

Supplementary Data

Using Diffusion Tensor Imaging and Mixed-Effects Models to Investigate Primary and Secondary White Matter Degeneration in Alzheimer's Disease and Mild Cognitive Impairment

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Supplementary Table 1
Diffusion results from all ROIs

Cerebellum	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.375	0.016	0.366	0.016	0.375	0.014	0.354	0.020	0.002
DR	0.582	0.026	0.601	0.031	0.599	0.038	0.532	0.203	0.052
DA	1.076	0.039	1.092	0.042	1.100	0.063	0.944	0.356	0.005
MD	0.746	0.028	0.765	0.033	0.766	0.045	0.767	0.054	0.060
Left Cingulum hippocampus	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.471	0.036	0.451	0.033	0.446	0.042	0.405	0.049	<0.0001
DR	0.572	0.067	0.597	0.052	0.617	0.073	0.718	0.152	<0.0001
DA	1.189	0.096	1.193	0.087	1.215	0.078	1.256	0.177	0.279
MD	0.778	0.073	0.796	0.058	0.816	0.070	0.897	0.158	0.001
Right Cingulum hippocampus	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.465	0.034	0.451	0.030	0.450	0.028	0.422	0.034	0.002
DR	0.566	0.062	0.597	0.048	0.609	0.050	0.697	0.139	<0.0001
DA	1.164	0.086	1.190	0.100	1.212	0.061	1.257	0.152	0.025
MD	0.766	0.066	0.795	0.060	0.810	0.050	0.884	0.142	<0.0005
Global ROI	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.426	0.018	0.415	0.019	0.420	0.021	0.392	0.031	<0.0001
DR	0.580	0.031	0.603	0.035	0.607	0.043	0.656	0.061	<0.0001
DA	1.146	0.030	1.163	0.034	1.182	0.041	1.201	0.042	<0.0001
MD	0.768	0.029	0.790	0.033	0.799	0.041	0.838	0.054	<0.0001
Left Parahippocampal pole	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.398	0.043	0.373	0.043	0.377	0.043	0.350	0.036	0.005
DR	0.640	0.066	0.682	0.051	0.697	0.107	0.821	0.194	<0.0001
DA	1.165	0.081	1.182	0.072	1.213	0.112	1.289	0.244	0.011
MD	0.815	0.066	0.848	0.051	0.869	0.106	0.977	0.210	<0.0001
Right Parahippocampal pole	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.373	0.040	0.356	0.046	0.364	0.031	0.343	0.049	0.130
DR	0.635	0.074	0.672	0.076	0.683	0.053	0.745	0.096	<0.0005
DA	1.103	0.096	1.133	0.092	1.167	0.090	1.196	0.155	0.025
MD	0.791	0.078	0.826	0.077	0.844	0.061	0.895	0.110	0.001
Forceps Minor	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.474	0.024	0.456	0.025	0.462	0.027	0.434	0.037	<0.0001
DR	0.546	0.037	0.571	0.039	0.584	0.049	0.618	0.065	<0.0001
DA	1.213	0.039	1.219	0.035	1.263	0.049	1.262	0.043	<0.0001
MD	0.768	0.036	0.787	0.035	0.810	0.047	0.833	0.055	<0.0001
Forceps Major	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.500	0.025	0.489	0.031	0.491	0.032	0.448	0.050	<0.0001
DR	0.543	0.033	0.566	0.047	0.564	0.052	0.634	0.092	<0.0001
DA	1.305	0.034	1.316	0.052	1.318	0.038	1.337	0.072	0.153
MD	0.797	0.028	0.816	0.042	0.815	0.043	0.869	0.080	<0.0001
Left Uncinate Fasciculus	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.425	0.023	0.411	0.020	0.415	0.026	0.391	0.045	0.001
DR	0.580	0.033	0.597	0.036	0.618	0.054	0.648	0.085	<0.0001
DA	1.144	0.034	1.145	0.043	1.193	0.058	1.185	0.064	<0.0005
MD	0.768	0.031	0.780	0.037	0.810	0.054	0.827	0.076	<0.0001
Right Uncinate Fasciculus	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.432	0.024	0.416	0.022	0.421	0.035	0.393	0.036	<0.0005
DR	0.570	0.034	0.598	0.036	0.602	0.056	0.635	0.070	<0.0001
DA	1.153	0.041	1.172	0.041	1.192	0.042	1.184	0.059	0.006
MD	0.764	0.033	0.790	0.035	0.799	0.049	0.818	0.064	<0.0005
Cerebral Peduncles	CON	SD	MCIa	SD	MCIa	SD	AD	SD	p-value
FA	0.706	0.025	0.702	0.025	0.705	0.023	0.675	0.024	0.006
DR	0.363	0.031	0.370	0.030	0.372	0.029	0.386	0.023	0.144
DA	1.423	0.057	1.436	0.072	1.441	0.052	1.364	0.053	0.013
MD	0.716	0.032	0.725	0.037	0.728	0.027	0.712	0.021	0.388

Supplementary Table 1
(Continued)

Cerebellum	CON	SD	MCI _{na}	SD	MCI _a	SD	AD	SD	p-value
Post. Limb of Internal Capsule	CON	SD	MCI _{na}	SD	MCI _a	SD	AD	SD	p-value
FA	0.694	0.036	0.686	0.024	0.691	0.037	0.664	0.039	0.110
DR	0.359	0.044	0.371	0.035	0.368	0.043	0.366	0.031	0.705
DA	1.306	0.055	1.321	0.071	1.326	0.050	1.208	0.062	<0.0001
MD	0.675	0.040	0.688	0.041	0.687	0.039	0.646	0.027	0.055
Superior long. Fasciculus	CON	SD	MCI _{na}	SD	MCI _a	SD	AD	SD	p-value
FA	0.536	0.041	0.548	0.043	0.566	0.034	0.537	0.064	0.133
DR	0.523	0.039	0.521	0.039	0.511	0.037	0.541	0.068	0.436
DA	1.260	0.073	1.299	0.069	1.319	0.050	1.320	0.082	0.006
MD	0.769	0.032	0.780	0.032	0.781	0.030	0.801	0.051	0.050
Inferior long. fasciculus	CON	SD	MCI _{na}	SD	MCI _a	SD	AD	SD	p-value
FA	0.583	0.041	0.582	0.046	0.574	0.036	0.580	0.082	0.935
DR	0.503	0.062	0.507	0.073	0.521	0.051	0.501	0.109	0.832
DA	1.366	0.095	1.358	0.099	1.380	0.111	1.301	0.100	0.263
MD	0.791	0.066	0.790	0.077	0.808	0.064	0.768	0.092	0.624

DR, DA, MD are $\times 10^{-3}$ mm² / sec; Abbreviations: SD, standard deviation; Con, Control, MCI_{na}, non-amnesic MCI, MCI_a, amnesic MCI, AD, Alzheimer's disease; Superior long. fasciculus, Superior longitudinal fasciculus; Inferior long. fasciculus, Inferior longitudinal fasciculus; DA, axial diffusion; MD, mean diffusion; DR, radial diffusion; FA, fractional anisotropy.; P-value is for the F-test of a General Linear Model.

Supplementary Table 2
Results from All Mixed Effects Models Examined

	Myelinating	Diffusion		AIC (WM)	AIC(GM)	p-value
		Index	Model			
Cerebellum	Late	FA	Mixed	-537.240	-537.070	N/S
		DR	WM	-1792.657	-1791.047	0.029
		DA	Mixed	-1718.835	-1718.835	N/S
Left Cingulum hippocampus	Late	MD	Mixed	-1774.005	-1774.789	N/S
		FA	Mixed	-374.682	-374.682	N/S
		DR	WM	-1633.891	-1633.632	0.047
Right Cingulum hippocampus	Late	DA	Mixed	-1567.235	-1568.245	N/S
		MD	Mixed	-1619.541	-1620.703	N/S
		FA	Mixed	-395.098	-394.896	N/S
Global ROI	Early+Late	DR	Mixed	-1661.972	-1663.664	N/S
		DA	Mixed	-1589.355	-1588.210	N/S
		MD	Mixed	-1619.541	-1620.703	N/S
Left Parahippocampal pole	Late	FA	Mixed	-510.955	-512.130	N/S
		DR	GM	-1781.575	-1783.837	0.039
		DA	Mixed	-1782.382	-3575.380	N/S
Right Parahippocampal pole	Late	MD	GM	-1793.409	-1790.421	0.026
		FA	Mixed	-342.564	-341.330	N/S
		DR	Mixed	-1616.931	-1613.786	N/S
Forceps Minor	Late	DA	WM	-1567.117	-1566.044	0.035
		MD	Mixed	-1610.898	-1608.224	N/S
		FA	Mixed	-345.572	-339.360	N/S
Forceps Major	Early	DR	Mixed	-1610.557	-1610.557	N/S
		DA	Mixed	-1548.564	-1549.495	N/S
		MD	Mixed	-1597.573	-1597.573	N/S
Left Uncinate Fasciculus	Late	FA	Mixed	-457.515	-457.964	N/S
		DR	Mixed	-1740.334	-1741.988	N/S
		DA	Mixed	-1740.264	-1738.585	N/S
Right Uncinate Fasciculus	Late	MD	Mixed	-1751.933	-1753.110	N/S
		FA	Mixed	-432.216	-433.206	N/S
		DR	Mixed	-1722.600	-1731.516	N/S
Cerebral Peduncles	Early	DA	Mixed	-1724.720	-1724.581	N/S
		MD	GM	-1748.697	-1751.753	0.025
		FA	Mixed	-468.720	-468.720	N/S
Post. Limb of Internal Capsule	Early	DR	Mixed	-1742.664	-1742.664	N/S
		DA	Mixed	-1728.415	-1726.929	N/S
		MD	Mixed	-1747.796	-1747.796	N/S
Superior long. fasciculus	Late	FA	Mixed	-456.165	-456.165	N/S
		DR	GM	-1749.470	-1751.335	0.049
		DA	Mixed	-1727.798	-1727.671	N/S
Inferior long. Fasciculus	Late	MD	Mixed	-1756.782	-1758.457	N/S
		FA	Mixed	-452.386	-450.879	N/S
		DR	GM	-1795.233	-1795.476	0.046
Inferior long. Fasciculus	Late	DA	Mixed	-1666.320	-1666.417	N/S
		MD	GM	-1798.328	-1790.390	0.003
		FA	Mixed	-382.484	-384.728	N/S
Superior long. fasciculus	Late	DR	Mixed	-1736.452	-1733.155	N/S
		DA	Mixed	-1665.547	1663.335	N/S
		MD	Mixed	-1744.931	-1740.812	N/S
Inferior long. Fasciculus	Late	FA	Mixed	-326.978	-326.978	N/S
		DR	Mixed	-1724.520	-1721.666	N/S
		DA	Mixed	-1623.802	-1625.213	N/S
Inferior long. Fasciculus	Late	MD	Mixed	-1781.323	-1781.490	N/S
		FA	Mixed	-328.665	-338.997	N/S
		DR	Mixed	-1641.195	-1642.087	N/S
Inferior long. Fasciculus	Late	DA	WM	-1575.338	-1568.175	0.004
		MD	WM	-1635.481	-1632.119	0.025

The threshold for significance is set at $p < 0.05$, and p-values are calculated by comparing the WM and GM models using the anova function in R. One model is determined to be significantly better than another when the Akaike Information Criterion (AIC) value is more negative, and where the p-value from the anova function is less than 0.05. Early and Late refer to whether the ROIs myelinate at an early or late ontogenetic stage. AIC (WM); this is the AIC value for the WM model. AIC (GM); this is the AIC value for the GM model.