(a)

Sc 2, 1 / 6
TSE/M

(b)

Sc 4, 1 / 17
TSE/M

(c)

Sc 3, 1 / 15
TSE/M

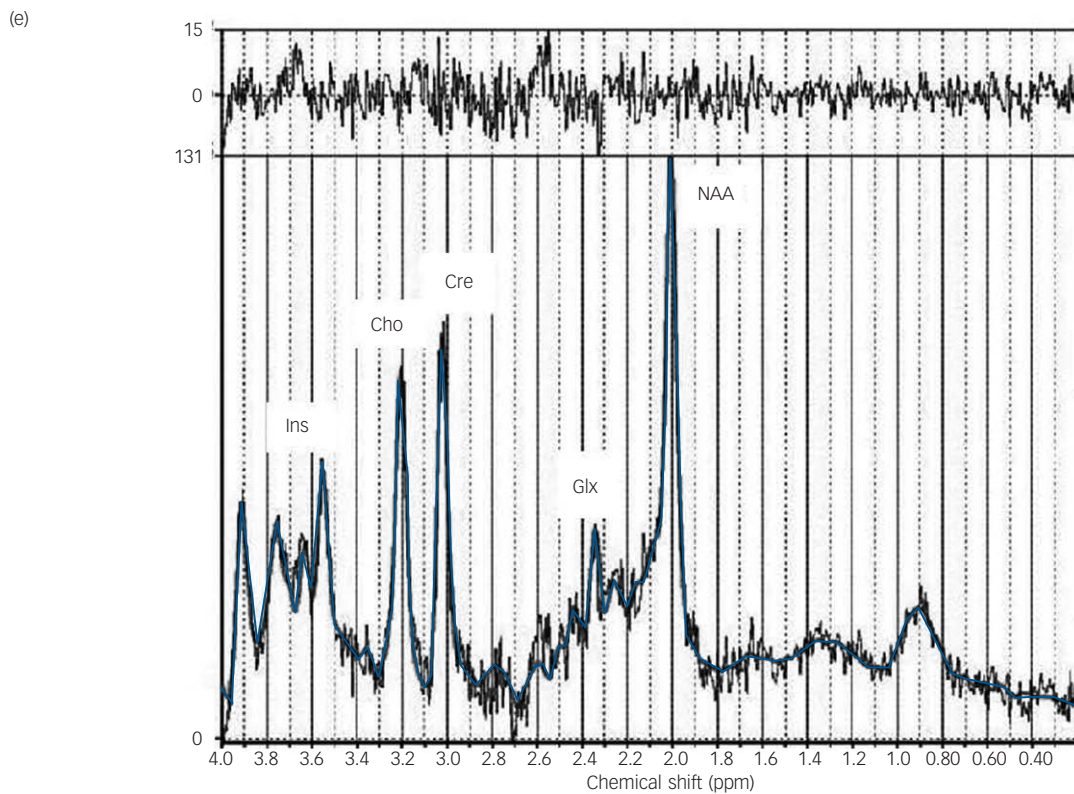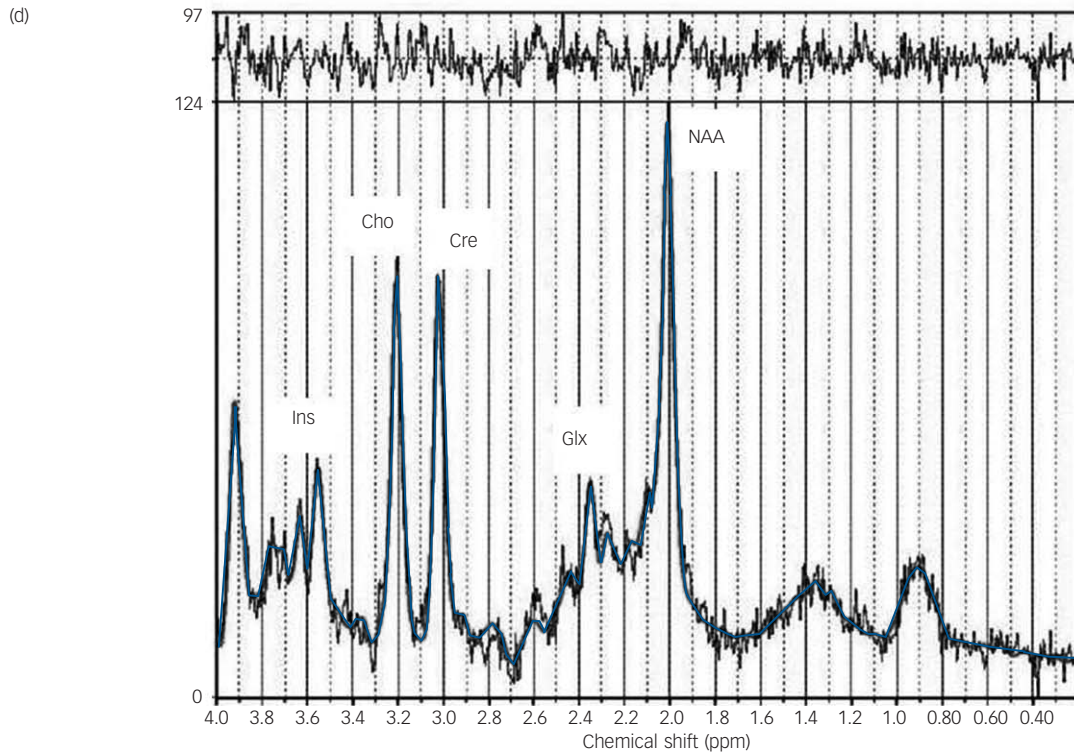**Fig. DS1**   a, b and c *(caption on next page)*.

Fig. DS1 T_2-weighted (a) sagittal, (b) axial and (c) coronal magnetic resonance images *(opposite)* showing the placement of the hippocampal proton magnetic resonance spectroscopy (^{1}H-MRS) voxel and sample ^{1}H-MRS spectra from (d) a participant with bipolar disorder and (e) a control.

Cho, cholines; Cre, creatine/phosphocreatine; Glx, glutamate/glutamine; Ins, inositols; NAA, *N*-acetylaspartate.

Online supplement DS1
Supplementary Patients and Methods

To convert the relative water-referenced Glx concentrations generated by LCModel to absolute concentrations in institutional millimolar units, the relative concentrations were multiplied by the mean voxel water concentration (WCONC) and correction factors accounting for water (ATTH2O) and Glx (ATTMET) signal T_1 and T_2 relaxation during the acquisition:

$$WCONC = 55556mM \times \left[WC_{wm} \times F_{wm} + WC_{gm} \times F_{gm} + WC_{csf} \times F_{csf}\right]$$

$$ATTH2O = F_{wm} \times \left[e^{-\frac{TE}{T2_{wm}}}\left(1 - e^{-\frac{TR}{T1_{wm}}}\right)\right] + F_{gm} \times \left[e^{-\frac{TE}{T2_{gm}}}\left(1 - e^{-\frac{TR}{T1_{gm}}}\right)\right] +$$
$$F_{csf} \times \left[e^{-\frac{TE}{T2_{csf}}}\left(1 - e^{-\frac{TR}{T1_{csf}}}\right)\right]$$

$$ATTMET = \frac{F_{wm}}{\left[e^{-\frac{TE}{T2_{wm}}}\left(1 - e^{-\frac{TR}{T1_{wm}}}\right)\right]} + \frac{F_{gm}}{\left[e^{-\frac{TE}{T2_{gm}}}\left(1 - e^{-\frac{TR}{T1_{gm}}}\right)\right]}$$

For WCONC and ATTH2O:
WC_{type} is the percent concentration wet weight of water in the tissue type (e.g. CSF is 99% water so $WC_{csf} = 0.99$)
F_{type} is the volume fraction of each tissue type (eg. if the voxel is composed of 70% WM, $F_{wm} = 0.70$)
TE is the echo time in seconds
$T2_{type}$ is the T_2 relaxation time in seconds of water protons in each tissue type
TR is the repetition time in seconds
$T1_{type}$ is the T_1 relaxation time in seconds of water protons in each tissue type

For ATTMET:
F_{type} is the volume fraction of each tissue type
TE is the echo time in seconds
$T2_{type}$ is the T_2 relaxation time in seconds of Glx in each tissue type
TR is the repetition time in seconds
$T1_{type}$ is the T_1 relaxation time in seconds of Glx in each tissue type
Note: there should not be any metabolites in the CSF so that tissue type is not included.

Table DS1: Mean total hippocampal volumes, tissue composition of the MRS voxel, and MRS data quality measures in BD patients and healthy participants

Volumes (mL)	Patients with BD (N=51)		Healthy participants (N=28)		*P*
	Overweight/ Obese (N=17)	Normal Weight (N=34)	Overweight/ Obese (N=6)	Normal Weight (N=22)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Mean total hippocampus (L+R hippocampus/2) [1]	3.76 (0.25)	3.90 (0.48)	4.11 (0.27)	4.02 (0.59)	.379
MRS voxel					
Mean hippocampal volume in voxel	2.39 (0.19)	2.38 (0.26)	2.53 (0.22)	2.50 (0.33)	.981
Mean hippocampal GM	2.15 (0.18)	2.13 (0.21)	2.27 (0.20)	2.26 (0.27)	.951
Mean hippocampal WM	0.24 (0.05)	0.24 (0.07)	0.26 (0.09)	0.24 (0.08)	.605
Mean non-hippocampal GM	1.62 (0.44)	1.60 (0.31)	1.52 (0.25)	1.52 (0.38)	.915
Mean non-hippocampal WM	2.52 (0.47)	2.55 (0.38)	2.49 (0.34)	2.53 (0.32)	.957
Mean CSF	0.22 (0.06)	0.22 (0.13)	0.21 (0.04)	0.20 (0.07)	.749
Data quality measures					
Signal-to-noise ratio (SNR)	8.43 (2.34)	8.08 (1.39)	7.42 (1.83)	8.43 (1.80)	.173
Full width at half maximum (FWHM), Hz	7.73 (1.43)	7.59 (1.48)	6.58 (0.75)	7.00 (1.24)	.455

"Mean total hippocampus" includes hippocampal GM and WM, both inside and outside the MRS voxel.

Since diagnosis and BMI could both impact hippocampal volume, the content of the voxel, and data quality measures, the p-values take both into account by showing the probability of diagnosis x BMI interactions – i.e. the probability that hippocampal volume, voxel content, and data quality values are distributed differently based on weight categories in patients and healthy participants.