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Data supplement

Table DS1 Cross-sectional voxel-based morphometry analysis of grey matter volume reductions in early at-risk mental state group (ARMS–E) *v.* control group, late at-risk mental state group (ARMS–L) *v.* control group and ARMS–E *v.* ARMS–L[a]

Region	Left *k* (%clust; %reg)	Right *k* (%clust; %reg)
T contrast: [controls>ARMS–E]		
Cluster 1: $k_c = 8404$, $P_{FWE} = 0.005$		
Temporal pole superior		95 (1.1; 0.9)
Temporal pole middle		118 (1.4; 1.2)
Temporal superior		153 (1.8; 0.6)
Parahippocampal		558 (6.6; 6.2)
Amygdala		730 (8.7; 36.8)
Temporal inferior		923 (11.0; 3.2)
Fusiform		1142 (13.6; 5.7)
Temporal middle		1293 (15.4; 3.7)
Hippocampus		1866 (22.2; 24.7)
Cluster 2: $k_c = 9418$, $P_{FWE} = 0.003$		
Amygdala	901 (9.6; 51.2)	
Hippocampus	266 (2.8; 3.6)	
Insula	140 (1.5; 0.9)	
Temporal inferior	3558 (37.8; 13.9)	
Temporal middle	1569 (16.7; 4.0)	
Temporal pole superior	95 (1.0; 0.9)	
Temporal superior	442 (4.7; 2.4)	
T contrast: [controls>ARMS–L]		
Cluster 1: $k_c = 126\,520$, $P_{FWE} < 0.001$		
Cingulum anterior	3265 (2.6; 29.2)	4482 (3.5; 42.7)
Cingulum middle	1005 (0.8; 6.5)	1224 (0.97; 7.0)
Frontal inferior opercular	2177 (1.7; 26.2)	98 (0.1; 0.9)
Frontal inferior orbital	3471 (2.7; 25.7)	1011 (0.8; 7.4)
Frontal inferior triangular	3457 (2.7; 17.1)	2796 (2.2; 16.3)
Frontal medial orbital	3719 (2.9; 64.7)	4666 (3.7; 68.1)
Frontal middle	8239 (6.5; 21.2)	12971 (10.3; 31.8)
Frontal middle orbital	2632 (2.1; 37.1)	3414 (2.7; 42.0)
Frontal superior	5465 (4.3; 19.0)	
Frontal superior medial	16786 (13.3; 70.1)	11329 (9.0; 66.4)
Frontal superior orbital	2238 (1.8; 29.1)	3129 (2.47; 39.2)
Insula	3040 (2.4; 20.5)	
Olfactory	162 (0.1;7.2)	111 (0.1;4.8)
Precentral	1477 (1.2; 5.2)	40 (0.0; 0.2)
Rectus	3684 (2.9; 54.1)	
Rolandic opercular	56 (0.0; 0.7)	
Supplementary motor area	3589 (2.8; 20.9)	2854 (2.3; 15.1)
Cluster 2: $k_c = 5832$, $P_{FWE} = 0.037$		
Postcentral	285 (4.9; 0.9)	
Supramarginal	239 (4.1; 2.4)	
Temporal middle	2818 (48.3; 7.1)	
Temporal superior	2414 (41.4; 13.1)	
Cluster 3: $k_c = 7409$, $P_{FWE} = 0.011$		
Amygdala		168 (2.3; 8.5)
Fusiform		2357 (31.8; 11.7)
Hippocampus		1847 (24.9; 24.4)
Parahippocampal		2691 (36.3; 29.7)
Cluster 4: $k_c = 7838$, $P_{FWE} = 0.008$		
Cingulum anterior		32 (0.4; 0.3)
Olfactory		281 (3.6; 12.2)
Caudate	1705 (21.8; 22.2)	1464 (18.7; 18.4)
Thalamus	120 (1.5; 1.4)	
Cluster 5: $k_c = 5513$, $P_{FWE} = 0.047$		
Paracentral lobule		57 (1.0; 0.9)
Parietal superior		3160 (57.3; 17.8)
Postcentral		1160 (21.0; 3.8)
Precuneus		1030 (18.7; 3.9)

(continued)

Table DS1 *(continued)*

Region	Left *k* (%clust; %reg)	Right *k* (%clust; %reg)
T contrast: [ARMS–E>ARMS–L]		
Cluster 1: $k_c = 9214$, $P_{FWE} = 0.003$		
Frontal inferior orbital	256 (2.8; 1.9)	
Frontal inferior triangular	674 (7.3; 3.3)	
Frontal middle	5783 (62.8; 14.9)	
Frontal middle orbital	1307 (14.2; 18.4)	
Frontal superior	867 (9.4; 3.0)	
Frontal superior orbital	317 (3.4; 4.1)	
Cluster 2: $k_c = 18\,558$, $P_{FWE} < 0.001$		
Cingulum anterior	1294 (7.0; 11.6)	1263 (6.8; 12.0)
Cingulum middle		70 (0.4; 0.4)
Frontal inferior orbital		24 (0.1; 0.2)
Frontal medial orbital		1822 (9.8; 26.6)
Frontal middle orbital	236 (1.3; 3.3)	
Frontal superior	413 (2.2; 1.4)	60 (0.3; 0.2)
Frontal superior medial	4454 (24; 18.6)	1746 (9.4; 10.2)
Frontal superior orbital	465 (2.5; 6.0)	1196 (6.4; 15.0)
Rectus	795 (4.3; 11.7)	752 (4.1; 12.6)
Supplementary motor area	134 (0.7; 0.8)	
Cluster 3: $k_c = 9377$, $P_{FWE} = 0.003$		
Frontal inferior triangular		425 (4.5; 2.5)
Frontal middle		5364 (57.2; 13.1)
Frontal superior		3575 (38.1; 11.0)

a. Clusters were characterised by their extent (k_c) and significance (P_{FWE}), corrected for non-stationarity. For anatomical regions within clusters, the number of voxels (*k*), the percentage of the cluster covered by the region (%clust) and the percentage of the region covered by the cluster (%reg) were reported. For additional information (effects sizes, percentage differences) see Table DS2.

Table DS2 Cross-sectional voxel-based morphometry analysis of grey matter volume reductions in the early at-risk mental state group (ARMS–E) *v.* control group, late at-risk mental state group (ARMS–L) *v.* control group and ARMS–E *v.* ARMS–L[a]

	Left hemisphere			Right hemisphere		
Regions	*t*-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)	*t*-value, maximum; mean (s.d.)	Cohen's *D* maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)
T contrast: [controls>ARMS–E]						
Cluster 1: $k_c = 8404$, $P_{FWE} = 0.005$						
Amygdala				3.30; 2.69 (0.22)	0.61; 0.50 (0.50)	5.0; 4.1 (0.5)
Fusiform				3.80; 2.87 (0.35)	0.70; 0.53 (0.53)	5.2; 4.3 (0.5)
Hippocampus				3.70; 2.91 (0.31)	0.69; 0.54 (0.54)	5.9; 4.4 (0.8)
Parahippocampal				3.50; 2.86 (0.30)	0.65; 0.53 (0.53)	5.4; 4.1 (0.6)
Temporal inferior				3.36; 2.76 (0.27)	0.62; 0.51 (0.51)	5.7; 4.5 (0.5)
Temporal middle				3.56; 2.77 (0.29)	0.66; 0.51 (0.51)	6.4; 4.7 (0.6)
Temporal pole middle				2.93; 2.55 (0.14)	0.54; 0.47 (0.47)	4.6; 4.2 (0.2)
Temporal pole superior				3.20; 2.58 (0.18)	0.59; 0.48 (0.48)	5.2; 3.8 (0.5)
Temporal superior				3.42; 2.70 (0.26)	0.63; 0.50 (0.50)	4.7; 3.4 (0.5)
Cluster 2: $k_c = 9418$; $P_{FWE} = 0.003$						
Amygdala	3.80; 2.87 (0.33)	0.65; 0.54 (0.06)	5.5; 4.3 (0.6)			
Hippocampus	3.56; 2.89 (0.31)	0.64; 0.51 (0.05)	5.3; 4.0 (0.5)			
Insula	3.71; 2.97 (0.39)	0.63; 0.50 (0.05)	4.6; 3.6 (0.5)			
Temporal inferior	3.85; 2.80 (0.3)	0.70; 0.51 (0.05)	5.7; 4.4 (0.6)			
Temporal middle	3.80; 2.82 (0.33)	0.60; 0.50 (0.04)	5.6; 4.2 (0.5)			
Temporal pole superior	3.73; 2.82 (0.29)	0.57; 0.49 (0.04)	4.1; 3.1 (0.3)			
Temporal superior	3.72; 2.90 (0.32)	0.65; 0.52 (0.05)	4.2; 3.2 (0.4)			
T contrast: [controls>ARMS–L]						
Cluster 1: $k_c = 126520$, $P_{FWE} < 0.001$						
Cingulum anterior	4.81; 2.95 (0.43)	0.74; 0.54 (0.06)	6.6; 4.4 (0.8)	4.77; 2.96 (0.43)	0.80; 0.56 (0.56)	6.7; 4.5 (0.8)
Cingulum middle	4.46; 2.95 (0.44)	0.72; 0.51 (0.06)	5.7; 3.5 (0.6)	4.43; 2.93 (0.44)	0.79; 0.55 (0.55)	5.5; 3.7 (0.6)
Frontal inferior opercular	4.60; 2.90 (0.39)	0.67; 0.51 (0.06)	7.1; 3.5 (0.8)	4.32; 2.92 (0.42)	0.62; 0.50 (0.50)	3.8; 3.1 (0.4)
Frontal inferior orbital	4.22; 2.92 (0.41)	0.75; 0.51 (0.06)	3.9; 2.9 (0.3)	4.14; 2.94 (0.41)	0.61; 0.49 (0.49)	3.8; 3.0 (0.4)
Frontal inferior triangular	4.59; 2.93 (0.39)	0.70; 0.52 (0.06)	5.7; 3.1 (0.5)	4.82; 2.95 (0.41)	0.81; 0.54 (0.54)	5.0; 3.2 (0.7)
Frontal medial orbital	4.18; 2.89 (0.38)	0.82; 0.58 (0.09)	5.4; 4.1 (0.7)	4.23; 2.91 (0.39)	0.79; 0.54 (0.54)	5.3; 3.9 (0.7)
Frontal middle	4.78; 2.94 (0.44)	0.83; 0.53 (0.07)	5.2; 3.1 (0.5)	4.81; 2.94 (0.43)	0.90; 0.55 (0.55)	5.8; 3.4 (0.6)
Frontal middle orbital	4.10; 2.87 (0.39)	0.73; 0.52 (0.06)	4.3; 2.9 (0.3)	4.13; 2.87 (0.39)	0.74; 0.55 (0.55)	4.6; 3.2 (0.5)
Frontal superior	4.51; 2.91 (0.41)	0.74; 0.51 (0.06)	5.3; 3.3 (0.6)	4.65; 2.96 (0.44)	0.77; 0.53 (0.53)	5.2; 3.5 (0.5)
Frontal superior medial	4.87; 2.95 (0.44)	0.90; 0.57 (0.09)	6.3; 3.8 (0.7)	4.72; 2.94 (0.42)	0.79; 0.56 (0.56)	6.2; 3.6 (0.7)
Frontal superior orbital	3.97; 2.88 (0.36)	0.66; 0.50 (0.05)	4.9; 3.2 (0.6)	4.14; 2.91 (0.38)	0.72; 0.54 (0.54)	4.7; 3.3 (0.5)
Insula	3.97; 2.80 (0.34)	0.68; 0.52 (0.06)	4.6; 3.4 (0.5)			
Olfactory	3.71; 3.10 (0.43)	0.56; 0.48 (0.03)	3.3; 2.9 (0.2)	3.76; 2.90 (0.45)	0.53; 0.46 (0.46)	3.3; 2.8 (0.2)
Precentral	4.13; 2.89 (0.37)	0.70; 0.53 (0.07)	7.1; 3.7 (1.0)	3.29; 2.71 (0.33)	0.52; 0.47 (0.47)	4.5; 3.9 (0.4)
Rectus	4.13; 2.85 (0.36)	0.78; 0.55 (0.07)	4.8; 3.3 (0.5)	4.16; 2.85 (0.36)	0.78; 0.56 (0.56)	4.7; 3.1 (0.5)
Rolandic opercular	3.53; 2.84 (0.32)	0.48; 0.45 (0.01)	3.3; 2.8 (0.1)			
Supplementary motor area	4.52; 2.98 (0.45)	0.75; 0.53 (0.07)	6.0; 3.9 (0.7)	4.56; 2.92 (0.41)	0.65; 0.50 (0.50)	5.5; 3.8 (0.5)
Cluster 2: $k_c = 5832$, $P_{FWE} = 0.037$						
Postcentral	3.94; 2.99 (0.42)	0.53; 0.47 (0.02)	2.8; 2.6 (0.1)			
Supramarginal	3.86; 2.90 (0.36)	0.55; 0.47 (0.03)	3.0; 2.7 (0.2)			
Temporal middle	3.63; 2.76 (0.28)	0.88; 0.60 (0.12)	9.7; 5.1 (1.7)			
Temporal superior	3.97; 2.86 (0.36)	0.73; 0.53 (0.07)	4.7; 3.4 (0.5)			
Cluster 3: $k_c = 7409$, $P_{FWE} = 0.011$						
Amygdala				3.08; 2.62 (0.18)	0.57; 0.49 (0.49)	4.2; 3.5 (0.3)
Fusiform				3.77; 2.85 (0.34)	0.7; 0.53 (0.53)	4.8; 3.5 (0.5)
Hippocampus				3.79; 2.75 (0.25)	0.71; 0.51 (0.51)	4.6; 3.7 (0.5)
Parahippocampal				3.97; 2.93 (0.41)	0.74; 0.54 (0.54)	4.7; 3.6 (0.4)
Cluster 4: k_c=7838, $P_{FWE} = 0.008$						
Caudate	4.08; 2.91 (0.39)	0.67; 0.53 (0.06)	5.6; 4.3 (0.7)	4.16; 2.94 (0.4)	0.67; 0.51 (0.51)	5.1; 4.1 (0.5)
Cingulum anterior				2.95; 2.64 (0.2)	0.56; 0.48 (0.48)	3.2; 2.8 (0.1)
Olfactory	3.56; 2.76 (0.25)	0.58; 0.48 (0.03)	4.1; 3.5 (0.4)	3.85; 2.79 (0.32)	0.64; 0.52 (0.52)	4.5; 3.5 (0.4)
Thalamus	3.75; 2.83 (0.34)	0.60; 0.49 (0.04)	4.5; 3.7 (0.4)			
Cluster 5: $k_c = 5513$, $P_{FWE} = 0.047$						
Paracentral lobule				3.19; 2.79 (0.22)	0.51; 0.47 (0.47)	3.4; 3.1 (0.2)
Parietal superior				3.76; 2.77 (0.29)	0.66; 0.50 (0.50)	4.6; 3.2 (0.3)
Postcentral				3.86; 2.84 (0.32)	0.57; 0.48 (0.48)	4.8; 3.4 (0.6)
Precuneus				3.68; 2.74 (0.27)	0.64; 0.50 (0.50)	3.6; 3.0 (0.3)

(continued)

Table DS2 *(continued)*

Regions	Left hemisphere			Right hemisphere		
	t-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)	*t*-value, maximum; mean (s.d.)	Cohen's *D* maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)
T contrast: [ARMS–E>ARMS–L]						
Cluster 1: $k_c = 9214$, $P_{FWE} = 0.003$						
Frontal inferior orbital	3.11; 2.54 (0.15)	0.58; 0.49 (0.04)	3.9; 3.3 (0.3)			
Frontal inferior triangular	3.45; 2.67 (0.23)	0.68; 0.52 (0.07)	6.6; 4.8 (1.1)			
Frontal middle	3.58; 2.74 (0.26)	0.78; 0.53 (0.08)	6.6; 4.4 (0.9)			
Frontal middle orbital	3.11; 2.57 (0.15)	0.64; 0.51 (0.05)	5.6; 3.8 (0.6)			
Frontal superior	3.45; 2.75 (0.26)	0.70; 0.50 (0.06)	6.0; 3.9 (0.9)			
Frontal superior orbital	2.94; 2.53 (0.14)	0.67; 0.52 (0.06)	5.7; 4.6 (0.5)			
Cluster 2: $k_c = 18558$, $P_{FWE} < 0.001$						
Cingulum anterior	3.55; 2.74 (0.27)	0.66; 0.51 (0.05)	8.7; 6.0 (1.1)	3.57; 2.84 (0.30)	0.66; 0.53 (0.53)	8.7; 5.8 (1.1)
Cingulum middle	2.41; 2.39 (0.02)	0.45; 0.44 (0.00)	3.9; 3.8 (0.1)	2.61; 2.46 (0.07)	0.49; 0.46 (0.46)	4.0; 3.5 (0.2)
Frontal inferior orbital	2.58; 2.47 (0.06)	0.48; 0.46 (0.01)	3.8; 3.6 (0.2)	2.62; 2.48 (0.08)	0.49; 0.46 (0.46)	4.0; 3.6 (0.2)
Frontal medial orbital	4.06; 2.97 (0.41)	0.75; 0.55 (0.08)	6.5; 5.1 (0.7)	3.62; 2.78 (0.31)	0.67; 0.52 (0.52)	6.4; 4.7 (0.7)
Frontal middle orbital	2.98; 2.58 (0.15)	0.55; 0.48 (0.03)	4.9; 4.0 (0.4)	3.53; 2.79 (0.28)	0.66; 0.52 (0.52)	5.3; 4.2 (0.5)
Frontal superior	3.04; 2.62 (0.16)	0.57; 0.49 (0.03)	5.0; 4.1 (0.4)	2.64; 2.47 (0.08)	0.49; 0.46 (0.46)	5.3; 4.1 (0.5)
Frontal superior medial	3.81; 2.75 (0.32)	0.71; 0.51 (0.06)	8.1; 4.7 (1.0)	3.36; 2.57 (0.16)	0.62; 0.48 (0.48)	7.7; 4.5 (0.8)
Frontal superior orbital	3.39; 2.63 (0.22)	0.63; 0.49 (0.04)	5.4; 3.9 (0.5)	3.49; 2.73 (0.23)	0.65; 0.51 (0.51)	6.3; 4.1 (0.5)
Rectus	3.19; 2.63 (0.18)	0.59; 0.49 (0.03)	5.4; 3.9 (0.6)	3.25; 2.60 (0.19)	0.61; 0.48 (0.48)	5.2; 3.4 (0.5)
Supplementary motor area	2.66; 2.44 (0.06)	0.49; 0.45 (0.01)	4.8; 3.8 (0.3)			
Cluster 3: $k_c = 9377$, $P_{FWE} = 0.003$						
Frontal inferior triangular				3.51; 2.72 (0.26)	0.68; 0.51 (0.51)	5.2; 4.0 (0.4)
Frontal middle				3.53; 2.63 (0.21)	0.65; 0.48 (0.48)	4.8; 3.7 (0.4)
Frontal superior				3.11; 2.57 (0.17)	0.53; 0.47 (0.47)	3.4; 3.0 (0.2)

a. Significant clusters were additionally characterised by the maximum; mean (s.d.) of *t*-values, effect sizes (Cohen's *D*) and percentage differences computed for the portions of the anatomical regions occupied by the clusters.

Table DS3 Cross-sectional voxel-based morphometry analysis of grey matter volume reductions in at-risk mental state group without subsequent disease transition (ARMS–NT) *v.* control group, at-risk mental state group with subsequent transition to psychosis (ARMS–T) *v.* control group and ARMS–T *v.* ARMS–NT[a]

Region	Left *k* (%clust; %reg)	Right *k* (%clust; %reg)
T contrast: [controls > ARMS–NT]		
Cluster 1: $k_c = 10\,925$, $P_{FWE} = 0.001$		
Frontal inferior opercular	395 (3.6; 4.8)	
Frontal inferior triangular	744 (6.8; 3.7)	
Frontal middle	3941 (36.1; 10.1)	
Frontal superior	187 (1.7; 0.7)	
Parietal inferior	16 (0.2; 0.1)	
Postcentral	3837 (35.1; 12.3)	
Precentral	1766 (16.2; 6.3)	
Cluster 2: $k_c = 20\,174$, $P_{FWE} < 0.001$		
Frontal inferior opercular		252 (1.3; 2.3)
Frontal inferior triangular		98 (0.5; 0.6)
Frontal middle		7379 (36.6; 18.1)
Frontal superior		2665 (13.2; 8.2)
Postcentral		2591 (12.8; 8.5)
Precentral		6139 (30.4; 22.7)
Supplementary motor area		693 (3.4; 3.7)
Supramarginal		308 (1.5; 2.0)
Cluster 3: $k_c = 22\,017$, $P_{FWE} < 0.001$		
Amygdala		1127 (5.1; 56.8)
Fusiform		2402 (10.9; 11.9)
Heschl		36 (0.2; 1.8)
Hippocampus		1745 (7.9; 23.1)
Insula		43 (0.2; 0.3)
Lingual		661 (3.0; 3.6)
Parahippocampal		2312 (10.5; 25.5)
Putamen		10 (0.1; 0.1)
Temporal inferior		3992 (18.1; 14.0)
Temporal middle		4180 (19.0; 11.9)
Temporal pole middle		153 (0.7; 1.6)
Temporal pole superior		185 (0.8; 1.7)
Temporal superior		3034 (13.8; 12.1)
T contrast: [controls > ARMS–T]		
Cluster 1: $k_c = 124\,078$, $P_{FWE} < 0.001$		
Caudate	388 (0.3; 5.0)	179 (0.1; 2.3)
Cingulum anterior	4753 (3.8; 42.4)	6399 (5.2; 60.9)
Cingulum middle	778 (0.6; 5.0)	796 (0.6; 4.5)
Frontal inferior opercular		109 (0.1; 1.0)
Frontal inferior orbital	894 (0.7; 6.6)	1106 (0.9; 8.1)
Frontal inferiortriangular	1780 (1.4; 8.8)	3131 (2.5; 18.2)
Frontal medial orbital	4356 (3.5; 75.7)	5377 (4.3; 78.5)
Frontal middle	6060 (4.9; 15.6)	11624 (9.4; 28.5)
Frontal middle orbital	2021 (1.6; 28.5)	3107 (2.5; 38.3)
Frontal superior	7733 (6.2; 26.9)	9392 (7.6; 28.9)
Frontal superior medial	15845 (12.8; 66.2)	13185 (10.6; 77.2)
Frontal superior orbital	2937 (2.4; 38.1)	2756 (2.2; 34.6)
Olfactory		152 (0.1; 6.6)
Paracentral lobule	555 (0.5; 5.1)	
Postcentral	1987 (1.6; 6.4)	
Precentral	2393 (1.9; 8.5)	613 (0.5; 2.3)
Rectus	2887 (2.3; 42.4)	2885 (2.3; 48.4)
Supplementary motor area	2957 (2.4; 17.2)	1908 (1 .5; 10.1)
T contrast: [ARMS–NT > ARMS–T]		
Cluster 1: $k_c = 34\,146$, $P_{FWE} < 0.001$		
Cingulum anterior	2592 (7.6; 23.1)	3100 (9.1; 29.5)
Cingulum middle	34 (0.1; 0.2)	122 (0.4; 0.7)
Frontal inferior orbital		135 (0.4; 1.0)
Frontal inferior triangular	92 (0.27; 0.6)	
Frontal medial orbital	2289 (6.7; 39.8)	2349 (6.9; 34.3)
Frontal middle	1402 (4.1; 3.6)	1159 (3.4; 2.8)
Frontal middle orbital	136 (0.4; 1.9)	750 (2.2; 9.2)
Frontal superior	1998 (5.85; 6.9)	2559 (7.49; 7.9)
Frontal superior medial	7008 (20.5; 29.3)	5947 (17.4; 34.8)
Frontal superior orbital	1163(3.4; 15.1)	744 (2.18; 9.3)
Rectus	192 (0.6; 2.8)	231 (0.7; 3.9)

a. Clusters were characterised by their extent (k_c) and significance (P_{FWE}), corrected for non-stationarity. For anatomical regions within clusters, the number of voxels (*k*), the percentage of the cluster covered by the region (%clust) and the percentage of the region covered by the cluster (%reg) were reported. For additional information (effects sizes, percentage differences) see Table DS4.

Table DS4 Cross-sectional voxel-based morphometry analysis of grey matter volume reductions in at-risk mental state group without subsequent disease transition (ARMS–NT) *v.* control group, at-risk mental state group with subsequent disease transition (ARMS–T) *v.* control group and ARMS–NT *v.* ARMS–T[a]

	Left hemisphere			Right hemisphere		
Regions	*t*-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)	*t*-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)
T contrast: [controls > ARMS–NT]						
Cluster 1: $k_c = 10\,925$, $P_{FWE} < 0.001$						
Frontal inferior opercular	4.15; 2.93 (0.47)	0.62; 0.54 (0.04)	4.1; 3.5 (0.3)			
Frontal inferior triangular	4.37; 2.92 (0.49)	0.73; 0.56 (0.07)	4.6; 3.6 (0.5)			
Frontal middle	4.66; 2.90 (0.44)	0.72; 0.53 (0.05)	7.5; 3.9 (1.1)			
Frontal superior	4.60; 3.01 (0.59)	0.65; 0.55 (0.05)	7.4; 5.9 (0.9)			
Parietal inferior	2.92; 2.77 (0.13)	0.49; 0.48 (0.01)	3.6; 3.3 (0.2)			
Postcentral	4.56; 2.81 (0.39)	1.01; 0.61 (0.12)	5.6; 3.8 (0.7)			
Precentral	4.65; 2.89 (0.48)	0.84; 0.53 (0.06)	4.8; 3.5 (0.5)			
Cluster 2: $k_c = 20\,174$, $P_{FWE} < 0.001$						
Frontal inferior opercular				3.84; 2.85 (0.37)	0.52; 0.49 (0.49)	4.3; 3.1 (0.3)
Frontal inferior triangular				3.39; 2.76 (0.29)	0.56; 0.50 (0.50)	3.2; 2.7 (0.2)
Frontal middle				4.65; 2.94 (0.48)	0.82; 0.58 (0.58)	10.3; 4.3 (1.3)
Frontal superior				4.41; 2.94 (0.45)	0.77; 0.55 (0.55)	7.9; 4.9 (0.9)
Postcentral				4.63; 2.91 (0.46)	0.73; 0.57 (0.57)	6.6; 4.2 (0.9)
Precentral				4.66; 2.93 (0.45)	1.01; 0.62 (0.62)	10.4; 4.9 (1.5)
Supplementary motor area				3.94; 2.87 (0.36)	0.55; 0.50 (0.50)	5.7; 5.0 (0.4)
Supramarginal				3.23; 2.58 (0.16)	0.66; 0.54 (0.54)	6.3; 4.3 (1.1)
Cluster 3: $k_c = 22\,017$, $P_{FWE} < 0.001$						
Amygdala				3.84; 3.06 (0.38)	0.76; 0.60 (0.60)	5.7; 4.5 (0.6)
Fusiform				4.66; 3.04 (0.55)	0.92; 0.60 (0.60)	7.2; 4.7 (1.1)
Heschl				2.70; 2.49 (0.10)	0.53; 0.49 (0.49)	3.6; 3.1 (0.3)
Hippocampus				3.69; 2.69 (0.25)	0.73; 0.53 (0.53)	5.4; 4.1 (0.7)
Insula				2.92; 2.52 (0.13)	0.57; 0.50 (0.50)	3.7; 3.3 (0.3)
Lingual				3.56; 2.77 (0.29)	0.70; 0.55 (0.55)	5.2; 4.1 (0.6)
ParaHippocampal				4.14; 2.82 (0.36)	0.82; 0.56 (0.56)	6.2; 3.9 (0.7)
Putamen				2.53; 2.44 (0.05)	0.50; 0.48 (0.48)	4.0; 3.9 (0.1)
Temporal inferior				3.77; 2.75 (0.28)	0.74; 0.54 (0.54)	5.9; 4.4 (0.6)
Temporal middle				4.35; 2.88 (0.47)	0.86; 0.57 (0.57)	8.1; 4.8 (1.1)
Temporal pole middle				3.44; 2.76 (0.32)	0.68; 0.54 (0.54)	6.1; 4.7 (0.6)
Temporal pole superior				3.55; 2.62 (0.28)	0.70; 0.52 (0.52)	6.1; 3.9 (0.6)
Temporal superior				4.41; 2.84 (0.44)	0.87; 0.56 (0.56)	7.1; 4.0 (0.9)
T contrast: [controls>ARMS–T]						
Cluster 1: $k_c = 124\,078$, $P_{FWE} < 0.001$						
Caudate	2.97; 2.56 (0.13)	0.59; 0.5 (0.03)	5.7; 4.8 (0.6)	2.87; 2.50 (0.10)	0.56; 0.49 (0.49)	5.0; 4.4 (0.3)
Cingulum anterior	4.30; 3.07 (0.41)	0.85; 0.6 (0.08)	8.5; 5.8 (1.0)	5.22; 3.38 (0.70)	1.03; 0.67 (0.67)	10.2; 6.5 (1.5)
Cingulum middle	3.06; 2.61 (0.15)	0.60; 0.52 (0.03)	5.1; 4.2 (0.3)	4.37; 2.92 (0.54)	0.86; 0.58 (0.58)	6.0; 4.4 (0.6)
Frontal inferior opercular				2.98; 2.63 (0.17)	0.59; 0.52 (0.52)	4.7; 3.7 (0.5)
Frontal inferior orbital	3.06; 2.58 (0.16)	0.60; 0.51 (0.03)	4.5; 3.4 (0.4)	3.39; 2.64 (0.20)	0.67; 0.52 (0.52)	4.7; 3.7 (0.5)
Frontal inferior triangular	3.43; 2.68 (0.25)	0.68; 0.53 (0.05)	5.5; 3.9 (0.7)	4.50; 2.91 (0.41)	0.89; 0.57 (0.57)	8.3; 4.5 (1.4)
Frontal medial orbital	4.25; 3.13 (0.45)	0.84; 0.62 (0.09)	7.8; 5.1 (0.8)	4.37; 3.01 (0.39)	0.86; 0.59 (0.59)	7.4; 5.1 (0.9)
Frontal middle	4.45; 2.79 (0.39)	0.88; 0.55 (0.08)	6.2; 3.9 (0.6)	4.90; 3.02 (0.51)	0.97; 0.60 (0.60)	8.4; 4.5 (1.0)
Frontal middle orbital	3.31; 2.66 (0.20)	0.65; 0.52 (0.04)	5.2; 3.5 (0.4)	4.02; 2.93 (0.40)	0.79; 0.58 (0.58)	7.0; 4.0 (0.7)
Frontal superior	4.61; 2.82 (0.35)	0.91; 0.56 (0.07)	7.1; 4.3 (0.7)	4.69; 2.91 (0.47)	0.92; 0.57 (0.57)	7.8; 4.5 (0.8)
Frontal superior medial	4.88; 3.17(0.53)	0.96; 0.62 (0.1)	8.1; 5.0 (1.1)	5.15; 3.25 (0.55)	1.01; 0.64 (0.64)	9.0; 5.1 (1.1)
Frontal superior orbital	3.70; 2.77 (0.30)	0.73; 0.55 (0.06)	6.6; 4.2 (0.8)	4.20; 2.92 (0.44)	0.83; 0.58 (0.58)	7.1; 4.4 (1.0)
Olfactory				2.92; 2.56 (0.14)	0.58; 0.50 (0.50)	5.2; 4.0 (0.4)
Paracentral lobule	3.35; 2.76 (0.25)	0.66; 0.54 (0.05)	7.9; 6.7 (0.6)			
Postcentral	3.83; 2.90 (0.36)	0.75; 0.57 (0.07)	5.5; 4.1 (0.6)			
Precentral	3.83; 2.78 (0.30)	0.75; 0.55 (0.06)	7.7; 5.3 (1.2)	2.99; 2.54 (0.13)	0.59; 0.50 (0.50)	6.9; 5.5 (0.6)
Rectus	3.97; 2.80 (0.35)	0.78; 0.55 (0.07)	5.4; 3.9 (0.5)	4.29; 2.94 (0.41)	0.84; 0.58 (0.58)	5.4; 3.7 (0.6)
Supplementary motor area	3.32; 2.67 (0.22)	0.65; 0.53 (0.04)	7.7; 4.7 (0.8)	3.37; 2.66 (0.21)	0.66; 0.52 (0.52)	7.7; 5.1 (0.9)

Table DS4 *(continued)*

Regions	Left hemisphere			Right hemisphere		
	t-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)	*t*-value, maximum; mean (s.d.)	Cohen's *D*, maximum; mean (s.d.)	Difference, %: maximum; mean (s.d.)
T contrast: [ARMS–NT>ARMS–T]						
Cluster 1: $k_c = 34146$, $P_{FWE}<0.001$						
Cingulum anterior	3.94; 2.88 (0.37)	0.78; 0.57 (0.07)	10.4; 7.2 (1.5)	4.37; 3.15 (0.49)	0.86; 0.62 (0.62)	10.6; 7.8 (1.4)
Cingulum middle	2.53; 2.42 (0.04)	0.50; 0.48 (0.01)	5.2; 4.7 (0.2)	3.18; 2.69 (0.24)	0.63; 0.53 (0.53)	5.7; 4.5 (0.4)
Frontal inferior orbital	3.40; 2.78 (0.29)	0.67; 0.55 (0.55)	6.0; 5.0 (0.6)			
Frontal inferior triangular	2.59; 2.44 (0.05)	0.51; 0.48 (0.01)	6.8; 5.0 (0.9)			
Frontal medial orbital	4.57; 3.00 (0.44)	0.90; 0.59 (0.09)	9.1; 6.1 (0.9)	3.55; 2.76 (0.24)	0.70; 0.54 (0.54)	7.6; 5.7 (0.8)
Frontal middle	3.73; 2.67 (0.30)	0.74; 0.53 (0.06)	6.8; 4.8 (0.6)	3.45; 2.66 (0.21)	0.68; 0.52 (0.52)	7.2; 5.0 (0.7)
Frontal middle orbital	2.84; 2.52 (0.13)	0.56; 0.50 (0.03)	5.5; 4.5 (0.3)	3.40; 2.65 (0.19)	0.67; 0.52 (0.52)	6.1; 4.6 (0.5)
Frontal superior	4.31; 2.78 (0.37)	0.85; 0.55 (0.07)	8.1; 5.2 (0.8)	4.05; 2.77 (0.37)	0.80; 0.55 (0.55)	7.8; 5.2 (0.8)
Frontal superior medial	4.25; 3.02 (0.46)	0.84; 0.59 (0.09)	10.3; 6.3 (1.4)	4.27; 2.95 (0.39)	0.84; 0.58 (0.58)	9.5; 6.1 (1.2)
Frontal superior orbital	4.55; 2.82 (0.48)	0.90; 0.56 (0.09)	8.5; 5.1 (1.1)	3.24; 2.68 (0.19)	0.64; 0.53 (0.53)	7.2; 5.1 (0.7)
Rectus	2.68; 2.45 (0.06)	0.53; 0.48 (0.01)	6.1; 4.5 (0.6)	2.93; 2.56 (0.13)	0.58; 0.50 (0.5)	6.0; 4.5 (0.6)

a. Significant clusters were additionally characterised by the maximum, mean (s.d.) of *t*-values, effect sizes (Cohen's *D*) and percentage differences computed for the portions of the anatomical regions occupied by the clusters.

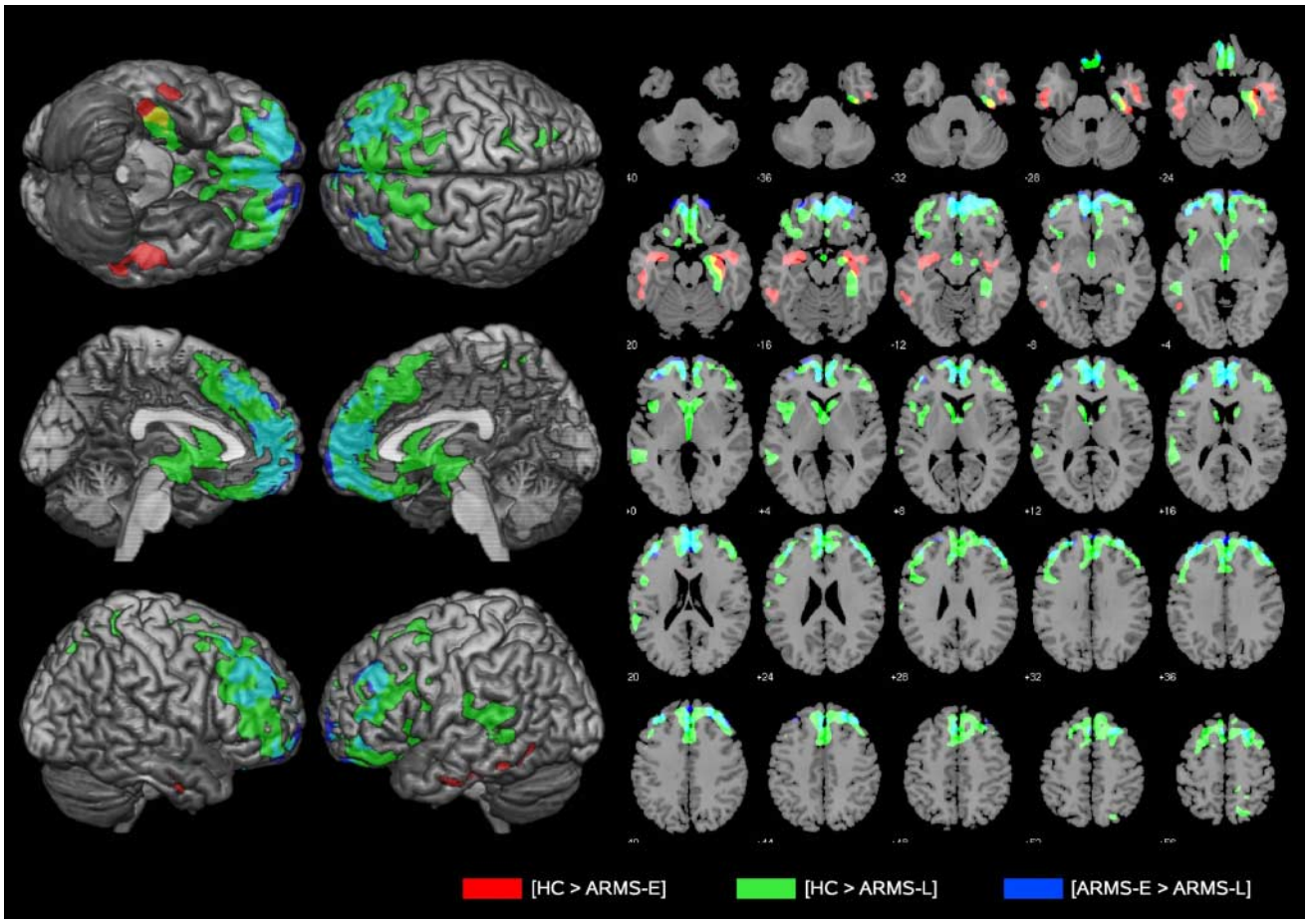


Fig. DS1 Significant clusters of grey matter volume reductions in ARMS–E *v.* control (HC) groups (red), ARMS–L *v.* control (HC) groups (green) and ARMS–L *v.* ARMS–E groups (blue).

The significant clusters of volume reduction ($P_{FWE} < 0.05$, primary threshold: $P_{uncorr} < 0.01$) detected in the *T* contrasts [HC > ARMS–E] (red), [HC > ARMS–L] (green) and [ARMS–E > ARMS–L] (blue) were overlaid on the MNI (Montreal Neurological Institute) single-subject anatomical template using the software packages MRIcron (C. Rohrden, www.sph.sc.edu/comd/rorden/mricron) and SPM5 ('slover' script of Matthew Brett) in order to visualise the anatomical localisation and spatial extent of between-group differences. Overlapping cluster regions show additive colours; yellow: [HC > ARMS–E] and [HC > ARMS–L]; magenta: [HC > ARMS–E] and [ARMS–E > ARMS–L]; cyan: [HC > ARMS–L] and [ARMS–E > ARMS–L]; white: all three *T* contrasts. ARMS–E, early at-risk mental state group; ARMS–L, late at-risk mental state group; HC, control group.

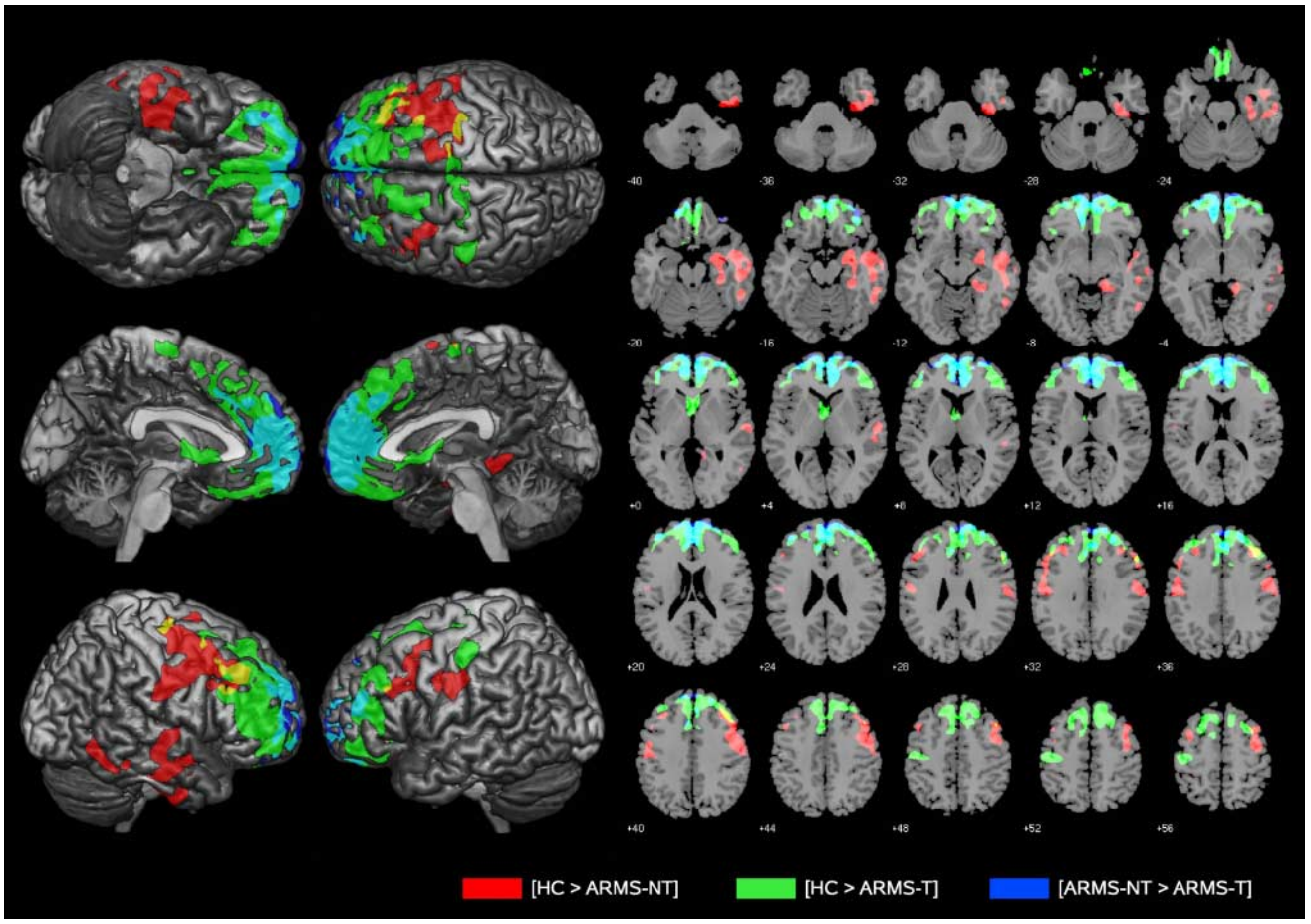


Fig. DS2 Significant clusters of grey matter volume reductions in ARMS–NT *v.* control (HC) groups (red), ARMS–T *v.* control (HC) groups (green) and ARMS–T *v.* ARMS–NT (blue)

The significant clusters of volume reduction ($P_{FWE} < 0.05$, primary threshold: $P_{uncorr} < 0.01$) detected in the *T* contrasts [HC > ARMS–NT] (red colour), [HC > ARMS–T] (green colour) and [ARMS–NT > ARMS–T] (blue colour) were overlaid on the MNI single subject anatomical template using the software packages MRIcron (C. Rohrden, www.sph.sc.edu/comd/rorden/mricron) and SPM5 ('slover' script of Matthew Brett) in order to visualise the anatomical localisation and spatial extent of between-group differences. Overlapping cluster regions show additive colours; yellow: [HC > ARMS–NT] and [HC > ARMS–T]; magenta: [HC > ARMS–NT] and [ARMS–NT > ARMS–T]; cyan: [HC > ARMS–T] and [ARMS–NT > ARMS–T]; white: all three *T* contrasts. ARMS–T, group with at-risk mental state and subsequent transition to psychosis; ARMS–NT, group with at-risk mental state and no subsequent transition to psychosis; HC, control group.

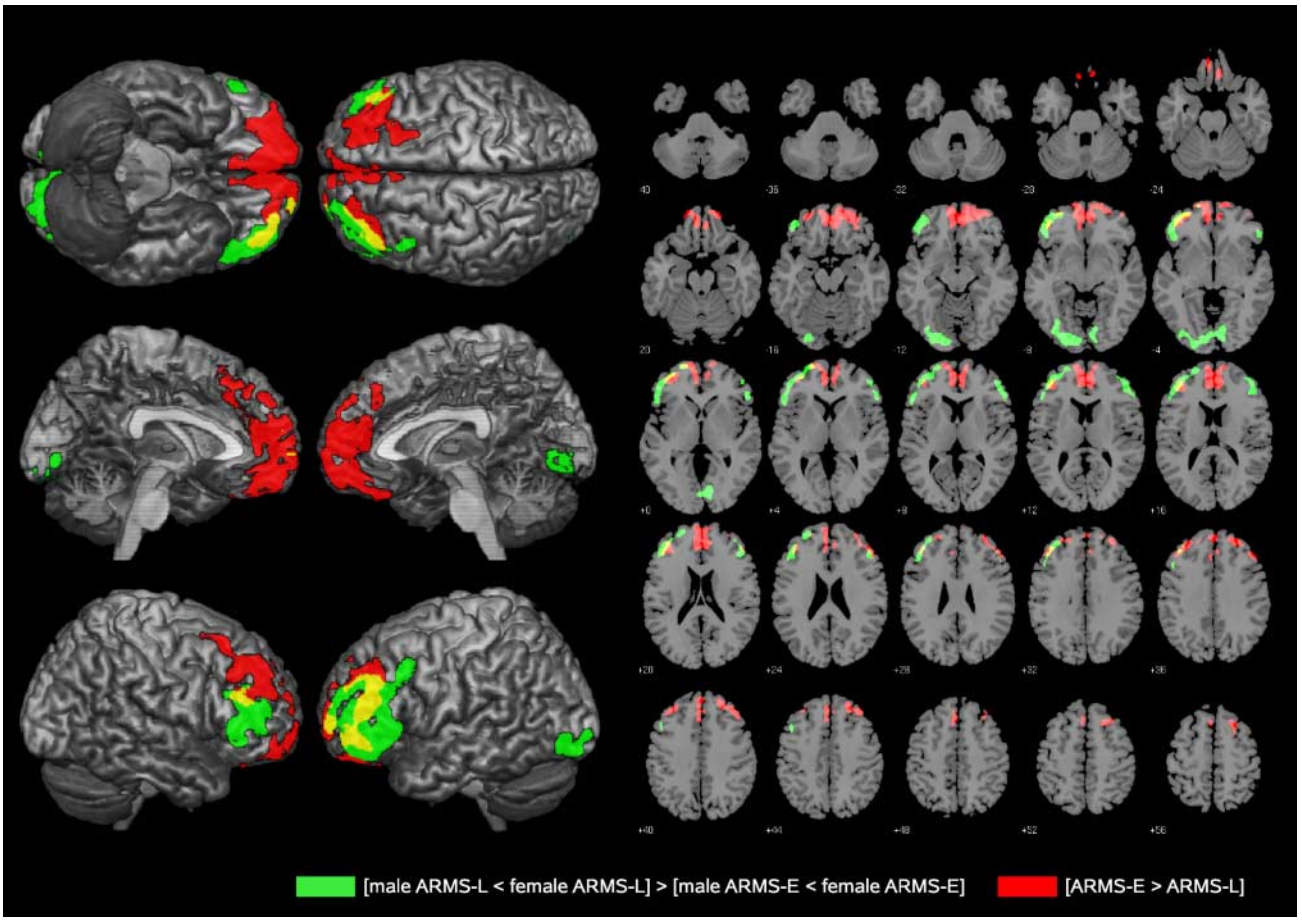
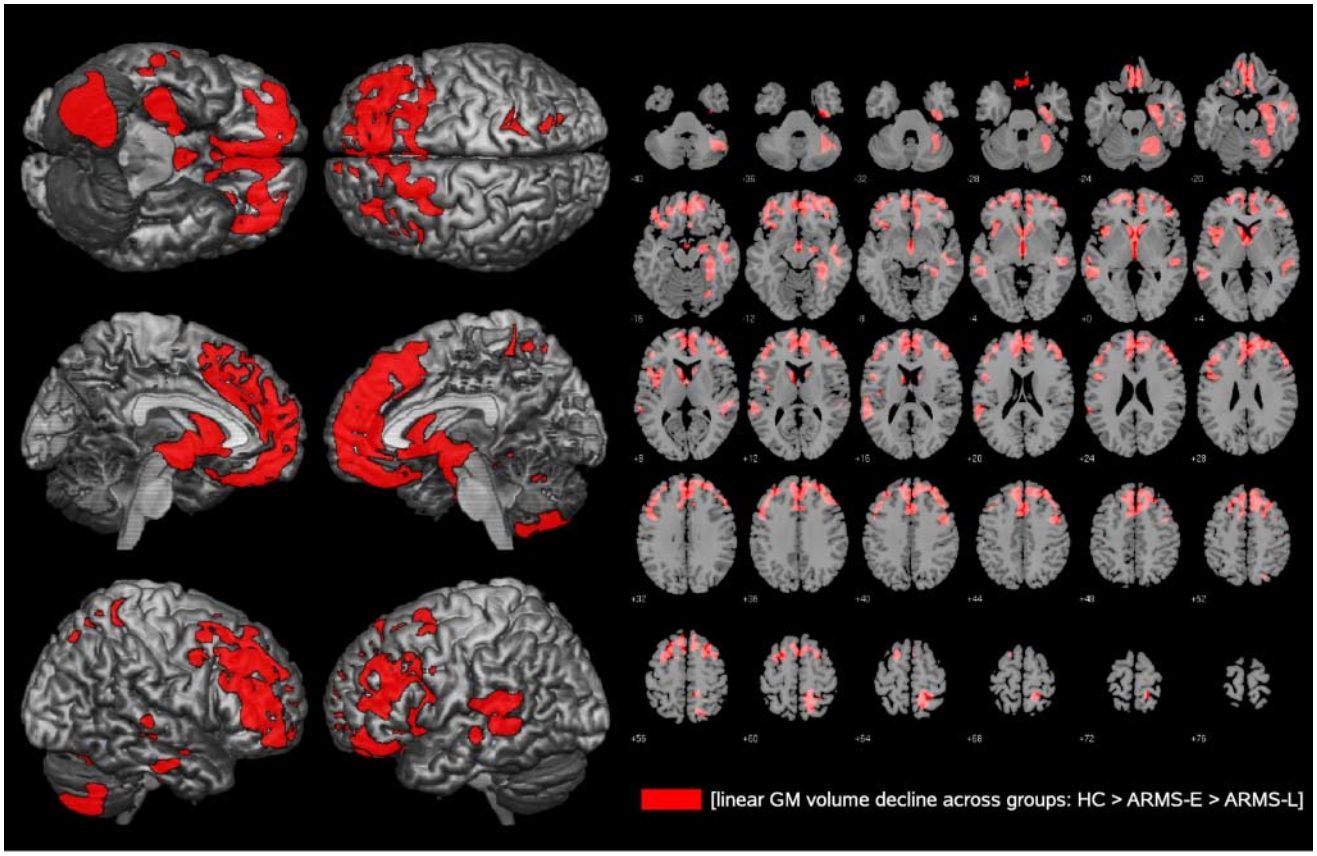


Fig. DS3 Voxel-based morphometry (VBM) interaction analysis: gender × ARMS group.

A two-factorial analysis of covariance was constructed with gender and ARMS group entered as factors and age defined as covariate of no interest in order to investigate possible gender effects on the grey matter volume differences detected by the *T* contrast [ARMS–E > ARMS–L]. Cluster-level inference was performed as in the main VBM analysis at $P_{FWE} < 0.05$, after applying a cluster-forming threshold of $P < 0.01$, uncorrected. The results were overlaid on the MNI single-subject anatomical template using the software packages MRIcron (C. Rohrden, www.sph.sc.edu/comd/rorden/mricron) and SPM5 ('slover' script of Matthew Brett). Green clusters indicate volume reductions in male *v.* female participants that were more pronounced in ARMS–L *v.* ARMS–E. Volume reductions detected in the main VBM analysis by the contrast [ARMS–E > ARMS–L] are shown in red. Regions of overlap between both contrasts appear in yellow and reveal regions where gender effects may have modulated the results of the main analysis. Sexual dimorphisms were more pronounced in the ARMS–L compared with the ARMS–E sample involving volume reductions in male ARMS–L participants that included the ventrolateral prefrontal cortex, bilaterally, and extended to the dorsolateral prefrontal cortex and the frontopolar cortex. Overlapping effects between red and green clusters were confined to the border region between the ventrolateral prefrontal cortex and the dorsolateral prefrontal cortex and were more pronounced on the left hemisphere. ARMS, at-risk mental state group; ARMS–E, early at-risk mental state group; ARMS–L, late at-risk mental state group.



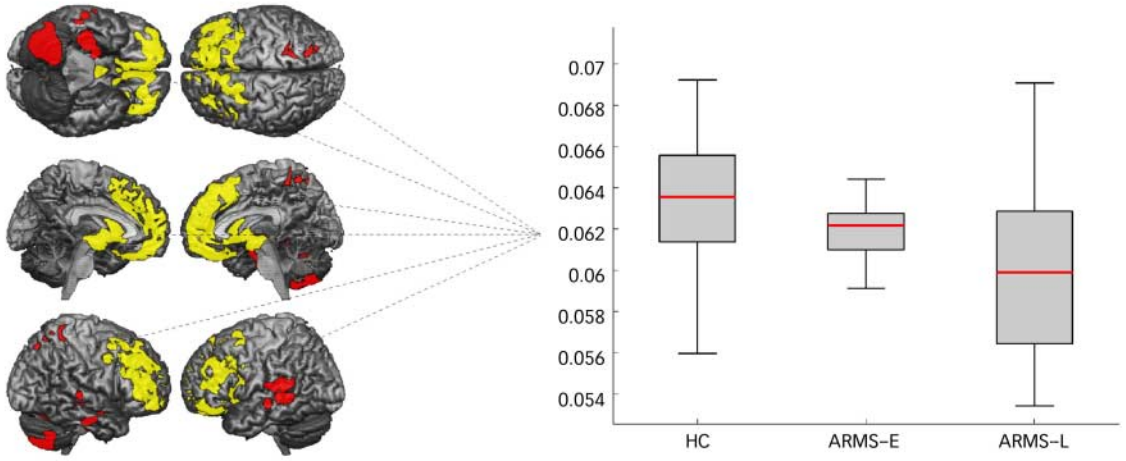


Fig. DS4 Analysis of linear correlations between grey matter volume and symptomatological proximity to psychosis.

A regressor coding the three study groups HC, ARMS–E and ARMS–L in a descending ranking of 3, 2, 1 was entered in a multiple regression design together with age and gender defined as nuisance regressors. Positive (HC > ARMS–E > ARMS–L) and negative (HC < ARMS–E < ARMS–L) correlations between grey matter volume and increasing symptomatological proximity to psychosis were assessed using a cluster-level inference at $P_{FWE} < 0.05$, after application of a cluster-forming threshold of $P < 0.01$, uncorrected. Upper part of the figure: Inverse relationships between grey matter volume and symptomatological proximity to psychosis (red clusters) were detected by the [HC > ARMS–E > ARMS–L] *T* contrast and displayed a large overlap with the anatomical regions identified by the contrast [HC > ARMS–L] of the main voxel-based morphometry analysis. Additional cortical regions included the right cerebellum, thalamus, left anterior insula, as well as the right posterior superior temporal gyrus, middle temporal and inferior temporal gyrus. Lower part of the figure: the first eigenvariate of the prefrontal cluster (yellow) was extracted by singular value decomposition across the entire study population. Box plots were used to display the descriptive statistics of this eigenvariate for each of the three study samples respectively. Grey matter volume declines increase from ARMS–E to ARMS–L, showing that the prefrontal areas detected by the [HC > ARMS–L] contrast seemed to be already affected in ARMS–E participants. ARMS–E, early at-risk mental state group; ARMS–L, late at-risk mental state group; HC, control group.

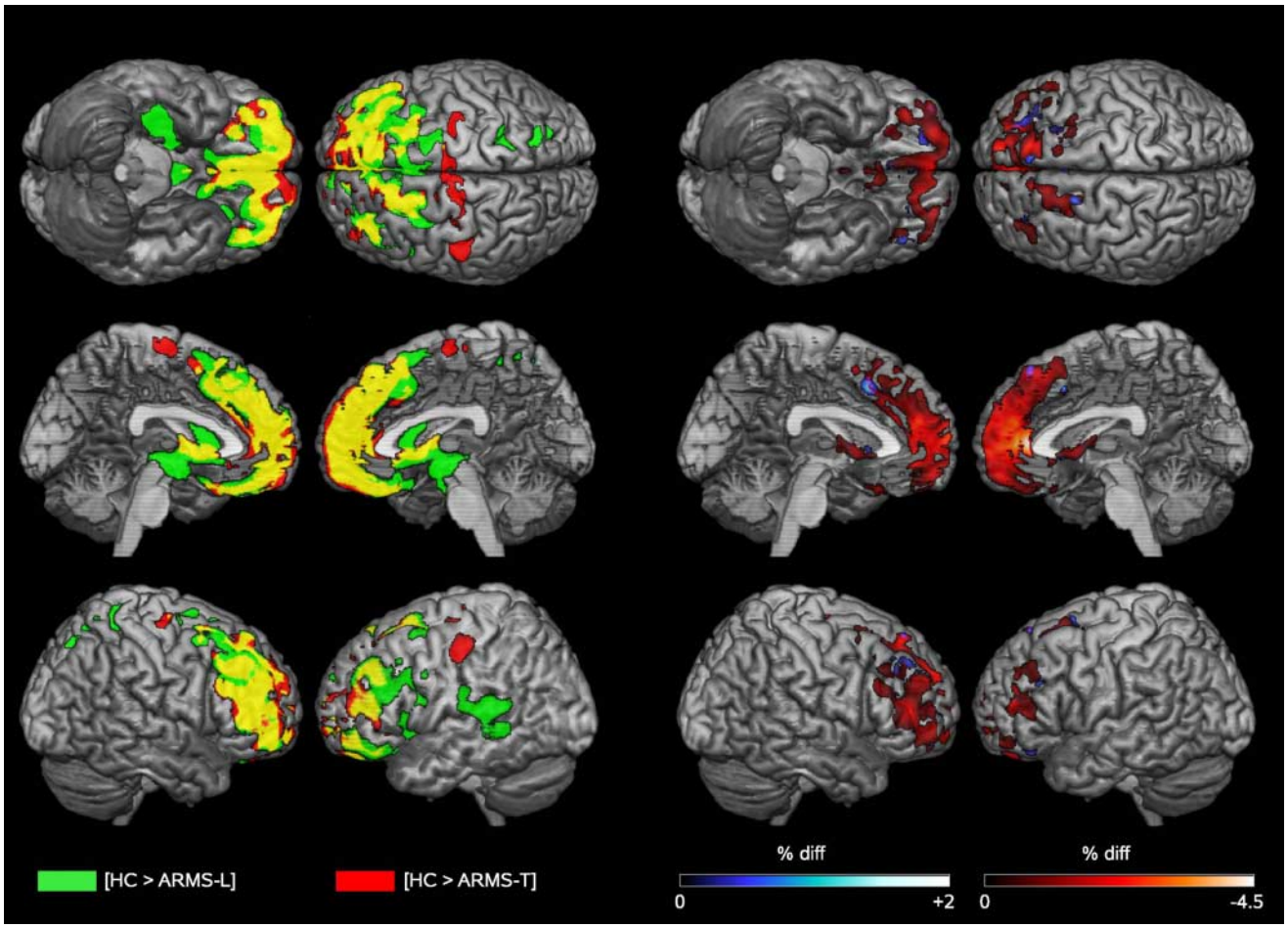


Fig. DS5 Analysis of grey matter volume reductions associated with vulnerability *v.* transition to psychosis.

Left part of the figure: significant clusters of grey matter volume reduction revealed by the *T* contrast [HC > ARMS–L] (green) were overlaid on the grey matter volume reduction clusters of the contrast [HC > ARMS–T] (red) in order to delineate the volume alterations in the ARMS–L sample that were predictive of a subsequent transition to psychosis (yellow). Yellow clusters were localised in the medial and lateral prefrontal as well as the orbitofrontal cortex and the anterior portions of the thalamus. The overlap of ARMS–L and ARMS–T was more pronounced in the right than in the left hemisphere. Right part of the figure: the percentage difference map of the [HC > ARMS–T] contrast was subtracted from the map of the [HC > ARMS–L] contrast in order to quantify the volumetric differences between ARMS–L and ARMS–T *v.* HC, respectively. Clusters appearing in warm colours indicate regions that spatially overlap ARMS–L and ARMS–T (yellow clusters of the left part of the figure), but that show more pronounced grey matter volume reductions in the ARMS–T than in the ARMS–L sample. The largest percentage differences were detected within the right medial prefrontal cortex, with maximum values in the anterior cingulated cortex (–4.5%), indicating that the ARMS–T participants had lower grey matter volumes in this cortical region than the ARMS–L participants. Only a few regions (small clusters within the right dorsolateral prefrontal cortex, left dorsomedial prefrontal cortex and orbitofrontal cortex, bilaterally) seemed to be affected by more pronounced grey matter volume reductions in the ARMS–L group compared with the ARMS–T group. ARMS–L, late at-risk mental state group; ARMS–T, group with at-risk mental state and subsequent transition to psychosis; HC, control group.