



King's Research Portal

DOI:

[10.1017/S0033291716002439](https://doi.org/10.1017/S0033291716002439)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Schmidt, A., Antoniadou, M., Allen, P., Egerton, A., Chaddock, C., Borgwardt, S. J., Fusar-Poli, P., Roiser, J. P., Howes, O. D., & McGuire, P. (2017). Longitudinal alterations in motivational salience processing in ultra high-risk subjects for psychosis. *Psychological Medicine*, 243-254. [PSM-D-16-00500R2].
<https://doi.org/10.1017/S0033291716002439>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

1. Results in healthy controls (n=13) and all subjects at ultra high-risk for psychosis (n=23).

Supplementary Table 1. Group effect across both visits during adaptive reward prediction.

Healthy controls > Ultra high-risk subjects					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.029 ^a	/†	12/4/-10	R	3.48
Ventral striatum*	0.038 ^a	/†	-14/8/-8	L	3.38
Calcarine sulcus	0.049 ^b	322†	12/-74/14	L	4.11
Cuneus			-2/-84/20	L	3.40
Calcarine sulcus			22/-70/6	R	3.38
Midbrain	0.048 ^b	311†	-6/-24/-10	L	4.10
Midbrain			6/-22/-10	R	3.61
Middle temporal gyrus	0.047 ^b	328†	-48/-54/-4	L	3.77
Superior temporal gyrus	0.7226 ^b	53	-46/12/-16	L	3.95
Cuneus	0.1292 ^b	223	-14/-74/24	L	3.92
Occipital gyrus			-26/-76/20	L	3.58
Calcarine sulcus	0.2111 ^b	175	-8/-78/6	L	3.77
Superior parietal gyrus	0.4378 ^b	105	-14/-70/44	L	3.77
Inferior frontal gyrus	0.2600 ^b	155	52/10/2	R	3.68
Insula			44/8/6	R	3.65
Cuneus	0.2546 ^b	157	18/-96/8	R	3.65
Calcarine sulcus			24/-86/6	R	3.56
Supramarginal gyrus	0.7971 ^b	41	54/-36/34	R	3.60

Middle cingulate cortex	0.5099 ^b	90	6/6/44	R	3.54
Inferior parietal gyrus	0.5334 ^b	35	-30/-44/36	L	3.52
Precentral gyrus	0.6493 ^b	65	-50/2/36	L	3.51
Ventral striatum	0.5412 ^b	84	12/0/8	R	3.43
Thalamus			12/-14/8	R	3.37
Insula	0.8032 ^b	40	-36/-4/12	L	3.41
Postcentral gyrus	0.7103 ^b	55	-20/-34/54	L	3.40
Paracentral gyrus			-14/-26/54	L	3.31
Ventral striatum	0.8513 ^b	32	-14/8/-8	L	3.38
Thalamus	0.8798 ^b	27	-4/-20/12	L	3.34

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level.

No significant effects were found for ultra high-risk subjects > healthy controls.

Supplementary Table 2. Time effect across both groups during adaptive reward prediction.

Follow-up activity > baseline activity					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral part of head of caudate nucleus*	0.0043 ^a	/†	-6/10/-2	L	4.09
Ventral part of head of caudate nucleus	0.0911 ^b	251	-6/10/-2	L	4.09
Cerebellum	0.8115 ^b	39	-4/-36/-46	L	3.84
Thalamus	0.026 ^b	383†	22/-18/12	R	3.79
Ventral striatum			14/0/8	R	3.49
Inferior temporal gyrus	0.8833 ^b	27	-40/-16/-22	L	3.60
Occipital gyrus	0.7544 ^b	48	26/-68/-4	R	3.58
Anterior cingulate cortex	0.6655 ^b	62	-18/34/14	L	3.57
Ventral striatum	0.8543 ^b	32	-14/-2/6	L	3.56
Inferior frontal gyrus	0.3252 ^b	131	46/6/14	R	3.55
Cerebellum	0.8239 ^b	37	2/-60/-6	R	3.53
Superior temporal gyrus	0.9104 ^b	37	40/-40/16	R	3.52
Lingual gyrus	0.8661 ^b	30	-20/-50/2	L	3.44
Insula	0.8115 ^b	39	28/34/8	R	3.31

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level. No significant effects were found for baseline > follow-up.

Supplementary Table 3. Group effect during adaptive reward prediction at baseline.

Healthy controls > Ultra high-risk subjects					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.025 ^a	/†	-16/6/-8	L	3.54
Parahippocampal gyrus	<0.0001 ^b	831†	-14/-36/-8	L	4.14
Cerebellum			2/-58/-10	L	3.89
Midbrain			-8/-30/-8	L	3.88
Middle temporal gyrus	0.042 ^b	325†	-46/-64/0	L	4.03
Superior temporal gyrus	0.8311 ^b	36	-46/14/-14	L	3.90
Precentral gyrus	0.3664 ^b	119	-48/-6/40	L	3.76
Insula	0.0735 ^b	269	44/6/-2	R	3.64
Ventral striatum	0.7222 ^b	53	-16/6/-8	L	3.54
Middle cingulate cortex	0.6773 ^b	60	-6/-12/40	L	3.52
Precentral gyrus	0.8556 ^b	32	46/-8/44	R	3.50
Supplementary Motor Cortex	0.2877 ^b	141	4/6/46	R	3.49
Middle cingulate cortex			10/10/40	R	3.44
Precentral gyrus	0.7868 ^b	43	54/-2/36	R	3.48
Ventral striatum	0.8904 ^b	26	26/-10/8	R	3.46
Insula	0.5791 ^b	76	-40/0/10	L	3.45
Calcarine sulcus	0.8123 ^b	39	-12/-80/6	L	3.41
Lingual gyrus			-6/-74/4	L	3.16
Ventral striatum	0.7416 ^b	50	-30/-10/-8	L	3.31

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level. No significant effects were found for ultra high-risk subjects > healthy controls.

Supplementary Table 4. Group effect during adaptive reward prediction at follow-up.

Healthy controls > Ultra high-risk subjects					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.021 ^a	/†	10/18/-2	R	3.60
Ventral striatum*	0.044 ^a	/†	-4/14/0	L	3.33
Anterior cingulate cortex	0.0617 ^b	293	-16/32/16	L	3.93
Inferior frontal gyrus			-32/20/18	L	3.76
Cerebellum	0.2488 ^b	157	-47/-52/-40	L	3.89
Ventral striatum	0.7477 ^b	49	10/18/-2	R	3.60
Middle cingulate cortex	0.8531 ^b	32	-18/-40/34	L	3.43
Thalamus	0.3540 ^b	124	-4/-12/12	L	3.40
Ventral striatum	0.7856 ^b	43	-4/14/0	L	3.33
Insula	0.9141 ^b	21	-26/-26/30	L	3.30
Cerebellum	0.8351 ^b	35	38/-48/-38	R	3.29
Occipital gyrus	0.9141 ^b	21	20/-94/10	R	3.26
Occipital gyrus	0.8763 ^b	28	-20/-86/14	L	3.24
Insula	0.9192 ^b	20	30/-24/28	R	3.21

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected. ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the voxel level. No significant effects were found for ultra high-risk subjects > healthy controls.

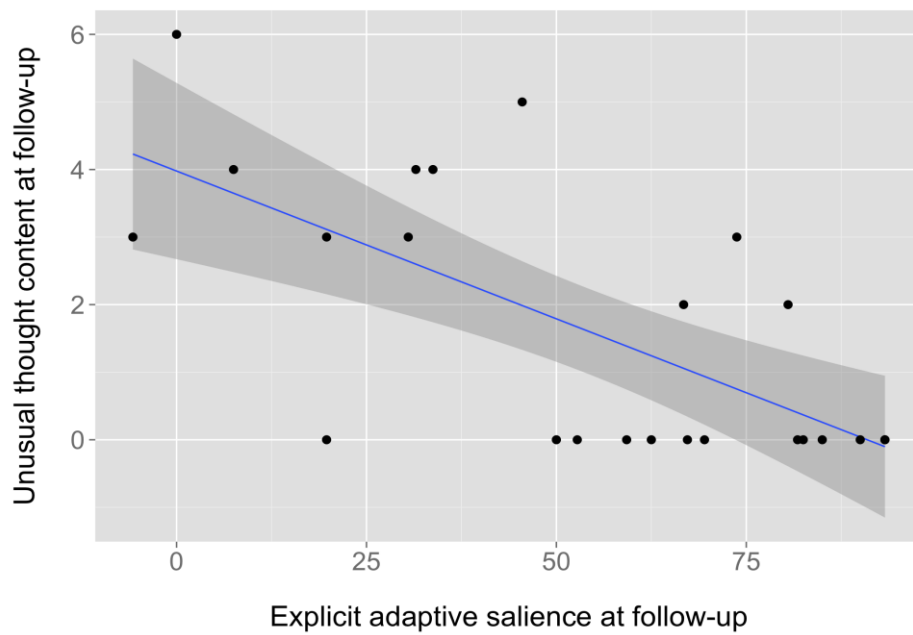
Supplementary Table 5. Negative correlation between longitudinal changes in activation during adaptive reward prediction and change in the severity of abnormal beliefs in ultra high-risk subjects.

Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.0171 ^a	/†	18/6/-6	R	3.73
Precentral gyrus	0.6126 ^b	69	20/-20/64	R	3.79
Ventral striatum	0.2033 ^b	160	18/6/-6	R	3.73
Supplementary Motor Cortex	0.026 ^b	340†	0/-16/58	R/L	3.65
Supplementary Motor Cortex			-10/-4/70	L	3.52
Supplementary Motor Cortex			4/-6/64	R	3.52

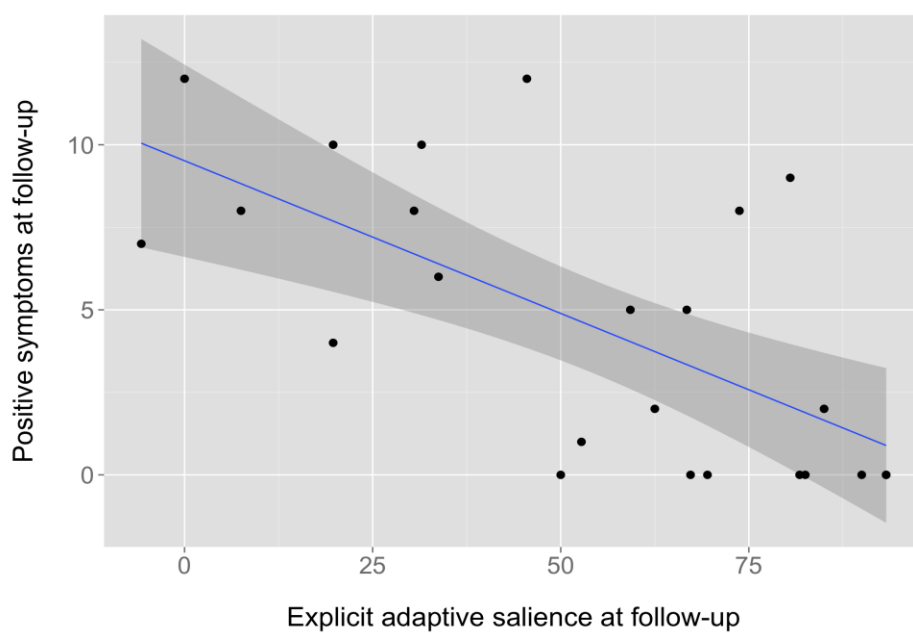
Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected. ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level. No significant positive correlations were found.

Supplementary Figure 1. Significant correlations in ultra high-risk subjects between explicit adaptive salience responses (visual analogue scale, VAS) and **(A)** unusual thought content ($r=-0.674$, $p<0.001$), **(B)** CAARMS positive symptoms ($r=-0.653$, $p<0.001$) and **(C)** global functioning (GAF) ($r=0.497$, $p=0.014$) at follow-up.

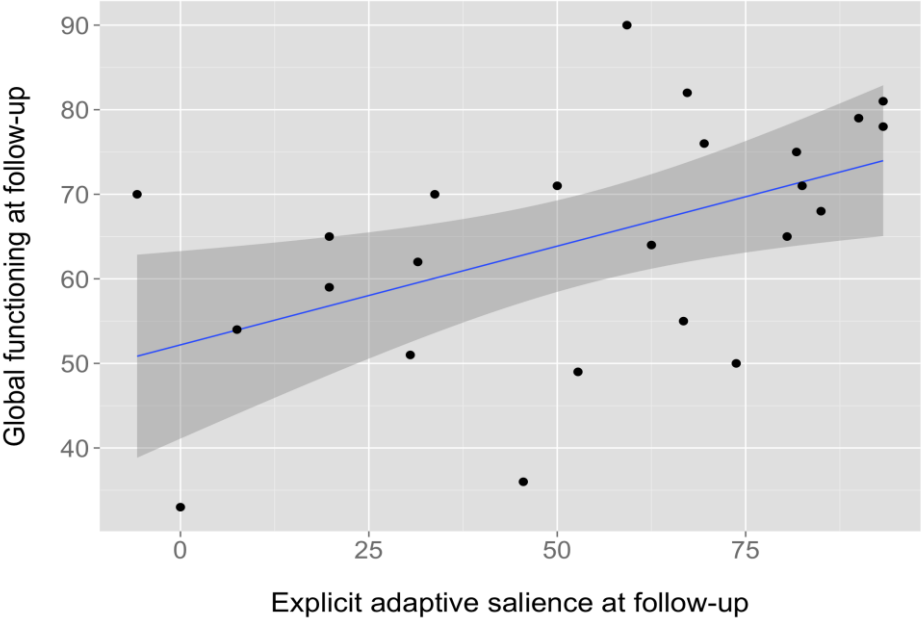
A)



B)



C)



2. Results in healthy controls (n=13) and subjects at ultra high-risk for psychosis who did not transit to psychosis (n=22).

A. Behavioural data

Aberrant attribution of salience

Across both visits, UHR subjects showed significantly higher implicit aberrant salience than HCs subjects ($F(1,33)=6.443$, $p=0.016$), and there was a trend for a group x time interaction ($F(1,33)=3.076$, $p=0.089$). There was also a trend for a group x time interaction for explicit aberrant salience ($F(1,33)=3.437$, $p=0.073$). Based on our *a priori* hypotheses we constructed linear contrasts at each time point to test for the predicted group differences in aberrant salience.

At baseline, UHR subjects were more likely than HCs to attribute salience to irrelevant cue features (explicit aberrant salience) ($F(1,33)=5.117$, $p=0.030$), but did not exhibit greater implicit aberrant salience than HCs ($F(1,33)=0.879$, $p=0.335$). At follow-up the group difference in explicit aberrant salience was no longer significant ($F(1,33)=0.073$, $p=0.789$), but HCs had significantly lower implicit aberrant scores than the UHR group ($F(1,33)=11.972$, $p=0.002$) due to a reduction in this measure over time.

Adaptive attribution of salience

Across both visits, the UHR group had lower implicit adaptive salience scores than HCs ($F(1,33)=11.603$, $p=0.002$), as well as lower explicit adaptive salience scores ($F(1,33)=5.763$, $p=0.02$). There was also a strong trend for a group x time interaction for explicit adaptive salience ($F(1,33)=4.086$, $p=0.051$).

At baseline, UHR subjects had significantly lower implicit adaptive salience than HCs ($F(1,33)=14.562$, $p=0.001$) and also exhibited significantly lower explicit adaptive salience ($F(1,33)=9.391$, $p=0.004$). Both of these group differences were no longer significant at follow-up

(implicit adaptive salience: $F(1,33)=3.642$, $p=0.065$; explicit adaptive salience: $F(1,33)=1.446$, $p=0.238$), due to improved scores in the UHR group together with relatively stable performance in HCs.

B. Activation during salience processing

Supplementary Table 6. Group effect across both visits during adaptive reward prediction.

Healthy controls > Ultra high-risk subjects without transition (n=22)					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.025 ^a	/†	12/2/8	R	3.54
Ventral striatum*	0.008 ^a	/†	-8/8/4	L	3.90
Midbrain	0.024 ^b	401†	-6/-24/-10	L	4.25
Midbrain			10/-24/-12	R	3.81
Calcarine sulcus	0.118 ^b	231	12/-74/14	R	4.05
Calcarine sulcus			22/-70/6	R	3.31
Superior temporal gyrus	0.619 ^b	70	-46/12/-16	L	4.02
Insula	0.514 ^b	89	-38/-4/12	L	3.97
Ventral striatum	0.393 ^b	115	-8/8/4	L	3.90
Cuneus	0.175 ^b	192	-14/-74/24	L	3.87
Occipital gyrus			-26/-76/20	L	3.55
Precentral gyrus	0.253 ^b	157	-50/2/36	L	3.80
			-44/-4/36	L	3.59
			-46/-6/50	L	3.25
Insula	0.253 ^b	157	44/8/8	R	3.80
Inferior frontal gyrus			52/10/2	R	3.60
Superior parietal gyrus	0.440 ^b	104	-14/-70/44	L	3.79
Postcentral gyrus	0.354 ^b	125	-20/-34/54	L	3.79
Middle temporal gyrus	0.070 ^b	284	-52/-58/-2	L	3.70
Calcarine sulcus	0.272 ^b	150	-8/-78/6	L	3.69

Middle cingulate cortex	0.205 ^b	177	6/6/44	R	3.68
Cuneus	0.350 ^b	126	18/-96/8	R	3.60
Occipital gyrus			26/-86/6	R	3.50
Calcarine sulcus			16/-100/0	R	3.47
Supramarginal gyrus	0.846 ^b	33	54/-36/34	R	3.55
Ventral striatum	0.573 ^b	78	12/2/8	R	3.54
Inferior parietal gyrus	0.908 ^b	22	-30/-44/36	L	3.47
Thalamus	0.840 ^b	34	12/-14/8	R	3.46
Supplementary Motor Cortex	0.785 ^b	43	2/-16/52	R	3.45
Middle cingulate cortex	0.760 ^b	47	-6/-10/40	L	3.41
Middle cingulate cortex			-10/-20/40	L	3.25
Ventral striatum	0.846 ^b	33	12/4/-10	R	3.41
Insula	0.816 ^b	38	-30/-22/10	L	3.41
Supplementary Motor Cortex	0.918 ^b	20	18/-22/52	R	3.37
Ventral striatum	0.840 ^b	34	-14/8/-8	L	3.34
Thalamus	0.912 ^b	21	-4/-20/12	L	3.34
Precentral gyrus	0.816 ^b	38	50/-4/44	R	3.33
Inferior frontal gyrus			56/8/26	R	3.31
Cuneus	0.869 ^b	29	-2/-86/20	L	3.32

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level.

No significant effects were found for ultra high-risk subjects > healthy controls.

Supplementary Table 7. Time effect across both groups (healthy controls + ultra high-risk subjects without transition) during adaptive reward prediction.

Follow-up activity > baseline activity					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral part of head of caudate nucleus*	0.006 ^a	/†	-4/16/-6	L	3.99
Ventral part of head of caudate nucleus	0.037 ^a	/†	19/12/-2	R	3.41
Ventral striatum	0.125 ^b	209	-4/-16/-6	L	3.99
Ventral striatum			-18/24/-8	L	3.55
Ventral striatum			-8/12/-12	L	3.43
Inferior frontal gyrus	0.132 ^b	211	46/6/14	R	3.85
Insula			38/-16/28	R	3.75
Thalamus	0.0074 ^b	513†	22/-18/12	R	3.85
Thalamus			18/-8/10	R	3.69
Ventral striatum			14/0/8	R	3.62
Insula	0.411 ^b	108	28/34/8	R	3.72
Inferior frontal gyrus			38/18/10	R	3.19
Lingual gyrus	0.626 ^b	68	2/-62/-6	R	3.71
Occipital gyrus	0.683 ^b	59	26/-68/-4	R	3.65
Cerebellum	0.868 ^b	30	-4/-36/-46	L	3.64
Middle frontal gyrus	0.578	76	-24/34/12	L	3.59
Inferior temporal gyrus	0.902	24	-40/-14/-24	L	3.59
Superior temporal gyrus	0.908 ^b	23	40/-40/16	R	3.59
Amygdala	0.923 ^b	20	-16/-6/-10	L	3.53
Lingual gyrus	0.923 ^b	20	-20/-50/2	L	3.45

Occipital gyrus			-34/-66/2	L	3.27
Ventral striatum	0.908 ^b	23	-14/-2/6	L	3.42
Ventral striatum	0.880 ^b	28	30/12/6	R	3.24
			24/18/6	R	3.15

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. ^{*}Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. [†] survives FWE correction for multiple comparisons at the cluster or voxel level. No significant effects were found for baseline > follow-up.

Supplementary Table 8. Group effect during adaptive reward prediction at baseline.

Healthy controls > Ultra high-risk subjects without conversion (n=22)					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.009 ^a	/†	-16/6/-10	L	3.87
Ventral striatum*	0.042 ^a	/†	14/2/8	R	3.37
Precentral gyrus	0.069 ^b	268	-50/0/38	L	4.37
Precentral gyrus			-42/-10/44	L	3.41
Postcentral gyrus			-44/-20/46	L	3.29
Parahippocampal gyrus	<0.0001 ^b	1117†	-12/-36/-8	L	4.32
Cerebellum			0/-40/-12	L	4.16
Midbrain			8/-30/-10	R	3.83
Superior temporal gyrus	0.014 ^b	428†	-46/14/-14	L	4.25
Ventral striatum			-16/6/-10	L	3.87
Ventral striatum			-24/-2/-10	L	3.81
Insula	0.106 ^b	228	-38/-2/12	L	4.17
Inferior frontal gyrus			-52/6/10	L	3.50
Middle temporal gyrus	0.052 ^b	295	-46/-64/0	L	4.08
Middle temporal gyrus			-44/-44/-2	L	3.37
Middle temporal gyrus			-50/-50/-4	L	3.24
Precentral gyrus	0.243 ^b	153	46/-8/44	R	4.00
Precentral gyrus			54/2/36	R	3.62
Precentral gyrus			56/8/30	R	3.51

Middle cingulate cortex	0.036 ^b	332 [†]	8/10/40	R	3.82
Ventral striatum	0.473 ^b	94	26/-10/8	R	3.82
Ventral striatum			22/-2/8	R	3.52
Ventral striatum			12/4/6	R	3.32
Middle cingulate cortex	0.270 ^b	144	-6/-12/40	L	3.74
Insula	0.048 ^b	304 [†]	44/6/-2	R	3.62
Insula			42/8/6	R	3.61
Inferior frontal gyrus			56/6/8	R	3.55
Precentral gyrus	0.893 ^b	26	-22/-28/52	L	3.43
Calcarine sulcus	0.876 ^b	29	-12/-80/6	L	3.38
Insula	0.910 ^b	23	-32/-22/10	L	3.34

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. ^{*}Small volume corrected. ^apeak-level FWE-corrected, ^bcluster-level FWE-corrected. [†] survives FWE correction for multiple comparisons at the cluster or voxel level. No significant effects were found for ultra high-risk subjects > healthy controls.

Supplementary Table 9. Group effect during adaptive reward prediction at follow-up.

Healthy controls > Ultra high-risk subjects without conversion (n=22)					
Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.025 ^a	/†	10/18/-2	R	3.53
Ventral striatum*	0.046 ^a	/†	-6/14/0	L	3.31
Anterior cingulate cortex	0.089 ^b	255	-16/32/16	L	3.86
Inferior frontal gyrus			-32/20/18	L	3.72
Ventral striatum			-20/14/20	L	3.42
Cerebellum	0.264 ^b	151	-46/-52/-40	L	3.82
Ventral striatum	0.811 ^b	39	10/18/-2	R	3.53
Middle cingulate cortex	0.914 ^b	21	-18/-40/34	L	3.38
Thalamus	0.446 ^b	102	-4/-12/12	L	3.35
Thalamus			-12/-4/10	L	3.32
Ventral striatum	0.754 ^b	48	-6/14/0	L	3.31
Insula	0.920 ^b	20	-26/-26/30	L	3.31
Cerebellum	0.899 ^b	24	38/-48/-38	R	3.24

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected. ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the voxel level. No significant effects were found for ultra high-risk subjects > healthy controls.

Supplementary Table 10. Negative correlation between longitudinal changes in activation during adaptive reward prediction and change in the severity of abnormal beliefs in ultra high-risk subjects who did not convert (n=22).

Region	P value	Cluster size	MNI co-ordinates (X/Y/Z)	R/L	Z value
Ventral striatum*	0.021 ^a	/†	18/6/-6	R	3.67
Supplementary Motor Cortex	0.001 ^b	671†	4/-6/62	R	4.18
Supplementary Motor Cortex			-8/-6/70	L	4.13
Supplementary Motor Cortex			-2/-14/58	L	3.41
Ventral striatum	0.174 ^b	171	32/0/2	R	3.75
Ventral striatum			18/6/-6	R	3.67
Ventral striatum	0.745 ^b	50	-30/-20/0	L	3.30
Ventral striatum			-26/-8/-4	L	3.18

Results are reported using a cluster-forming threshold $p < 0.001$ uncorrected, with an extent threshold of 20 voxels. *Small volume corrected. ^apeak-level FWE-corrected. ^bcluster-level FWE-corrected. † survives FWE correction for multiple comparisons at the cluster or voxel level. No significant positive correlations were found.