Functional connectivity modeling of consistent cortico-striatal degeneration in Huntington's disease

- Supplementary data -

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Figure S-1 Overview on workflow with applied techniques and related research questions

Figure S-2 Functional characterization by behavioral domains and paradigm classes of **a** premanifest striatal (*yellow*) and MOG (*blue*) atrophy seeds; **b** manifest striatal (*yellow*), IFJ (*green*) and M1 (*red*) atrophy seeds. Bar plots show significant associations (at $p<0.05$, Bonferroni corrected for multiple comparison) of a behavioral domains and paradigm class from BrainMap meta-data given observed brain activity (and *vice versa*); x-axis indicates relative probability values.

Table S-1 Meta-analytic connectivity modeling and resting-state connectivity of consistent striatal degeneration in HD

	MNI co-ordinates						MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area	k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area
MACM map of left and right striatal seeds						***Resting-state connectivity of left and right striatal seeds***					
16,407	12	10	0	R	Caudate nucleus	28,592	8	10	4	R	Caudate nucleus
	-12	8	2	L	Caudate nucleus		-12	10	6	L	Caudate nucleus
	18	8	2	R	Pallidum, Putamen		22	6	-8	R	Putamen, Pallidum
	-20	4	4	L	Putamen, Pallidum		-18	14	-4	L	Putamen, Pallidum
	-32	20	2	L	Insula		26	-4	2	R	Pallidum
	34	22	-2	R	Insula					L/R	Thalamus [prefrontal, temporal, parietal,
	-12	-16	6	L	Thalamus [prefrontal,temporal,parietal,pre-/motor]						premotor, motor, somatosensory]
	10	-16	6	R	Thalamus [prefrontal,temporal,parietal,premotor]					L/R	Amygdala [SF, LB, CM]
				L/R	Amygdala [SF, CM]					L/R	Insula [Ig1, Ig2]
	50	12	2	R/L	Inferior frontal [BA 44, 45], middle frontal gyrus					L/R	Inferior frontal gyrus [BA 44, 45]
				R	Precentral gyrus, PMC [BA 6]					L	Middle and superior frontal gyrus
	-52	8	32	L	Precentral gyrus, PMC [BA 6], M1 [BA 4a,p]					L/R	Precentral gyrus, PMC [BA6], M1 [4a, 4p]
	-30	-54	50	L	IPS [hIP1-3], SPL [7A,7PC], IPC [PFt], SI [BA 2,3b]					L/R	SMA [BA6], Anterior and middle cingulate cortex
3,135	0	10	48	L/R	SMA [BA 6]					L/R	Heschl's gyrus [TE 1.0, 1.1]
	0	2	54	L/R	Middle cingulate cortex					R	Parietal operculum [OP2]
500	36	-46	46	R	IPS [hIP1-3], SPL [7A]					L/R	Cerebellum [Lobule I-IV]
271	-56	-22	22	L	IPC [PFop], parietal operculum [OP1]	210	38	-84	-40	R	Cerebellum [Lobule VIIa Crus I, II]
132	60	-36	20	R	IPC [PF, PFcm]	201	32	-68	-30	R	Cerebellum [Lobule VIIa Crus I]
57	62	-28	4	R	Superior temporal gyrus		34	-56	-32	R	Cerebellum [Lobule VI]
502	-28	-60	-26	L	Cerebellum [Lobule VI], Fusiform gyrus,	158	-48	-62	52	L	IPC [PFm, PGa, PF]
					inferior occipital gyrus	72	56	-60	44	R	IPC [PFm, PGa], Angular gyrus
293	26	-64	-24	R	Cerebellum [Lobule VI]	101	-42	58	-6	L	Middle Orbital Gyrus
Conjunction: MACM & Resting-state maps of left and right striatal seeds											
10,156	-6	5	9	L/R	Caudate nucleus, Putamen, Pallidum					L/R	Insula
				L/R	Thalamus [prefrontal,temporal,parietal,premotor]					L/R	Inferior frontal gyrus [BA 44, 45]
				L	Thalamus [motor]					L/R	PMC [BA 6], M1 [BA 4a]
				L/R	Amygdala [SF]	2,524	6	24	22	L/R	Middle cingulate cortex, SMA [BA6]

Results are cluster-level FWE corrected at $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$); k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI: primary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-2 Meta-analytic connectivity modeling and resting-state connectivity of cortical and striatal seeds in premanifest HD

	MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic region
MACM map of right MOG and striatal seeds					
717	-16	2	14	L	Caudate nucleus
	-20	2	10	L	Putamen
	-14	2	0	L	Pallidum
	-28	20	4	L	Anterior insula
320	18	8	2	R	Pallidum
	14	10	4	R	Caudate nucleus; putamen
472	36	20	2	R	Anterior insula; inferior frontal gyrus, p.orbitalis
430	-52	10	24	L	Inferior frontal gyrus, p.opercularis [BA 44]
	-40	4	30	L	Precentral gyrus
246	48	10	28	R	Inferior frontal gyrus, p opercularis [BA 44]
	50	6	34	R	Precentral gyrus
200	26	-4	60	R	Superior frontal gyrus
	42	0	56	R	Middle frontal gyrus
137	50	30	20	R	Inferior frontal gyrus, p triangularis
	42	38	24	R	Middle frontal gyrus
449	2	12	50	L/R	SMA [BA 6]
1,287	32	-70	32	R	Middle occipital gyrus
	34	-46	46	R	IPS [hIP3,2]; SI [BA 2]
	28	-64	52	R	SPL [7A, 7PC]
597	-26	-62	52	L	SPL [BA 7A]; IPS [hIP3]
	-28	-68	36	L	Middle occipital gyrus; Superior occipital gyrus
***Resting-state connectivity* of right MOG and striatal seeds**					
822	-50	8	22	L	Inferior frontal gyrus, p.opercularis [BA 44]
	-32	-8	52	L	Precentral gyurs
	-42	-4	56	L	PMC [BA6]
	-22	-2	58	L	Superior frontal gyrus
439	54	8	20	R	Inferior frontal gyrus, p.opercularis [BA 44]
	56	8	36	R	Precentral gyrus
	42	-2	52	R	Middle frontal gyrus
	26	-6	64	R	Superior frontal gyrus; PMC [BA6]
207	-58	-34	46	L	IPC [PF, PFt]
169	60	-28	42	R	IPC [PF, PFt]
162	-46	32	10	L	Inferior frontal gyrus, p.triangularis [BA45]
114	54	34	10	R	Inferior frontal gyrus, p.triangularis [BA45]
74	28	-72	-54	R	Cerebellum [Lobule VII]
Conjunction: MACM & Resting-state maps of right MOG ∩ striatal seeds					
195	-50	8	22	L	Inferior frontal gyrus, p. opercularis [BA 44]
	-54	4	36	L	Precentral gyrus
59	56	8	36	R	Precentral gyrus, inferior frontal gyrus

Results are cluster-level FWE corrected at $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$); k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI: primary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-3 Meta-analytic connectivity modeling of cortical and striatal seeds in manifest HD

	MNI co-ordinates						MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area	k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area
MACM map of IFJ ∩ striatal seeds						***MACM map of M1 ∩ striatal seeds***					
10,354	-14	4	10	L	Caudate nucleus	7,550	-20	6	4	L	Putamen; pallidum
	14	6	8	R	Caudate nucleus		-14	4	10	L	Caudate nucleus
	-18	4	6	L	Putamen; pallidum		-34	24	0	L	Insula; parietal operculum, SII [OP1]
	22	6	4	R	Putamen		-50	6	32	L	Inferior frontal gyrus [BA 44]
	16	2	2	R	Pallidum		-26	-6	56	L	Middle frontal gyrus; PMC [BA 6]
	10	-14	10	R/L	Thalamus [prefrontal, temporal]		-36	-22	54	L	M1 [BA 4a, p]; SI [BA 3b, 3a, 2]
	-34	22	0	L	Anterior Insula		-42	-40	42	L	IPS [hIP1-3]; IPC [PFt; PFop]; SPL [7A; 7PC]
	34	22	-4	R	Anterior Insula	2,883	24	8	2	R	Putamen; caudate nucleus
	-44	8	30	L	Inferior frontal gyrus [BA 44,45]; PMC [BA 6]; Middle frontal gyrus		18	-4	-4	R	Pallidum
							10	-16	6	R	Thalamus [Prefrontal, temporal, premotor]
	46	8	28	R	Inferior frontal [BA 44,45]; middle frontal gyrus		34	22	-2	R	Insula
2,187	-2	12	50	L/R	SMA [BA 6]		58	10	24	R	Inferior frontal gyrus [BA 44]
	4	30	38	R/L	Middle cingulate cortex	263	50	34	26	R	Inferior and middle frontal gyrus
	2	28	40	R/L	Superior medial gyrus	475	-14	-18	6	L	Thalamus [Prefrontal, parietal, premotor, motor]
1,713	-30	-54	48	L	IPS [hIP1-3]; superior/middle occipital gyrus	2,034	-2	2	56	L/R	SMA [BA 6]
	-24	-66	48	L	SPL [7A, 7PC, 7P]		12	4	40	L/R	Middle cingulate cortex
	-44	-36	44	L	IPC [PFt, PF]; SI [BA 2]	1,127	40	-4	58	R	PMC [BA 6]
695	36	-46	44	R	IPS [hIP1-3]; SPL [7A, 7PC]; SI [BA 2]		38	-16	52	R	M1 [BA 4a, 4p]
241	-52	-42	10	L	Middle temporal gyrus		40	-42	58	R	SI [BA 2,3b]
539	-30	-62	-26	L	Cerebellum [lobule VI]		34	-50	44	R	IPS [hIP1-3]; IPC [PFt]
	-42	-64	-14	L	Fusiform gyrus		32	-64	54	R	SPL [7A, 7PC]; Superior occipital gyrus
157	28	-50	-24	R	Cerebellum [lobule VI]; fusiform gyrus	347	58	-20	22	R	Parietal operculum, SII [OP1]
							62	-34	22	R	IPC [PF, PFt, PFop]; SI [BA 2,1]
						244	-44	-58	-14	L	Inferior occipital gyrus; fusiform gyrus
Contrast: MACM map of IFJ ∩ striatum > M1 ∩ striatum						***Contrast: MACM map of M1 ∩ striatum > IFJ ∩ striatum***					
601	-16	-6	18	L	Caudate nucleus	106	26	-10	6	R	Putamen
	12	-2	16	R	Caudate nucleus		26	-4	-2	R	Pallidum
	-4	-18	14	L	Thalamus [temporal, prefrontal]	312	-32	-6	2	L	Putamen
	4	-10	10	R	Thalamus [temporal, prefrontal]		-22	-6	-6	L	Pallidum
2,066	-42	6	22	L	Inferior frontal gyrus [BA 44,45]; anterior insula		-32	-8	12	L	Insula
	-38	40	18	L	Middle temporal gyrus		-44	2	10	L	Rolandic operculum
	-48	14	-4	L	Temporal pole, anterior insula	155	-16	-24	4	L	Thalamus [parietal, motor, premotor, prefrontal]
	-50	0	48	L	Precentral gyrus	2,247	-32	-12	60	L	PMC [BA 6]; M1 [BA 4p, 4a]; SI [BA 2, 3b,a, 1]
1,022	46	6	26	R	Inferior frontal gyrus [BA 44]		-36	-44	38	L	IPS [hIP1-3]
	44	4	42	R	Precentral gyrus, MFG		-56	-28	20	L	IPC [PFop, PFt]
290	44	28	-2	R	Inferior frontal gyrus [BA 45]		-62	-18	22	L	Parital operculum, SII [OP4, OP1]
				R	Anterior Insula		-20	0	54	L	Superior frontal gyrus
266	42	40	20	R	Middle frontal gyrus	460	38	-16	52	R	M1 [BA 4a, 4p]; SI [BA 3b, 2]; PMC [BA 6]
1,068	0	20	36	L/R	Middle cingulate cortex; Superior medial gyrus	305	60	-18	26	R	IPC [PFt, PFop, PF]; parietal operculum [OP1]
	0	10	62	L/R	SMA [BA 6]		58	-20	44	R	SI [BA 2, 1]
593	-26	-52	44	L	IPS [hIP3]	716	-6	-6	54	L	SMA [BA 6]
	-24	-74	44	L	SPL [7A, 7P]; superior occipital gyrus		12	-4	60	R	SMA [BA 6]
163	36	-58	54	R	SPL [7A]; IPS [hIP3]		-10	4	38	L	Middle cingulate cortex
174	-50	-50	6	L	Middle Temporal gyrus	233	-56	6	24	L	Inferior frontal gyurs [BA 44]; PMC [BA 6]
160	-34	-64	-24	L	Cerebellum [Lobule VI]; Fusiform gyrus	165	62	10	18	R	Inferior frontal gyrus [BA 44]; precentral gyrus

Results are cluster-level FWE corrected at $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$), $p<0.05$ (uncorrected) for contrast analysis; k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI/II: primary/secondary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-4 Resting-state connectivity of cortical and striatal seeds in manifest HD

	MNI co-ordinates						MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area	k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area
IFJ ∩ striatal seeds						***M1 ∩ striatal seeds***					
3,256	-32	20	0	L	Anterior insula	5,191	-4	-8	64	L	SMA [BA 6], Middle cingulate cortex
	-58	16	14	L	Inferior frontal gyrus, p.opercularis [BA 44]		8	-4	54	R	SMA [BA 6], Middle cingulate cortex
	-54	22	12	L	Inferior frontal gyrus, p.triangularis [BA 45]		-20	-12	64	L	Precentral gyrus, PMC [BA6]; M1 [4a]
	-44	34	-8	L	Inferior frontal gyrus, p.orbitalis		22	-20	64	R	Precentral gyrus, PMC [BA6]; M1 [4a,4p];SI [3b]
	-54	-2	44	L	Precentral gyrus, PMC [BA 6]	1,360	-58	10	16	L	Inferior frontal gyrus, p. opercularis [BA 44]
2,452	-4	8	54	L	SMA [BA 6]		-50	32	12	L	Inferior frontal gyrus, p. triangularis [BA 45]
	6	6	60	R	SMA [BA 6]		-54	-2	44	L	Precentral gyrus, PMC [BA 6]
	-2	26	40	L	Superior medial gyrus		-46	32	32	L	Middle frontal gyrus
	6	42	34	R	Superior medial gyrus	1,158	34	-14	10	R	Posterior Insula [Ig2, Ig1]
	12	12	34	R	Middle cingulate cortex		62	-16	2	R	Superior temporal gyrus
1,396	32	20	0	R	Anterior Insula		36	-12	4	R	Putamen
	56	2	44	R	Precentral gyrus, PMC [BA 6]		46	-20	10	R	Heschl's gyrus [TE 1.0,1.1,1.2,3]; SII [OP2,1]
	56	16	10	R	Inferior frontal gyrus, p. opercularis [BA 44]	954	-32	-22	10	L	Posterior Insula [Ig2, Ig1]
	58	24	2	R	Inferior frontal gyrus, p.triangularis [BA 45]		-32	4	-2	L	Putamen
	50	6	14	R	Rolandic operculum		-46	-34	14	L	IPC [PFcm]
411	-34	14	54	L	Middle frontal gyrus		-42	-20	14	L	Parietal operdulum,SII [OP1,2,3]
	-38	-10	56	L	Precentral gyrus, PMC [BA 6]	587	58	2	34	R	Precentral gyrus, PMC [BA6]
303	-18	-4	16	L	Thalamus [prefrontal]		60	2	38	R	Precentral gyrus
	-14	0	14	L	Caudate nucleus		56	6	14	R	Inferior frontal gyrus [BA 44]
	-18	8	0	L	Putamen	164	-20	-20	4	L	Thalamus
156	18	-2	16	R	Caudate nucleus	152	18	-18	2	R	Thalamus
						152	-60	-16	2	L	Superior temporal gyrus
							-58	-10	2	L	Heschl's gyrus [TE1.2,3]
						103	52	-18	60	R	Postcentral gyrus, SI [BA 1]
							46	-8	60	R	Precentral gyrus, PMC [BA6]
Contrast: IFJ ∩ striatum > M1 ∩ striatum						***Contrast: M1 ∩ striatum > IFJ ∩ striatum***					
1,269	-32	22	-2	L	Anterior insula	2,035	-20	-12	64	L/R	Precentral gyrus, PMC [BA 6],
	-54	22	12	L	Inferior frontal gyrus, p.triangularis [BA 45]		-10	-36	72	L/R	M1 [4a]; right M1 [4p], SI [3b]
	-52	16	10	L	Inferior frontal gyrus, p.opercularis [BA 44]		2	-14	56	L/R	SMA [BA 6]
	-44	34	-8	L	Inferior frontal gyrus, p.orbitalis	1086	34	-14	10	R	Posterior insula [Ig2,1]
866	40	24	-4	R	Anterior insula		62	-16	2	R	Superior temporal gyrus; SII [OP2,1]
	56	16	10	R	Inferior frontal gyrus, p. opercularis [BA 44]		68	-24	2	R	Heschl's gyrus [TE 1.0,1.1,1.2,3]
	58	24	2	R	Inferior frontal gyrus, p.triangularis [BA 45]		36	-8	2	R	Putamen
	54	32	-8	R	Inferior frontal gyrus, p.orbitalis	644	-32	-22	10	L	Insula [Ig1,2]
595	0	10	54	L	SMA [BA6]		-46	-34	14	L	IPC [PFcm]
	6	8	58	R	SMA [BA6]		-42	-20	14	L	Parietal operculum [OP1,2,3]
	0	32	38	L	Superior medial gyrus		-32	6	-2	L	Putamen
	8	12	44	R	Middle cingulate cortex	163	-20	-20	4	L	Thalamus [somatosensory, motor, premotor, prefrontal]
164	-14	0	14	L	Caudate nucleus						
	-22	-2	12	L	Putamen	152	18	-18	2	R	Thalamus [somatosensory, premotor, motor, prefrontal, parietal]
	-20	-12	20	L	Thalamus [prefrontal]						
124	18	-2	16	R	Caudate nucleus	152	-60	-16	2	L	Superior temporal gyrus
							-58	-10	2	L	Heschl's gyrus [TE1.2,3]
						106	-22	18	52	L	Superior frontal gyrus, Middle frontal gyrus

Results are cluster-level FWE corrected at $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$; for contrast analysis: masked with $p<0.05$, uncorrected); k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI/II: primary/secondary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-5 Conjunction between MACM and resting-state connectivity maps of cortical and striatal seeds in manifest HD

	MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic region
Manifest HD: IFJ ∩ striatal seeds					
217	-16	-6	18	L	Caudate nucleus
	-18	8	0	L	Putamen
77	16	-2	16	R	Caudate nucleus
1,334	-32	20	0	L	Anterior insula
	-56	14	12	L	Inferior frontal gyrus [BA 44]
	-48	24	12	L	Inferior frontal gyrus
	-54	-2	44	L	Precentral gyrus, PMC [BA 6]
561	54	16	10	R	Inferior frontal gyrus [BA 44]
	40	24	-4	R	Anterior insula
	52	2	42	R	Precentral gyrus
1,481	-4	8	54	L	SMA [BA 6]; middle cingulate cortex
	-2	26	40	L	Superior medial gyrus
	6	6	60	R	SMA [BA 6]; middle cingulate cortex
144	-38	-10	56	L	Precentral gyrus, PMC [BA 6]
				L	Middle frontal gyrus
Manifest HD: M1 ∩ striatal seeds					
107	-10	-20	-2	L	Thalamus [prefrontal, premotor, motor]
46	14	-18	4	R	Thalamus [prefrontal, premotor]
415	-36	-2	8	L	Insula
	-32	-8	2	L	Putamen
181	-58	10	18	L	Inferior frontal gyrus [BA 44]
171	56	6	14	R	Inferior frontal gyrus [BA 44]
	60	6	24	R	Precentral gyrus
1,032	-4	-8	64	L	SMA [BA 6]
	8	-4	58	R	SMA [BA 6]
	-4	24	42	L	Superior medial gyrus
325	-26	-16	66	L	Precentral gyrus, PMC [BA 6]
	-40	-16	50	L	Precentral gyrus; M1 [BA 4a]
	-26	-2	54	L	Middle frontal gyrus
215	-54	-2	44	L	Precentral gyrus, PMC [BA 6]

Results are cluster-level FWE corrected at $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$); k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI: primary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-6 Contrast maps between MOG-striatal and IFJ-striatal connectivity

	MNI co-ordinates						MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area	k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area
MACM: Contrast (MOG ∩ striatum) > (IFJ ∩ striatum)						***Resting-state connectivity: Contrast (MOG ∩ striatum) > (IFJ ∩ striatum)***					
783	32	-74	26	R	Middle occipital gyrus	207	-58	-34	46	L	IPC [PF,PFt]
224	-28	-82	32	L	Middle occipital gyrus	136	62	-26	34	R	IPC [PF,PFt]
						91	42	-2	52	R	Middle frontal gyrus
							48	4	50	R	Precentral gyrus
MACM: Contrast (MOG ∩ striatum) < (IFJ ∩ striatum)						***Resting-state connectivity: Contrast (MOG ∩ striatum) < (IFJ ∩ striatum)***					
1,038	-42	8	24	L	Inferior frontal gyrus, p. opercularis [BA 44]	2,274	-4	8	54	L	SMA [BA 6]
	-38	30	20	L	Inferior frontal gyrus, p. triangularis [BA 45]		6	6	60	R	SMA [BA 6]
				L	Precentral gyrus [BA 6]		-2	26	40	L	Superior medial gyrus
1,019	-22	4	6	L	Putamen; Pallidum		6	14	42	R	Middle cingulate cortex
	-44	20	0	L	Inferior frontal gyrus [BA 44, 45]	2,246	-32	20	0	L	Anterior insula
	-44	10	-8	L	Anterior insula		-58	16	14	L	Inferior frontal gyrus, p.opercularis [BA 44]
697	-30	-54	42	L	IPS [hIP3,2,1]		-54	22	12	L	Inferior frontal gyrus, p.triangularis [BA 45]
	-44	-36	46	L	IPC [PFt], BA2		-44	34	-8	L	Inferior frontal gyrus, p.orbitalis
	-16	-68	44	L	SPL [7A,7PC]	1,062	56	2	44	R	Precentral gyrus, PMC [BA 6]
653	34	20	-10	R	Anterior insula		56	16	10	R	Inferior frontal gyrus, p.opercularis [BA 44]
	22	6	8	R	Putamen					R	Inferior frontal gyrus, p.triangularis [BA 45]
	48	30	2	R	Inferior frontal gyrus, p. triangularis [BA 45]		36	18	0	R	Anterior insula
555	42	10	34	R	Inferior frontal gyrus, p. opercularis [BA 44]	303	-14	0	14	L	Caudate nucleus
					Precentral gyrus		-18	8	0	L	Putamen; Pallidum
524	2	22	40	L/R	Superior medial gyrus		-20	-12	20	L	Thalamus [prefrontal]
	12	12	60	R	SMA [BA 6]	211	-44	0	46	L	Precentral gyrus
	-8	14	56	L	SMA [BA 6]		-54	18	34	L	Inferior frontal gyrus, p.opercularis [BA 44]
	-6	28	28	L/R	Mid-cingulate cortex		-50	28	32	L	Inferior frontal gyrus, p.triangularis [BA 45]
392	12	-10	10	R	Thalamus [prefrontal, temporal];		-50	18	42	L	Middle frontal gyrus
					caudate nucleus	177	-56	-2	42	L	Precentral gyrus, PMC [BA 6]
171	-56	-44	8	L	Middle temporal gyrus	153	18	-2	16	R	Caudate nucleus
	-56	-42	16	L	Superior temporal gyrus		18	8	2	R	Pallidum
						144	-38	-10	56	L	Precentral gyrus, PMC [BA 6]
						96	-34	14	54	L	Middle frontal gyurs

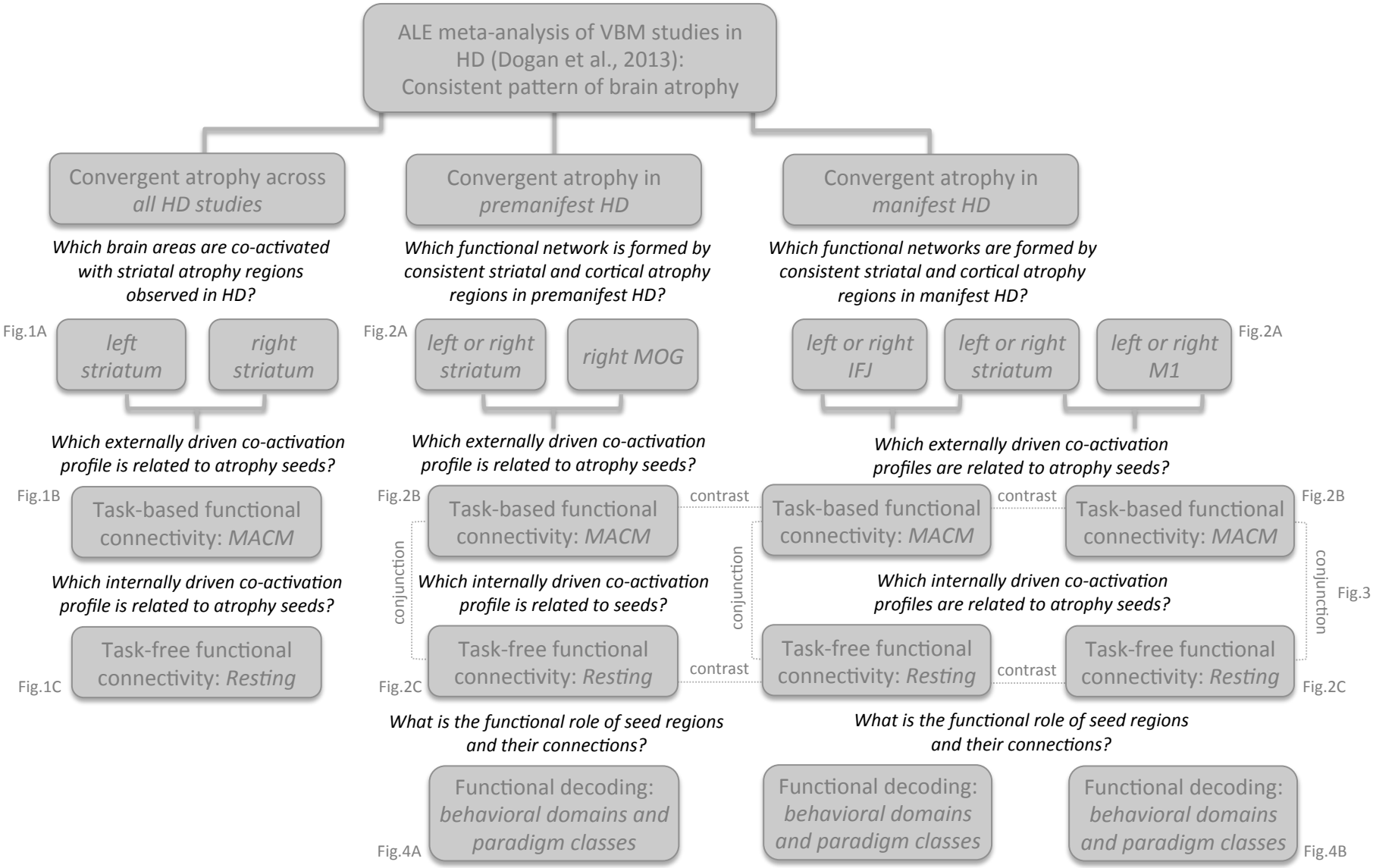
k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI: primary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Table S-7 Contrast maps between MOG-striatal and M1-striatal connectivity

	MNI co-ordinates						MNI co-ordinates				
k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area	k_E	x	y	z	Lat.	Macroanatomical and cytoarchitectonic area
MACM: Contrast (MOG ∩ striatum) > (M1 ∩ striatum)						***Resting-state connectivity: Contrast (MOG ∩ striatum) > (M1 ∩ striatum)***					
757	32	-74	26	R	Middle occipital gyrus	207	-58	-34	46	L	IPC [PF,PFt]
216	-28	-80	28	L	Middle occipital gyrus	136	62	-26	34	R	IPC [PF,PFt]
117	24	-60	48	R	SPL [7A]	103	42	-2	52	R	Middle frontal gyrus
113	-24	-62	54	L	SPL [7A]		48	4	50	R	Precentral gyrus
MACM: Contrast (MOG ∩ striatum) < (M1 ∩ striatum)						***Resting-state connectivity: Contrast (MOG ∩ striatum) < (M1 ∩ striatum)***					
1,834	-36	-44	38	L	IPS [hIP1-3]	4,959	-4	-8	64	L	SMA [BA 6], M1 [4a]
	-52	-26	32	L	IPC [PFt, PFop]		8	-4	58	R	SMA [BA 6], M1 [4a, 4p], SI [3b]
	-48	-24	22	L	Parietal operculum [OP1]		-8	-8	50	L	Middle cingulate cortex
	-26	-16	66	L	Precentral gyrus, PMC [BA6], M1 [4p,4a]	1,158	34	-14	10	R	Insula [Ig2, Ig1]
	-40	-44	60	L	Postcentral gyrus, SI [BA 2,3b,3a]		62	-16	2	R	Superior temporal gyrus
729	-26	2	4	L	Putamen		36	-8	2	R	Putamen
	-48	-2	10	L	Insula, rolandic operculum		68	-24	2	R	Heschl's g. [TE1.0,1.1,3], parietal operc. [OP2,1]
479	-4	-4	52	L	SMA [BA 6]	954	-36	-2	8	L	Insula [Ig2,Ig1]
	8	4	64	R	SMA [BA 6]		-46	-34	14	L	IPC [PFcm]
436	28	6	6	R	Putamen		-42	-20	14	L	Parietal operculum [OP1-3]
	36	20	-8	R	Insula		-20	10	-2	L	Putamen
394	40	-28	54	R	Postcentral gyrus, SI [BA 3b,2]	532	-58	10	16	L	Inferior frontal gyrus, p.opercularis [BA 44]
	46	-30	44	R	IPC [PFt]		-52	32	10	L	Inferior frontal gyrus, p.triangularis [BA 45]
	34	-22	52	R	Precentral gyrus, M1 [4p,4a]	431	58	2	34	R	Precentral gyrus, PMC [BA6]
	32	-16	52	R	Precentral gyrus, PMC [BA6]		56	6	14	R	Inferior frontal gyrus, p.opercularis [BA 44]
149	64	-22	18	R	Parietal operculum [OP1]	186	-56	-2	42	L	Precentral gyrus, PMC [BA6]
	64	-30	18	R	IPC [PF, PFop]	164	-20	-20	4	L	Thalamus
104	54	18	8	R	Inferior frontal gyrus, p.opercularis [BA 44]	152	18	-18	2	R	Thalamus
						152	-60	-16	2	L	Superior temporal gyrus
							-58	-10	2	L	Heschl's gyrus [TE1.2,3]
						113	-52	20	32	L	Inferior frontal gyrus [BA 44, 45]
							-46	32	30	L	Middle frontal gyrus
						97	52	-18	60	R	Postcentral gyrus, SI [BA 1]
							44	-6	58	R	Precentral gyurs, PMC [BA 6]

k_E: cluster extent; Lat.: laterality; L: left; R: right; BA: Brodmann Area; SI: primary somatosensory cortex; PMC: premotor cortex; SMA: supplementary motor area; M1: primary motor cortex; SI: primary somatosensory cortex; IPS: intraparietal sulcus; IPC: inferior parietal cortex; SPL: superior parietal lobule.

Figure S-1 – Overview on workflow with applied techniques and related research questions



Abbreviations: HD, Huntington's disease; ALE, anatomical likelihood estimation; VBM, voxel-based morphometry; MOG, middle occipital gyrus; IFJ, inferior frontal junctions; M1, primary motor cortex; MACM, meta-analytic connectivity modeling.

Figure S-2 – Functional characterization by behavioral domains and paradigm classes of premanifest and manifest atrophy seeds