**Supplementary material**

***Participants and methods***

*Participants*

Inclusion criteria for patients were: 18-45 years of age, fulfilled diagnostic criteria for schizophrenia spectrum disorder according to International Classification of Diseases, 10th revision (schizophrenia, schizoaffective disorder, non-organic psychosis), first presentation to clinical services for psychosis, lifetime antipsychotic-naïve with no previous treatment with antipsychotic medication or central nervous system stimulants, no use of antidepressants in the preceding 30 days, and legally competent.

Exclusion criteria for all participants were: substance abuse or dependence in the preceding three months (except smoking), pregnancy, history of major head injury with loss of consciousness exceeding five minutes, neurological or severe medical disorders, and contraindication to MRI. Occasional use of benzodiazepines was accepted to ensure sleep at night but only >12 hours before an examination. Information on alcohol, cannabis, nicotine, and drug use was self-reported and confirmed using a urine test (Rapid Response, Jepsen Healthcare).

Patients included had their first presentation to clinical services for psychosis. Most of the patients were diagnosed a few days or weeks before inclusion, however, some patients were diagnosed several months before, but not previously treated with antipsychotics. For the majority of patients (N=29), the duration of untreated psychosis was < 30 weeks, and for few patients (N=13) the duration of untreated psychosis was >100 weeks. The median duration of untreated psychosis for the whole group of patients was (median, 25%-75% percentile) 26 weeks (16 – 104 weeks).

HC did not report any personal or family history of neurological, psychiatric or medical disorders and were matched to patients regarding sex, age, and parental educational background. HC had no current or prior psychiatric illness. HC were excluded if they were at high risk of psychosis as assessed with the Comprehensive Assessment of At-Risk Mental States (Yung, Yuen, Phillips, Francey, & McGorry, 2003).

Diagnoses were confirmed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN version 2.1)(Wing, J.K., Babor, T., Brugha, T., Burke, J., Cooper, J.E., Giel, R., Jablenski, A., Regier, D. & Sartorius, 1990).

*Monetary incentive delay task*

A modified monetary incentive delay task was used to elicit neural responses on anticipation of motivational salient stimuli and on outcome evaluation.In order to secure that participants understood the task, and that the task was completely clear to all, participants were carefully informed about the task, the meaning of the cues, the importance of button press, the possibility of monetary gain, and were given five minutes to practice the game before MRI acquisition.

The trial was programmed to an adaptive hit rate of 66%, which participants were not informed about.

The task lasted 12 minutes and consisted of 72 interactive trials evenly distributed between neutral trials and trials with the possibility of winning or losing money. Each cue was presented 24 times. In each trial, participants were presented initially with a cue indicating the trial condition. The initial cue on the screen either represented a trial with possibility of winning money (arrow pointing up), a trial with possibility of losing money (arrow pointing down) or a neutral trial (arrow pointing up and down). The initial cue was followed by a waiting phase (cross on the screen), and subsequently a target cue (white box on the screen), where participants pressed a button as fast as possible, expecting to win or avoid losses (see Figure 1). Afterwards, the trial outcome appeared on the screen. In possible win trials, participants gained 7 Euro on a hit and 0 Euro on a miss. In possible loss trials, participants earned 0 Euro on a hit and lost 7 Euro on a miss. Neutral trials resulted in 0 Euro every time. Upon completion of the data acquisition, participants received the amount of money they had won.

To obtain measures during anticipation of motivational salience, we defined a contrast showing the overall motivational salience, i.e., a joint effect of anticipated motivational salience during presentation of cues representing trials with possible win and possible loss versus neutral cues. To obtain measures during negative outcome evaluation (NOE), we defined a contrast showing miss outcome versus neutral outcome. For explorative analyses of positive outcome, we defined a contrast showing hit outcome versus neutral outcome. See Supplementary Figure S3 for task design.

The monetary incentive delay task was used to elicit neural responses on anticipation during motivational salient stimuli and on outcome evaluation in regions of interest, which have previously been shown to be activated by similar tasks. To ensure that the task worked as expected e.g. activated the regions of interest during responses to motivational salient stimuli and outcome evaluation in healthy controls, analyses on the group of healthy controls were performed for each ROI and contrast.

*MRS voxel placement*

Levels of glutamate were acquired using PRESS, where unsuppressed water reference spectra were acquired separate as built-in sequences in the PRESS sequence. To avoid signal interference during acquisition, a lipid saturation band was placed to cover the scalp and a water saturation band to cover the circle of Willis.

Placement of voxels in the left thalamus and dorsal ACC was positioned manually using anatomical information from the T1-weighted image and placed to minimize the amount of cerebral spinal fluid (CSF). The thalamus voxel was manually placed on the axial slice so that it only covered thalamic brain tissue and to minimize the amount of CSF. The ACC voxel was manually placed on the sagittal slice, where the voxel was aligned with the corpus callosum and placed with a voxel corner lying on a line going through the extremities of the corpus callosum (Figure S1). As shown in Supplementary Figure S1, there was a good overlap of voxel placement between subjects in the thalamus and ACC.

*Shimming, field homogeneity, and eddy-current correction*

Shimming was done automatically using the second order pencil beam. Shimming was evaluated by measuring the spectral linewidth. The MRS sequence was repeated if the linewidth was >10Hz for the voxel in thalamus and >7Hz for the ACC voxel. Field homogeneity was evaluated by full-width half-maximum values and reported in Table S1 as well as the signal-to-noise ratio (SNR). Eddy-current correction was automatically performed on the metabolite data by the scanner.

*MRS analysis*

Glutamate output, as reported by the LCModel, was used in the analyses; however, the glutamate measure at 3T cannot reliably be separated from glutamine, which means that it reflects glutamate-glutamine rather than glutamate. Glutamate levels were estimated in institutional units, i.e., glutamate was corrected for partial volume CSF contamination. To perform this correction, we began by segmenting the structural image into white matter (WM) and gray matter (GM) using segment in Statistical Parametric Mapping 12. Next, we co-registered the voxel mask and the structural image and used FSL tools to extract the tissue fractions within the voxel.

We used the equation:

glutamate IU= glutamate\*(WM+GM+1.55\*CSF)/(WM+GM) (Stone et al., 2012)

where WM and GM are fractions of WM and GM in the spectroscopic voxel, and CSF is a CSF fraction in the voxel, calculated as 1-(WM+GM) (Stone et al., 2012). We found no group difference in GM between FEP and HC, however, glutamate measures were also corrected for GM using the following formula:

glutamate IUadjusted = glutamate IU\*(GM/(GM+WM))

where glutamate IUadjusted is glutamate concentrations in institutional units corrected for CSF content and the fraction of grey matter.

Measures of glutamate IU and glutamate IUadjusted are provided in Table S1.

*Regions of interest in the right hemisphere*

For explorative analyses parameter estimates were extracted from ROIs in the right hemisphere. The striatal ROIs in the right hemisphere were defined as a 6 mm radius spherical region centered in the MNI coordinates: 10, 12, 8 (right caudate), and 10, 14, -6 (right accumbens). The ROIs in right ACC, right DLPFC and right thalamus were defined as a 5 mm radius spherical region centered in MNI coordinates 5, 39, 20 (right ACC), 46, 38, 8 (right DLPFC) and 7, -17, 5 (right thalamus).

**Supplementary Figure S1. Spectra and mean voxel placement in the left thalamus and anterior cingulate cortex for all subjects**

Picture 1

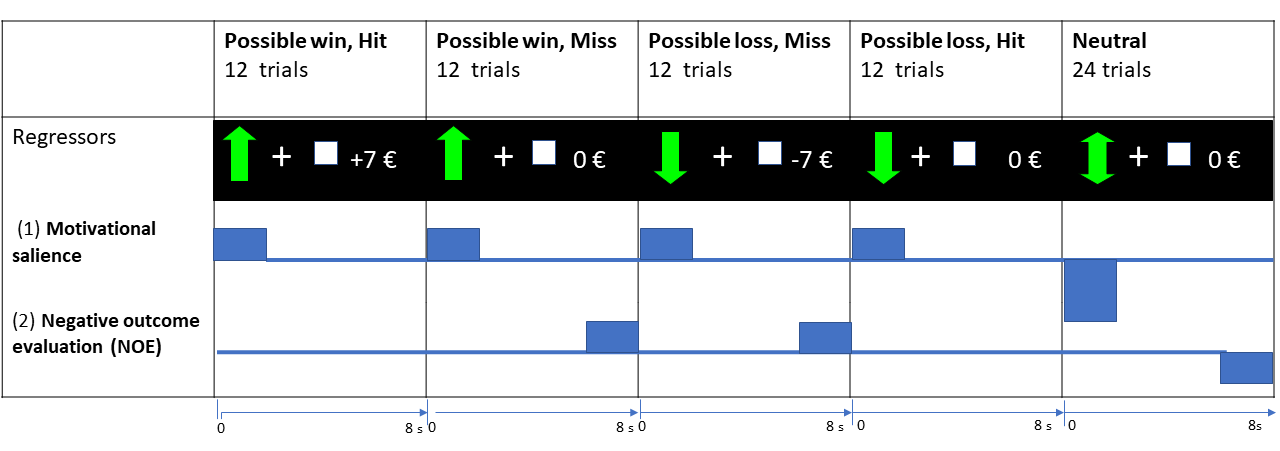
Mean voxel position in the sagittal, coronal and axial plane is shown for all subject in model space for the left thalamus in A, the dorsal anterior cingulate cortex in B, and representative spectra from LCModel are shown for the left thalamus in C, and for anterior cingulate cortex in D. For the spectra; the black line indicates the output whereas the red line shows the fit done by LCModel to estimate the concentration of major metabolites including glutamate with a peak around 2.35 ppm.

**Supplementary Figure S2. Overlay of MRS voxel placement in the left thalamus and ACC and fMRI ROIS in the left thalamus and ACC**

Picture 1

The figure illustrates mean spectroscopic voxel placement in the left thalamus (blue) and ACC (green), and their overlay with fMRI ROI in the left thalamus (yellow) and ACC (red). MRS: magnetic resonance spectroscopy, ACC: anterior cingulate cortex, fMRI: functional magnetic resonance imaging, ROI: region of interest.

**Supplementary Figure S3. Task design and regressors of interest**



The figure illustrates task design and regressors of interest, which contrasted (1) Motivational salience and (2) Negative outcome evaluation. Motivational salience was a contrast of joint effect of anticipation to win or loss vs neutral. Negative outcome evaluation was a contrast of outcome miss vs outcome neutral. The duration of each trial was approximately 8 seconds. A trial started with a cue representing the trial condition (green arrow), followed by a waiting phase (whit cross) and a target cue (white box) where participants pressed a button as fast as possible, expecting to win (hit) or avoid losses(hit). Afterward the trial outcome was presented on the screen. In possible win trials, participants gained +7 Euro on a hit and 0 Euro on a miss. In possible loss trials participants earned 0 Euro on a hit and lost -7 Euro on a miss. Neutral trials resulted in 0 Euro every time.

***Supplementary Results***

*Behavioral results*

There was a group difference in response time with patients having a higher response time e.g. reacting more slowly for conditions with possible win (T(101)=2.7, p=0.007, CI: 0.003, 0.019) and possible loss (T(101)=2.7, p=0.008, CI:0.004, 0.025) but not for neutral conditions (T(101)=1.2, p=0.24, CI: -0.004, 0.017), see Table S7. In patients, there was a significant difference in response time between possible win and neutral condition (mean difference= 0.0149±0.0169, p=0.0001, CI:0.010, 0.019) and between possible loss and neutral condition (mean difference=0.011±0.0277, p=0.006, CI:-0.018, -0.003), but not between possible win and possible loss condition (mean difference=-0.003±0.027, p=0.34, CI:-0.11, 0.004). This imply that the group of patients understood the task.

Likewise, for the group of healthy controls there was a significant difference in response time between possible win and neutral condition (mean difference=0.019±0.019, p=0.0001, CI: 0.014, 0.025) and between possible loss and neutral condition (mean difference= 0.019±0.024, p=0.0001, CI:-0.025, -0.012), but not between possible win and possible loss condition (mean difference=-0.0003±0.016, p=0.88, CI:-0.005, 0.004), see Table S7 for mean response time for each condition in each group.

There was no group difference in hit rate for each of the conditions, see Table S7.

*Analyses on assessing task activity in fMRI contrasts in regions of interest in healthy controls*

To assess whether the task activated the ROIs in HC e.g. worked as expected, analyses were performed on parameter estimates extracted from left ROIs in HC using one sample t-test, and showed a significant activation during motivational salience in the accumbens (p=0.003) and caudate (p=0.04), but not in the DLPFC (p=0.08), ACC (p=0.62) and thalamus (p=0.87). During negative outcome evaluation (NOE) there was a significant activity in accumbens (p=0.04), caudate (p=0.009), DLPFC (p=0.004), ACC (p=0.009) but not in the thalamus (p=0.69), see Table S5 for mean activity and confidence interval. Explorative analyses during positive outcome (PO) evaluation showed significant activity in HC in the caudate (p=0.002) and DLPFC (p=0.002), but not in the ACC (p=0.07), thalamus (p=0.24) or accumbens (p=0.71), see Table S5 for mean activity and confidence interval.

*MRS quality assessment*

Spectral quality was initially assessed by visual inspection according to the LCModel guidelines. Individual metabolic peaks were excluded if the Cramér Rao lower bound (CRLB) was above 20%. In Thalamus, 4 spectra (1 FEP, 3 HC) were excluded after visual inspection. For the remaining 99 spectra, they all had CRLB<20% and no glutamate data were excluded. In ACC, 3 spectra (3 FEP, 0 HC) were excluded after visual inspection. For the remaining 100 spectra, they all had CRLB<20% and no glutamate data were excluded.

For the MRS acquisitions in thalamus and ACC, the signal to noise ratio and FWHM are provided in Table S1.

There was a small but significant group difference between FWHM values for ACC in FEP compared with HC (FEP: 0.0284±0.005, HC: 0.0257±0.006, p=0.025), but all FWHM values were below 0.086 ppm which is used as a the cut-off value in the LC Model manual. Measures of Cramér-Rao lower bounds (CRLB) over the total sample (N=103) in ACC was mean 5.24 ± 0.9 (minimum 4 and maximum 12), and in thalamus mean 10.71 ±3.9 (minimum 7 and maximum 32). For measures of CRLB in the sample included in the analyses e.g. in the sample without those subjects that are not in accordance with the quality criterion, CRLB was in ACC (N=100) mean 5.17 ±0.5 (minimum 4 and maximum 9), and in thalamus (N=99) mean 10.1 ± 2.2 (minimum 7 and maximum 19) . Measures of CRLB in HC and FEP without subjects that are not in accordance with the quality criterion are provided in Table S1.

For the excluded MRS spectra in thalamus (4 spectra), 3 was excluded due to visual inspection and CRLB>20%, and 1 was excluded due to visual inspection only. For the 4 excluded spectra in thalamus, the mean SNR was 6.75.

For excluded MRS spectra in ACC (3 spectra), all were excluded due to visual inspection, and the mean SNR was 19**.**

*Main effects of covariates*

For glutamatergic measures in thalamus, there was no main effect of age (p=0.35), but a main effect of sex (p=0.024) and smoking status (p=0.003). For measures in ACC, there was a main effect of age (p=0.003) but no main effect of sex (p=0.09) or smoking status (p=0.92). There was no significant interaction between group and sex (thalamus: p=0.12; ACC: p=0.68), age (thalamus: p=0.63, ACC: p=0.96), and smoking status (thalamus: p=0.51, ACC: p=0.89). For mean values, 95% confidence interval and glutamate measures corrected for content of gray matter, see Supplementary Table S1.

*Glutamate levels adjusted for gray matter fraction in left thalamus and ACC in FEP and HC*

There was no group difference in glutamate levels when corrected for voxel content of gray matter, see Table S1, nor when controlled for covariates (thalamus: p= 0.05; ACC: p=0.23). There was no main effect of age (thalamus: p=0.72, ACC: p=0.05), sex (thalamus: p=0.08, ACC: p=0.06) or smoking status (thalamus: p=0.11, ACC: p=0.51).

*Association between motivational salience or NOE signal and glutamate levels adjusted for GM*

No significant correlations were found between glutamate levels corrected for gray matter fractions and motivational salience or NOE signaling in FEP or in HC, see Table S3. There was no main effect of sex, age or smoking status on the association between glutamate measures adjusted for GM and motivational salience or NOE signaling and including covariates in regression analyses did not affect the results.

*Glx IU levels in left thalamus and ACC in FEP and HC*

There was no group difference between FEP and HC in Glx IU levels in left thalamus (FEP: 9.69±1.6, HC: 9.80±1.5; T(97)=-0.35, p= 0.73, CI: -0.73, 0.50) or in ACC (FEP: 13.41±1.3, HC: 13.60±1.0; T(98)=-0.86, p=0.39, CI: -0.50, 0.22), nor when controlled for covariates (left thalamus: p=0.91, ACC: p=0.43).

*Association between motivational salience or NOE signal and glx IU levels*

No significant correlations were found between glx IU levels in left thalamus or ACC and motivational salience or negative outcome evaluation (NOE) signaling, see Table S4. There was no main effect of sex, age or smoking status on the association between glx IU levels and motivational salience or NOE signaling and including covariates in regression analyses did not affect the results.

*FMRI analyses on negative outcome evaluation signaling for ROIs in the right hemisphere*

For the negative outcome evaluation (NOE) signal, there was a group difference with FEP having higher signal (higher contrast parameter estimates) in the right caudate (T(101)=3.1, p=0.003, CI:0.05, 0.24) and in the right DLPFC (T(101)=2.9, p=0.004, CI: 0.06, 0.33), but not in the right accumbens (T(101)=2.4, p=0.02, CI: 0.02, 0.22), the right thalamus (T(101)=2.1, p=0.04, CI:0.01, 0.23), or the right ACC (T(101)=2.2, p=0.03, CI:0.02, 0.28), see Table S1. There were no significant correlations between glutamatergic measures and NOE signal on ROIs in the right hemisphere, see Table S2, Table S3 and Table S4*.*

*FMRI analyses on positive outcome signaling*

Explorative analyses on positive outcome (PO) signaling (hit outcome versus neutral outcome) showed no group difference for ROIs in the left or right hemisphere, see Table S1. Explorative additional analyses showed no correlation between PO and glutamatergic measures, see Table S2, Table S3 and Table S4.

*FMRI analyses on neutral outcome*

Additional explorative analyses on neutral outcome showed no group difference in the left caudate (FEP: 0.016±0.77, HC: 0.141±0.48, T(101)=-0.9, p=0.33, CI: -0.37, 0.13), left DLPFC (FEP: 0.231±0.92, HC: 0.420±0.65, T(101)=-1.2, p=0.64, CI: -0.50, 0.12), right caudate (FEP:-0.043±0.70, HC:0.123±0.46, T(101)=-1.4, p=0.16, CI: -0.39, 0.06) or right DLPFC (FEP: 0.210±0.85, HC: 0.263±0.45, T(101)=-0.40, p=0.69, CI:-0.32, 0.21).

*Correlations between PANSS scores and imaging measures in FEP*

Explorative correlations in the group of FEP between imaging measures of the predefined ROIs and PANSS total score, PANSS positive score, PANSS negative score and PANSS general scores showed no significant correlations, however, a trend level was found between PANSS positive score and motivational salience signal in the left caudate, and between PANSS positive score and positive outcome in the left accumbens. See Table S6 for correlation coefficients and p-values.

**Supplementary Figure S4. Whole-brain activation of healthy controls and antipsychotic-naïve patients with first-episode psychosis during contrast of motivational salience and negative outcome evaluation and group comparison**

Picture 3

Panel A shows negative outcome evaluation signal in healthy controls (HC), panel B shows negative outcome evaluation signal in first-episode psychosis patients (FEP), panel C shows group difference in negative outcome evaluation signal (FEP>HC), panel D shows group difference in negative outcome evaluation signal (HC>FEP), panel E shows motivational salience contrast signal in HC, panel F shows motivational salience contrast signal in FEP, panel G show group difference in motivational salience contrast signal (FEP>HC), panel H shows group difference in motivational salience contrast signal (HC>FEP). The resulting z-statistic images were thresholded using clusters determined by Z>2.3 and corrected significance threshold of p=0.05

**Supplementary Table S1. Behavioral measures, negative outcome evaluation, positive outcome, motivational salience signal, glutamate levels in thalamus and ACC, fractions in the voxels and spectral quality**

|  |  |  |  |
| --- | --- | --- | --- |
|  | FEP(N= 51) | HC(N= 52) | Statistics |
| Behavioral data |  |  |  |
| Monetary gain, euros ± SD | 76 ± 25 | 76 ± 24 | T(101)=0.10a, p=0.99, CI:-9.6, 9.7 |
| Hit rate % ± SD | 70.2 ± 4.2 | 70.0 ± 4.4 | T(101)=0.14a, p=0.89, CI:-1.5, 1.7 |
| Negative outcome evaluation signal |  |  |  |
| Left Caudate ± SD | 0.09 ± 0.28 | -0.09 ± 0.25 | T(101)=3.4a, **p=0.001**, CI:0.08, 0.28 |
| Left Accumbens ± SD | 0.03 ± 0.29 | -0,07 ± 0.24 | T(101)=1.8a, p=0.07, CI:-0.009, 0.20 |
| Left Dorsolateral prefrontal cortex ± SD | 0.08 ± 0.4 | -0.13 ± 0.3 | T(101)=3.1a, **p=0.003**, CI:0.07, 0.34 |
| Left Thalamus ± SD | 0.12±0.3 | 0.02±0.3 | T(101)=1.87a, p=0.063, CI:-0.006, 0.21 |
| Left ACC ± SD | 0.16±0.25 | 0.08±0.21 | T(101)=1.7a, p=0.09, CI:-0.01, 0.17 |
| Right Caudate ± SD | 0.08±0.26 | -0.06±0.22 | T(101)=3.1, **p=0.003**, CI:0.05, 0.24 |
| Right Accumbens ± SD | 0.08±0.28 | -0.03±0.22 | T(101)=2.4, p=0.02, CI:0.02, 0.22 |
| Right Dorsolateral prefrontal cortex ±SD | 0.21±0.43 | 0.01±0.20 | T(101)=2.9, p=0.004, CI:0.06, 0.33 |
| Right Thalamus ± SD | 0.16±0.28 | 0.04±0.29 | T(101)=2.1, p=0.04, CI:0.01, 0.23 |
| Right ACC ± SD | 0.31±0.42 | 0.16±0.23 | T(101)=2.2, p=0.03, CI:0.02, 0.28 |
| Motivational salience signal |  |  |  |
| Left Caudate ± SD | 0.01 ± 0.21 | 0.05 ± 0.16 | T(101)=-0.9a, p=0.35, CI:-0.11, 0.04 |
| Left Accumbens ± SD | 0.02 ± 0.16 | 0.07 ± 0.15 | T(101)=-1.3a, p=0.18, CI:-0.10, 0.02 |
| Left Dorsolateral prefrontal cortex ± SD | -0.06 ± 0.19 | -0.06 ± 0.24 | T(101)=-0.08a, p=0.94, CI:-0.09, 0.08 |
| Left Thalamus ± SD | -0.014±0.20 | -0.004±0.20 | T(101)=-0.25a, p=0.80, CI:-0.09, 0.07 |
| Left ACC ± SD | -0.01±0.19 | -0.01±0.13 | T(101)=-0.02a, p=0.98, CI:-0.06, 0.06 |
| Right Caudate ± SD | 0.01±0.21 | 0.07±0.19 | T(101)=-1.5a, p=0.13, CI: -0.14, 0.02 |
| Right Accumbens ± SD | 0.004±0.17 | 0.03±0.17 | T(101)=-0.9, p=0.36, CI:-0.09, 0.03 |
| Right Dorsolateral prefrontal cortex ± SD | -0.06±0.22 | -0.003±0.19 | T(101)=-1.4, p=0.16, CI:-0.14, 0.02 |
| Right Thalamus ± SD | -0.03±0.19 | -0.01±0.18 | T(101)=-0.4, p=0.69, CI: -0.08, 0.06 |
| Right ACC ± SD | 0.004±0.21 | -0.01±0.16 | T(101)=0.3, p=0.77, CI:-0.06, 0.08 |
| Positive outcome signal |  |  |  |
| Left Caudate ± SD | -0.027±0.27 | -0.106±0.23 | T(101)=1.6, p=0.11, CI: -0.02, 0.18 |
| Left Accumbens ± SD | 0.03±0.20 | -0.010±0.20 | T(101)=1.0, p=0.31, CI: -0.04, 0.12 |
| Left Dorsolateral prefrontal cortex ± SD | -0.047±0.26 | -0.116±0.26 | T(101)=1.3, p=0.18, CI: -0.03, 0.17 |
| Left Thalamus ± SD | 0.007±0.20 | -0.039±0.24 | T(101)=1.1, p=0.28, CI: -0.04, 0.13 |
| Left ACC ± SD | 0.082±0.24 | 0.042±0.17 | T(101)=0.9, p=0.34, CI: -0.04, 0.12 |
| Right Caudate ± SD | -0.029±0.25 | -0.086±0.22 | T(101)=1.2, p=0.23, CI: -0.03, 0.15 |
| Right Accumbens ± SD | 0.076±0.20 | 0.002±0.21 | T(101)=1.8, p=0.07, CI:-0.005, 0.15 |
| Right Dorsolateral prefrontal cortex ± SD | 0.077±0.19 | -0.017±0.19 | T(101)=2.5, p=0.014, CI:0.02, 0.17 |
| Right Thalamus ± SD | 0.067±0.24 | 0.002±0.19 | T(101)=1.5, p=0.12, CI:-0.02, 0.15 |
| Right ACC ± SD | 0.154±0.29 | 0.087±0.18 | T(101)=1.4, p=0.16, CI:-0.03, 0.16 |
| Glutamate in thalamus IU ± SD | 6.85 ± 0.9 | 6.74 ± 0.8 | T(97)=0.39a p=0.53, CI:-0.24, 0.47 |
| Glutamate in thalamus IUadjusted ± SD | 0.6868±0.38 | 0.5614±0.22 | T(97)=2.0a, p=0.05, CI:0.001, 0.25 |
| FWHM (ppm) ± SD | 0.0465±0.007 | 0.0462±0.007 | T(97)=0.17a, p=0.86, CI:-0.002, 0.003 |
| Signal to noise ration± SD | 16.1±3.9 | 16.5±3.7 | T(97)=-0.48a, p=0.63, CI:-1.9, 1.2 |
| CRLB (%) of glutamate ± SD | 10.1 ± 2 | 10.3 ± 2.7 | T(97)=-0.48a, p=0.63, CI:-0.9, 0.87 |
| Gray matter fraction ± SD | 0.10 ± 0.05 | 0.08 ± 0.03 | Z= -1.3b, p=0.19 |
| White matter fraction ± SD | 0.89 ± 0.05 | 0.92 ± 0.03 | Z= -1.3b, p=0.19 |
| CSF fraction ± SD | 0.002 ± 0.002 | 0.001± 0.001 | Z= -0.83b, p=0.41 |
| Glutamate in ACC IU ± SD | 10.2 ± 0.77 | 10.4 ± 0.64 | T(98)=0.98a, p=0.32, CI:-0.42, 0.14 |
| Glutamate in ACC IUadjusted ± SD | 8.34 ± 0.78 | 8.51 ± 0.73 | T(98)=-1.1, p=0.26, CI:-0.47, 0.13 |
| FWHM (ppm) ± SD | 0.0284±0.005 | 0.0257±0.006 | T(98)=2.3a, p=0.025, CI:0.0003, 0.005 |
| Signal to noise ratio ± SD | 32.2±2.3 | 32.1±2.6 | T(98)=0.18a, p=0.86,CI:-0.88, 1.1 |
| CRLB (%) of glutamate ± SD | 5.3 ± 1.1 | 5.2 ± 0.5 | T(98)=1.0a, p=0.30,CI:-0.16, 0.52 |
| Gray matter fraction ± SD | 0.69 ± 0.03 | 0.69 ± 0.02 | T(98)=-0.7a, p=0.49, CI:-0.01, 0.006 |
| White matter fraction ± SD | 0.16 ± 0.03 | 0.15 ± 0.03 | T(98)=0.79a, p=0.43, CI:-0.007, 0.02 |
| Cerebral spinal fluid fraction ± SD | 0.15 ± 0.03 | 0.15 ± 0.02 | T(98)=-0.3a, p=0.77, CI:-0.01, 0.008 |

Table S1 shows behavioral data, estimates of negative outcome evaluation, motivational salience signal, positive outcome signal and measures of glutamatergic levels, fractions of the voxels and spectral quality. A significant group difference was found between FEP and HC in negative outcome evaluation signal in the left caudate (p=0.001) and DLPFC (p=0.003). FEP: First episode psychosis patients, HC: Healthy controls, SD: standard deviation, ACC: anterior cingulate cortex, IU: Institutional Units, IUadjusted: glutamate measures adjusted for content of cerebral spinal fluid and grey matter fractions, FWHM: full-width half-maximum, Ppm: parts per million, CRLB: Cramer-Rao lower bound. aindependent t-test, bMann-Whitney U test. CI: 95%confindence interval of the difference.

**Supplementary Table S2. Regression coefficients, p-values and confidence interval between levels of glutamate and motivational salience or negative outcome evaluation or positive outcome signaling in antipsychotic-naïve first-episode psychosis and healthy controls**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Glutamate IUACC** | | | | | | **Glutamate IU Thalamus** | | | | | |
| FEP | | | HC | | | FEP | | | HC | | |
| Beta | P- value | 95%CI | Beta | p-value | 95%CI | Beta | p-value | 95%CI | Beta | p-value | 95%CI |
| **Main regression analyses**  **NOE signal** | | | | | | | | | |  | | |
| Left Caudate | -0.01 | 0.94 | -0.29, 0.28 | 0.21 | 0.15 | -0.07, 0.48 | -0.40 | **0.004** | -0.64, -0.13 | 0.13 | 0.37 | -0.16, 0.43 |
| Left DLPFC | 0.10 | 0.54 | -0.21, 0.39 | -0.05 | 0.74 | -0.35, 0.22 | -0.39 | **0.005** | -0.66, -0.13 | 0.11 | 0.46 | -0.18, 0.4 |
| **Explorative regression analyses**  **Motivational salience signal** | | | | | | | | | |  | | |
| Left Accumbens | 0.07 | 0.65 | -0.22, 0.36 | 0.32 | 0.02 | 0.05, 0.059 | 0.08 | 0.56 | -0.21, 0.38 | -0.20 | 0.16 | -0.49, 0.09 |
| Left Caudate | 0.21 | 0.16 | -0.08, 0.47 | -0.13 | 0.35 | -0.41, 0.15 | 0.24 | 0.09 | -0.04, 0.49 | -0.13 | 0.39 | 0.42, 0.17 |
| Left Thalamus | 0.12 | 0.41 | -0.17, 0.42 | 0.36 | 0.008 | 0.09, 0.63 | -0.04 | 0.84 | -0.33, 0.25 | 0.56 | 0.70 | -0.23, 0.34 |
| Left DLPFC | -0.22 | 0.13 | -0.49, 0.06 | -0.09 | 0.53 | -0.37, 0.19 | 0.32 | 0.02 | 0.05, 0.59 | 0.23 | 0.11 | -0.05, 0.52 |
| Left ACC | 0.06 | 0.69 | -0.23, 0.34 | 0.12 | 0.38 | -0.16, 0.41 | 0.01 | 0.49 | -0.19, 0.39 | 0.09 | 0.53 | -0.20, 0.39 |
| **NOE signal** | | | | | | | | | |  | | |
| Left Accumbens | 0.10 | 0.51 | -0.20, 0.40 | 0.15 | 0.29 | -0.13, 0.43 | -0.23 | 0.10 | -0.52, 0.05 | -0.08 | 0.59 | -0.37, 0.21 |
| Left Thalamus | 0.04 | 0.79 | -0.26, 0.35 | -0.21 | 0.14 | -0.49, 0.07 | -0.39 | 0.005 | -0.66, -0.12 | 0.01 | 0.93 | -0.27, 0.30 |
| Left ACC | 0.14 | 0.35 | -0.16, 0.44 | 0.03 | 0.85 | -0.26, 0.31 | -0.23 | 0.11 | -0.51, 0.05 | 0.18 | 0.23 | -0.11, 0.45 |
| **Explorative regression analyses**  **Motivational salience signal** | | |  |  |  |  |  |  |  |  |  |  |
| Right Accumbens | 0.16 | 0.26 | -0.12, 0.45 | 0.18 | 0.20 | -0.10, 0.46 | 0.15 | 0.31 | -0.14, 0.44 | 0.17 | 0.24 | -0.12, 0.46 |
| Right Caudate | 0.11 | 0.46 | -0.17, 0.37 | -0.10 | 0.47 | -0.38, 0.18 | 0.12 | 0.40 | -0.15, 0.37 | 0.001 | 1.0 | -0.29, 0.29 |
| Right Thalamus | 0.01 | 0.94 | -0.29, 0.31 | 0.15 | 0.30 | -0.14, 0.43 | -0.02 | 0.91 | -0.30, 0.27 | 0.21 | 0.14 | -0.08, 0.51 |
| Right DLPFC | 0.14 | 0.35 | -0.16, 0.44 | -0.10 | 0.53 | -0.37, 0.19 | -0.03 | 0.86 | -0.31, 0.27 | 0.01 | 0.96 | -0.29, 0.31 |
| Right ACC | 0.17 | 0.26 | -0.12, 0.45 | 0.18 | 0.20 | -0.10, 0.46 | 0.03 | 0.83 | -0.26, 0.32 | 0.03 | 0.82 | -0.26, 0.33 |
| **NOE signal** |  |  |  |  |  |  |  |  |  |  |  |  |
| Right Accumbens | 0.02 | 0.92 | -0.29, 0.32 | -0.02 | 0.91 | -0.30, 0.27 | -0.23 | 0.11 | -0.52, 0.05 | -0.09 | 0.54 | -0.39, 0.21 |
| Right Caudate | 0.04 | 0.97 | -0.29, 0.29 | 0.27 | 0.05 | 0.001, 0.55 | -0.24 | 0.09 | -0.50, 0.04 | 0.04 | 0.77 | 0.26, 0.35 |
| Right Thalamus | 0.06 | 0.68 | -0.24, 0.36 | -0.08 | 0.55 | -0.37, 0.20 | -0.41 | 0.004 | -0.68, -0.15 | 0.07 | 0.62 | -0.22, 0.36 |
| Right DLPFC | 0.14 | 0.36 | -0.16, 0.44 | -0.03 | 0.81 | -0.32, 0.25 | -0.34 | 0.015 | -0.61, -0.07 | 0.07 | 0.62 | -0.22, 0.37 |
| Right ACC | 0.13 | 0.37 | -0.17, 0.43 | -0.11 | 0.43 | -0.39, 0.17 | -0.26 | 0.07 | -0.54, 0.02 | 0.09 | 0.53 | -0.21, 0.39 |
| **Explorative regression analyses** | | |  |  |  |  |  |  |  |  |  |  |
| **UPO signal** |  |  |  |  |  |  |  |  |  |  |  |  |
| Left Accumbens | 0.16 | 0.29 | -0.15, 0.49 | 0.004 | 0.98 | -0.25, 0.26 | -0.28 | 0.04 | -0.60, -0.01 | -0.12 | 0.41 | -0.40, 0.16 |
| Left Caudate | -0.09 | 0.56 | -0.42, 0.23 | 0.19 | 0.18 | -0.09, 0.46 | -0.18 | 0.20 | -0.50, 0.11 | 0.13 | 0.38 | -0.17, 0.43 |
| Left Thalamus | 0.11 | 0.48 | -0.23, 0.47 | -0.21 | 0.14 | -0.40, 0.06 | -0.23 | 0.11 | -0.58, 0.06 | 0.13 | 0.39 | -0.15, 0.38 |
| Left DLPFC | 0.12 | 0.43 | -0.19, 0.44 | -0.002 | 0.98 | -0.26, 0.26 | -0.37 | 0.01 | -0.66, -0.10 | 0.12 | 0.41 | -0.17, 0.40 |
| Left ACC | 0.11 | 0.47 | -0.17, 0.37 | 0.17 | 0.23 | -0.13, 0.50 | -0.25 | 0.09 | -0.47, 0.03 | 0.25 | 0.09 | -0.05, 0.66 |
| Right Accumbens | 0.06 | 0.69 | -0.26, 0.40 | 0.12 | 0.41 | -0.15, 0.36 | -0.30 | 0.03 | -0.62, -0.03 | -0.21 | 0.14 | -0.46, 0.07 |
| Right Caudate | 0.08 | 0.60 | -0.24, 0.42 | 0.25 | 0.08 | -0.03, 0.51 | -0.03 | 0.98 | -0.31, 0.30 | 0.08 | 0.57 | -0.21, 0.38 |
| Right Thalamus | 0.13 | 0.38 | -0.16, 0.42 | -0.10 | 0.53 | -0.38, 0.20 | -0.19 | 0.18 | -0.45, 0.09 | 0.13 | 0.36 | -0.17, 0.47 |
| Right DLPFC | 0.09 | 0.54 | -0.23, 0.44 | -0.02 | 0.88 | -0.28, 0.24 | -0.22 | 0.13 | -0.54, 0.07 | 0.08 | 0.60 | -0.21, 0.35 |
| Right ACC | 0.15 | 0.32 | -0.14, 0.41 | 0.20 | 0.15 | -0.10, 0.59 | -0.08 | 0.61 | -0.32, 0.19 | 0.07 | 0.66 | -0.30, 0.47 |

Table S2 show associations between signaling of motivational salience or negative outcome evaluation or positive outcome for regions of interest in the left and the right hemisphere and levels of glutamate in first-episode psychosis patients and healthy controls. Associations were performed using regression analyses. A significant negative correlation was found in patients between negative outcome evaluation (NOE) signal in the caudate and glutamate levels in the thalamus (beta=-0.40, p=0.004) and a significant negative correlation between NOE signal in DLPFC and thalamic glutamate levels (beta=-0.39, p=0.005) when corrected for multiple comparisons (p<0.006). IU: institutional units, NOE: negative outcome evaluation, ACC: anterior cingulate cortex, FEP: first episode psychosis patients, HC: healthy controls, DLPFC: dorsolateral prefrontal cortex, PO: positive outcome, CI: confidence interval

**Supplementary Table S3. Regression coefficients, p-values and confidence interval between levels of glutamate corrected for gray matter and motivational salience or negative outcome evaluation or positive outcome signaling in antipsychotic-naïve patients with first-episode psychosis and healthy controls**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Glutamate IU adjusted ACC** | | | | | | **Glutamate IUadjusted Thalamus** | | | | | | |
| FEP | | | HC | | | FEP | | | | HC | | |
| Beta | P- value | 95%CI | Beta | p-value | 95%CI | Beta | p-value | 95%CI | Beta | | p-value | 95%CI |
| **Main regression analyses**  **NOE signal** | | | | | | | | | | | | | |
| Left Caudate | 0.12 | 0.42 | -0.17, 0.40 | 0.12 | 0.39 | -0.16, 0.40 | -0.19 | 0.20 | -0.46, 0.09 | | 0.27 | 0.06 | -0.02, 0.56 |
| Left DLPFC | 0.14 | 0.34 | -0.16, 0.44 | -0.01 | 0.94 | -0.32, 0.25 | -0.25 | 0.084 | -0.53, 0.04 | | 0.16 | 0.27 | -0.09, 0.49 |
| **Explorative regression analyses**  **Motivational salience signal** | | | | | | | | | | | | |  |
| Left Accumbens | 0.08 | 0.58 | -0.21, 0.37 | 0.32 | 0.02 | 0.05, 0.59 | 0.28 | 0.05 | 0.005, 0.56 | | -0.28 | 0.05 | -0.56, 0.005 |
| Left Caudate | 0.09 | 0.52 | -0.19, 0.36 | -0.09 | 0.53 | -0.37, 0.19 | 0.27 | 0.06 | -0.007, 0.52 | | -0.07 | 0.62 | -0.37, 0.22 |
| Left Thalamus | 0.16 | 0.27 | -0.13, 0.46 | 0.39 | 0.004 | 0.13, 0.65 | 0.18 | 0.21 | -0.11, 0.47 | | 0.16 | 0.36 | -0.13, 0.44 |
| Left DLPFC | -0.24 | 0.11 | -0.50, 0.05 | 0.02 | 0.86 | -0.26, 0.31 | 0.11 | 0.46 | -0.18, 0.40 | | -0.13 | 0.37 | -0.42, 0.16 |
| Left ACC | 0.04 | 0.79 | -0.25, 0.33 | 0.16 | 0.26 | -0.12, 0.44 | 0.10 | 0.50 | -0.19, 0.39 | | -0.15 | 0.31 | -0.44, 0.14 |
| **NOE signal** | | | | | | | | | | | | |  |
| Left Accumbens | 0.12 | 0.44 | -0.18, 0.41 | 0.09 | 0.51 | -0.19, 0.38 | -0.11 | 0.43 | -0.41, 0.18 | | 0.21 | 0.16 | -0.08, 0.49 |
| Left Thalamus | 0.14 | 0.35 | -0.16, 0.44 | -0.18 | 0.19 | -0.47, 0.09 | -0.18 | 0.22 | -0.47, 0.11 | | 0.09 | 0.53 | -0.19, 0.38 |
| Left ACC | 0.18 | 0.21 | -0.11, 0.48 | -0.03 | 0.84 | -0.31, 0.26 | 0.03 | 0.84 | -0.26, 0.32 | | 0.16 | 0.27 | -0.13, 0.44 |
| **Explorative regression analyses** | | |  |  |  |  |  |  |  | |  |  |  |
| **Motivational salience signal** | | | |  |  |  |  |  |  | |  |  |  |
| Right Accumbens | 0.18 | 0.21 | -0.10, 0.47 | 0.25 | 0.07 | -0.24, 0.53 | -0.03 | 0.82 | -0.30, 0.28 | | -0.07 | 0.65 | -0.36, 0.23 |
| Right Caudate | 0.013 | 0.93 | -0.26, 0.28 | -0.08 | 0.57 | -0.36, 0.20 | 0.15 | 0.30 | -0.12, 0.39 | | -0.23 | 0.11 | -0.52, 0.05 |
| Right Thalamus | 0.04 | 0.79 | -0.25, 0.34 | 0.22 | 0.12 | -0.06, 0.49 | 0.10 | 0.47 | -0.18, 0.39 | | 0.23 | 0.12 | -0.06, 0.52 |
| Right DLPFC | 0.17 | 0.25 | -0.13, 0.47 | -0.18 | 0.90 | -0.30, 0.27 | -0.12 | 0.40 | -0.42, 0.17 | | 0.05 | 0.75 | -0.35, 0.25 |
| Right ACC | 0.03 | 0.86 | -0.27, 0.32 | -0.05 | 0.71 | -0.34, 0.23 | 0.20 | 0.16 | -0.08, 0.49 | | -0.19 | 0.19 | -0.48, 0.10 |
| **NOE signal** |  |  |  |  |  |  |  |  |  | |  |  |  |
| Right Accumbens | 0.08 | 0.57 | -0.22, 0.38 | -0.03 | 0.85 | -0.31, 0.26 | -0.17 | 0.25 | -0.46, 0.12 | | 0.06 | 0.69 | -0.24, 0.36 |
| Right Caudate | 0.15 | 0.32 | -0.15, 0.43 | 0.21 | 0.13 | -0.06, 0.49 | -0.15 | 0.29 | -0.42, 0.13 | | 0.17 | 0.24 | -0.12, 0.47 |
| Right Thalamus | 0.14 | 0.34 | -0.15, 0.44 | -0.08 | 0.57 | -0.36, 0.20 | -0.25 | 0.08 | -0.54, 0.03 | | 0.21 | 0.13 | -0.07, 0.50 |
| Right DLPFC | 0.14 | 0.33 | -0.15, 0.44 | -0.05 | 0.70 | -0.34, 0.23 | -0.20 | 0.16 | -0.48, 0.08 | | 0.08 | 0.58 | -0.21, 0.38 |
| Right ACC | 0.16 | 0.27 | -0.13, 0.47 | -0.12 | 0.38 | -0.41, 0.16 | -0.04 | 0.77 | -0.33, 0.25 | | 0.23 | 0.11 | -0.05, 0.53 |
| **Explorative regression analyses** | | |  |  |  |  |  |  |  | |  |  |  |
| **PO signal** |  |  |  |  |  |  |  |  |  | |  |  |  |
| Left Accumbens | 0.16 | 0.28 | -0.14, 0.47 | -0.08 | 0.59 | -0.34, 0.20 | -0.03 | 0.84 | -0.39, 0.31 | | 0.07 | 0.64 | -0.15, 0.25 |
| Left Caudate | 0.10 | 0.49 | -0.20, 0.41 | 0.10 | 0.48 | -0.20, 0.40 | 0.05 | 0.74 | -0.29, 0.42 | | 0.09 | 0.53 | -0.14, 0.28 |
| Left Thalamus | 0.19 | 0.20 | -0.12, 0.53 | -0.19 | 0.17 | -0.42, 0.07 | 0.08 | 0.56 | -0.27, 0.49 | | 0.05 | 0.72 | -0.16, 0.23 |
| Left DLPFC | 0.12 | 0.43 | -0.18, 0.42 | -0.02 | 0.89 | -0.30, 0.26 | -0.13 | 0.38 | -0.49, 0.19 | | 0.07 | 0.64 | -0.15, 0.25 |
| Left ACC | 0.16 | 0.28 | -0.12, 0.39 | 0.07 | 0.62 | -0.26, 0.43 | 0.09 | 0.53 | -0.21, 0.39 | | 0.25 | 0.09 | -0.04, 0.48 |
| Right Accumbens | 0.11 | 0.46 | -0.19, 0.42 | 0.06 | 0.67 | -0.22, 0.33 | 0.01 | 0.95 | -0.35, 0.37 | | 0.001 | 0.99 | -0.20, 0.20 |
| Right Caudate | 0.23 | 0.12 | -0.06, 0.54 | 0.19 | 0.17 | -0.09, 0.49 | 0.17 | 0.25 | -0.15, 0.55 | | 0.04 | 0.80 | -0.19, 0.24 |
| Right Thalamus | 0.18 | 0.21 | -0.10, 0.44 | -0.10 | 0.48 | -0.42, 0.20 | 0.04 | 0.79 | -0.28, 0.36 | | 0.19 | 0.19 | -0.08, 0.38 |
| Right DLPFC | 0.12 | 0.40 | -0.18, 0.44 | -0.07 | 0.60 | -0.35, 0.21 | -0.13 | 0.35 | -0.53, 0.19 | | -0.03 | 0.84 | -0.22, 0.18 |
| Right ACC | 0.18 | 0.22 | -0.10, 0.41 | 0.11 | 0.45 | -0.23, 0.51 | 0.16 | 0.26 | -0.13, 0.46 | | 0.39 | 0.006 | 0.11, 0.62 |

Table S3 show associations between signaling of motivational salience or negative outcome evaluation for regions of interest in the left and in the right hemisphere and levels of glutamate in concentration of institutional units corrected for gray matter content in spectroscopic voxels in first-episode psychosis patients and healthy controls. Associations were performed using regression analyses. IUadjusted: glutamate IU levels adjusted for gray matter, IU: institutional units, NOE: negative outcome evaluation, ACC: anterior cingulate cortex, FEP: antipsychotic-naïve patients with first-episode psychosis, HC: healthy controls, DLPFC: dorsolateral prefrontal cortex, CI: confidence interval, PO: positive outcome.

**Supplementary Table S4. Regression coefficients, p-values and confidence interval between levels of glx IU and motivational salience or negative outcome evaluation or positive outcome signaling in antipsychotic-naïve patients with first-episode psychosis and healthy controls**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Glx IUACC** | | | | | | **Glx IU Thalamus** | | | | | |
| FEP | | | HC | | | FEP | | | HC | | |
| Beta | P- value | 95%CI | Beta | p-value | 95%CI | Beta | p-value | 95%CI | Beta | p-value | 95%CI |
| **Main regression analyses**  **NOE signal** | | | | | | | | | | | |  |
| Left Caudate | -0.02 | 0.88 | -0.31, 0.27 | 0.15 | 0.30 | -0.14, 0.43 | -0.17 | 0.24 | -0.44, 0.11 | 0.07 | 0.60 | -0.22, 0.37 |
| Left DLPFC | 0.04 | 0.78 | -0.26, 0.34 | 0.13 | 0.37 | -0.15, 0.41 | -0.22 | 0.13 | -0.50, 0.07 | 0.18 | 0.22 | -0.12, 0.46 |
| **Explorative regression analyses**  **Motivational salience signal** | | | | | | | | | | | |  |
|  |
| Left Accumbens | 0.11 | 0.46 | -0.18, 0.40 | 0.19 | 0.19 | -0.10, 0.46 | 0.12 | 0.40 | -0.17, 0.41 | -0.21 | 0.14 | -0.50, 0.07 |
| Left Caudate | 0.27 | 0.07 | -0.02, 0.51 | -0.08 | 0.58 | -0.36, 0.21 | 0.19 | 0.18 | -0.08, 0.45 | -0.10 | 0.51 | -0.39, 0.20 |
| Left Thalamus | 0.10 | 0.49 | -0.19, 0.40 | 0.26 | 0.06 | -0.01, 0.54 | -0.03 | 0.85 | -0.32, 0.27 | 0.01 | 0.96 | -0.28, 0.29 |
| Left DLPFC | -0.19 | 0.19 | -0.46, 0.10 | 0.05 | 0.74 | -0.24, 0.33 | 0.19 | 0.18 | -0.09, 0.48 | 0.24 | 0.09 | -0.04, 0.53 |
| Left ACC | 0.09 | 0.56 | -0.20, 0.37 | 0.01 | 0.95 | -0.27, 0.29 | 0.02 | 0.88 | -0.27, 0.31 | 0.10 | 0.51 | -0.20, 0.39 |
| **NOE signal** | | | | | | | | | | | |  |
| Left Accumbens | 0.02 | 0.91 | -0.28, 0.32 | 0.11 | 0.45 | -0.18, 0.39 | -0.21 | 0.14 | -0.50, 0.07 | -0.01 | 0.93 | -0.31, 0.28 |
| Left Thalamus | 0.04 | 0.81 | -0.27, 0.34 | -0.11 | 0.45 | -0.39, 0.17 | -0.24 | 0.09 | -0.53, 0.04 | 0.11 | 0.47 | -0.18, 0.39 |
| Left ACC | 0.08 | 0.59 | -0.22, 0.38 | 0.11 | 0.43 | -0.17, 0.39 | -0.07 | 0.62 | -0.36, 0.22 | 0.07 | 0.63 | -0.22, 0.36 |
| **Explorative regression analyses** | | | |  |  |  |  |  |  |  |  |  |
| **Motivational salience signal** | | |  |  |  |  |  |  |  |  |  |  |
| Right Accumbens | 0.11 | 0.44 | -0.18, 0.40 | 0.10 | 0.46 | -0.18, 0.39 | -0.04 | 0.79 | -0.33, 0.25 | 0.05 | 0.74 | -0.25, 0.34 |
| Right Caudate | 0.11 | 0.44 | -0.16, 0.37 | 0.02 | 0.90 | -0.26, 0.30 | 0.03 | 0.84 | -0.23, 0.29 | -0.001 | 0.97 | -0.30, 0.29 |
| Right Thalamus | -0.03 | 0.82 | -0.33, 0.27 | 0.15 | 0.28 | -0.13, 0.43 | -0.14 | 0.32 | -0.43, 0.14 | 0.26 | 0.08 | -0.03, 0.55 |
| Right DLPFC | 0.10 | 0.49 | -0.19, 0.40 | -0.05 | 0.75 | -0.32, 0.24 | -0.10 | 0.49 | -0.39, 0.19 | 0.01 | 0.96 | -0.29, 0.31 |
| Right ACC | -0.03 | 0.81 | -0.32, 0.26 | -0.07 | 0.61 | -0.36, 0.21 | 0.004 | 0.98 | -0.29, 0.29 | 0.02 | 0.91 | -0.28, 0.31 |
| **NOE signal** |  |  |  |  |  |  |  |  |  |  |  |  |
| Right Accumbens | 0.03 | 0.83 | -0.27, 0.33 | -0.01 | 0.94 | -0.30, 0.27 | 0.01 | 0.94 | -0.28, 0.30 | 0.02 | 0.91 | -0.28, 0.31 |
| Right Caudate | 0.04 | 0.78 | -0.25, 0.33 | 0.19 | 0.16 | -0.08, 0.48 | -0.04 | 0.80 | -0.31, 0.25 | 0.007 | 0.96 | -0.29, 0.31 |
| Right Thalamus | 0.06 | 0.67 | -0.24, 0.36 | -0.04 | 0.76 | -0.33, 0.24 | -0.21 | 0.14 | -0.50, 0.07 | 0.13 | 0.39 | -0.17, 0.41 |
| Right DLPFC | 0.09 | 0.52 | -0.20, 0.40 | 0.11 | 0.43 | -0.17, 0.39 | -0.10 | 0.47 | -0.39, 0.19 | 0.07 | 0.62 | -0.22, 0.37 |
| Right ACC | 0.07 | 0.63 | -0.23, 0.38 | -0.03 | 0.83 | -0.31, 0.26 | -0.13 | 0.35 | -0.43, 0.15 | 0.10 | 0.50 | -0.20, 0.40 |
| **Explorative regression analyses** | | | |  |  |  |  |  |  |  |  |  |
| **PO signal** |  |  |  |  |  |  |  |  |  |  |  |  |
| Left Accumbens | 0.02 | 0.88 | -0.31, 0.35 | 0.05 | 0.70 | -0.20, 0.30 | -0.38 | 0.007 | -0.68, -0.11 | -0.03 | 0.83 | -0.31, 0.25 |
| Left Caudate | -0.13 | 0.39 | -0.47, 0.19 | 0.15 | 0.28 | -0.13, 0.43 | -0.22 | 0.13 | -0.53, 0.07 | 0.13 | 0.38 | -0.17, 0.44 |
| Left Thalamus | 0.13 | 0.40 | -0.20, 0.50 | -0.10 | 0.48 | -0.32, 0.15 | -0.18 | 0.22 | -0.52, 0.12 | 0.22 | 0.14 | -0.07, 0.46 |
| Left DLPFC | 0.01 | 0.93 | -0.31, 0.34 | 0.10 | 0.50 | -0.17, 0.34 | -0.30 | 0.03 | -0.59, -0.03 | 0.18 | 0.22 | -0.11, 0.45 |
| Left ACC | 0.02 | 0.90 | -0.26, 0.29 | 0.10 | 0.49 | -0.21, 0.43 | -0.21 | 0.15 | -0.43, 0.07 | 0.19 | 0.20 | -0.13, 0.60 |
| Right Accumbens | 0.04 | 0.81 | -0.29, 0.37 | 0.13 | 0.36 | -0.14, 0.37 | 0.15 | 0.31 | -0.46, 0.15 | -0.07 | 0.66 | -0.34, 0.22 |
| Right Caudate | 0.07 | 0.65 | -0.26, 0.41 | 0.20 | 0.16 | -0.08, 0.46 | -0.03 | 0.83 | -0.34, 0.27 | 0.09 | 0.55 | -0.21, 0.39 |
| Right Thalamus | 0.10 | 0.50 | -0.20, 0.39 | -0.02 | 0.90 | -0.31, 0.27 | -0.12 | 0.42 | -0.38, 0.16 | 0.24 | 0.10 | -0.05, 0.58 |
| Right DLPFC | 0.06 | 0.68 | -0.27, 0.41 | -0.004 | 0.98 | -0.26, 0.26 | -0.05 | 0.72 | -0.37, 0.25 | 0.11 | 0.46 | -0.18, 0.39 |
| Right ACC | 0.05 | 0.72 | -0.23, 0.33 | 0.09 | 0.52 | -0.23, 0.46 | -0.11 | 0.46 | -0.34, 0.16 | 0.10 | 0.53 | -0.27, 0.52 |

Table S4 shows associations between signaling of motivational salience ornegative outcome evaluation or positive outcome for regions of interest in the left and the right hemisphere and levels of glutamate+glutamine (Glx) in concentration of institutional units in first-episode psychosis patients and healthy controls. Associations were performed using regression analyses. Glx: levels of glutamate+glutamine, IU: concentration in institutional units, FEP: first episode psychosis patients, HC: healthy controls, NOE: negative outcome evaluation, PO: positive outcome, ACC: anterior cingulate cortex, DLPFC: dorsolateral prefrontal cortex, CI: confidence interval.

**Supplementary Table S5. Assessment of task activity on ROIs in healthy controls**

|  |  |  |
| --- | --- | --- |
|  | **Healthy Controls (N= 52)** | **Statistics** |
| **Negative outcome evaluation signal** |  |  |
| **Left Caudate** ± SD | -0.09 ± 0.25 | T(51)=-2.7a, **p=0.009**, CI:-0.16, -0.03 |
| **Left Accumbens** ± SD | -0,07 ± 0.24 | T(51)=-2.0a, **p=0.04**, CI:-0.13, -0.002 |
| **Left Dorsolateral prefrontal cortex** ± SD | -0.13 ± 0.3 | T(51)=-3.0a, **p=0.004**, CI:-0.21, -0.04 |
| **Left Thalamus** ± SD | 0.02±0.3 | T(51)=0.4a, p=0.0.68, CI:-0.007, 0.10 |
| **Left ACC** ± SD | 0.08±0.21 | T(51)=2.7a, **p=0.009**, CI:0.02, 0.14 |
| **Motivational salience signal** |  |  |
| **Left Caudate** ± SD | 0.05 ± 0.16 | T(51)=2.1a, **p=0.039**, CI:0.002, 0.09 |
| **Left Accumbens** ± SD | 0.07 ± 0.15 | T(51)=3.1a, **p=0.003**, CI:0.02, 0.11 |
| **Left Dorsolateral prefrontal cortex** ± SD | -0.06 ± 0.24 | T(51)=-0.-1.7a, p=0.08, CI:-0.12, 0.007 |
| **Left Thalamus** ± SD | -0.004±0.20 | T(51)=-0.2a, p=0.87, CI:-0.06, 0.05 |
| **Left ACC** ± SD | -0.01±0.13 | T(51)=--0.5a, p=0.62, CI:-0.05, 0.03 |
| **Positive outcome signal** |  |  |
| **Left Caudate** ± SD | -0.106±0.23 | T(51)=-3.4a, **p=0.002**, CI: -0.17, -0.04 |
| **Left Accumbens** ± SD | -0.010±0.20 | T(51)=-0.4a, p=0.72, CI: -0.07, 0.05 |
| **Left Dorsolateral prefrontal cortex** ± SD | -0.116±0.26 | T(51)=-3.2a, **p=0.002**, CI: -0.19, -0.04 |
| **Left Thalamus** ± SD | -0.039±0.24 | T(51)=-1.1a, p=0.24, CI: -0.10, 0.03 |
| **Left ACC** ± SD | 0.042±0.17 | T(51)=1.8a, p=0.07, CI: -0.004, 0.09 |

Table S5 shows mean activity in ROIs of healthy controls on negative outcome evaluation, motivational salience signal and positive outcome evaluation for ROIs in the left hemisphere. ACC: anterior cingulate cortex, SD: standard deviation, CI: 95% confidence interval, One sample t-testa

**Supplementary Table S6.** **Correlation between PANSS scores and imaging measures**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PANSS Total** | | **PANSS Positive** | | **PANSS Negative** | | **PANSS General** | |
| r | P value | r | P value | r | P value | R | P value |
| **NOE signal** | | | | | | | | |
| Left Accumbens | -0.13 | 0.38 | 0.02 | 0.89 | -0.14 | 0.33 | -0.13 | 0.33 |
| Left Caudate | 0.17 | 0.24 | 0.18 | 0.22 | 0.11 | 0.45 | 0.14 | 0.33 |
| Left Thalamus | 0.06 | 0.66 | 0.07 | 0.61 | -0.13 | 0.38 | 0.14 | 0.32 |
| Left DLPFC | 0.15 | 0.28 | 0.03 | 0.82 | 0.16 | 0.27 | 0.16 | 0.25 |
| Left ACC | -0.08 | 0.58 | -0.08 | 0.57 | 0.02 | 0.89 | 0.16 | 0.25 |
| Right Accumbens | 0.09 | 0.54 | 0.10 | 0.50 | 0.02 | 0.87 | 0.14 | 0.34 |
| Right Caudate | 0.19 | 0.19 | 0.12 | 0.40 | 0.18 | 0.22 | 0.17 | 0.21 |
| Right Thalamus | -0.13 | 0.93 | 0.007 | 0.96 | -0.07 | 0.61 | 0.03 | 0.82 |
| Right DLPFC | 0.03 | 0.82 | 0.04 | 0.78 | -0.08 | 0.58 | 0.12 | 0.39 |
| Right ACC | -0.13 | 0.92 | -0.07 | 0.64 | 0.05 | 0.72 | 0.008 | 0.96 |
| **Motivational salience signal** | | | | | | | | |
| Left Accumbens | 0.14 | 0.33 | 0.03 | 0.82 | 0.10 | 0.48 | 0.21 | 0.13 |
| Left Caudate | 0.06 | 0.67 | -0.25 | 0.07 | 0.10 | 0.48 | 0.09 | 0.52 |
| Left Thalamus | 0.04 | 0.76 | -0.04 | 0.81 | 0.07 | 0.62 | 0.12 | 0.39 |
| Left DLPFC | 0.05 | 0.76 | 0.13 | 0.38 | 0.04 | 0.76 | -0.04 | 0.97 |
| Left ACC | 0.10 | 0.48 | -0.17 | 0.25 | 0.10 | 0.47 | 0.23 | 0.11 |
| Right Accumbens | -0.13 | 0.37 | -0.10 | 0.52 | 0.006 | 0.97 | -0.19 | 0.18 |
| Right Caudate | -0.02 | 0.87 | -0.18 | 0.20 | 0.01 | 0.94 | -0.001 | 0.99 |
| Right Thalamus | 0.09 | 0.52 | 0.13 | 0.35 | 0.05 | 0.75 | 0.12 | 0.39 |
| Right DLPFC | 0.10 | 0.44 | 0.01 | 0.92 | 0.22 | 0.13 | 0.04 | 0.81 |
| Right ACC | 0.007 | 0.96 | -0.07 | 0.61 | 0.04 | 0.77 | 0.05 | 0.74 |
| **PO signal** | | | | | | | | |
| Left Accumbens | -0.10 | 0.51 | -0.27 | 0.07 | -0.02 | 0.88 | -0.03 | 0.84 |
| Left Caudate | 0.08 | 0.54 | 0.06 | 0.69 | 0.09 | 0.50 | 0.11 | 0.45 |
| Left Thalamus | 0.05 | 0.70 | 0.07 | 0.63 | -0.03 | 0.81 | 0.07 | 0.59 |
| Left DLPFC | -0.06 | 0.69 | -0.10 | 0.53 | 0.03 | 0.98 | -0.06 | 0.67 |
| Left ACC | -0.05 | 0.71 | 0.006 | 0.96 | 0.05 | 0.74 | -0.13 | 0.36 |
| Right Accumbens | 0.06 | 0.64 | 0.004 | 0.98 | 0.01 | 0.92 | 0.17 | 0.25 |
| Right Caudate | 0.19 | 0.19 | 0.18 | 0.22 | 0.19 | 0.18 | 0.17 | 0.24 |
| Right Thalamus | 0.03 | 0.81 | -0.04 | 0.79 | 0.08 | 0.56 | 0.04 | 0.77 |
| Right DLPFC | 0.19 | 0.16 | 0.12 | 0.41 | 0.11 | 0.41 | 0.25 | 0.08 |
| Right ACC | -0.09 | 0.53 | -0.10 | 0.94 | -0.01 | 0.93 | -0.14 | 0.34 |

Table S6 shows correlation between PANSS scores and imaging measures. PANSS: positive and negative syndrome scale, r: correlation coefficient, NOE: negative outcome evaluation, PO: positive outcome evaluation, ACC: anterior cingulate cortex, DLPFC: dorso lateral prefrontal cortex.

**Supplementary Table S7. Behavioral measures in the group of patients and healthy controls**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **FEP** | **HC** | **Statistics** |
| **Response time, seconds mean±SD** |  |  |  |
| Possible win | 0.198±0.02 | 0.187±0.02 | T(101)=2.7, p=0.007, CI: 0.003, 0.019 |
| Possible loss | 0.202±0.03 | 0.187±0.02 | T(101)=2.7, p=0.008, CI:0.004, 0.025 |
| Neutral | 0.213±0.03 | 0.206±0.03 | T(101)=1.2, p=0.24, CI: -0.004, 0.017 |
| **Hit rate %, mean±SD** |  |  |  |
| Possible win | 72±6.6 | 74±7.5 | T(101)=-1.4, p=0.16, CI: -4.7, 0.79 |
| Possible loss | 73±8.0 | 74±8.9 | T(101)=-0.55, p=0.58, CI: -4.3, 2.4 |
| Neutral | 65±6.7 | 63±8.7 | T(101)=1.8, p=0.06, CI:0.04, 6.10 |

Supplementary Table S7 shows behavioral measures in the group of patients and healthy controls with mean response time and hit rate for each of the conditions possible win, possible loss and neutral. SD: standard deviation, CI: 95 % confidence interval.

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