[32]	Cross-sectional	T1 MRI	HC: n=49 (66 ± 7.2) SCD: n=24 (67 ± 6.1)	Basal forebrain	—	SCD showed a total reduction in volume of the chBFN, with largest effect sizes in the Ch1/2 and Ch4p subdivisions.

(Cont'd...)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Platero *et al.* (2019)[33]	Cross-sectional	T1 MRI	HC: n=70 (70.3 ± 4.5) SCD: n=87 (71.7 ± 5.1) MCI: n=137 (73.9 ± 5.0) AD: n=13 (75.6 ± 5.0)	Limbic region (HP)	—	SCD showed no significant differences in the volume of HP compared to HC.
Fu *et al.* (2021)[34]	Cross-sectional	T1 MRI	HC: n=42 (64.2 ± 6.2) SCD: n=35 (64.5 ± 7.3) aMCI: n=43 (67.5 ± 10.0) AD: n=41 (68.9 ± 7.86)	Limbic region, cerebellum, and diencephalon	—	SCD (lateral ventricle and cerebellum-WM), aMCI (lateral ventricle, pallidum, HP, amygdala, accumbens, and ventral diencephalon), and AD (lateral-ventricle, cerebellum-cortical pallidum, thalamus, HP, amygdala, accumbens, and ventral DC) showed altered asymmetries of volume, surface area, and shape.
Yasuno *et al.* (2015)[35]	Cross-sectional	DTI	HC: n=30 (72.2 ± 4.8) SCD: n=23 (69.6 ± 8.0)	External capsule and limbic region	compensation	SCD showed lower FA of the superior longitudinal fasciculus at the left external capsule and higher FA in the left cingulum.
Li *et al.* (2016)[36]	Cross-sectional	DTI	HC: n=37 (65.1 ± 6.8) SCD: n=27 (65.3 ± 8.0) aMCI: n=35 (69.2 ± 8.6) AD: n=25 (68.3 ± 9.4)	Widespread WM	—	SCD showed widespread WM alterations with decreased FA, increased MD and RD compared to HC, and localized WM alterations, with increased AxD similar to aMCI and AD.
Shu *et al.* (2018)[37]	Cross-sectional	DTI	HC: n=51 (62.2 ± 9.1) SCD: n=36 (63.5 ± 8.7)	Frontal region and thalamus	—	SCD showed less global and local efficiency and diminished rich-club and local connections, which were associated with impaired memory performance.
Yan *et al.* (2018)[38]	Cross-sectional	DTI	HC: n=62 (63.3 ± 8.1) SCD: n=47 (65.3 ± 8.4) aMCI: n=60 (67.3 ± 9.4) d-AD: n=55 (70.9 ± 9.8)	Peripheral regions	—	SCD, MCI, and AD showed similar patterns of disrupted peripheral regions and reduced connectivity. MCI and AD also showed reduced structural connectivity among rich club nodes.
Viviano *et al.* (2019)[39]	Cross-sectional	DTI	HC: n=48 (66.96 ± 8.79) SCD: n=35 (68.51 ± 7.66)	Limbic region	—	SCD showed no differences in cingulum or uncinate diffusion measures compared to HC.
Ohlhauser *et al.* (2019)[40]	Cross-sectional	DTI	HC: n=44 (72.49 ± 6.37) SCD: n=30 (72.94 ± 4.79)	Widespread WM	—	SCD showed lower WM integrity, which was associated with executive function.
Brueggen *et al.* (2019)[41]	Cross-sectional	DTI	HC: n=93 (68.5 ± 5.1) SCD: n=98 (71.3 ± 5.9) MCI: n=45 (72.3 ± 5.7) AD: n=35 (73.5 ± 6.8)	Widespread WM	—	SCD showed higher MD and lower FA and mode in several WM regions. AD and MCI showed higher MD and lower FA and MO in extensive regions, including the corpus callosum and temporal brain regions.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Du *et al.* (2001)[42]	Cross-sectional	T1 MRI	HC: n=40 (75.1 ± 4.3) MCI: n=36 (75.1 ± 8.2) AD: n=29 (75.8 ± 5.1)	Limbic region (ERC and HP)	—	AD and MCI showed reduced ERC and HP volumes, cortical GM loss, and ventricular enlargement compared to HC.
Dickerson *et al.* (2001)[43]	Longitudinal (77 months)	T1 MRI	HC: n=34 (70.3 ± 6.6) non-demented: n=28 (68.6 ± 8.6) AD: n=16 (71.4 ± 9.1)	Limbic region (ERC and HP)	—	Both patient groups showed entorhinal and HP atrophy. Entorhinal volume was a better predictor of conversion.
Pennanen *et al.* (2004)[44]	Cross-sectional	T1 MRI	HC: n=59 (72.7 ± 4.3) MCI: n=65 (72.8 ± 4.5) AD: n=48 (71.1 ± 8.1)	Limbic region (ERC and HP)	—	MCI showed more ERC volume loss, whereas AD showed more HP volume loss.
Pennanen *et al.* (2005)[45]	Cross-sectional	T1 MRI	HC: n=32 (74 ± 4) MCI: n=51 (72 ± 5)	Limbic region (MTL)	—	MCI showed unilateral atrophy in the MTL on the right side.
Stoub *et al.* (2006)[46]	Cross-sectional	T1 MRI	HC: n=50 (78.1 ± 6.0) MCI: n=40 (77.9 ± 7.5)	Limbic region (HP)	—	MCI showed decreased HP volume and parahippocampal WM volume, which contributed to memory dysfunction.
deJong *et al.* (2008)[47]	Cross-sectional	T1 MRI	MC: n=70 (66 ± 13) pAD: n=69 (77 ± 7.4)	Limbic region (HP), putamen, and thalamus	—	Probable AD showed reduced volumes in HP, putamen, and thalamus, which were associated with cognitive decline.
Thomann *et al.* (2008)[48]	Cross-sectional	T1 MRI	HC: n=20 (71.5 ± 5.8) MCI: n=20 (71.8 ± 4.9) AD: n=20 (71.6 ± 3.8)	Cerebellum	—	AD showed smaller posterior cerebellar lobes compared to HC, which were associated with poorer cognitive performance.
Balthazar *et al.* (2009)[49]	Cross-sectional	T1 MRI	HC: n=16 (69.12 ± 7.55) aMCI: n=17 (68.29 ± 9.93) AD: n=15 (74.26 ± 6.33)	Limbic region (parahippocampus) and thalamus	—	aMCI showed similar but less intense GM atrophy compared to AD and no WM atrophy.
Muth *et al.* (2010)[50]	Cross-sectional	T1 MRI	HC: n=46 (63.4 ± 6.4) aMCI: n=26 (67.6 ± 6.7) AD: n=12 (72.6 ± 6.6)	Basal forebrain	—	HC showed the largest substantia innominate volume followed by aMCI and AD patients.
Cherubini *et al.* (2010)[51]	Cross-sectional	T1 MRI DTI	HC: n=30 (67.9 ± 7.4) aMCI: n=30 (66.8 ± 6.0) AD: n=30 (68.7 ± 7.8)	Limbic region, thalamus, and basal ganglia	—	HP and thalamus decreased progressively from HC through MCI to AD. MD increased in the bilateral HP, amygdala, and right caudate. No differences in FA.
Evans *et al.* (2010)[52]	Longitudinal (12 months)	T1 MRI	HC: n=131 (76.0 ± 5.1) MCI: n=231 (74.4 ± 7.1) AD: n=99 (75.3 ± 6.9)	Whole brain	—	MCI and AD showed brain atrophy and ventricular expansion.
Serra *et al.* (2010)[53]	Cross-sectional	T1 MRI DTI	HC: n=13 (64.1 ± 10.5) aMCI: n=16 (72.4 ± 7.5) AD: n=9 (72.5 ± 6.5)	Temporal region	—	AD showed widespread GM atrophy. WM atrophy was mainly located in the temporal lobe.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Choo *et al.* (2010)[54]	Cross-sectional	T1 MRI DTI	HC: n=18 (70.7 ± 5.2) MCI: n=19 (71.6 ± 7.1) AD: n=19 (71.1 ± 5.1)	Limbic region	—	MCI and AD showed decreased PCC and ERC volumes. MCI showed decreased FA in PH-C, whereas AD showed decreased FA in PC-C and PH-C.
Scola *et al.* (2010)[55]	Longitudinal (2 years)	T1 MRI DTI	HC: n=20 (56-75) aMCI: n=19 (52-79) AD: n=21 (56-79)	Temporal, occipital, parietal, and frontal regions	—	AD-spectrum patients showed a trend of increased MD, decreased FA, and GM atrophy. The severity of microstructural damage within and beyond MTL was associated with an increased short-term risk of developing AD.
Zhang *et al.* (2011)[56]	Cross-sectional	T1 MRI	HC: n=243 (77.8 ± 4.5) naMCI: n=55 (78.2 ± 4.6) aMCI: n=81 (79.2 ± 4.7)	Basal forebrain	—	Basal forebrain atrophy was insignificant in the prediction of MCI.
Tondelli *et al.* (2012)[57]	Longitudinal (10 years)	T1 MRI	HC: n=40 (76.07 ± 5.69) MCI: n=32 (77.10 ± 5.22) AD: n=8 (79.39 ± 5.01)	Limbic region; orbitofrontal, and parietal lobes	—	Preclinical AD and MCI showed reduced brain volume in MTL, posterior cingulate/precuneus, and orbitofrontal cortex.
Trzepacz *et al.* (2013)[58]	Longitudinal (24 months)	T1 MRI	cMCI: n=122 (74.6 ± 6.9) sMCI: n=177 (74.4 ± 7.8) AD: n=163 (75.3 ± 7.5)	Limbic region; frontal, parietal, and insular lobes	—	Agitation and aggression in AD and MCI were associated with greater atrophy of frontal, insular, amygdala, cingulate, and HP regions.
Leung *et al.* (2013)[59]	Longitudinal (36 months)	T1 MRI	HC: n=205 (76.0 ± 5.1) MCI: n=352 (75.0 ± 7.2) AD: n=156 (74.9 ± 7.7)	Limbic region (HP)	—	MCI that progressed to AD in 3 years showed acceleration of HP loss.
Velayudhan *et al.* (2013)[60]	Longitudinal (1 year)	T1 MRI	HC: n=99 (74.56 ± 5.14) MCI: n=106 (74.00 ± 5.64) AD: n=120 (74.82 ± 6.21)	Limbic region (HP and ERC)	—	AD showed smaller ERC thickness as well as HP and whole-brain volumes. AD with thinner ERC showed lower cognition and higher disease severity and predicted greater cognitive decline.
Nir *et al.* (2015)[61]	Longitudinal (6 months)	T1 MRI DTI	HC: n=29 (71.8 ± 7.5) MCI: n=30 (73.4 ± 5.2)	Frontal, parietal, temporal, and occipital regions	—	Decreased clustering and lower nodal betweenness centrality were associated with greater atrophy.
Yi *et al.* (2016)[62]	Longitudinal (2 years)	T1 MRI	HC: n=181 (65 ± 8) MCI: n=201 (70 ± 9) AD: n=391 (69 ± 9)	Limbic region (HP) and basal forebrain	—	Loss of HP and nucleus accumbens volumes were associated with increased risk of progression from MCI to AD.
Krumm *et al.* (2016)[63]	Cross-sectional	T1 MRI	HC: n=46 (74.78 ± 7.09) aMCI: n=23 (76.08 ± 8.26) HC: n=31 (78.10 ± 5.58) AD: n=34 (78.89 ± 5.24)	Limbic region (ERC) and PRC	—	aMCI and AD showed ERC and medial PRC atrophy compared to HC. AD also showed lateral PRC atrophy.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Yang *et al.* (2016)[64]	Cross-sectional	T1 MRI	mild MCI: n=33 (60.5 ± 7) moderate MCI: n=57 (62.8 ± 6) severe MCI: n=35 (66.5 ± 8)	Temporal region	—	aMCI showed progressive GM atrophy in the right lingual gyrus, which was associated with poor cognitive function that progressively declined in three stages.
Gong *et al.* (2017)[65]	Cross-sectional	T1 MRI DTI	HC: n=18 (73.2 ± 5.5) aMCI: n=18 (75.0 ± 6.9) AD: n=18 (73.7 ± 4.2)	Temporal, parietal, and frontal regions	—	Early MCI showed more regions with diffusional abnormalities than atrophies in deep GM, contrary to late AD.
Matsuoka *et al.* (2020)[66]	Longitudinal (41 months)	T1 MRI	pMCI: n=68 (74.1 ± 7.3) sMCI: n=169 (72.5 ± 7.5)	Diencephalon	—	MCI showed pineal volume reduction and is a predictor of AD conversion.
Lin *et al.* (2020)[67]	Cross-sectional	T1 MRI	HC: n=230 (76.12 ± 5.02) MCI: n=399 (74.94 ± 7.48) AD: n=193 (75.53 ± 7.48)	Cerebellum	—	HC, MCI, and AD showed progressive decreases in cerebellar volume. MCI showed a negative association between cerebellar volume and cognitive function.
Dutt *et al.* (2020)[68]	Longitudinal (10 years)	T1 MRI	HC: n=814 (73.49 ± 6.76) MCI: n=542 (73.54 ± 7.35) AD: n=273 (75.12 ± 7.74)	Brainstem	—	MCI and AD showed smaller midbrain volumes when normalizing to whole brainstem volume, and smaller midbrain, locus coeruleus, pons, and whole brainstem volumes when normalizing to total intracranial volume.
Bernstein *et al.* (2021)[69]	Cross-sectional	T1 MRI	HC: n=125 (73.42 ± 6.25) EMCI: n=212 (70.60 ± 7.16) LMCI: n=114 (71.81 ± 7.93) AD: n=89 (74.06 ± 7.74)	Thalamus	—	Late MCI and AD showed smaller anteroventral, mediodorsal, pulvinar, medial geniculate, and centromedian nuclei, whereas early MCI showed smaller mediodorsal, pulvinar, and medial geniculate nuclei compared to HC.
Zeng *et al.* (2021)[70]	Longitudinal (2 years)	T1 MRI	HC: n=102 (73.64 ± 6.05) sMCI: n=52 (72.92 ± 7.38) pMCI: n=29 (72.56 ± 7.43)	Limbic region (HP)	—	pMCI showed smaller volume than sMCI in bilateral subiculum, molecular layer, molecular and granule cell layers of the dentate gyrus, cornu ammonis 4, and right tail as well as faster volume loss in bilateral subiculum and molecular layer.
Sheng *et al.* (2021)[71]	Cross-sectional	T1 MRI	HC: n=34 (72.38 ± 0.87) MCI: n=70 (73.78 ± 0.84) AD: n=40 (74.85 ± 1.37)	Temporal and frontal regions	Compensation	Patients showed higher nodal and edge properties, which were associated with impaired memory function.
Rose *et al.* (2000)[72]	Cross-sectional	DTI	HC: n=9 (72 ± 0.7) pAD: n=11 (70 ± 0.6)	Corpus callosum, cingulum, *et al.*	—	Probable AD showed reduction in the integrity of association WM fiber tracts.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Medina *et al.* (2006)[73]	Cross-sectional	DTI	HC: n=21 (77.3 ± 10.1) MCI: n=14 (78.0 ± 5.6) AD: n=14 (77.4 ± 6.8)	Posterior WM regions	—	MCI and AD showed reduced FA compared to HC in multiple posterior WM regions.
Huang and Auchus (2007)[74]	Cross-sectional	DTI	HC: n=6 (71.17 ± 5.74) MCI: n=8 (74.75 ± 8.55) AD: n=4 (73.75 ± 6.08)	Frontal, temporal, and parietal regions	—	MCI and AD showed microstructural WM changes in frontal, temporal, and parietal regions.
Zhou *et al.* (2008)[75]	Cross-sectional	DTI	HC: n=13 (65.92 ± 12.11) MCI: n=10 (68.89 ± 9.61) AD: n=11 (73.91 ± 11.00)	Limbic region	—	AD showed decreased fiber connections between HP and PCC, whereas MCI showed reduced numbers of fiber derived from PCC and HP to the whole brain.
Damoiseaux *et al.* (2009)[76]	Cross-sectional	DTI	HC: n=22 (70.7 ± 6.0) MCI: n=8 (73.9 ± 4.9) AD: n=16 (69.5 ± 6.7)	Temporal lobe	—	AD showed decreased FA only in the left ATL compared to HC.
Chen *et al.* (2009)[77]	Cross-sectional	DTI	HC: n=16 (69.0 ± 8.4) aMCI: n=13 (73.2 ± 9.3) AD: n=11 (76.7 ± 8.5)	Frontal and parietal regions	—	aMCI and early AD showed impaired executive function, which was associated with frontal and parietal periventricular WM changes.
Mielke *et al.* (2009)[78]	Longitudinal (3 months)	DTI	HC: n=25 (74.3 ± 7.1) MCI: n=25 (75.8 ± 5.3) AD: n=25 (75.6 ± 7.0)	Fornix, cingulum bundle, and splenium	—	AD showed lowed FA than NC at baseline and 3 months in the fornix and anterior portion of the cingulum bundle.
Teipel *et al.* (2010)[79]	Longitudinal (16 months)	DTI	HC: n=11 (67.4 ± 7.7) aMCI: n=14 (73.1 ± 7.4)	Corpus callosum	—	MCI showed decreased FA in the anterior corpus callosum.
Liu *et al.* (2011)[80]	Cross-sectional	DTI	HC: n=19 (75.0 ± 6.0) MCI: n=27 (75.0 ± 6.0) AD: n=17 (76.0 ± 7.0)	Limbic region, cerebellum, *et al.*	—	AD showed decreased FA in the neurofiber tracts compared to HC. The FA values of MCI were in between HC and AD.
Bozok *et al.* (2012)[81]	Cross-sectional	DTI	HC: n=16 (65.9 ± 8.5) MCI: n=23 (70.8 ± 7.9) AD: n=21 (71.6 ± 10.6)	Limbic region	—	MCI and AD showed disruption of limbic WM pathways.
Garcés *et al.* (2014)[82]	Cross-sectional	DTI	HC: n=31 (70.8 ± 4.2) MCI: n=26 (72.5 ± 6.7)	Limbic and parietal regions	—	MCI showed reduced FA along the reconstructed WM pathways connecting DMN regions.
Wang *et al.* (2014)[83]	Cross-sectional	DTI	HC: n=26 (73.8 ± 6.7) aMCI: n=40 (76.4 ± 7.6) AD: n=24 (78.3 ± 5.7)	Corpus callosum	—	aMCI and AD showed callosal degeneration.
Daianu *et al.* (2015)[84]	Cross-sectional	DWI	HC: n=50 (72.6 ± 6.1) early MCI: n=72 (72.4 ± 7.9) late MCI: n=38 (72.6 ± 5.6) AD: n=42 (75.5 ± 8.9)	Whole brain	—	Network disruptions predominated in the low-degree regions of the connectome in patients.
Mito *et al.* (2018)[85]	Cross-sectional	DTI	HC: n=56 (75.0 ± 7.0) early MCI: n=48 (72.0 ± 7.0) late MCI: n=35 (73.0 ± 8.0) AD: n=31 (73.0 ± 7.0)	Limbic and parietal regions	—	AD showed WM loss in the fiber pathways associated with DMN. MCI showed subtle axonal reduction within the posterior cingulum.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Gozdas *et al.* (2020)[86]	Cross-sectional	DTI	HC: n=23 (72.3 ± 6.2) aMCI: n=25 (73.4 ± 6.28)	Limbic region and corpus callosum	—	aMCI showed WM alterations specifically on the right cingulum cingulate, right cingulum HP, and anterior corpus callosum compared to HC.
Kuang *et al.* (2020)[87]	Cross-sectional	DTI	HC: n=33 (74.18 ± 8.28) MCI: n=77 (74.22 ± 6.73) AD: n=40 (72.45 ± 5.60)	Whole brain	—	AD and MCI showed decreased network integration and increased network segregation compared to HC.
Yang *et al.* (2021)[88]	Cross-sectional	DWI	MCI: n=85 (76.9 ± 8.09) AD: n=40 (74.8 ± 10.7)	Forceps minor, *et al.*	—	AD showed decreased FA and increased MD and RD in forceps minor, corticospinal tract, and inferior fronto-occipital fasciculus.
Laakso *et al.* (2000)[89]	Longitudinal (3 years)	T1 MRI	HC: n=8 (70 ± 5) AD: n=27 (69 ± 8)	Limbic region (HP)	—	AD showed statistically non-significant trend of accelerated HP volume loss compared to HC.
Rémy *et al.* (2005)[90]	Cross-sectional	TI MRI	HC: n=11 (65.9 ± 5.7) AD: n=8 (72.2 ± 10.8)	Temporal and parietal regions	—	AD showed GM atrophy in the MTL and inferior parietal/superior temporal associative areas.
DiPaola *et al.* (2007)[91]	Cross-sectional	T1 MRI	HC: n=18 (65.4 ± 10.6) AD: n=18 (64.3 ± 10.2)	MTL, parietal, frontal, and thalamus	—	AD showed GM volume reduction in the MTL, parietal, and frontal areas bilaterally as well as the left anterior thalamic nuclei.
Zarei *et al.* (2010)[92]	Cross-sectional	T1 MRI DTI	HC: n=22 (70.7 ± 6.0) AD: n=16 (69.5 ± 6.7)	Thalamus	—	AD showed bilateral regional atrophy in the dorsal-medial part of the thalamus and smaller internal medullary lamina.
Domoto-Reilly *et al.* (2012)[93]	Cross-sectional	T1 MRI	HC: n=183 (75.8 ± 5.1) AD: n=145 (75.7 ± 7.4)	Temporal lobe	—	Naming impairment in AD was associated with the left ATL atrophy.
Smits *et al.* (2014)[94]	Cross-sectional	T1 MRI	AD: n=329 (67 ± 8)	Limbic region (MTL)	—	MTL atrophy was associated with poor performance in memory, language, and attention. Posterior atrophy was associated with poor performance in visuospatial and executive functioning.
Cho *et al.* (2014)[95]	Longitudinal (3 years)	T1 MRI	HC: n=14 (67.1 ± 7.6) AD: n=36 (70.2 ± 8.0)	Basal ganglia	—	AD showed volumetric decline in caudate nucleus and putamen, which was associated with cognitive decline in frontal function.
Cavedo *et al.* (2014)[96]	Cross-sectional	T1 MRI	HC (young): n=18 (62.8 ± 4.7) HC (old): n=18 (75.1 ± 3.4) EOAD: n=18 (62.5 ± 4.4) LOAD: n=18 (77.5 ± 5.0)	Limbic region (amygdala and HP)	—	LOAD showed greater atrophy in amygdala and HP than EOAD.

(*Cont'd...*)

Table S1. ***(Continued).***

Authors (year)	Design	Modality	Subject (mean age ± SD)	Associated regions	Compensation	Main findings
Phillips *et al.* (2016)[97]	Cross-sectional	T1 MRI DTI	HC: n=47 (69.23 ± 4.45) AD: n=44 (71.02 ± 5.84)	Limbic region (HP), temporal, and frontal	—	AD showed increased AD and RD across most of the superficial WM.
Ji *et al.* (2021)[98]	Cross-sectional	T1 MRI	HC: n=27 (77.00 ± 7.3) AD-VM: n=27 (75.26 ± 6.2) AD-M: n=27 (77.07 ± 6.1)	Brainstem	—	AD-M showed bilateral loss in the pons and the left part of the midbrain compared to HC. AD-M showed greater loss in the left midbrain than AD-VM.
Yang *et al.* (2021)[99]	Cross-sectional	T1 MRI	HC: n=68 (75.87 ± 8.74) AD: n=68 (76.51 ± 7.04)	Limbic region (HP), basal ganglia, and thalamus	—	AD showed different connections between bilateral HP and bilateral thalamus, bilateral putamen, and between the left HP and the right caudate compared to HC.
Kavcic *et al.* (2008)[100]	Cross-sectional	DTI	HC: n=18 (75.39 ± 7.09) AD: n=14 (74.93 ± 5.91)	Posterior cerebral areas	—	WM changes in early AD were concentrated in posterior cerebral areas.
Rose *et al.* (2008)[101]	Cross-sectional	DTI	HC: n=13 (75.8 ± 6.5) AD: n=13 (76.8 ± 5.2)	Limbic region	—	AD showed increased MD (mainly in the posterior cingulate gyrus) and reduced FA.
Lo *et al.* (2010)[102]	Cross-sectional	DTI	HC: n=30 (70.07 ± 6.37) AD: n=25 (79.40 ± 5.89)	Frontal region	—	AD showed reduced nodal efficiency in WM network (mainly in the frontal regions) compared to HC.
Mayo *et al.* (2017)[103]	Longitudinal (1 year)	DTI	HC: n=33 (74.1 ± 6.5) AD: n=34 (76.9 ± 7.7)	Limbic region	—	AD showed reduced FA and increased MD in the hippocampal cingulum compared to HC.
Toniolo *et al.* (2020)[104]	Cross-sectional	DTI	HC: n=25 (67.2 ± 6.7) AD: n=50 (70.5 ± 4.5)	Cerebellum	—	AD showed lower FA and higher RD in MCP, SCPL, and SCPR, higher MD in SCPR and SCPL, as well as higher AxD in SCPL.
Luo *et al.* (2021)[105]	Cross-sectional	DTI	HC (young): n=64 (59.7 ± 2.5) HC (old): n=46 (72.4 ± 3.8) EOAD: n=31 (60.58 ± 3.3) LOAD: n=45 (74.3 ± 4.6)	Limbic region, corpus callosum, and thalamus	—	EOAD showed lower FD in splenium of corpus callosum, limbic tracts, cingulum bundles, and posterior thalamic radiation, as well as higher FC in splenium of corpus callosum, dorsal cingulum, and posterior thalamic radiation. LOAD showed lower FD and FC.

ACC, anterior cingulate cortex; AD, Alzheimer's disease; AD-M, mild AD; AD-VM, very mild AD; aMCI, amnestic MCI; ATL, anterior temporal lobe; AxD, axial diffusivity; cMCI, MCI converter; CSF, cerebrospinal fluid; chBFN, cholinergic basal forebrain nuclei; DMN, default mode network; DTI, diffusion tensor imaging; EOAD, early-onset AD; ERC, entorhinal cortex; FA, fractional anisotropy; FC, fiber bundle cross-section; FD, fiber density; GM, gray matter; HC, healthy control; HMCI, high sum of box score MCI; HP, hippocampus; LMCI, low sum of box score MCI; LOAD, late-onset AD; MCI, mild cognitive impairment; MCP, middle cerebellar peduncle; MD, mean diffusivity; MTL, medial temporal lobe; MRI, magnetic resonance imaging; naMCI, non-amnestic MCI; pAD, prodromal AD; PCC, posterior cingulate cortex; PC-C, posterior cingulate cingulum; PH-C, parahippocampal cingulum; pMCI, progressive MCI; PRC, perirhinal cortex; RD, radial diffusivity; SCD, subjective cognitive decline; SCPL/SCPR, left and right superior cerebellar peduncles; sMCI, stable MCI; WM, white matter

Table S2. Summary of functional connectivity studies in AD-spectrum patients.

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Rodda *et al.* (2009)[106]	Cross-sectional	Task-fMRI	HC: n=10 (68.0 ± 13.5) SCD: n=10 (64.2 ± 5.6)	Temporal, parietal occipital, and frontal	Compensation	SCD showed increased activation in left MTL, left PFC, and occipitoparietal and medial frontal cortex.
Erk *et al.* (2011)[107]	Cross-sectional	Task-fMRI	HC: n=20 (66.8 ± 5.4) SCD: n=19 (68.4 ± 5.7)	Limbic system (HP) and frontal region	Compensation	SCD showed reduced activation in right HP and increased activation in right dorsolateral PFC during episodic memory recall.
Dumas *et al.* (2013)[108]	Cross-sectional	Task-fMRI	HC: n=11 (56.8 ± 1.9) SCD: n=12 (57.1 ± 2.3)	Frontal, parietal, and limbic system	Compensation	SCD showed greater activation in middle frontal gyrus, precuneus, and cingulate gyrus during working memory.
Wang *et al.* (2013)[109]	Cross-sectional	Task-fMRI	HC: n=16 (70.7 ± 6.0) SCD: n=23 (70.1 ± 7.3) MCI: n=18 (73.7 ± 9.1)	Limbic system (HP)	—	SCD and MCI showed decreased DMN connectivity in the right HP compared to HC but greater connectivity than MCI.
Hafkemeijer *et al.* (2013)[10]	Cross-sectional	rs-fMRI	HC: n=29 (71.3 ± 3.4) SCD: n=25 (71.4 ± 9.2)	Limbic system, temporal, parietal, and occipital regions	Compensation	SCD showed increased FC in the DMN (HP, thalamus, PCC, cuneus, precuneus, and superior temporal gyrus) and medial visual network (ACC, PCC, cuneus, and precuneus).
Yasuno *et al.* (2015)[35]	Cross-sectional	rs-fMRI	HC: n=30 (72.2 ± 4.8) SCD: n=23 (69.6 ± 8.0)	Limbic system (ACC) and frontal region	—	SCD showed reduced FC in between RSC and other cortical midline structures of dorsomedial PFC and ACC.
Sun *et al.* (2016)[20]	Cross-sectional	rs-fMRI	HC: n=61 (64.11 ± 8.59) SCD: n=25 (65.52 ± 6.12)	Parietal, temporal, and occipital regions; cerebellum	Compensation	SCD showed higher ALFF values in bilateral inferior parietal lobule, right inferior and middle occipital gyrus, right superior temporal gyrus, and right cerebellum posterior lobe.
Dillen *et al.* (2016)[110]	Cross-sectional	rs-fMRI	HC: n=25 (62.4 ± 7.0) SCD: n=27 (65.7 ± 7.9) AD: n=24 (71.0 ± 6.2)	Limbic system, frontal, and occipital	Compensation	SCD showed higher FC from RSC to frontal cortex. Prodromal AD showed higher FC from RSC to the occipital cortex and from PCC to the lingual gyrus.
Dillen *et al.* (2017)[111]	Cross-sectional	rs-fMRI	HC: n=25 (62.4 ± 7.0) SCD: n=28 (65.8 ± 7.8) pAD: n=25 (70.8 ± 6.2)	Limbic system, frontal, and parietal	—	SCD and prodromal AD showed an anterior-posterior disconnection and a HP decoupling from posterior DMN.
Hayes *et al.* (2017)[112]	Cross-sectional	Task-fMRI	HC: n=41 (67.5 ± 9.1) SCD: n=23 (68.6 ± 8.2)	Parietal, occipital, and limbic system (PCC)	—	SCD showed lower subsequent memory effects in occipital lobe, superior parietal lobe, and PCC.
Dong *et al.* (2018)[113]	Cross-sectional	rs-fMRI	HC: n=39 (82.89 ± 4.13) SCD: n=39 (83 ± 4.43)	Frontal, parietal, and occipital regions; limbic system	Compensation	SCD showed detectable changes in FC strength.
Verfaillie *et al.* (2018)[114]	Longitudinal (1 year)	rs-fMRI	HC: n=29 (65 ± 6) SCD: n=30 (65 ± 6)	Temporal region and limbic system (PCC)	Compensation	SCD showed higher connectivity between posterior DMN and the medial temporal memory system.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Viviano *et al.* (2019)[39]	Cross-sectional	rs-fMRI	HC: n=48 (66.96 ± 8.79) SCD: n=35 (68.51 ± 7.66)	Limbic system and parietal region	—	SCD showed lower FC across regions of the putative posterior memory system, specifically retrosplenial-precuneus FC.
Parker *et al.* (2020)[115]	Cross-sectional	T1 MRI rs-fMRI	HC: n=23 (74.3 ± 5.0) SCD: n=23 (72.9 ± 5.4)	Limbic system, frontal, temporal, and occipital regions	Compensation	SCD showed increased FC in DMN and decreased FC in bilateral frontal pole, caudate, angular gyrus, and lingual gyrus.
Chen *et al.* (2020)[116]	Cross-sectional	rs-fMRI	HC: n=64 (73.23 ± 6.69) SCD: n=66 (71.28 ± 5.45)	Frontal, temporal, and parietal regions	Compensation	SCD showed higher nodal topological properties mainly in DMN and increased local and medium range connectivity between bilateral PHG and other DMN-related regions.
Yang *et al.* (2020)[117]	Cross-sectional	rs-fMRI	HC: n=55 (63.41 ± 8.0) SCD: n=43 (65.09 ± 8.7) aMCI: n=52 (68.06 ± 9.3) AD: n=44 (70.98 ± 10.0)	Parietal and occipital regions; cerebellum	Compensation	The fractional ALFF values presented with a decreasing trend as the disease progressed.
Khan *et al.* (2020)[118]	Cross-sectional	rs-fMRI	HC: n=34 (75.3 ± 6.3) SCD: n=24 (71.9 ± 5.3) EMCI: n=43 (71.1 ± 6.9) LMCI: n=31 (71.2 ± 7.7) AD: n=23 (72.9 ± 7.7)	Limbic system and parietal region (precuneus)	—	AD showed decreased FC in anterior precuneus, dorsal PCC, and central precuneus compared to HC. The FC of the central precuneus was associated with disease severity and specific deficits in memory and executive function across the entire AD spectrum.
Sharma *et al.* (2021)[119]	Cross-sectional	rs-fMRI	HC: n=26 (71.42 ± 7.3) SCD: n=23 (70.70 ± 5.5)	Limbic system	—	SCD showed disrupted FC between the posterior DMN and parahippocampal gyrus.
Machulda *et al.* (2003)[120]	Cross-sectional	Task-fMRI	HC: n=11 (79.3) MCI: n=9 (76.5) AD: n=9 (79.6)	Limbic system (MTL)	—	MCI and AD showed less MTL activation on memory task but similar activation on sensory task compared to HC.
Dannhauser *et al.* (2005)[121]	Cross-sectional	Task-fMRI	HC: n=10 (68.0 ± 13.5) aMCI: n=10 (72.0 ± 7.7)	Frontal region	—	aMCI showed attenuated PFC activation, which was associated with the functional network subserving divided attention.
Rosano *et al.* (2005)[122]	Cross-sectional	Task-fMRI	HC: n=8 (81.5) MCI: n=8 (79.5)	Parietal and frontal regions	Compensation	MCI showed greater activation in posterior parietal and dorsolateral prefrontal cortex.
Rombouts *et al.* (2005)[123]	Cross-sectional	rs-fMRI	HC: n=41 (63.1 ± 5.2) MCI: n=28 (74.0 ± 7.5) AD: n=18 (74.1 ± 8.0)	Frontal, parietal, and limbic system	—	MCI showed less deactivation in DMN (anterior frontal cortex, precuneus, and PCC) than HC but more than AD during tasks.
Celone *et al.* (2006)[124]	Cross-sectional	Task-fMRI	HC: n=15 (75.5 ± 6.0) LMCI: n=15 (75.1 ± 7.1) HMCI: n=12 (80.0 ± 4.5) AD: n=10 (77.6 ± 8.0)	Limbic system (HP) and parietal region	Compensation	Less impaired MCI showed hyperactivation in HP and greater deactivation in parietal regions compared to HC. More impaired MCI and AD showed hypoactivation in HP and loss of deactivation in parietal regions.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Johnson *et al.* (2006)[125]	Cross-sectional	Task-fMRI	HC: n=14 (72.5 ± 5.7) aMCI: n=14 (73.7 ± 6.9)	Limbic system (PCC, HP)	—	MCI showed less activity in PCC during recognition of previous items and in the right HP during encoding of novel items.
Kircher *et al.* (2007)[126]	Cross-sectional	Task-fMRI	HC: n=29 (67.8 ± 5.4) MCI: n=21 (69.7 ± 7.0)	Limbic system (MTL)	Compensation	MCI showed increased activation in MTL during successful encoding compared to HC.
Hämäläinen *et al.* (2007)[127]	Cross-sectional	Task-fMRI	HC: n=21 (71.2 ± 4.9) MCI: n=14 (72.4 ± 7.3) AD: n=15 (73.1 ± 6.7)	Limbic system (MTL) and fusiform region	MCI: Compensation AD: Decompensation	MCI showed increased activation in posterior MTL and fusiform regions, which was absent in AD.
Sorg *et al.* (2007)[128]	Cross-sectional	rs-fMRI	HC: n=16 (68.1 ± 3.8) aMCI: n=24 (69.3 ± 8.1)	Limbic system (HP and PCC)	—	MCI showed the loss of FC between both hippocampi in the MTLs and the posterior cingulate of the DMN.
Zhou *et al.* (2008)[75]	Cross-sectional	rs-fMRI	HC: n=13 (65.92 ± 12.11) MCI: n=10 (68.89 ± 9.61) AD: n=11 (73.91 ± 11.00)	Limbic system (HP and PCC)	—	MCI and AD showed reduced connectivity from both the PCC and HP to the whole brain and between these two regions.
Dannhauser *et al.* (2008)[129]	Cross-sectional	Task-fMRI	HC: n=10 (68 ± 13.5) MCI: n=10 (72 ± 7.7)	Frontal region	—	aMCI revealed decreased activation in left ventrolateral PFC compared to HC.
Woodard *et al.* (2009)[130]	Cross-sectional	Task-fMRI	HC: n=19 (75.1 ± 5.9) MCI: n=19 (75.4 ± 6.9)	Limbic system, temporoparietal, and frontal regions	Compensation	MCI showed greater changes in MTL, temporoparietal junction, posterior cingulate/precuneus, and frontal regions.
Qi *et al.* (2010)[131]	Cross-sectional	rs-fMRI	HC: n=14 (70.4 ± 5.8) aMCI: n=14 (71.8 ± 7.3)	Frontal, parietal, and temporal regions	Compensation	aMCI showed increased activity in left PFC, inferior parietal lobule, and middle temporal gyrus compared to HC.
Bosch *et al.* (2010)[132]	Cross-sectional	Task-fMRI	HC: n=15 (72.20 ± 5.8) aMCI: n=15 (74.63 ± 6.9) AD: n=15 (75.27 ± 5.7)	Frontal, parietal, and occipital regions; limbic system	Compensation	aMCI and AD showed positive correlations between cognitive reserve measures and activation in speech processing areas, as well as greater deactivations in DMN.
Gili *et al.* (2011)[133]	Cross-sectional	T1 MRI rs-fMRI	HC: n=10 (64.1 ± 10.5) aMCI: n=10 (71.2 ± 4.1) AD: n=11 (71.9 ± 7.9)	Limbic system (PCC)	—	aMCI showed reduced connectivity in PCC with the absence of GM atrophy, which was detectable in AD.
Lenzi *et al.* (2011)[134]	Cross-sectional	Task-fMRI	HC: n=14 (64.3) MCI: n=15 (72.5)	Temporal and frontal regions	Compensation	aMCI showed greater activation in left inferior temporal, right superior temporal, and right dorsal precentral gyrus.
Bai *et al.* (2011)[135]	Longitudinal (20 months)	rs-fMRI	HC: n=18 (70.3 ± 4.7) aMCI: n=26 (71.4 ± 4.3)	Cerebellum	—	aMCI showed decreased functional connections to the posterior cerebellar lobe.
Wang *et al.* (2011)[136]	Cross-sectional	rs-fMRI	HC: n=22 (66.55 ± 7.67) MCI: n=16 (69.38 ± 7.00) AD: n=16 (69.56 ± 7.65)	Parietal, temporal, and frontal regions; basal ganglia	Compensation	AD and MCI showed decreased activity in medial parietal lobe and lentiform nucleus but increased activity in lateral temporal regions and superior frontal and parietal regions.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Binnewijzend *et al.* (2012)[137]	Cross-sectional	rs-fMRI	HC: n=43 (69 ± 7) MCI: n=23 (71 ± 8) AD: n=39 (67 ± 8)	Limbic system (PCC) and parietal region	—	AD showed lower FC in the DMN (precuneus and PCC) compared with HC, independent of cortical atrophy.
Agosta *et al.* (2012)[138]	Cross-sectional	rs-fMRI	HC: n=13 (68.5 ± 6.9) aMCI: n=12 (69.1 ± 7.4) AD: n=13 (74.5 ± 9.7)	Parietal and frontal regions	Compensation	aMCI showed reduced precuneus connectivity in the DMN compared to HC. AD showed opposing connectivity effects in the DMN and frontal networks.
Liang *et al.* (2012)[139]	Cross-sectional	rs-fMRI	HC: n=16 (67.19 ± 8.38) MCI: n=16 (68.50 ± 7.77)	Parietal region	Compensation	MCI showed altered connectivity in the DMN, ECN, and SN compared to HC.
Zamboni *et al.* (2013)[140]	Cross-sectional	Task-fMRI rs-fMRI	HC: n=25 (75.1 ± 7.3) MCI: n=25 (74.8 ± 7.2) AD: n=30 (74.9 ± 6.0)	Limbic system (HP) and frontal region	Compensation	Compared to HC and AD, MCI showed HP hyperactivation. AD showed increased frontal activation during a memory task, overlapping with increased frontal connectivity during rest.
Zamboni *et al.* (2013)[141]	Cross-sectional	Task-fMRI	HC: n=17 (75.5 ± 4.8) MCI: n=17 (76.2 ± 5.9) AD: n=17 (76.7 ± 5.4)	Frontal and temporal cortices	—	Decreased functional activation of medial prefrontal and anterior temporal cortices was associated with impaired self-awareness in AD.
Liu *et al.* (2014)[142]	Cross-sectional	rs-fMRI	HC: n=21 (65.0 ± 8.1) MCI: n=18 (70.2 ± 7.9) mAD: n=17 (66.1 ± 8.3) sAD: n=18 (65.4 ± 8.6)	Frontal and parietal regions	—	Severe AD showed attenuated FC particularly between regions that were separated by a greater physical distance.
Neufang *et al.* (2014)[143]	Cross-sectional	rs-fMRI Task-fMRI	HC: n=16 (68.1 ± 3.8) pAD: n=15 (68.5 ± 6.6)	Frontal region	—	Prodromal AD showed disrupted prediction of effective connectivity by functional connectivity.
Pasquini *et al.* (2015)[144]	Cross-sectional	rs-fMRI	HC: n=22 (66.3 ± 9.0) MCI: n=22 (65.3 ± 8.7) AD: n=21 (72.3 ± 8.6)	Limbic system	Compensation	AD showed increased HP local connectivity, which was negatively correlated with decreased HP global connectivity.
Xie *et al.* (2015)[145]	Cross-sectional	T1 MRI rs-fMRI	HC: n=26 (70.31 ± 4.8) aMCI: n=30 (72.57 ± 4.8)	Frontal, parietal, and temporal lobes	—	aMCI showed reduced GM volumes and decreased intrinsic FC in the frontal-parietal lobe and MTL, which affected the cognitive function.
Vasavada *et al.* (2015)[146]	Cross-sectional	T1 MRI Task-fMRI	HC: n=27 (69.5 ± 10.4) MCI: n=21 (73.2 ± 9.0) AD: n=15 (71.9 ± 11.9)	Limbic system	Decompensation	MCI and AD showed decreased volume and activation in the HP and primary olfactory cortex.
Wang *et al.* (2015)[147]	Cross-sectional	rs-fMRI	HC: n=27 (69.2 ± 6.5) MCI: n=27 (73.8 ± 7.8) AD: n=35 (72.4 ± 8.5)	Temporal, occipital, and frontal regions	MCI: Compensation AD: Decompensation	MCI and AD showed decreased connectivity in the DMN and sensorimotor network. The connectivity in the control network increased in MCI but sharply decreased in AD.
Serra *et al.* (2016)[148]	Longitudinal (2 years)	T1 MRI rs-fMRI	HC: n=26 (70.6 ± 5.3) cMCI: n=14 (72.3 ± 7.0) sMCI: n=17 (68.6 ± 9.4)	Frontotemporal and parietal areas	Compensation	Converters showed GM atrophy in the frontotemporal areas and increased connectivity in the precuneus.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Zhu *et al.* (2016)[149]	Cross-sectional	rs-fMRI	HC: n=35 (63.8 ± 6.7) aMCI: n=20 (65.7 ± 10.7) AD: n=25 (67.8 ± 8.6)	Frontal and parietal regions; limbic system	MCI: Compensation AD: Decompensation	aMCI and AD showed intranetwork functional disruptions within the DAN and ECN. Disrupted intranetwork connectivity of the DMN and anti-correlation between the DAN and the DMN was observed in AD.
Papma *et al.* (2017)[150]	Cross-sectional	T1 MRI Task-fMRI	MCI: n=27 (73.9 ± 4.9)	Limbic system (PCC, HP)	—	MCI showed a relationship between PCC and HP activation without any differences in the HP structure during episodic memory.
Serra *et al.* (2017)[151]	Cross-sectional	rs-fMRI	HC: n=25 (68.5 ± 6.7) aMCI: n=61 (70.4 ± 9.0) AD: n=68 (71.6 ± 6.7)	Frontal, parietal, and temporal regions; cerebellum	Compensation	aMCI with high cognitive reserve showed increased connectivity in frontoparietal nodes and decreased connectivity in frontotemporocerebellar nodes.
Sullivan *et al.* (2019)[152]	Cross-sectional	rs-fMRI	HC: n=71 (74.10 ± 6.71) MCI: n=91 (71.96 ± 7.76)	Frontal, parietal, and limbic system	Decompensation	MCI showed intrinsic network dedifferentiation, which did not follow a compensatory-like pattern in HC.
Therriault *et al.* (2019)[153]	Cross-sectional	rs-fMRI	HC: n=95 (78.3 ± 7.5) MCI: n=33 (79.4 ± 7.6) AD: n=49 (77.4 ± 8.2)	Limbic system (HP)	—	Reduced rostral-caudal HP convergence strength was observed in early MCI to AD, independent of HP atrophy.
Yan *et al.* (2020)[154]	Cross-sectional	T1 MRI rs-fMRI	HC: n=42 (65.81 ± 6.14) MCI: n=38 (68.89 ± 8.46) AD: n=22 (67.68 ± 7.17)	Limbic system (HP)	—	Patients showed reduced GM volume and functional connectivity compared to NC in CA1, CA2/3/dentate gyrus, and subiculum (AD < MCI < NC).
Pagen *et al.* (2020)[155]	Cross-sectional	rs-fMRI	HC: n=18 (64.56 ± 3.4) aMCI: n=18 (65.11 ± 4.5)	Cerebellum	—	aMCI showed lower anti-correlation between the cerebellar DMN and several cerebral DMN regions compared to HC.
Soman *et al.* (2020)[156]	Cross-sectional	rs-fMRI	HC: n=31 (65.1 ± 6.7) MCI: n=30 (65.7 ± 6.0) AD: n=30 (67.2 ± 4.8)	Frontal and parietal regions; cerebellum	Compensation	AD showed widespread network hypoconnectivity involving DMN and FPN compared to MCI non-convertors.
Wang *et al.* (2020)[157]	Cross-sectional	T1 MRI rs-fMRI DTI	HC: n=41 (68.6 ± 6.7) aMCI: n=34 (69.5 ± 8.8) AD: n=44 (69.9 ± 8.9)	Limbic system (HP)	—	AD and aMCI showed decreased GM volume, reduced FC between the bilateral hippocampi and several brain regions in DMN and control network, as well as damaged integrity of the fornix body.
Langella *et al.* (2021)[158]	Cross-sectional	rs-fMRI	HC: n=39 (75.13 ± 6.25) EMCI: n=54 (72.41 ± 6.0) LMCI: n=37 (73.14 ± 7.4)	Limbic system (HP)	Compensation	MCI showed lower functional hippocampal redundancy.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Xiong *et al.* (2021)[159]	Cross-sectional	rs-fMRI	HC: n=12 (64.00 ± 6.18) MCI: n=12 (64.33 ± 7.01)	Temporal, fusiform gyrus, and SMA	Compensation	The degree centrality of the left inferior temporal gyrus was lower in MCI but was higher in the right fusiform gyrus and left SMA.
Luo *et al.* (2021)[160]	Cross-sectional	rs-fMRI	HC: n=33 (66.82 ± 6.43) MCI: n=27 (69.30 ± 7.42) AD: n=24 (70.79 ± 8.86)	Frontal gyrus and cerebellum	Compensation	AD and MCI showed altered graph metrics of the frontal gyrus and cerebellum.
Wang *et al.* (2021)[161]	Cross-sectional	rs-fMRI	HC: n=46 (74 ± 6.) MCI: n=85 (71 ± 8) AD: n=31 (73 ± 7)	Frontal, parietal, and limbic system	—	AD and MCI showed decreased multilayer participation coefficient, increased number of intralayer nodes, and decreased number of interlayer nodes.
Prvulovic *et al.* (2002)[162]	Cross-sectional	Task-fMRI	HC: n=14 (63.7 ± 4.8) AD: n=14 (69.2 ± 9.9)	Occipitotemporal, and parietal regions	Compensation	AD showed reduced activity in the superior parietal lobule and increased activity in occipitotemporal cortical regions, which were associated with superior parietal lobule atrophy.
Sperling *et al.* (2003)[163]	Cross-sectional	Task-fMRI	HC: n=10 (74.1 ± 7.3) AD: n=7 (80.6 ± 6.9)	Limbic system and parietal regions	Compensation	AD showed less activation in HP formation but greater activation in medial parietal and posterior cingulate regions.
Grossman *et al.* (2003)[164]	Cross-sectional	Task-fMRI	HC: n=16 (73.9 ± 3.6) AD: n=11 (73.0 ± 4.9)	Temporal and parietal regions	Compensation	AD showed reduced activation in the left posterolateral temporal-inferior parietal cortex and increased activation in the left temporal cortex.
Rémy *et al.* (2005)[90]	Cross-sectional	Task-fMRI	HC: n=11 (65.9 ± 5.7) AD: n=8 (72.2 ± 10.8)	Temporal, parietal, and frontal regions	Compensation	AD showed reduced activation in the MTL and inferior parietal/superior temporal area and increased activation in the left prefrontal region.
Wang *et al.* (2006)[165]	Cross-sectional	rs-fMRI	HC: n=13 (69.5 ± 5.7) AD: n=13 (70.1 ± 6.7)	Limbic system and frontal regions	Compensation	AD showed disrupted FC between right HP and a set of regions but increased FC between the left HP and right lateral PFC.
Wang *et al.* (2007)[166]	Cross-sectional	rs-fMRI	HC: n=14 (69.6 ± 5.5) AD: n=14 (70.2 ± 6.3)	Frontal, parietal, and occipital regions	Compensation	AD showed anterior-posterior disconnection, increased within-lobe FC, and decreased negative correlations between two intrinsically anti-correlated networks.
He *et al.* (2007)[167]	Cross-sectional	rs-fMRI	HC: n=14 (69.6 ± 5.5) AD: n=14 (70.1 ± 6.4)	Limbic system; occipital and parietal regions	Compensation	AD showed decreased activation in PCC/precuneus but increased activation in bilateral cuneus, right lingual gyrus, and left fusiform gyrus.
Vannini *et al.* (2008)[168]	Cross-sectional	Task-fMRI	HC: n=13 (68.7 ± 7.8) AD: n=13 (68.9 ± 6.9)	Temporal regions	Compensation	AD showed decreased activation in several networks and increased task demand-independent activation in the right middle temporal gyrus.

(*Cont'd...*)

Table S2. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age ± SD)	Associated regions	Compensation	Main findings
Peters *et al.* (2009)[169]	Cross-sectional	rs-fMRI	HC: n=16 (76.0 ± 6.1) AD: n=16 (77.1 ± 6.6)	Frontal, parietal, and limbic system	Compensation	AD showed decreased activation in the left supramarginal gyrus and right middle frontal gyrus but increased activation in the left parahippocampus and HP, underlying memory over short delays.
Wu *et al.* (2011)[170]	Cross-sectional	rs-fMRI	HC: n=16 (65.1 ± 9.2) AD: n=15 (64.0 ± 8.3)	Frontal, parietal, and temporal regions; limbic system	—	AD showed decreased FC and altered effective connectivity within the DMN.
Li *et al.* (2012)[171]	Cross-sectional	rs-fMRI	HC: n=16 (65 ± 9.20) AD: n=15 (64 ± 8.27)	Frontal, temporal, and parietal regions	—	AD showed disrupted DAN and preserved VAN compared to HC.
Damoiseaux *et al.* (2012)[172]	Longitudinal (4 years)	rs-fMRI	HC: n=18 (62.7 ± 10.3) AD: n=21 (64.2 ± 8.7)	Frontal and parietal regions	Compensation	Early AD showed decreased FC in posterior DMN and increased FC in anterior and ventral DMN at baseline, as well as decreased FC across all default mode systems at follow-up.
Liu *et al.* (2012)[173]	Cross-sectional	rs-fMRI	HC: n=18 (64.9 ± 8.4) AD: n=18 (63.7 ± 8.6)	Widespread regions	Compensation	AD showed decreased interactions in RSNs. The causal connectivity was weaker in DMN and auditory network but stronger in memory and executive control network.
Schwindt *et al.* (2013)[174]	Cross-sectional	rs-fMRI Task-fMRI	HC: n=18 (71.0 ± 7.4) AD: n=16 (72.2 ± 9.9)	Parietal region and limbic system	—	AD showed reduction in the capacity for DMN modulation.
Toussaint *et al.* (2014)[175]	Cross-sectional	rs-fMRI	HC: n=19 (61 ± 1) AD: n=20 (62 ± 9)	Parietal region and limbic system (PCC)	Decompensation	AD showed decreased anteroposterior (precuneus-PCC) integration within the DMN compared to elderly controls.
Xia *et al.* (2014)[176]	Cross-sectional	rs-fMRI	HC: n=38 (68.39 ± 7.78) AD: n=32 (71.25 ± 8.63)	Limbic system (PCC) and parietal region	Compensation	AD showed disruptions in three subregions of the posteromedial cortex compared to HC.
Gu *et al.* (2020)[177]	Cross-sectional	rs-fMRI	HC: n=26 (75.7 ± 6.2) AD: n=26 (74.6 ± 6.5)	Frontal and temporal regions	Compensation	AD showed abnormal dynamic FC mainly in the frontal and temporal cortices.
Olivito *et al.* (2020)[178]	Cross-sectional	rs-fMRI	HC: n=30 (69.3 ± 7.1) AD: n=26 (74.5 ± 2.2)	Temporal region and cerebellum	—	AD showed an increase in FC between the cerebellar dentate nucleus and regions of the lateral temporal lobe.

ACC, anterior cingulate cortex; AD, Alzheimer's disease; ALFF, amplitude of low-frequency fluctuation; aMCI, amnestic MCI; DAN, dorsal attention network; DMN, default mode network; ECN, executive control network; FC, functional connectivity; GM, gray matter; HP, hippocampus; MCI, mild cognitive impairment; MTL, medial temporal lobe; PCC, posterior cingulate cortex; PFC, prefrontal cortex; PHG, parahippocampal gyrus; RSC, retrosplenial cortex; RSN, resting state network; SCD, subjective cognitive decline; SMA, supplementary motor area; SN, salience network; VAN, ventral attention network.

Table S3. Summary of white matter hyperintensity studies in AD-spectrum patients.

Authors (year)	Design	Modality	Sample (mean age±SD)	Associated regions	Main findings
Bracco *et al.* (2005)[179]	Cross-sectional	T2/PD/FLAIR MRI	AD: n=86 (71.9±7.3)	Periventricular	Periventricular WMHs in AD showed an association with executive function, while deep WMHs showed an association with history of mood depression.
Chen *et al.* (2006)[180]	Cross-sectional	T2/PD MRI	HC: n=14 (75±4) MCI: n=15 (74±7) AD: n=27 (76±6)	Frontal, temporal, and parieto-occipital regions	AD showed the greatest total WMH volume, followed by MCI and HC.
Bombois *et al.* (2007)[181]	Cross-sectional	T2/FLAIR MRI	MCI: n=170 (68.1)	Periventricular and lobar WM	Periventricular and lobar WMHs in MCI were significantly associated with executive dysfunction.
Carmichael *et al.* (2010)[182]	Longitudinal (1 year)	T1/T2/PD MRI	HC: n=224 (76±4.8) MCI: n=391 (75±7.5) AD: n=189 (76±7.5)	Whole brain	MCI and AD showed higher WMH volumes and greater 1 year increases compared to HC. Higher WMH volume at baseline was associated with greater subsequent declines in global cognition.
Prasad *et al.* (2011)[183]	Longitudinal (18 months)	T2/FLAIR MRI	cMCI: n=23 (78.4±10.7) sMCI: n=56 (60.2±12.6)	Periventricular and deep subcortical	MCI that progressed to AD showed greater periventricular and deep subcortical WMH.
Guzman *et al.* (2013)[184]	Cross-sectional	T1/T2/PD MRI	aMCI: n=199 (74.50±7.55)	Temporal regions	WMH volumes were associated with smaller entorhinal cortex volume.
van der Vlies *et al.* (2013)[185]	Cross-sectional	T2/FLAIR MRI	AD: n=107 (72±8)	Temporal regions	Temporal WMH was associated with impaired memory, whereas frontal WMH was associated with slower mental speed.
Defrancesco *et al.* (2013)[186]	Cross-sectional	T2 MRI	cMCI: n=31 (76.3±6.7) sMCI: n=29 (70.7±7.3)	Periventricular	MCI converters showed more white matter lesions in periventricular regions.
Makino *et al.* (2014)[187]	Cross-sectional	FLAIR MRI	aMCI: n=40 (76.08±6.56) AD: n=160 (77.01±6.87)	Periventricular	Small periventricular WMHs were significantly associated with poor performances in categorical verbal fluency in aMCI.
Kandiah *et al.* (2015)[188]	Cross-sectional	T1/T2 MRI	HC: n=165 (67.66±6.23) MCI: n=103 (67.83±6.66) mAD: n=141 (71.38±8.63) m-sAD: n=68 (74.62±8.47)	Periventricular and deep subcortical	From CN to MCI to AD, WMH increased significantly. MCI and mild AD showed the greatest association between WMH and MTA.
Lindemer *et al.* (2015)[189]	Longitudinal (18 months)	T1/T2/PD MRI	HC: n=104 (76.6±5.8) cMCI: n=115 (75.2±6.9) sMCI: n=116 (75.6±6.8) AD: n=124 (77.0±5.7)	Whole brain	AD have higher WM signal abnormality volume than MCI. MCI converters showed faster lesion quality decline than non-converters.
Taylor *et al.* (2017)[190]	Cross-sectional	T1/T2/PD MRI/rs-fMRI	HC (Aβ-): n=24 (74.7±6.6) HC (Aβ+): n=14 (74.8±6.5) MCI: n=42 (72.4±6.7) AD: n=22 (73.2±6.9)	Frontal and temporal regions	High WMH volume was associated with reduced FC in connected DMN areas.
Nestor *et al.* (2017)[191]	Cross-sectional	T1/T2/PD MRI	HC1: n=84 (72±8) AD1: n=154 (75±8) HC2: n=28 (72±7) AD2: n=36 (74±8)	Whole brain	SVD burden was associated with reduced posterior cingulate corticocortical GM network integrity and subneocorticocortical hub network integrity in AD.

(*Cont'd...*)

Table S3. ***(Continued).***

Authors (year)	Design	Modality	Sample (mean age±SD)	Associated regions	Main findings
van Rooden *et al.* (2018)[192]	Cross-sectional	T1/T2/FLAIR MRI	HC: n=42 (68±9.2) SCD: n=25 (68±9.1)	Whole brain	SCD showed greater WMHs compared to HC.
Vipin *et al.* (2018)[193]	Cross-sectional	T1/FLAIR MRI	HC: n=51 (66.23±5.66) MCI: n=35 (66.25±5.92) AD: n=30 (69.07±7.89)	Whole brain	AD showed the highest total WMH volume but MCI showed the strongest association between cognitive impairment and lower GM volume.
Chen *et al.* (2018)[194]	Longitudinal (2 years)	T1/T2/FLAIR MRI	HC: n=57 (62.3±7.2) dMCI: n=40 (66.7±8.3) aMCI: n=53 (68.4±7.8) AD: n=50 (73.0±9.5)	Periventricular region	Compared to HC, AD showed higher periventricular WMH, especially in the occipital caps, which was also found to be associated with MTA.
Damulina *et al.* (2019)[195]	Longitudinal (2 years)	T2/FLAIR MRI	HC: n=130 (73.78) AD: n=130 (74.63)	Periventricular regions	AD showed a higher likelihood of WMH in bilateral periventricular location, which had no significant association with cognitive decline.
Misquitta *et al.* (2020)[196]	Longitudinal (5 years)	T1/T2/FLAIR MRI	HC: n=225 (75.58±6.65) MCI: n=315 (73.21±7.93) AD: n=121 (75.77±7.38)	Whole brain	MCI and AD showed greater WMH load, which contributed to neuropsychiatric sub-syndromes.
Caillaud *et al.* (2020)[197]	Cross-sectional	T2/PD/FLAIR MRI	HC: n=30 (71.9±5.7) SCD: n=67 (72.3±5.1) MCI: n=29 (76.3±5.3)	Whole brain	All groups showed a correlation between WMH and performance on executive tests.
Bangen *et al.* (2020)[198]	Longitudinal (4 years)	T2/PD/FLAIR MRI	HC: n=301 (75.97±6.16) aMCI: n=232 (73.78±6.97) naMCI: n=85 (77.07±6.44)	Temporal and occipital regions	naMCI showed greater baseline occipital WMH compared to aMCI. Greater WMH in temporal and occipital regions was associated with faster functional decline.
Hirao *et al.* (2021)[199]	Longitudinal (2 years)	T2/FLAIR MRI	MCI: n=24 (76.7±5.8)	Deep subcortical regions	Deep WMH progression was closely associated with a decline in frontal lobe function and semantic memory.

AD, Alzheimer's disease; aMCI, amnestic MCI; cMCI, MCI converter; dMCI, dysexecutive MCI; DMN, default mode network; ECN, executive control network; FC, functional connectivity; FLAIR, fluid-attenuated inversion recovery; GM, gray matter; HC, healthy control; m-sAD, moderate-severe AD; mAD, mild AD; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; MTA, medial temporal lobe atrophy; naMCI, non-amnestic MCI; PD, proton density; rs-fMRI, resting-state functional MRI; SCD, subjective cognitive decline; sMCI, stable MCI; SVD, small vessel disease; WMH, white matter hyperintensity

References

1. Saykin AJ, Wishart HA, Rabin LA, *et al.*, 2006, Older adults with cognitive complaints show brain atrophy similar to that of amnestic MCI. *Neurology*, 67 (5): 834–842.

   https://doi.org/10.1212/01.wnl.0000234032.77541.a2

2. Jessen F, Feyen L, Freymann K, *et al.*, 2006, Volume reduction of the entorhinal cortex in subjective memory impairment. *Neurobiol Aging*, 27 (12): 1751–1756.

   https://doi.org/10.1016/j.neurobiolaging.2005.10.010

3. Tepest R, Wang L, Csernansky JG, *et al.*, 2008, Hippocampal surface analysis in subjective memory impairment, mild cognitive impairment and alzheimer's dementia. *Dement Geriatr Cogn Disord*, 26 (4): 323–329.

   https://doi.org/10.1159/000161057

4. Striepens N, Scheef L, Wind A, *et al.*, 2010, Volume loss of the medial temporal lobe structures in subjective memory impairment. *Dement Geriatr Cogn Disord*, 29 (1): 75–81.

   https://doi.org/10.1159/000264630

5. Nunes T, Fragata I, Ribeiro F, *et al.*, 2010, The outcome of elderly patients with cognitive complaints but normal neuropsychological tests. *J Alzheimers Dis*, 19 (1): 137–145.

   https://doi.org/10.3233/jad-2010-1210

6. Shen L, Saykin AJ, Kim S, *et al.*, 2010, Comparison of manual and automated determination of hippocampal volumes in MCI and early AD. *Brain Imaging Behav*, 4 (1): 86–95.

   https://doi.org/10.1007/s11682-010-9088-x

7. Stewart R, Godin O, Crivello F, *et al.*, 2011, Longitudinal neuroimaging correlates of subjective memory impairment: 4-year prospective community study. *Br J Psychiatry*,

198 (3): 199–205.

https://doi.org/10.1192/bjp.bp.110.078683

8. Scheef L, Spottke A, Daerr M, *et al*., 2012, Glucose metabolism, gray matter structure, and memory decline in subjective memory impairment. *Neurology*, 79 (13): 1332–1339.

https://doi.org/10.1212/WNL.0b013e31826c1a8d

9. Selnes P, Fjell AM, Gjerstad L, *et al*., 2012, White matter imaging changes in subjective and mild cognitive impairment. *Alzheimers Dement*, 8 (5 Suppl): S112–121.

https://doi.org/10.1016/j.jalz.2011.07.001

10. Hafkemeijer A, Altmann-Schneider I, Oleksik AM, *et al*., 2013, Increased functional connectivity and brain atrophy in elderly with subjective memory complaints. *Brain Connect*, 3 (4): 353–362.

https://doi.org/10.1089/brain.2013.0144

11. Kim MJ, Seo SW, Kim GH, *et al*., 2013, Less depressive symptoms are associated with smaller hippocampus in subjective memory impairment. *Arch Gerontol Geriatr*, 57 (1): 110–115.

https://doi.org/10.1016/j.archger.2013.01.005

12. Peter J, Scheef L, Abdulkadir A, *et al*., 2014, Gray matter atrophy pattern in elderly with subjective memory impairment. *Alzheimers Dement*, 10 (1): 99–108.

https://doi.org/10.1016/j.jalz.2013.05.1764

13. Kiuchi K, Kitamura S, Taoka T, *et al*., 2014, Gray and white matter changes in subjective cognitive impairment, amnestic mild cognitive impairment and alzheimer's disease: A voxel-based analysis study. *PLoS One*, 9 (8).

https://doi.org/10.1371/journal.pone.0104007

14. Perrotin A, de Flores R, Lamberton F, *et al*., 2015, Hippocampal subfield volumetry and 3D surface mapping in subjective cognitive decline. *J Alzheimers Dis*, 48 Suppl 1: S141–150.

https://doi.org/10.3233/jad-150087

15. Meiberth D, Scheef L, Wolfsgruber S, *et al*., 2015, Cortical thinning in individuals with subjective memory impairment. *J Alzheimers Dis*, 45 (1): 139–146.

https://doi.org/10.3233/jad-142322

16. Cherbuin N, Sargent-Cox K, Easteal S, *et al*., 2015, Hippocampal atrophy is associated with subjective memory decline: The PATH through life study. *Am J Geriatr Psychiatry*, 23 (5): 446–455.

https://doi.org/10.1016/j.jagp.2014.07.009

17. Cantero JL, Iglesias JE, Van Leemput K, *et al*., 2016, Regional hippocampal atrophy and higher levels of plasma amyloid-beta are associated with subjective memory complaints in nondemented elderly subjects. *J Gerontol A Biol Sci Med Sci*, 71 (9): 1210–1215.

https://doi.org/10.1093/gerona/glw022

18. Verfaillie SCJ, Tijms B, Versteeg A, *et al*., 2016, Thinner temporal and parietal cortex is related to incident clinical progression to dementia in patients with subjective cognitive decline. *Alzheimers Dement (Amst)*, 5: 43-52.

https://doi.org/10.1016/j.dadm.2016.10.007

19. Hong YJ, Kim CM, Jang EH, *et al*., 2016, White matter changes may precede gray matter loss in elderly with subjective memory impairment. *Dement Geriatr Cogn Disord*, 42 (3–4): 227–235.

https://doi.org/10.1159/000450749

20. Sun Y, Dai Z, Li Y, *et al*., 2016, Subjective cognitive decline: Mapping functional and structural brain changes-A combined resting-state functional and structural MR imaging study. *Radiology*, 281 (1): 185–192.

https://doi.org/10.1148/radiol.2016151771

21. Rogne S, Vangberg T, Eldevik P, *et al*., 2016, Magnetic resonance volumetry: Prediction of subjective memory complaints and mild cognitive impairment, and associations with genetic and cardiovascular risk factors. *Dement Geriatr Cogn Dis Extra*, 6 (3): 529–540.

https://doi.org/10.1159/000450885

22. Perrotin A, La Joie R, de La Sayette V, *et al*., 2017, Subjective cognitive decline in cognitively normal elders from the community or from a memory clinic: Differential affective and imaging correlates. *Alzheimers Dement*, 13 (5): 550–560.

https://doi.org/10.1016/j.jalz.2016.08.011

23. Ryu SY, Lim EY, Na S, *et al*., 2017, Hippocampal and entorhinal structures in subjective memory impairment: A combined MRI volumetric and DTI study. *Int Psychogeriatr*, 29 (5): 785–792.

https://doi.org/10.1017/s1041610216002349

24. Tijms BM, ten Kate M, Gouw AA, *et al*., 2018, Gray matter networks and clinical progression in subjects with predementia alzheimer's disease. *Neurobiol Aging*, 61: 75–81.

https://doi.org/10.1016/j.neurobiolaging.2017.09.011

25. Verfaillie SCJ, Slot RER, Dicks E, *et al*., 2018, A more randomly organized grey matter network is associated with deteriorating language and global cognition in individuals with subjective cognitive decline. *Hum Brain Mapp*, 39 (8): 3143–3151.

https://doi.org/10.1002/hbm.24065

26. Verfaillie SCJ, Slot RE, Tijms BM, *et al*., 2018, Thinner cortex in patients with subjective cognitive decline is associated with steeper decline of memory. *Neurobiol Aging*, 61: 238–244.

https://doi.org/10.1016/j.neurobiolaging.2017.09.009

27. Sanchez-Benavides G, Grau-Rivera O, Suarez-Calvet M, *et al*., 2018, Brain and cognitive correlates of subjective cognitive decline-plus features in a population-based cohort. *Alzheimers Res Ther*, 10 (1): 123.

https://doi.org/10.1186/s13195-018-0449-9

28. Fan LY, Lai YM, Chen TF, *et al*., 2018, Diminution of context association memory structure in subjects with subjective cognitive decline. *Hum Brain Mapp*, 39 (6): 2549–2562.

https://doi.org/10.1002/hbm.24022

29. Yue L, Wang T, Wang J, *et al*., 2018, Asymmetry of hippocampus and amygdala defect in subjective cognitive decline among the community dwelling Chinese. *Front Psychiatry*, 9: 226.

https://doi.org/10.3389/fpsyt.2018.00226

30. Niemantsverdriet E, Ribbens A, Bastin C, *et al*., 2018, A retrospective belgian multi-center MRI biomarker study in alzheimer's disease (REMEMBER). *J Alzheimers Dis*, 63 (4): 1509–1522.

https://doi.org/10.3233/jad-171140

31. Zhao W, Wang X, Yin C, *et al*., 2019, Trajectories of the hippocampal subfields atrophy in the alzheimer's disease: A structural imaging study. *Front Neuroinform*, 13: 13.

https://doi.org/10.3389/fninf.2019.00013

32. Scheef L, Grothe MJ, Koppara A, *et al*., 2019, Subregional volume reduction of the cholinergic forebrain in subjective cognitive decline (SCD). *Neuroimage Clin*, 21: 101612.

https://doi.org/10.1016/j.nicl.2018.101612

33. Platero C, Lopez ME, Del Carmen Tobar M, *et al*., 2019, Discriminating alzheimer's disease progression using a new hippocampal marker from T1-weighted MRI: The local surface roughness. *Hum Brain Mapp*, 40 (5): 1666–1676.

https://doi.org/10.1002/hbm.24478

34. Fu Z, Zhao M, Wang X, *et al*., 2021, Altered neuroanatomical asymmetries of subcortical structures in subjective cognitive decline, amnestic mild cognitive impairment, and alzheimer's disease. *J Alzheimers Dis*, 79 (3): 1121–1132.

https://doi.org/10.3233/jad-201116

35. Yasuno F, Kazui H, Yamamoto A, *et al*., 2015, Resting-state synchrony between the retrosplenial cortex and anterior medial cortical structures relates to memory complaints in subjective cognitive impairment. *Neurobiol Aging*, 36 (6): 2145–2152.

https://doi.org/10.1016/j.neurobiolaging.2015.03.006

36. Li XY, Tang ZC, Sun Y, *et al*., 2016, White matter degeneration in subjective cognitive decline: A diffusion tensor imaging study. *Oncotarget*, 7 (34): 54405–54414.

https://doi.org/10.18632/oncotarget.10091

37. Shu N, Wang X, Bi Q, *et al*., 2018, Disrupted topologic efficiency of white matter structural connectome in individuals with subjective cognitive decline. *Radiology*, 286 (1): 229–238.

https://doi.org/10.1148/radiol.2017162696

38. Yan T, Wang W, Yang L, *et al*., 2018, Rich club disturbances of the human connectome from subjective cognitive decline to alzheimer's disease. *Theranostics*, 8 (12): 3237–3255.

https://doi.org/10.7150/thno.23772

39. Viviano RP, Hayes JM, Pruitt PJ, *et al*., 2019, Aberrant memory system connectivity and working memory performance in subjective cognitive decline. *Neuroimage*, 185: 556–564.

https://doi.org/10.1016/j.neuroimage.2018.10.015

40. Ohlhauser L, Parker AF, Smart CM, *et al*., 2019, White matter and its relationship with cognition in subjective cognitive decline. *Alzheimers Dement (Amst)*, 11: 28–35.

https://doi.org/10.1016/j.dadm.2018.10.008

41. Brueggen K, Dyrba M, Cardenas-Blanco A, *et al*., 2019, Structural integrity in subjective cognitive decline, mild cognitive impairment and alzheimer's disease based on multicenter diffusion tensor imaging. *J Neurol*, 266 (10): 2465–2474.

https://doi.org/10.1007/s00415-019-09429-3

42. Du AT, Schuff N, Amend D, *et al*., 2001, Magnetic resonance imaging of the entorhinal cortex and hippocampus in mild cognitive impairment and alzheimer's disease. *J Neurol Neurosurg Psychiatry*, 71 (4): 441–447.

https://doi.org/10.1136/jnnp.71.4.441

43. Dickerson BC, Goncharova I, Sullivan MP, *et al*., 2001, MRI-derived entorhinal and hippocampal atrophy in incipient and very mild alzheimer's disease. *Neurobiol Aging*, 22 (5): 747–754.

https://doi.org/10.1016/s0197-4580 (01)00271-8

44. Pennanen C, Kivipelto M, Tuomainen S, *et al*., 2004, Hippocampus and entorhinal cortex in mild cognitive impairment and early AD. *Neurobiol Aging*, 25 (3): 303–310.

https://doi.org/10.1016/s0197-4580 (03)00084-8

45. Pennanen C, Testa C, Laakso MP, *et al*., 2005, A voxel based morphometry study on mild cognitive impairment. *J Neurol Neurosurg Psychiatry*, 76 (1): 11–14.

https://doi.org/10.1136/jnnp.2004.035600

46. Stoub TR, deToledo-Morrell L, Stebbins GT, *et al*., 2006, Hippocampal disconnection contributes to memory dysfunction in individuals at risk for alzheimer's disease. *Proc Natl Acad Sci U S A*, 103 (26): 10041–10045.

https://doi.org/10.1073/pnas.0603414103

47. de Jong LW, van der Hiele K, Veer IM, *et al*., 2008, Strongly reduced volumes of putamen and thalamus in alzheimer's

disease: An MRI study. *Brain*, 131 (Pt 12): 3277–3285.

https://doi.org/10.1093/brain/awn278

48. Thomann PA, Schläfer C, Seidl U, *et al*., 2008, The cerebellum in mild cognitive impairment and alzheimer's disease a structural MRI study. *J Psychiatr Res*, 42 (14): 1198–1202.

https://doi.org/10.1016/j.jpsychires.2007.12.002

49. Balthazar ML, Yasuda CL, Pereira FR, *et al*., 2009, Differences in grey and white matter atrophy in amnestic mild cognitive impairment and mild alzheimer's disease. *Eur J Neurol*, 16 (4): 468–474.

https://doi.org/10.1111/j.1468-1331.2008.02408.x

50. Muth K, Schönmeyer R, Matura S, *et al*., 2010, Mild cognitive impairment in the elderly is associated with volume loss of the cholinergic basal forebrain region. *Biol Psychiatry*, 67 (6): 588–591.

https://doi.org/10.1016/j.biopsych.2009.02.026

51. Cherubini A, Péran P, Spoletini I, *et al*., 2010, Combined volumetry and DTI in subcortical structures of mild cognitive impairment and alzheimer's disease patients. *J Alzheimers Dis*, 19 (4): 1273–1282.

https://doi.org/10.3233/jad-2010-091186

52. Evans MC, Barnes J, Nielsen C, *et al*., 2010, Volume changes in alzheimer's disease and mild cognitive impairment: Cognitive associations. *Eur Radiol*, 20 (3): 674–682.

https://doi.org/10.1007/s00330-009-1581-5

53. Serra L, Cercignani M, Lenzi D, *et al*., 2010, Grey and white matter changes at different stages of alzheimer's disease. *J Alzheimers Dis*, 19 (1): 147–159.

https://doi.org/10.3233/jad-2010-1223

54. Choo IH, Lee DY, Oh JS, *et al*., 2010, Posterior cingulate cortex atrophy and regional cingulum disruption in mild cognitive impairment and alzheimer's disease. *Neurobiol Aging*, 31 (5): 772–779.

https://doi.org/10.1016/j.neurobiolaging.2008.06.015

55. Scola E, Bozzali M, Agosta F, *et al*., 2010, A diffusion tensor MRI study of patients with MCI and AD with a 2-year clinical follow-up. *J Neurol Neurosurg Psychiatry*, 81 (7): 798–805.

https://doi.org/10.1136/jnnp.2009.189639

56. Zhang H, Trollor JN, Wen W, *et al*., 2011, Grey matter atrophy of basal forebrain and hippocampus in mild cognitive impairment. *J Neurol Neurosurg Psychiatry*, 82 (5): 487–493.

https://doi.org/10.1136/jnnp.2010.217133

57. Tondelli M, Wilcock GK, Nichelli P, *et al*., 2012, Structural MRI changes detectable up to ten years before clinical alzheimer's disease. *Neurobiol Aging*, 33 (4): 825.e825–836.

https://doi.org/10.1016/j.neurobiolaging.2011.05.018

58. Trzepacz PT, Yu P, Bhamidipati PK, *et al*., 2013, Frontolimbic atrophy is associated with agitation and aggression in mild cognitive impairment and alzheimer's disease. *Alzheimers Dement*, 9 (5 Suppl): S95–S104.e101.

https://doi.org/10.1016/j.jalz.2012.10.005

59. Leung KK, Bartlett JW, Barnes J, *et al*., 2013, Cerebral atrophy in mild cognitive impairment and alzheimer disease: Rates and acceleration. *Neurology*, 80 (7): 648–654.

https://doi.org/10.1212/WNL.0b013e318281ccd3

60. Velayudhan L, Proitsi P, Westman E, *et al*., 2013, Entorhinal cortex thickness predicts cognitive decline in alzheimer's disease. *J Alzheimers Dis*, 33 (3): 755–766.

https://doi.org/10.3233/jad-2012-121408

61. Nir TM, Jahanshad N, Toga AW, *et al*., 2015, Connectivity network measures predict volumetric atrophy in mild cognitive impairment. *Neurobiol Aging*, 36 Suppl 1 (1): S113–120.

https://doi.org/10.1016/j.neurobiolaging.2014.04.038

62. Yi HA, Möller C, Dieleman N, *et al*., 2016, Relation between subcortical grey matter atrophy and conversion from mild cognitive impairment to alzheimer's disease. *J Neurol Neurosurg Psychiatry*, 87 (4): 425–432.

https://doi.org/10.1136/jnnp-2014-309105

63. Krumm S, Kivisaari SL, Probst A, *et al*., 2016, Cortical thinning of parahippocampal subregions in very early alzheimer's disease. *Neurobiol Aging*, 38: 188–196.

https://doi.org/10.1016/j.neurobiolaging.2015.11.001

64. Yang C, Sun X, Tao W, *et al*., 2016, Multistage grading of amnestic mild cognitive impairment: The associated brain gray matter volume and cognitive behavior characterization. *Front Aging Neurosci*, 8: 332.

https://doi.org/10.3389/fnagi.2016.00332

65. Gong NJ, Chan CC, Leung LM, *et al*., 2017, Differential microstructural and morphological abnormalities in mild cognitive impairment and alzheimer's disease: Evidence from cortical and deep gray matter. *Hum Brain Mapp*, 38 (5): 2495–2508.

https://doi.org/10.1002/hbm.23535

66. Matsuoka T, Oya N, Yokota H, *et al*., 2020, Pineal volume reduction in patients with mild cognitive impairment who converted to alzheimer's disease. *Psychiatry Clin Neurosci*, 74 (11): 587–593.

https://doi.org/10.1111/pcn.13103

67. Lin CY, Chen CH, Tom SE, *et al*., 2020, Cerebellar volume is associated with cognitive decline in mild cognitive impairment: Results from ADNI. *Cerebellum*, 19 (2): 217–225.

https://doi.org/10.1007/s12311-019-01099-1

68. Dutt S, Li Y, Mather M, *et al*., 2020, Brainstem volumetric integrity in preclinical and prodromal alzheimer's disease. *J Alzheimers Dis*, 77 (4): 1579–1594.

https://doi.org/10.3233/jad-200187

69. Bernstein AS, Rapcsak SZ, Hornberger M, *et al*., 2021, Structural changes in thalamic nuclei across prodromal and clinical alzheimer's disease. *J Alzheimers Dis*, 82 (1): 361–371.

https://doi.org/10.3233/jad-201583

70. Zeng Q, Li K, Luo X, *et al*., 2021, Distinct atrophy pattern of hippocampal subfields in patients with progressive and stable mild cognitive impairment: A longitudinal MRI study. *J Alzheimers Dis*, 79 (1): 237–247.

https://doi.org/10.3233/jad-200775

71. Sheng X, Chen H, Shao P, *et al*., 2021, Brain structural network compensation is associated with cognitive impairment and alzheimer's disease pathology. *Front Neurosci*, 15: 630278.

https://doi.org/10.3389/fnins.2021.630278

72. Rose SE, Chen F, Chalk JB, *et al*., 2000, Loss of connectivity in alzheimer's disease: An evaluation of white matter tract integrity with colour coded MR diffusion tensor imaging. *J Neurol Neurosurg Psychiatry*, 69 (4): 528–530.

https://doi.org/10.1136/jnnp.69.4.528

73. Medina D, DeToledo-Morrell L, Urresta F, *et al*., 2006, White matter changes in mild cognitive impairment and AD: A diffusion tensor imaging study. *Neurobiol Aging*, 27 (5): 663–672.

https://doi.org/10.1016/j.neurobiolaging.2005.03.026

74. Huang J, Auchus AP, 2007, Diffusion tensor imaging of normal appearing white matter and its correlation with cognitive functioning in mild cognitive impairment and alzheimer's disease. *Ann N Y Acad Sci*, 1097: 259–264.

https://doi.org/10.1196/annals.1379.021

75. Zhou Y, Dougherty JH Jr., Hubner KF, *et al*., 2008, Abnormal connectivity in the posterior cingulate and hippocampus in early alzheimer's disease and mild cognitive impairment. *Alzheimers Dement*, 4 (4): 265–270.

https://doi.org/10.1016/j.jalz.2008.04.006

76. Damoiseaux JS, Smith SM, Witter MP, *et al*., 2009, White matter tract integrity in aging and alzheimer's disease. *Hum Brain Mapp*, 30 (4): 1051–1059.

https://doi.org/10.1002/hbm.20563

77. Chen TF, Chen YF, Cheng TW, *et al*., 2009, Executive dysfunction and periventricular diffusion tensor changes in amnesic mild cognitive impairment and early alzheimer's disease. *Hum Brain Mapp*, 30 (11): 3826–3836.

https://doi.org/10.1002/hbm.20810

78. Mielke MM, Kozauer NA, Chan KC, *et al*., 2009, Regionally-specific diffusion tensor imaging in mild cognitive impairment and alzheimer's disease. *Neuroimage*, 46 (1): 47–55.

https://doi.org/10.1016/j.neuroimage.2009.01.054

79. Teipel SJ, Meindl T, Wagner M, *et al*., 2010, Longitudinal changes in fiber tract integrity in healthy aging and mild cognitive impairment: A DTI follow-up study. *J Alzheimers Dis*, 22 (2): 507–522.

https://doi.org/10.3233/jad-2010-100234

80. Liu Y, Spulber G, Lehtimäki KK, *et al*., 2011, Diffusion tensor imaging and tract-based spatial statistics in alzheimer's disease and mild cognitive impairment. *Neurobiol Aging*, 32 (9): 1558–1571.

https://doi.org/10.1016/j.neurobiolaging.2009.10.006

81. Bozoki AC, Korolev IO, Davis NC, *et al*., 2012, Disruption of limbic white matter pathways in mild cognitive impairment and alzheimer's disease: A DTI/FDG-PET study. *Hum Brain Mapp*, 33 (8): 1792–1802.

https://doi.org/10.1002/hbm.21320

82. Garcés P, Angel Pineda-Pardo J, Canuet L, *et al*., 2014, The default mode network is functionally and structurally disrupted in amnestic mild cognitive impairment - a bimodal MEG-DTI study. *Neuroimage Clin*, 6: 214–221.

https://doi.org/10.1016/j.nicl.2014.09.004

83. Wang PN, Chou KH, Chang NJ, *et al*., 2014, Callosal degeneration topographically correlated with cognitive function in amnestic mild cognitive impairment and alzheimer's disease dementia. *Hum Brain Mapp*, 35 (4): 1529–1543.

https://doi.org/10.1002/hbm.22271

84. Daianu M, Jahanshad N, Nir TM, *et al*., 2015, Rich club analysis in the alzheimer's disease connectome reveals a relatively undisturbed structural core network. *Hum Brain Mapp*, 36 (8): 3087–3103.

https://doi.org/10.1002/hbm.22830

85. Mito R, Raffelt D, Dhollander T, *et al*., 2018, Fibre-specific white matter reductions in alzheimer's disease and mild cognitive impairment. *Brain*, 141 (3): 888–902.

https://doi.org/10.1093/brain/awx355

86. Gozdas E, Fingerhut H, Chromik LC, *et al*., 2020, Focal white matter disruptions along the cingulum tract explain cognitive decline in amnestic mild cognitive impairment (aMCI). *Sci Rep*, 10 (1): 10213.

https://doi.org/10.1038/s41598-020-66796-y

87. Kuang L, Gao Y, Chen Z, *et al*., 2020, White matter brain network research in alzheimer's disease using persistent features. *Molecules*, 25 (11): 2472.

https://doi.org/10.3390/molecules25112472

88. Yang FPG, Bal SS, Lee JF, *et al*., 2021, White matter differences

in networks in elders with mild cognitive impairment and alzheimer's disease. *Brain Connect*, 11 (3): 180–188.

https://doi.org/10.1089/brain.2020.0767

89. Laakso MP, Lehtovirta M, Partanen K, *et al*., 2000, Hippocampus in alzheimer's disease: A 3-year follow-up MRI study. *Biol Psychiatry*, 47 (6): 557–561.

https://doi.org/10.1016/s0006-3223 (99)00167-5

90. Rémy F, Mirrashed F, Campbell B, *et al*., 2005, Verbal episodic memory impairment in alzheimer's disease: A combined structural and functional MRI study. *Neuroimage*, 25 (1): 253–266.

https://doi.org/10.1016/j.neuroimage.2004.10.045

91. Di Paola M, Macaluso E, Carlesimo GA, *et al*., 2007, Episodic memory impairment in patients with alzheimer's disease is correlated with entorhinal cortex atrophy. A voxel-based morphometry study. *J Neurol*, 254 (6): 774–781.

https://doi.org/10.1007/s00415-006-0435-1

92. Zarei M, Patenaude B, Damoiseaux J, *et al*., 2010, Combining shape and connectivity analysis: An MRI study of thalamic degeneration in alzheimer's disease. *Neuroimage*, 49 (1): 1–8.

https://doi.org/10.1016/j.neuroimage.2009.09.001

93. Domoto-Reilly K, Sapolsky D, Brickhouse M, *et al*., 2012, Naming impairment in alzheimer's disease is associated with left anterior temporal lobe atrophy. *Neuroimage*, 63 (1): 348–355.

https://doi.org/10.1016/j.neuroimage.2012.06.018

94. Smits LL, Tijms BM, Benedictus MR, *et al*., 2014, Regional atrophy is associated with impairment in distinct cognitive domains in alzheimer's disease. *Alzheimers Dement*, 10 (5 Suppl): S299–305.

https://doi.org/10.1016/j.jalz.2013.06.007

95. Cho H, Kim JH, Kim C, *et al*., 2014, Shape changes of the basal ganglia and thalamus in alzheimer's disease: A three-year longitudinal study. *J Alzheimers Dis*, 40 (2): 285–295.

https://doi.org/10.3233/jad-132072

96. Cavedo E, Pievani M, Boccardi M, *et al*., 2014, Medial temporal atrophy in early and late-onset alzheimer's disease. *Neurobiol Aging*, 35 (9): 2004–2012.

https://doi.org/10.1016/j.neurobiolaging.2014.03.009

97. Phillips OR, Joshi SH, Piras F, *et al*., 2016, The superficial white matter in alzheimer's disease. *Hum Brain Mapp*, 37 (4): 1321–1334.

https://doi.org/10.1002/hbm.23105

98. Ji X, Wang H, Zhu M, *et al*., 2021, Brainstem atrophy in the early stage of alzheimer's disease: A voxel-based morphometry study. *Brain Imaging Behav*, 15 (1): 49–59.

https://doi.org/10.1007/s11682-019-00231-3

99. Yang C, Ren J, Li W, *et al*., 2021, Individual-level morphological hippocampal networks in patients with alzheimer's disease. *Brain Cogn*, 151: 105748.

https://doi.org/10.1016/j.bandc.2021.105748

100. Kavcic V, Ni H, Zhu T, *et al*., 2008, White matter integrity linked to functional impairments in aging and early alzheimer's disease. *Alzheimers Dement*, 4 (6): 381–389.

https://doi.org/10.1016/j.jalz.2008.07.001

101. Rose SE, Janke AL, Chalk JB, 2008, Gray and white matter changes in alzheimer's disease: A diffusion tensor imaging study. *J Magn Reson Imaging*, 27 (1): 20–26.

https://doi.org/10.1002/jmri.21231

102. Lo CY, Wang PN, Chou KH, *et al*., 2010, Diffusion tensor tractography reveals abnormal topological organization in structural cortical networks in alzheimer's disease. *J Neurosci*, 30 (50): 16876–16885.

https://doi.org/10.1523/jneurosci.4136-10.2010

103. Mayo CD, Mazerolle EL, Ritchie L, *et al*., 2017, Longitudinal changes in microstructural white matter metrics in alzheimer's disease. *Neuroimage Clin*, 13: 330–338.

https://doi.org/10.1016/j.nicl.2016.12.012

104. Toniolo S, Serra L, Olivito G, *et al*., 2020, Cerebellar white matter disruption in alzheimer's disease patients: A diffusion tensor imaging study. *J Alzheimers Dis*, 74 (2): 615–624.

https://doi.org/10.3233/jad-191125

105. Luo X, Wang S, Jiaerken Y, *et al*., 2021, Distinct fiber-specific white matter reductions pattern in early- and late-onset alzheimer's disease. *Aging (Albany N Y)*, 13 (9): 12410–12430.

https://doi.org/10.18632/aging.202702

106. Rodda JE, Dannhauser TM, Cutinha DJ, *et al*., 2009, Subjective cognitive impairment: Increased prefrontal cortex activation compared to controls during an encoding task. *Int J Geriatr Psychiatry*, 24 (8): 865–874.

https://doi.org/10.1002/gps.2207

107. Erk S, Spottke A, Meisen A, *et al*., 2011, Evidence of neuronal compensation during episodic memory in subjective memory impairment. *Arch Gen Psychiatry*, 68 (8): 845–852.

https://doi.org/10.1001/archgenpsychiatry.2011.80

108. Dumas JA, Kutz AM, McDonald BC, *et al*., 2013, Increased working memory-related brain activity in middle-aged women with cognitive complaints. *Neurobiol Aging*, 34 (4): 1145–1147.

https://doi.org/10.1016/j.neurobiolaging.2012.08.013

109. Wang Y, Risacher SL, West JD, *et al*., 2013, Altered default mode network connectivity in older adults with cognitive complaints and amnestic mild cognitive impairment. *J Alzheimers Dis*, 35 (4): 751–760.

https://doi.org/10.3233/jad-130080

110. Dillen KNH, Jacobs HIL, Kukolja J, *et al*., 2016, Aberrant functional connectivity differentiates retrosplenial cortex from posterior cingulate cortex in prodromal alzheimer's disease. *Neurobiol Aging*, 44: 114–126.

https://doi.org/10.1016/j.neurobiolaging.2016.04.010

111. Dillen KNH, Jacobs HIL, Kukolja J, *et al*., 2017, Functional disintegration of the default mode network in prodromal alzheimer's disease. *J Alzheimers Dis*, 59 (1): 169–187.

https://doi.org/10.3233/jad-161120

112. Hayes JM, Tang L, Viviano RP, *et al*., 2017, Subjective memory complaints are associated with brain activation supporting successful memory encoding. *Neurobiol Aging*, 60: 71–80.

https://doi.org/10.1016/j.neurobiolaging.2017.08.015

113. Dong C, Liu T, Wen W, *et al*., 2018, Altered functional connectivity strength in informant-reported subjective cognitive decline: A resting-state functional magnetic resonance imaging study. *Alzheimers Dement (Amst)* 10: 688–697.

https://doi.org/10.1016/j.dadm.2018.08.011

114. Verfaillie SCJ, Binette AP, Vachon-Presseau E, *et al*., 2018, Subjective cognitive decline is associated with altered default mode network connectivity in individuals with a family history of alzheimer's disease. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 3 (5): 463–472.

https://doi.org/10.1016/j.bpsc.2017.11.012

115. Parker AF, Smart CM, Scarapicchia V, *et al*., 2020, Identification of earlier biomarkers for alzheimer's disease: A multimodal neuroimaging study of individuals with subjective cognitive decline. *J Alzheimers Dis*, 77 (3): 1067–1076.

https://doi.org/10.3233/jad-200299

116. Chen H, Sheng X, Luo C, *et al*., 2020, The compensatory phenomenon of the functional connectome related to pathological biomarkers in individuals with subjective cognitive decline. *Transl Neurodegener*, 9 (1): 21.

https://doi.org/10.1186/s40035-020-00201-6

117. Yang L, Yan Y, Li Y, *et al*., 2020, Frequency-dependent changes in fractional amplitude of low-frequency oscillations in alzheimer's disease: A resting-state fMRI study. *Brain Imaging Behav*, 14 (6): 2187–2201.

https://doi.org/10.1007/s11682-019-00169-6

118. Khan W, Amad A, Giampietro V, *et al*., 2020, The heterogeneous functional architecture of the posteromedial cortex is associated with selective functional connectivity differences in alzheimer's disease. *Hum Brain Mapp*, 41 (6): 1557–1572.

https://doi.org/10.1002/hbm.24894

119. Sharma N, Murari G, Vandermorris S, *et al*., 2021, Functional connectivity between the posterior default mode network and parahippocampal gyrus is disrupted in older adults with subjective cognitive decline and correlates with subjective memory ability. *J Alzheimers Dis*, 82 (1): 435–445.

https://doi.org/10.3233/jad-201579

120. Machulda MM, Ward HA, Borowski B, *et al*., 2003, Comparison of memory fMRI response among normal, MCI, and alzheimer's patients. *Neurology*, 61 (4): 500–506.

https://doi.org/10.1212/01.wnl.0000079052.01016.78

121. Dannhauser TM, Walker Z, Stevens T, *et al*., 2005, The functional anatomy of divided attention in amnestic mild cognitive impairment. *Brain*, 128 (Pt 6): 1418–1427.

https://doi.org/10.1093/brain/awh413

122. Rosano C, Aizenstein HJ, Cochran JL, *et al*., 2005, Event-related functional magnetic resonance imaging investigation of executive control in very old individuals with mild cognitive impairment. *Biol Psychiatry*, 57 (7): 761–767.

https://doi.org/10.1016/j.biopsych.2004.12.031

123. Rombouts SA, Barkhof F, Goekoop R, *et al*., 2005, Altered resting state networks in mild cognitive impairment and mild alzheimer's disease: An fMRI study. *Hum Brain Mapp*, 26 (4): 231–239.

https://doi.org/10.1002/hbm.20160

124. Celone KA, Calhoun VD, Dickerson BC, *et al*., 2006, Alterations in memory networks in mild cognitive impairment and alzheimer's disease: An independent component analysis. *J Neurosci*, 26 (40): 10222–10231.

https://doi.org/10.1523/jneurosci.2250-06.2006

125. Johnson SC, Schmitz TW, Moritz CH, *et al*., 2006, Activation of brain regions vulnerable to alzheimer's disease: The effect of mild cognitive impairment. *Neurobiol Aging*, 27 (11): 1604–1612.

https://doi.org/10.1016/j.neurobiolaging.2005.09.017

126. Kircher TT, Weis S, Freymann K, *et al*., 2007, Hippocampal activation in patients with mild cognitive impairment is necessary for successful memory encoding. *J Neurol Neurosurg Psychiatry*, 78 (8): 812–818.

https://doi.org/10.1136/jnnp.2006.104877

127. Hämäläinen A, Pihlajamäki M, Tanila H, *et al*., 2007, Increased fMRI responses during encoding in mild cognitive impairment. *Neurobiol Aging*, 28 (12): 1889–1903.

https://doi.org/10.1016/j.neurobiolaging.2006.08.008

128. Sorg C, Riedl V, Mühlau M, *et al*., 2007, Selective changes of resting-state networks in individuals at risk for alzheimer's disease. *Proc Natl Acad Sci U S A*, 104 (47): 18760–18765.

https://doi.org/10.1073/pnas.0708803104

129. Dannhauser TM, Shergill SS, Stevens T, *et al*., 2008, An fMRI

study of verbal episodic memory encoding in amnestic mild cognitive impairment. *Cortex*, 44 (7): 869–880.

https://doi.org/10.1016/j.cortex.2007.04.005

130. Woodard JL, Seidenberg M, Nielson KA, *et al*., 2009, Semantic memory activation in amnestic mild cognitive impairment. *Brain*, 132 (Pt 8): 2068–2078.

https://doi.org/10.1093/brain/awp157

131. Qi Z, Wu X, Wang Z, *et al*., 2010, Impairment and compensation coexist in amnestic MCI default mode network. *Neuroimage*, 50 (1): 48–55.

https://doi.org/10.1016/j.neuroimage.2009.12.025

132. Bosch B, Bartrés-Faz D, Rami L, *et al*., 2010, Cognitive reserve modulates task-induced activations and deactivations in healthy elders, amnestic mild cognitive impairment and mild alzheimer's disease. *Cortex*, 46 (4): 451–461.

https://doi.org/10.1016/j.cortex.2009.05.006

133. Gili T, Cercignani M, Serra L, *et al*., 2011, Regional brain atrophy and functional disconnection across alzheimer's disease evolution. *J Neurol Neurosurg Psychiatry*, 82 (1): 58–66.

https://doi.org/10.1136/jnnp.2009.199935

134. Lenzi D, Serra L, Perri R, *et al*., 2011, Single domain amnestic MCI: A multiple cognitive domains fMRI investigation. *Neurobiol Aging*, 32 (9): 1542–1557.

https://doi.org/10.1016/j.neurobiolaging.2009.09.006

135. Bai F, Liao W, Watson DR, *et al*., 2011, Mapping the altered patterns of cerebellar resting-state function in longitudinal amnestic mild cognitive impairment patients. *J Alzheimers Dis*, 23 (1): 87–99.

https://doi.org/10.3233/jad-2010-101533

136. Wang Z, Yan C, Zhao C, *et al*., 2011, Spatial patterns of intrinsic brain activity in mild cognitive impairment and alzheimer's disease: A resting-state functional MRI study. *Hum Brain Mapp*, 32 (10): 1720–1740.

https://doi.org/10.1002/hbm.21140

137. Binnewijzend MA, Schoonheim MM, Sanz-Arigita E, *et al*., 2012, Resting-state fMRI changes in alzheimer's disease and mild cognitive impairment. *Neurobiol Aging*, 33 (9): 2018–2028.

https://doi.org/10.1016/j.neurobiolaging.2011.07.003

138. Agosta F, Pievani M, Geroldi C, *et al*., 2012, Resting state fMRI in alzheimer's disease: Beyond the default mode network. *Neurobiol Aging*, 33 (8): 1564–1578.

https://doi.org/10.1016/j.neurobiolaging.2011.06.007

139. Liang P, Wang Z, Yang Y, *et al*., 2012, Three subsystems of the inferior parietal cortex are differently affected in mild cognitive impairment. *J Alzheimers Dis*, 30 (3): 475–487.

https://doi.org/10.3233/jad-2012-111721

140. Zamboni G, Wilcock GK, Douaud G, *et al*., 2013, Resting functional connectivity reveals residual functional activity in alzheimer's disease. *Biol Psychiatry*, 74 (5): 375–383.

https://doi.org/10.1016/j.biopsych.2013.04.015

141. Zamboni G, Drazich E, McCulloch E, *et al*., 2013, Neuroanatomy of impaired self-awareness in alzheimer's disease and mild cognitive impairment. *Cortex*, 49 (3): 668–678.

https://doi.org/10.1016/j.cortex.2012.04.011

142. Liu Y, Yu C, Zhang X, *et al*., 2014, Impaired long distance functional connectivity and weighted network architecture in alzheimer's disease. *Cereb Cortex*, 24 (6): 1422–1435.

https://doi.org/10.1093/cercor/bhs410

143. Neufang S, Akhrif A, Riedl V, *et al*., 2014, Predicting effective connectivity from resting-state networks in healthy elderly and patients with prodromal alzheimer's disease. *Hum Brain Mapp*, 35 (3): 954–963.

https://doi.org/10.1002/hbm.22226

144. Pasquini L, Scherr M, Tahmasian M, *et al*., 2015, Link between hippocampus' raised local and eased global intrinsic connectivity in AD. *Alzheimers Dement*, 11 (5): 475–484.

https://doi.org/10.1016/j.jalz.2014.02.007

145. Xie C, Bai F, Yuan B, *et al*., 2015, Joint effects of gray matter atrophy and altered functional connectivity on cognitive deficits in amnestic mild cognitive impairment patients. *Psychol Med*, 45 (9): 1799–1810.

https://doi.org/10.1017/s0033291714002876

146. Vasavada MM, Wang J, Eslinger PJ, *et al*., 2015, Olfactory cortex degeneration in alzheimer's disease and mild cognitive impairment. *J Alzheimers Dis*, 45 (3): 947–958.

https://doi.org/10.3233/jad-141947

147. Wang P, Zhou B, Yao H, *et al*., 2015, Aberrant intra- and inter-network connectivity architectures in alzheimer's disease and mild cognitive impairment. *Sci Rep*, 5: 14824.

https://doi.org/10.1038/srep14824

148. Serra L, Cercignani M, Mastropasqua C, *et al*., 2016, Longitudinal changes in functional brain connectivity predicts conversion to alzheimer's disease. *J Alzheimers Dis*, 51 (2): 377–389.

https://doi.org/10.3233/jad-150961

149. Zhu H, Zhou P, Alcauter S, *et al*., 2016, Changes of intranetwork and internetwork functional connectivity in alzheimer's disease and mild cognitive impairment. *J Neural Eng*, 13 (4): 046008.

https://doi.org/10.1088/1741-2560/13/4/046008

150. Papma JM, Smits M, de Groot M, *et al*., 2017, The effect of hippocampal function, volume and connectivity on posterior cingulate cortex functioning during episodic

memory fMRI in mild cognitive impairment. *Eur Radiol*, 27 (9): 3716–3724.

https://doi.org/10.1007/s00330-017-4768-1

151. Serra L, Mancini M, Cercignani M, *et al*., 2017, Network-based substrate of cognitive reserve in alzheimer's disease. *J Alzheimers Dis*, 55 (1): 421–430.

https://doi.org/10.3233/jad-160735

152. Sullivan MD, Anderson JAE, Turner GR, *et al*., 2019, Intrinsic neurocognitive network connectivity differences between normal aging and mild cognitive impairment are associated with cognitive status and age. *Neurobiol Aging*, 73: 219–228.

https://doi.org/10.1016/j.neurobiolaging.2018.10.001

153. Therriault J, Wang S, Mathotaarachchi S, *et al*., 2019, Rostral-caudal hippocampal functional convergence is reduced across the alzheimer's disease spectrum. *Mol Neurobiol*, 56 (12): 8336–8344.

https://doi.org/10.1007/s12035-019-01671-0

154. Yan S, Zheng C, Cui B, *et al*., 2020, Multiparametric imaging hippocampal neurodegeneration and functional connectivity with simultaneous PET/MRI in alzheimer's disease. *Eur J Nucl Med Mol Imaging*, 47 (10): 2440–2452.

https://doi.org/10.1007/s00259-020-04752-8

155. Pagen LHG, van de Ven VG, Gronenschild E, *et al*., 2020, Contributions of cerebro-cerebellar default mode connectivity patterns to memory performance in mild cognitive impairment. *J Alzheimers Dis*, 75 (2): 633–647.

https://doi.org/10.3233/jad-191127

156. Soman SM, Raghavan S, Rajesh PG, *et al*., 2020, Does resting state functional connectivity differ between mild cognitive impairment and early alzheimer's dementia? *J Neurol Sci*, 418: 117093.

https://doi.org/10.1016/j.jns.2020.117093

157. Wang P, Zhou B, Yao H, *et al*., 2020, Aberrant hippocampal functional connectivity is associated with fornix white matter integrity in alzheimer's disease and mild cognitive impairment. *J Alzheimers Dis*, 75 (4): 1153–1168.

https://doi.org/10.3233/jad-200066

158. Langella S, Sadiq MU, Mucha PJ, *et al*., 2021, Lower functional hippocampal redundancy in mild cognitive impairment. *Transl Psychiatry*, 11 (1): 61.

https://doi.org/10.1038/s41398-020-01166-w

159. Xiong J, Yu C, Su T, *et al*., 2021, Altered brain network centrality in patients with mild cognitive impairment: An fMRI study using a voxel-wise degree centrality approach. *Aging (Albany N Y)*, 13 (11): 15491–15500.

https://doi.org/10.18632/aging.203105

160. Luo Y, Sun T, Ma C, *et al*., 2021, Alterations of brain networks in alzheimer's disease and mild cognitive impairment: A resting state fMRI study based on a population-specific brain template. *Neuroscience*, 452: 192–207.

https://doi.org/10.1016/j.neuroscience.2020.10.023

161. Wang X, Cui X, Ding C, *et al*., 2021, Deficit of cross-frequency integration in mild cognitive impairment and alzheimer's disease: A multilayer network approach. *J Magn Reson Imaging*, 53 (5): 1387–1398.

https://doi.org/10.1002/jmri.27453

162. Prvulovic D, Hubl D, Sack AT, *et al*., 2002, Functional imaging of visuospatial processing in alzheimer's disease. *Neuroimage*, 17 (3): 1403–1414.

https://doi.org/10.1006/nimg.2002.1271

163. Sperling RA, Bates JF, Chua EF, *et al*., 2003, fMRI studies of associative encoding in young and elderly controls and mild alzheimer's disease. *J Neurol Neurosurg Psychiatry*, 74 (1): 44–50.

https://doi.org/10.1136/jnnp.74.1.44

164. Grossman M, Koenig P, Glosser G, *et al*., 2003, Neural basis for semantic memory difficulty in alzheimer's disease: An fMRI study. *Brain*, 126 (Pt 2): 292–311.

https://doi.org/10.1093/brain/awg027

165. Wang L, Zang Y, He Y, *et al*., 2006, Changes in hippocampal connectivity in the early stages of alzheimer's disease: Evidence from resting state fMRI. *Neuroimage*, 31 (2): 496–504.

https://doi.org/10.1016/j.neuroimage.2005.12.033

166. Wang K, Liang M, Wang L, *et al*., 2007, Altered functional connectivity in early alzheimer's disease: A resting-state fMRI study. *Hum Brain Mapp*, 28 (10): 967–978.

https://doi.org/10.1002/hbm.20324

167. He Y, Wang L, Zang Y, *et al*., 2007, Regional coherence changes in the early stages of alzheimer's disease: A combined structural and resting-state functional MRI study. *Neuroimage*, 35 (2): 488–500.

https://doi.org/10.1016/j.neuroimage.2006.11.042

168. Vannini P, Lehmann C, Dierks T, *et al*., 2008, Failure to modulate neural response to increased task demand in mild alzheimer's disease: fMRI study of visuospatial processing. *Neurobiol Dis*, 31 (3): 287–297.

https://doi.org/10.1016/j.nbd.2008.04.013

169. Peters F, Collette F, Degueldre C, *et al*., 2009, The neural correlates of verbal short-term memory in alzheimer's disease: An fMRI study. *Brain*, 132 (Pt 7): 1833–1846.

https://doi.org/10.1093/brain/awp075

170. Wu X, Li R, Fleisher AS, *et al*., 2011, Altered default mode network connectivity in alzheimer's disease--a resting functional MRI and Bayesian network study. *Hum Brain*

Mapp, 32 (11): 1868–1881.

https://doi.org/10.1002/hbm.21153

171. Li R, Wu X, Fleisher AS, *et al*., 2012, Attention-related networks in alzheimer's disease: A resting functional MRI study. *Hum Brain Mapp*, 33 (5): 1076–1088.

https://doi.org/10.1002/hbm.21269

172. Damoiseaux JS, Prater KE, Miller BL, *et al*., 2012, Functional connectivity tracks clinical deterioration in alzheimer's disease. *Neurobiol Aging*, 33 (4): 828.e819–830.

https://doi.org/10.1016/j.neurobiolaging.2011.06.024

173. Liu Z, Zhang Y, Bai L, *et al*., 2012, Investigation of the effective connectivity of resting state networks in alzheimer's disease: A functional MRI study combining independent components analysis and multivariate Granger causality analysis. *NMR Biomed*, 25 (12): 1311–1320.

https://doi.org/10.1002/nbm.2803

174. Schwindt GC, Chaudhary S, Crane D, *et al*., 2013, Modulation of the default-mode network between rest and task in alzheimer's Disease. *Cereb Cortex*, 23 (7): 1685–1694.

https://doi.org/10.1093/cercor/bhs160

175. Toussaint PJ, Maiz S, Coynel D, *et al*., 2014, Characteristics of the default mode functional connectivity in normal ageing and alzheimer's disease using resting state fMRI with a combined approach of entropy-based and graph theoretical measurements. *Neuroimage*, 101: 778–786.

https://doi.org/10.1016/j.neuroimage.2014.08.003

176. Xia M, Wang Z, Dai Z, *et al*., 2014, Differentially disrupted functional connectivity in posteromedial cortical subregions in alzheimer's disease. *J Alzheimers Dis*, 39 (3): 527–543.

https://doi.org/10.3233/jad-131583

177. Gu Y, Lin Y, Huang L, *et al*., 2020, Abnormal dynamic functional connectivity in alzheimer's disease. *CNS Neurosci Ther*, 26 (9): 962–971.

https://doi.org/10.1111/cns.13387

178. Olivito G, Serra L, Marra C, *et al*., 2020, Cerebellar dentate nucleus functional connectivity with cerebral cortex in alzheimer's disease and memory: A seed-based approach. *Neurobiol Aging*, 89: 32–40.

https://doi.org/10.1016/j.neurobiolaging.2019.10.026

179. Bracco L, Piccini C, Moretti M, *et al*., 2005, Alzheimer's disease: Role of size and location of white matter changes in determining cognitive deficits. *Dement Geriatr Cogn Disord*, 20 (6): 358–366.

https://doi.org/10.1159/000088562

180. Chen YF, Wang H, Chu Y, *et al*., 2006, Regional quantification of white matter hyperintensity in normal aging, mild cognitive impairment, and alzheimer's disease. *Dement Geriatr Cogn Disord*, 22 (2): 177–184.

https://doi.org/10.1159/000094785

181. Bombois S, Debette S, Delbeuck X, *et al*., 2007, Prevalence of subcortical vascular lesions and association with executive function in mild cognitive impairment subtypes. *Stroke*, 38 (9): 2595–2597.

https://doi.org/10.1161/strokeaha.107.486407

182. Carmichael O, Schwarz C, Drucker D, *et al*., 2010, Longitudinal changes in white matter disease and cognition in the first year of the alzheimer disease neuroimaging initiative. *Arch Neurol*, 67 (11): 1370–1378.

https://doi.org/10.1001/archneurol.2010.284

183. Prasad K, Wiryasaputra L, Ng A, *et al*., 2011, White matter disease independently predicts progression from mild cognitive impairment to alzheimer's disease in a clinic cohort. *Dement Geriatr Cogn Disord*, 31 (6): 431–434.

https://doi.org/10.1159/000330019

184. Guzman VA, Carmichael OT, Schwarz C, *et al*., 2013, White matter hyperintensities and amyloid are independently associated with entorhinal cortex volume among individuals with mild cognitive impairment. *Alzheimers Dement*, 9 (5 Suppl): S124–131.

https://doi.org/10.1016/j.jalz.2012.11.009

185. van der Vlies AE, Staekenborg SS, Admiraal-Behloul F, *et al*., 2013, Associations between magnetic resonance imaging measures and neuropsychological impairment in early and late onset alzheimer's disease. *J Alzheimers Dis*, 35 (1): 169–178.

https://doi.org/10.3233/jad-121291

186. Defrancesco M, Marksteiner J, Deisenhammer E, *et al*., 2013, Impact of white matter lesions and cognitive deficits on conversion from mild cognitive impairment to alzheimer's disease. *J Alzheimers Dis*, 34 (3): 665–672.

https://doi.org/10.3233/jad-122095

187. Makino T, Umegaki H, Suzuki Y, *et al*., 2014, Relationship between small cerebral white matter lesions and cognitive function in patients with alzheimer's disease and amnestic mild cognitive impairment. *Geriatr Gerontol Int*, 14 (4): 819–826.

https://doi.org/10.1111/ggi.12176

188. Kandiah N, Chander RJ, Ng A, *et al*., 2015, Association between white matter hyperintensity and medial temporal atrophy at various stages of alzheimer's disease. *Eur J Neurol*, 22 (1): 150–155.

https://doi.org/10.1111/ene.12546

189. Lindemer ER, Salat DH, Smith EE, *et al*., 2015, White matter signal abnormality quality differentiates mild cognitive impairment that converts to alzheimer's disease from nonconverters. *Neurobiol Aging*, 36 (9): 2447–2457.

https://doi.org/10.1016/j.neurobiolaging.2015.05.011

190. Taylor ANW, Kambeitz-Ilankovic L, Gesierich B, *et al*., 2017, Tract-specific white matter hyperintensities disrupt neural network function in alzheimer's disease. *Alzheimers Dement*, 13 (3): 225–235.

https://doi.org/10.1016/j.jalz.2016.06.2358

191. Nestor SM, Mišić B, Ramirez J, *et al*., 2017, Small vessel disease is linked to disrupted structural network covariance in alzheimer's disease. *Alzheimers Dement*, 13 (7): 749–760.

https://doi.org/10.1016/j.jalz.2016.12.007

192. van Rooden S, van den Berg-Huysmans AA, Croll PH, *et al*., 2018, Subjective cognitive decline is associated with greater white matter hyperintensity volume. *J Alzheimers Dis*, 66 (3): 1283–1294.

https://doi.org/10.3233/jad-180285

193. Vipin A, Foo HJL, Lim JKW, *et al*., 2018, Regional white matter hyperintensity influences grey matter atrophy in mild cognitive impairment. *J Alzheimers Dis*, 66 (2): 533–549.

https://doi.org/10.3233/jad-180280

194. Chen YC, Tsao HH, Chu YC, *et al*., 2018, Exploring the spectrum of subcortical hyperintensities and cognitive decline. *J Neuropsychiatry Clin Neurosci*, 30 (2): 130–138.

https://doi.org/10.1176/appi.neuropsych.17050099

195. Damulina A, Pirpamer L, Seiler S, *et al*., 2019, White matter hyperintensities in alzheimer's disease: A lesion probability mapping study. *J Alzheimers Dis*, 68 (2): 789–796.

https://doi.org/10.3233/jad-180982

196. Misquitta K, Dadar M, Louis Collins D, *et al*., 2020, White matter hyperintensities and neuropsychiatric symptoms in mild cognitive impairment and alzheimer's disease. *Neuroimage Clin*, 28: 102367.

https://doi.org/10.1016/j.nicl.2020.102367

197. Caillaud M, Hudon C, Boller B, *et al*., 2020, Evidence of a relation between hippocampal volume, white matter hyperintensities, and cognition in subjective cognitive decline and mild cognitive impairment. *J Gerontol B Psychol Sci Soc Sci*, 75 (7): 1382–1392.

https://doi.org/10.1093/geronb/gbz120

198. Bangen KJ, Thomas KR, Weigand AJ, *et al*., 2020, Pattern of regional white matter hyperintensity volume in mild cognitive impairment subtypes and associations with decline in daily functioning. *Neurobiol Aging*, 86: 134–142.

https://doi.org/10.1016/j.neurobiolaging.2019.10.016

199. Hirao K, Yamashita F, Tsugawa A, *et al*., 2021, Association of white matter hyperintensity progression with cognitive decline in patients with amnestic mild cognitive impairment. *J Alzheimers Dis*, 80 (2): 877–883.

https://doi.org/10.3233/jad-201451