

On-line Appendix

Results

Control Values

The control values displayed a significant change with time in 3 regions, as shown in On-line Table 5. In the left thalamus and the left caudate nucleus, a significant decrease in mean MTR was seen; in the right putamen, a significant increase in mean MTR was observed. To ensure that our most significant longitudinal finding, namely MTR peak height of the right putamen, was not affected by the potential influence of calibration, we also examined the difference with time of this value without calibration to controls. As expected, the MTR peak height from the right putamen in the premanifest far from onset group also displayed a very significant ($P = .005$) increase during the 2-year follow-up.

Premanifest versus Manifest in 4 Group Division

When the 2 premanifest and 2 manifest groups were combined, there were 6 noteworthy increases: the MTR peak height of the right putamen ($P = .010$), MTR peak height of the left pallidum ($P = .001$), MTR peak height of cortical gray matter ($P = .024$), mean MTR of the left amygdala ($P = .024$), and mean MTR of the right thalamus ($P = .048$). Furthermore, a decrease was seen in mean MTR of the left caudate nucleus ($P = .030$); and in the manifest HD group, the left and right amygdalae showed a decrease in mean MTR (left amygdala, $P = .042$; right amygdala, $P = .025$). However, when the Bonferroni correction for multiple testing was applied, only the increase in MTR peak height of the left pallidum remained statistically significant.

On-line Table 1: MTI-derived values in 14 different regions on both baseline and follow-up visit for the premanifest HD A and premanifest HD B group

	Premanifest A				P	Premanifest B				P
	Baseline		Follow-Up			Baseline		Follow-Up		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
White matter										
Peak height	1.144	0.161	1.176	0.223	.567	1.092	0.258	1.188	0.134	.172
Mean MTR	0.387	0.013	0.389	0.010	.249	0.388	0.017	0.388	0.010	.903
Cortical gray matter										
Peak height	0.752	0.107	0.796	0.109	.091	0.685	0.136	0.727	0.111	.152
Mean MTR	0.326	0.014	0.329	0.013	.079	0.325	0.012	0.319	0.013	.020 ^a
Caudate right										
Peak height	0.852	0.133	0.910	0.184	.320	0.849	0.182	0.838	0.169	.804
Mean MTR	0.339	0.018	0.346	0.020	.049 ^a	0.333	0.031	0.340	0.025	.353
Caudate left										
Peak height	0.974	0.245	1.046	0.085	.367	0.964	0.199	1.013	0.146	.480
Mean MTR	0.357	0.021	0.351	0.016	.308	0.359	0.024	0.346	0.022	.062
Putamen right										
Peak height	1.132	0.235	1.375	0.206	0.003 ^a	1.338	0.354	1.409	0.241	.396
Mean MTR	0.329	0.015	0.335	0.012	.160	0.330	0.031	0.334	0.021	.312
Putamen left										
Peak height	1.291	0.199	1.340	0.181	.614	1.298	0.314	1.433	0.295	.091
Mean MTR	0.352	0.013	0.356	0.015	.119	0.353	0.031	0.356	0.024	.494
Pallidum right										
Peak height	1.569	0.333	1.740	0.272	.112	1.617	0.318	1.701	0.285	.400
Mean MTR	0.381	0.006	0.382	0.007	.740	0.382	0.021	0.387	0.013	.300
Pallidum left										
Peak height	1.471	0.285	1.721	0.218	.032 ^a	1.528	0.310	1.709	0.223	.086
Mean MTR	0.386	0.010	0.386	0.009	.958	0.383	0.019	0.392	0.013	.094
Thalamus right										
Peak height	1.013	0.139	1.083	0.159	.142	1.003	0.204	0.999	0.167	.946
Mean MTR	0.359	0.015	0.367	0.018	.047 ^a	0.352	0.028	0.359	0.021	.398
Thalamus left										
Peak height	1.166	0.279	1.197	0.098	.717	1.116	0.222	1.196	0.167	.332
Mean MTR	0.372	0.018	0.380	0.014	.090	0.371	0.020	0.375	0.020	.467
Amygdala right										
Peak height	1.297	0.116	1.405	0.191	.050 ^a	1.259	0.327	1.279	0.240	.837
Mean MTR	0.357	0.017	0.358	0.011	.817	0.364	0.027	0.351	0.019	.164
Amygdala left										
Peak height	1.530	0.190	1.613	0.212	.236	1.304	0.231	1.486	0.325	.064
Mean MTR	0.374	0.016	0.370	0.015	.506	0.377	0.026	0.364	0.018	.200
Hippocampus right										
Peak height	1.346	0.219	1.298	0.224	.586	1.164	0.266	1.198	0.288	.637
Mean MTR	0.360	0.015	0.363	0.009	.635	0.365	0.021	0.355	0.017	.124
Hippocampus left										
Peak height	1.010	0.195	1.059	0.170	.558	0.888	0.188	1.088	0.197	.037 ^a
Mean MTR	0.381	0.022	0.387	0.018	.347	0.380	0.018	0.373	0.013	.317
Whole brain										
Peak height	0.923	0.123	0.963	0.141	.198	0.864	0.181	0.936	0.094	.118
Mean MTR	0.352	0.013	0.355	0.011	.110	0.353	0.013	0.350	0.010	.297

^a Significant finding at $P < .05$.

On-line Table 2: MTI-derived values in 14 different regions on both baseline and follow-up visit for the manifest HD 1 and manifest HD 2 group

	Manifest 1				<i>P</i>	Manifest 2				<i>P</i>
	Baseline		Follow-Up			Baseline		Follow-Up		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
White matter										
Peak height	0.747	0.274	0.824	0.243	.388	0.866	0.263	0.916	0.245	.560
Mean MTR	0.372	0.025	0.384	0.013	.121	0.380	0.016	0.379	0.014	.713
Cortical gray matter										
Peak height	0.589	0.174	0.587	0.137	.961	0.602	0.127	0.632	0.097	.239
Mean MTR	0.319	0.014	0.316	0.015	.264	0.311	0.017	0.311	0.013	.928
Caudate right										
Peak height	0.726	0.234	0.704	0.182	.762	0.777	0.204	0.703	0.200	.371
Mean MTR	0.331	0.034	0.344	0.039	.321	0.323	0.034	0.339	0.032	.123
Caudate left										
Peak height	0.784	0.240	0.798	0.156	.852	0.833	0.244	0.898	0.236	.311
Mean MTR	0.339	0.045	0.338	0.045	.930	0.346	0.039	0.346	0.037	.999
Putamen right										
Peak height	0.877	0.326	1.018	0.287	.152	0.961	0.282	1.082	0.334	.221
Mean MTR	0.330	0.029	0.338	0.024	.276	0.329	0.018	0.323	0.029	.455
Putamen left										
Peak height	0.941	0.332	1.037	0.178	.415	1.029	0.295	1.177	0.275	.106
Mean MTR	0.346	0.026	0.352	0.031	.720	0.360	0.015	0.353	0.033	.348
Pallidum right										
Peak height	1.178	0.466	1.325	0.359	.203	1.307	0.409	1.356	0.394	.714
Mean MTR	0.396	0.039	0.389	0.018	.565	0.384	0.021	0.394	0.019	.146
Pallidum left										
Peak height	1.138	0.366	1.240	0.211	.321	1.237	0.364	1.370	0.282	.268
Mean MTR	0.376	0.047	0.396	0.026	.237	0.399	0.012	0.392	0.023	.308
Thalamus right										
Peak height	0.825	0.297	0.826	0.208	.988	0.874	0.234	0.838	0.205	.667
Mean MTR	0.349	0.035	0.360	0.038	.396	0.335	0.042	0.358	0.028	.079
Thalamus left										
Peak height	0.884	0.311	0.901	0.183	.856	0.933	0.285	0.993	0.280	.477
Mean MTR	0.346	0.054	0.367	0.045	.230	0.354	0.044	0.373	0.038	.214
Amygdala right										
Peak height	1.076	0.366	1.100	0.336	.875	1.131	0.277	1.080	0.325	.536
Mean MTR	0.361	0.019	0.333	0.029	.036 ^a	0.351	0.024	0.349	0.017	.686
Amygdala left										
Peak height	1.128	0.344	1.298	0.388	.102	1.198	0.265	1.121	0.228	.434
Mean MTR	0.377	0.042	0.345	0.036	.157	0.369	0.020	0.354	0.015	.022 ^a
Hippocampus right										
Peak height	0.974	0.264	0.976	0.233	.994	1.097	0.235	0.948	0.249	.131
Mean MTR	0.372	0.036	0.344	0.022	.073	0.354	0.027	0.359	0.018	.576
Hippocampus Left										
Peak height	0.717	0.226	0.798	0.181	.142	0.957	0.256	1.062	0.232	.350
Mean MTR	0.394	0.045	0.364	0.029	.150	0.389	0.017	0.379	0.020	.284
Whole brain										
Peak height	0.661	0.217	0.696	0.184	.579	0.719	0.174	0.762	0.153	.428
Mean MTR	0.343	0.016	0.347	0.014	.098	0.342	0.016	0.343	0.012	.728

^a Significant finding at $P < .05$.

On-line Table 3: Volumetric analysis of 14 brain regions in premanifest HD^a

	Premanifest A				<i>P</i>	Premanifest B				<i>P</i>
	Baseline		Follow-Up			Baseline		Follow-Up		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Caudate right	3.907	0.428	3.705	0.482	.004	3.897	0.339	3.739	0.353	.001 ^b
Caudate left	3.797	0.395	3.651	0.406	.001 ^b	3.713	0.359	3.576	0.376	.002 ^b
Putamen right	4.832	0.619	4.680	0.603	.009	4.582	0.497	4.397	0.525	.001 ^b
Putamen left	4.916	0.502	4.748	0.544	.006	4.681	0.556	4.483	0.586	.002 ^b
Pallidum right	2.056	0.173	2.069	0.207	.555	2.009	0.155	1.952	0.142	.067
Pallidum left	1.931	0.205	1.890	0.226	.199	1.995	0.134	1.925	0.175	.081
Thalamus right	8.155	0.545	8.122	0.468	.566	7.718	0.637	7.595	0.741	.044
Thalamus left	8.492	0.595	8.452	0.554	.474	7.833	0.659	7.777	0.722	.382
Amygdala right	1.689	0.242	1.672	0.222	.821	1.799	0.268	1.793	0.306	.891
Amygdala left	1.772	0.266	1.752	0.259	.578	1.711	0.229	1.733	0.234	.626
Hippocampus right	5.519	0.385	5.411	0.431	.033	5.204	0.470	5.252	0.619	.497
Hippocampus left	5.315	0.358	5.392	0.319	.034	4.925	0.750	4.962	0.853	.552
White matter	673.9	36.2	667.2	34.0	.028	647.2	46.2	637.0	44.4	.014
Whole brain	1486.4	38.7	1477.3	33.2	.208	1445.7	72.9	1429.0	73.4	.036

^a Volumes (cubic millimeters) of 14 VOIs on both baseline and follow-up.

^b Significant finding after Bonferroni correction ($P < .0033$).

On-line Table 4: Volumetric analysis of 14 brain regions in manifest HD^a

	Manifest 1				<i>P</i>	Manifest 2				<i>P</i>
	Baseline		Follow-Up			Baseline		Follow-Up		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Caudate right	3.290	0.530	3.165	0.621	.046	3.302	0.495	3.223	0.624	.219
Caudate left	3.178	0.478	3.002	0.481	.019	3.094	0.472	2.916	0.515	.001 ^b
Putamen right	4.002	0.603	3.839	0.602	.009	3.518	0.325	3.296	0.392	.012
Putamen left	4.176	0.548	3.962	0.593	.004	3.455	0.479	3.285	0.437	.003 ^b
Pallidum right	1.834	0.086	1.790	0.058	.029	1.845	0.248	1.751	0.226	.014
Pallidum left	1.866	0.207	1.793	0.201	.117	1.769	0.288	1.679	0.324	.141
Thalamus right	7.603	0.703	7.427	0.661	.003 ^b	7.285	0.593	7.207	0.435	.352
Thalamus left	7.745	0.729	7.567	0.728	.001 ^b	7.358	0.897	7.176	0.892	.018
Amygdala right	1.643	0.258	1.732	0.194	.257	1.623	0.149	1.633	0.279	.918
Amygdala left	1.654	0.311	1.676	0.357	.707	1.638	0.106	1.594	0.115	.295
Hippocampus right	5.127	0.511	5.063	0.374	.354	4.961	0.579	4.807	0.578	.018
Hippocampus left	5.096	0.591	5.033	0.556	.557	4.542	0.440	4.446	0.550	.233
White matter	632.9	52.9	619.4	53.9	.001 ^b	633.8	35.8	616.1	34.8	.009
Whole brain	1396.6	95.3	1371.9	93.8	.001 ^b	1383.1	77.8	1350.6	81.4	.001 ^b

^a Volumes (cubic millimeters) of 14 VOIs on both baseline and follow-up.

^b Significant finding after Bonferroni correction ($P < .0033$).

On-line Table 5: Control values of MTR parameters

Control Group (<i>n</i> = 25)			Mean	SD
White matter	MTR peak height	Baseline	1.109	0.220
		Follow-up	1.125	0.231
	Mean MTR	Baseline	0.391	0.012
		Follow-up	0.394	0.012
Cortical gray matter	MTR peak height	Baseline	0.769	0.119
		Follow-up	0.735	0.132
	Mean MTR	Baseline	0.329	0.013
		Follow-up	0.330	0.014
Caudate nucleus right	MTR peak height	Baseline	0.799	0.192
		Follow-up	0.830	0.224
	Mean MTR	Baseline	0.349	0.026
		Follow-up	0.343	0.025
Caudate nucleus left	MTR peak height	Baseline	0.892	0.188
		Follow-up	0.831	0.198
	Mean MTR	Baseline	0.369	0.018
		Follow-up	0.354 ^a	0.018
Putamen right	MTR peak height	Baseline	1.257	0.372
		Follow-up	1.240	0.271
	Mean MTR	Baseline	0.340	0.019
		Follow-up	0.351 ^a	0.017
Putamen left	MTR peak height	Baseline	1.337	0.268
		Follow-up	1.266	0.265
	Mean MTR	Baseline	0.360	0.015
		Follow-up	0.357	0.016
Pallidum right	MTR peak height	Baseline	1.494	0.343
		Follow-up	1.435	0.230
	Mean MTR	Baseline	0.382	0.015
		Follow-up	0.388	0.014
Pallidum left	MTR peak height	Baseline	1.601	0.301
		Follow-up	1.490	0.268
	Mean MTR	Baseline	0.386	0.014
		Follow-up	0.388	0.014
Thalamus right	MTR peak height	Baseline	0.988	0.261
		Follow-up	0.936	0.236
	Mean MTR	Baseline	0.369	0.021
		Follow-up	0.350	0.021
Thalamus left	MTR peak height	Baseline	1.067	0.226
		Follow-up	1.003	0.251
	Mean MTR	Baseline	0.383	0.020
		Follow-up	0.368 ^a	0.016
Amygdala right	MTR peak height	Baseline	1.329	0.295
		Follow-up	1.287	0.289
	Mean MTR	Baseline	0.360	0.020
		Follow-up	0.363	0.025
Amygdala left	MTR peak height	Baseline	1.475	0.307
		Follow-up	1.328	0.369
	Mean MTR	Baseline	0.370	0.021
		Follow-up	0.370	0.026
Hippocampus right	MTR peak height	Baseline	1.240	0.309
		Follow-up	1.194	0.273
	Mean MTR	Baseline	0.366	0.019
		Follow-up	0.371	0.020
Hippocampus left	MTR peak height	Baseline	0.981	0.247
		Follow-up	0.929	0.222
	Mean MTR	Baseline	0.386	0.015
		Follow-up	0.391	0.017
Whole brain	MTR peak height	Baseline	0.917	0.152
		Follow-up	0.906	0.156
	Mean MTR	Baseline	0.356	0.011
		Follow-up	0.359	0.012

^a Significant finding after Bonferroni correction ($P < .0033$).