

On-line Table 1: Comparison of subcortical volumes and MD values across groups^a

Region	CN	HD	PreHD	EarlyHD	MidadvHD	P Value
Volume (mL)						
Left						
Caudate	3.5 ± 0.4	2.4 ± 0.6	2.9 ± 0.4	2.2 ± 0.3	1.9 ± 0.3	<.001, ^b <.001, ^c <.001, ^d .08 ^e
Putamen	4.9 ± 0.4	3.2 ± 0.7	3.8 ± 0.7	3.0 ± 0.5	2.5 ± 0.4	<.001, <.001, .001, .022
Accumbens	0.5 ± 0.1	0.3 ± 0.1	0.4 ± 0.1	0.3 ± 0.1	0.28 ± 0.1	<.001, .001, .25, .08
Pallidum	2.1 ± 0.2	1.4 ± 0.3	1.6 ± 0.2	1.3 ± 0.3	1.1 ± 0.2	<.001, <.001, <.001, .087
Amygdala	1.5 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	1.3 ± 0.2	1.0 ± 0.2	<.001, .005, .6, .008
Thalamus	8.1 ± 0.7	7.0 ± 0.9	7.5 ± 0.9	6.9 ± 0.6	6.4 ± 1.1	<.001, .03, .07, .31
Hippocampus	4.2 ± 0.4	3.7 ± 0.4	3.8 ± 0.4	3.7 ± 0.3	3.3 ± 0.4	<.001, .008, .5, .024
Right						
Caudate	3.6 ± 0.4	2.6 ± 0.5	3.0 ± 0.4	2.4 ± 0.4	2.2 ± 0.3	<.001, <.001, .001, .13
Putamen	4.9 ± 0.4	3.2 ± 0.7	3.7 ± 0.7	2.9 ± 0.4	2.5 ± 0.6	<.001, <.001, .001, .07
Accumbens	0.6 ± 0.07	0.4 ± 0.09	0.5 ± 0.09	0.4 ± 0.07	0.3 ± 0.08	<.001, .006, <.001, .036
Pallidum	2.1 ± 0.2	1.4 ± 0.3	1.7 ± 0.2	1.3 ± 0.2	1.1 ± 0.3	<.001, <.001, .039, .043
Amygdala	1.6 ± 0.2	1.4 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.1 ± 0.2	<.001, .018, .39, .012
Thalamus	7.4 ± 0.7	6.5 ± 0.7	6.6 ± 0.7	6.6 ± 0.6	6.0 ± 0.8	<.001, .003, .94, .07
Hippocampus	4.3 ± 0.3	3.7 ± 0.5	3.9 ± 0.5	3.8 ± 0.3	3.2 ± 0.4	<.001, .02, .44, .006
MD (μm ² /ms)						
Left						
Caudate	0.77 ± 0.03	0.88 ± 0.09	0.82 ± 0.02	0.89 ± 0.08	0.95 ± 0.1	<.001, <.001, .001, .25
Putamen	0.75 ± 0.02	0.87 ± 0.09	0.79 ± 0.04	0.89 ± 0.08	0.97 ± 0.09	<.001, <.001, <.001, .06
Accumbens	0.83 ± 0.04	0.87 ± 0.07	0.88 ± 0.04	0.85 ± 0.08	0.89 ± 0.1	.015, .001, .24, .3
Pallidum	0.75 ± 0.04	0.78 ± 0.08	0.74 ± 0.04	0.78 ± 0.05	0.82 ± 0.1	.12, .69, .06, .26
Amygdala	0.86 ± 0.06	0.89 ± 0.07	0.89 ± 0.07	0.89 ± 0.06	0.88 ± 0.08	.10, .22, .9, .72
Thalamus	0.81 ± 0.02	0.85 ± 0.05	0.83 ± 0.03	0.87 ± 0.04	0.86 ± 0.06	<.001, .048, .01, .71
Hippocampus	1.08 ± 0.05	1.19 ± 0.09	1.15 ± 0.07	1.20 ± 0.09	1.24 ± 0.1	<.001, .002, .11, .34
Right						
Caudate	0.85 ± 0.03	0.94 ± 0.08	0.89 ± 0.03	0.96 ± 0.06	1.0 ± 0.1	<.001, .001, .001, .16
Putamen	0.79 ± 0.02	0.91 ± 0.09	0.84 ± 0.04	0.92 ± 0.07	1.0 ± 0.09	<.001, <.001, <.001, .06
Accumbens	0.86 ± 0.05	0.84 ± 0.07	0.88 ± 0.04	0.82 ± 0.08	0.83 ± 0.09	.25, .18, .008, .64
Pallidum	0.81 ± 0.05	0.83 ± 0.06	0.81 ± 0.04	0.82 ± 0.07	0.87 ± 0.08	.61, .35, .09, .10
Amygdala	0.84 ± 0.03	0.87 ± 0.06	0.87 ± 0.03	0.86 ± 0.06	0.91 ± 0.1	.04, .039, .49, .10
Thalamus	0.84 ± 0.02	0.87 ± 0.06	0.86 ± 0.07	0.87 ± 0.05	0.88 ± 0.07	.022, .25, .68, .79
Hippocampus	1.08 ± 0.05	1.15 ± 0.07	1.13 ± 0.06	1.15 ± 0.06	1.18 ± 0.09	<.001, .024, .24, .35

^a Values are expressed as mean ± standard deviation.

^b CN vs HD.

^c CN vs preHD.

^d PreHD vs earlyHD.

^e EarlyHD vs midadvHD.

On-line Table 2: Associations between imaging indicators and clinical variables within preHD and earlyHD groups^a

Clinical Variable	Significant Clinical-Imaging Correlations	
	PreHD	EarlyHD
DBS	MD_L_precentral ($r = 0.71, P < .01$), MD_R_precuneus ($r = 0.53, P = .04$), MD_Ls_caudate ($r = 0.57, P = .03$)	Cth_L_superior-parietal ($r = -0.52, P = .04$), MD_Ls_hippocampus ($r = 0.57, P = .02$)
Estimated yr to onset	MD_L_precentral ($r = -0.59, P = .02$), MD_Rs_caudate ($r = -0.57, P = .03$), Vol_Ls_pallidum ($r = 0.53, P = .04$)	NA
TFC	MD_Ls_putamen ($r = -0.61, P = .01$), MD_Ls_amygdala ($r = -0.79, P < .01$)	MD_R_superior-parietal ($r = -0.55, P = .03$), MD_R_precentral ($r = -0.64, P = .01$), Cth_R_superior-parietal ($r = 0.61, P = .01$), Cth_R_superior-temporal ($r = 0.65, P = .01$), Cth_R_superior-frontal ($r = 0.69, P < .01$), Cth_L_inferior-parietal ($r = 0.52, P = .04$), Cth_L_postcentral ($r = 0.58, P = .02$), Cth_L_superior-frontal ($r = 0.64, P = .01$), Cth_L_superior-parietal ($r = 0.51, P = .04$), Cth_L_supramarginal ($r = 0.51, P = .04$), Cth_L_superior-frontal-anterior ($r = 0.56, P = .03$), MD_L_superior-temporal ($r = -0.50, P = .05$), MD_L_lateral-orbitofrontal-cortex ($r = -0.54, P = .03$)
UHDRS_TMS	MD_L_entorhinal ($r = 0.78, P < .01$), MD_R_entorhinal ($r = 0.76, P < .01$), MD_Ls_thalamus ($r = 0.63, P = .01$), MD_Ls_putamen ($r = 0.55, P = .03$), MD_Ls_pallidum ($r = 0.54, P = .04$), MD_Rs_amygdala ($r = 0.65, P = .01$), Vol_Ls_putamen ($r = -0.64, P = .01$), Vol_Ls_hippocampus ($r = -0.52, P = .05$), Vol_Rs_putamen ($r = -0.60, P = .02$)	MD_R_cuneus ($r = 0.54, P = .03$), MD_R_superior-temporal ($r = 0.55, P = .03$), MD_R_superior-parietal ($r = 0.53, P = .04$), MD_R_precentral ($r = 0.55, P = .03$), Cth_R_superior-parietal ($r = -0.56, P = .03$), Cth_R_superior-temporal ($r = -0.66, P = .01$), Cth_R_superior-frontal ($r = -0.75, P < .01$), Cth_L_inferior-parietal ($r = -0.52, P = .04$), Cth_L_superior-frontal ($r = -0.65, P = .01$), Cth_L_superior-frontal-anterior ($r = -0.62, P = .01$), MD_L_pericalcarine ($r = 0.53, P = .04$), MD_L_superior-temporal ($r = 0.56, P = .02$), MD_L_lateral-orbitofrontal-cortex ($r = 0.60, P = .01$), MD_Ls_putamen ($r = 0.64, P = .01$), MD_Ls_hippocampus ($r = 0.53, P = .04$)
Cogscore	MD_L_entorhinal ($r = -0.54, P = .04$), MD_Rs_caudate ($r = -0.63, P = .01$), MD_Rs_hippocampus ($r = -0.59, P = .02$), Vol_Ls_caudate ($r = 0.52, P = .04$), Vol_Rs_caudate ($r = 0.52, P = .05$)	Cth_R_superior-parietal ($r = 0.55, P = .03$), Cth_R_superior-temporal ($r = 0.55, P = .04$), Cth_R_superior-frontal ($r = 0.81, P < .01$), Cth_L_superior-parietal ($r = 0.54, P = .04$), MD_Ls_putamen ($r = -0.62, P = .01$), MD_Ls_hippocampus ($r = -0.73, P < .01$), MD_Rs_putamen ($r = -0.65, P = .01$), MD_Rs_hippocampus ($r = -0.62, P = .01$)
Apathy score	MD_Ls_thalamus ($r = 0.58, P = .02$), MD_Ls_caudate ($r = 0.73, P < .01$)	MD_Ls_hippocampus ($r = 0.54, P = .03$), MD_Rs_putamen ($r = 0.54, P = .03$), MD_Rs_hippocampus ($r = 0.70, P < .01$)
FAS		MD_Rs_hippocampus ($r = -0.51, P = .04$)
SDMT	MD_Ls_accumbens ($r = -0.56, P = .03$), MD_Rs_pallidum ($r = -0.55, P = .03$), Vol_Rs_pallidum ($r = 0.57, P = .03$)	Cth_R_superior-frontal ($r = 0.50, P = .05$), MD_Ls_putamen ($r = -0.50, P = .05$), MD_Ls_hippocampus ($r = -0.64, P = .01$), MD_Ls_accumbens ($r = -0.54, P = .03$), MD_Rs_putamen ($r = -0.56, P = .02$), MD_Rs_hippocampus ($r = -0.52, P = .04$)
Semantic fluency		MD_Rs_putamen ($r = -0.55, P = .03$), MD_Rs_hippocampus ($r = -0.50, P = .05$), Vol_Ls_caudate ($r = 0.51, P = .04$), Vol_Rs_caudate ($r = 0.56, P = .03$)

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On-line Table 2: Continued

Clinical Variable	Significant Clinical-Imaging Correlations	
	PreHD	EarlyHD
Stroop Color	MD_L_superior-temporal ($r = -0.54, P = .04$), MD_L_superior-frontal ($r = -0.55, P = .04$), MD_R_rostral midfrontal ($r = -0.55, P = .03$), MD_R_precentral ($r = -0.62, P = .01$)	MD_R_cuneus ($r = -0.63, P = .01$), MD_R_superior-temporal ($r = -0.61, P = .01$), MD_R_superior-parietal ($r = -0.55, P = .03$), MD_R_precuneus ($r = -0.56, P = .02$), MD_R_precentral ($r = -0.60, P = .01$), Cth_R_superior-parietal ($r = 0.56, P = .03$), Cth_R_superior-temporal ($r = 0.53, P = .03$), Cth_R_superior-frontal ($r = 0.69, P < .01$), Cth_L_superior-frontal ($r = 0.54, P = .03$), MD_L_pericalcarine ($r = -0.62, P = .01$), MD_L_superior-temporal ($r = -0.61, P = .01$), MD_L_lateral-orbitofrontal-cortex ($r = -0.58, P = .02$), MD_L_caudate middle frontal ($r = -0.59, P = .02$), MD_L_superior-parietal ($r = -0.53, P = .04$), MD_Ls_thalamus ($r = -0.50, P = .05$), MD_Ls_putamen ($r = -0.77, P < .01$), MD_Ls_hippocampus ($r = -0.65, P = .01$), MD_Rs_thalamus ($r = -0.62, P = .01$), MD_Rs_caudate ($r = -0.56, P = .02$), MD_Rs_putamen ($r = -0.70, P < .01$), Vol_Rs_accumbens ($r = 0.53, P = .04$)
Stroop-Word	MD_Ls_hippocampus ($r = -0.57, P = .03$), Vol_Ls_caudate ($r = 0.63, P = .01$), Vol_Rs_caudate ($r = 0.60, P = .02$)	MD_R_superior-parietal ($r = -0.51, P = .04$), MD_R_precentral ($r = -0.51, P = .04$), Cth_R_superior-parietal ($r = 0.56, P = .03$), Cth_R_superior-frontal ($r = 0.63, P = .01$), Cth_L_superior-parietal ($r = 0.62, P = .01$), MD_Ls_putamen ($r = -0.60, P = .01$), MD_Ls_hippocampus ($r = -0.60, P = .01$), MD_Ls_accumbens ($r = -0.52, P = .04$), MD_Rs_putamen ($r = -0.71, P < .01$), MD_Rs_hippocampus ($r = -0.52, P = .04$), MD_Rs_accumbens ($r = -0.55, P = .03$), Vol_Rs_accumbens ($r = 0.52, P = .04$)
TMT B-A	MD_Ls_putamen ($r = 0.55, P = .03$)	MD_Ls_accumbens ($r = -0.52, P = .04$), Vol_Ls_palladium ($r = -0.51, P = .04$)
TMT cognitive flexibility	MD_L_rostral midfrontal ($r = -0.60, P = .02$)	

Note:—Vol indicates volume; NA, not applicable; R, right; L, left; Ls, left subcortical; Rs, right subcortical; TFC, Total Functional Capacity; TMS, Total Motor Score; Cogscore, Cognitive Score; FAS, F-A-S test of verbal fluency.

^aThe set of clusters and subcortical structures were previously described in the text.

On-line Table 3: Associations between imaging indicators and clinical variables within preHD and earlyHD groups^a

Clinical Variable	Significant Clinical-Imaging Correlations, Controlling for Caudate Atrophy	
	PreHD	EarlyHD
DBS	MD_L_precentral ($r = 0.65, P = .02$)	MD_Ls_caudate ($r = 0.86, P = .03$), MD_Ls_accumbens ($r = 0.93, P = .01$), MD_Rs_accumbens ($r = 0.93, P = .01$)
Estimated yr to onset TFC	MD_Ls_putamen ($r = -0.60, P = .03$), MD_Ls_amygdala ($r = -0.79, P < .01$)	NA Cth_R_superior-temporal ($r = 0.84, P = .04$), Cth_L_postcentral ($r = 0.84, P = .04$), Cth_L_superior-frontal ($r = 0.90, P = .01$)
UHDRS_TMS	MD_L_entorhinal ($r = 0.69, P = .01$), MD_R_entorhinal ($r = 0.70, P = .01$), MD_Rs_amygdala ($r = 0.69, P = .01$)	MD_R_precentral ($r = 0.84, P = .04$), Cth_R_superior-temporal ($r = -0.88, P = .02$), Cth_R_superior-frontal ($r = -0.85, P = .03$), MD_Ls_putamen ($r = 0.97, P < .01$), MD_Rs_putamen ($r = 0.90, P = .01$), MD_Rs_amygdala ($r = 0.91, P = .01$)
Cogscore	MD_Rs_caudate ($r = -0.60, P = .03$), MD_Rs_hippocampus ($r = -0.56, P = .05$)	MD_Ls_putamen ($r = -0.90, P = .01$), MD_Ls_hippocampus ($r = -0.86, P = .03$), MD_Rs_putamen ($r = -0.94, P = .01$)
Apathy score	MD_Ls_thalamus ($r = 0.60, P = .03$), MD_Ls_caudate ($r = 0.71, P = .01$)	MD_Ls_hippocampus ($r = 0.85, P = .03$), MD_Rs_accumbens ($r = 0.85, P = .03$), Vol_Ls_hippocampus ($r = 0.90, P = .02$)
FAS		Cth_L_inferior-parietal ($r = -0.85, P = .03$), Cth_L_postcentral ($r = -0.88, P = .02$), Cth_L_superior-frontal ($r = -0.83, P = .04$)
SDMT Semantic fluency	MD_Ls_accumbens ($r = -0.62, P = .02$) MD_L_precentral ($r = -0.56, P = .05$)	MD_Rs_putamen ($r = -0.86, P = .03$) MD_Ls_putamen ($r = -0.83, P = .04$), MD_Ls_hippocampus ($r = -0.88, P = .02$), MD_Rs_putamen ($r = -0.92, P = .01$), MD_Rs_accumbens ($r = -0.87, P = .02$), Vol_Ls_hippocampus ($r = -0.83, P = .04$), Vol_Rs_amygdala ($r = -0.88, P = .02$)
Stroop Color	MD_L_superior-temporal ($r = -0.58, P = .04$), MD_R_precentral ($r = -0.62, P = .03$)	MD_R_cuneus ($r = -0.83, P = .04$), MD_R_superior-temporal ($r = -0.86, P = .03$), MD_R_superior-parietal ($r = -0.94, P = .01$), MD_R_precuneus ($r = -0.91, P = .01$), MD_R_precentral ($r = -0.94, P = .01$), Cth_R_superior-parietal ($r = 0.88, P = .02$), Cth_R_superior-temporal ($r = 0.82, P = .05$), MD_L_pericalcarine ($r = -0.85, P = .03$), MD_L_superior-temporal ($r = -0.90, P = .01$), MD_L_lateral-orbitofrontal-cortex ($r = -0.91, P = .01$), MD_L_caudal middle frontal ($r = -0.92, P = .01$), MD_L_superior-parietal ($r = -0.91, P = .01$), MD_Ls_thalamus ($r = -0.85, P = .03$), MD_Ls_caudate ($r = -0.84, P = .04$), MD_Ls_putamen ($r = -0.92, P = .01$), MD_Ls_hippocampus ($r = -0.88, P = .02$), MD_Rs_putamen ($r = -0.97, P < .01$)
Stroop-Word TMT (parts B-A) TMT cognitive flexibility	MD_Ls_putamen ($r = 0.56, P = .04$) MD_L_rostral midfrontal ($r = -0.60, P = .03$), MD_Rs_accumbens ($r = -0.56, P = .05$)	MD_Ls_amygdala ($r = -0.84, P = .04$) Vol_Rs_hippocampus ($r = 0.86, P = .03$)

Note:—TFC indicates Total Functional Capacity; TMS, Total Motor Score; Cogscore, Cognitive Score; FAS, F-A-S test of verbal fluency; Vol, volume.

^a The set of clusters and subcortical structures were previously described in the text.