Fig. 1

Probability maps showing significant
dose-dependent changes in BOLD signal

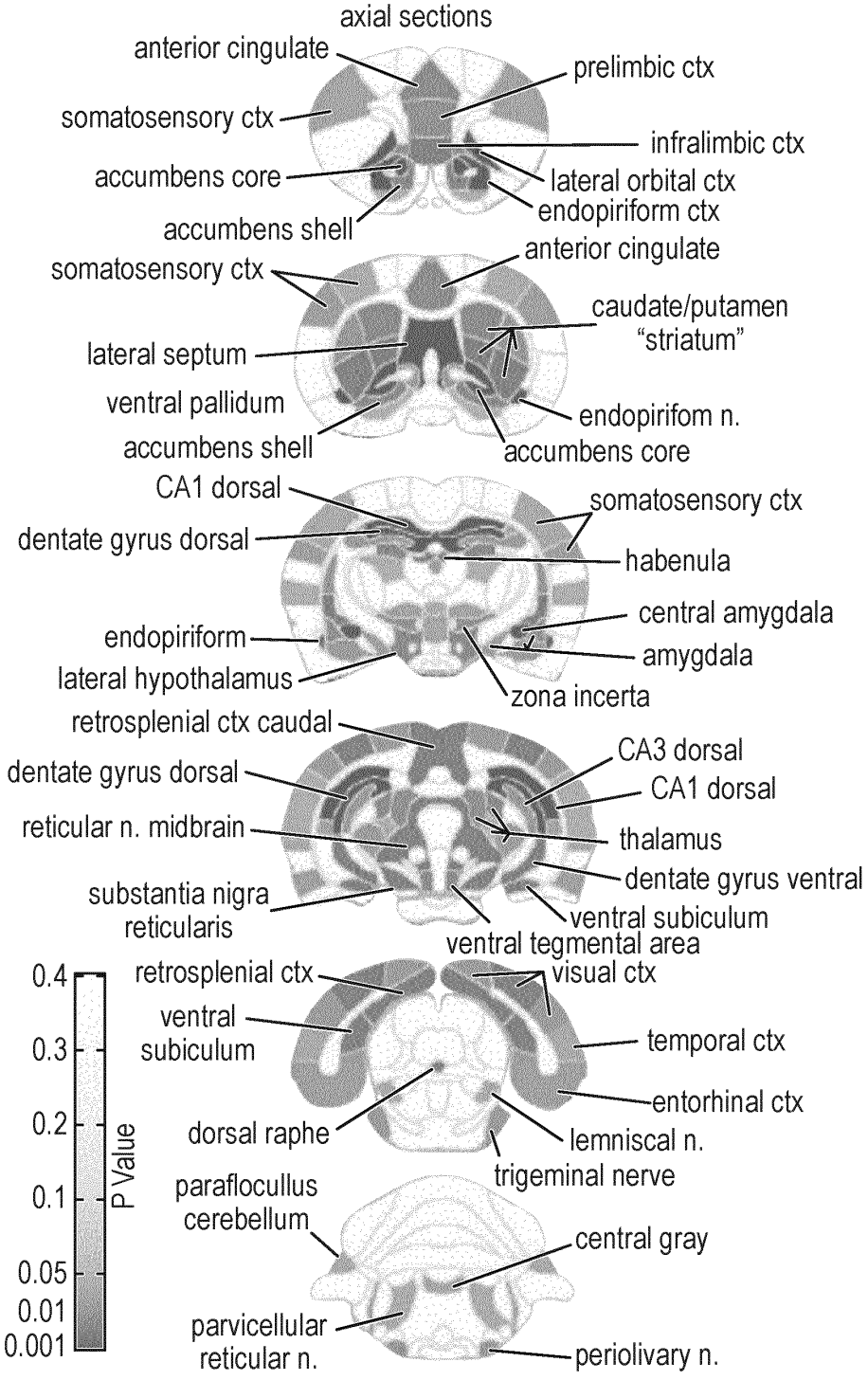


Fig. 2

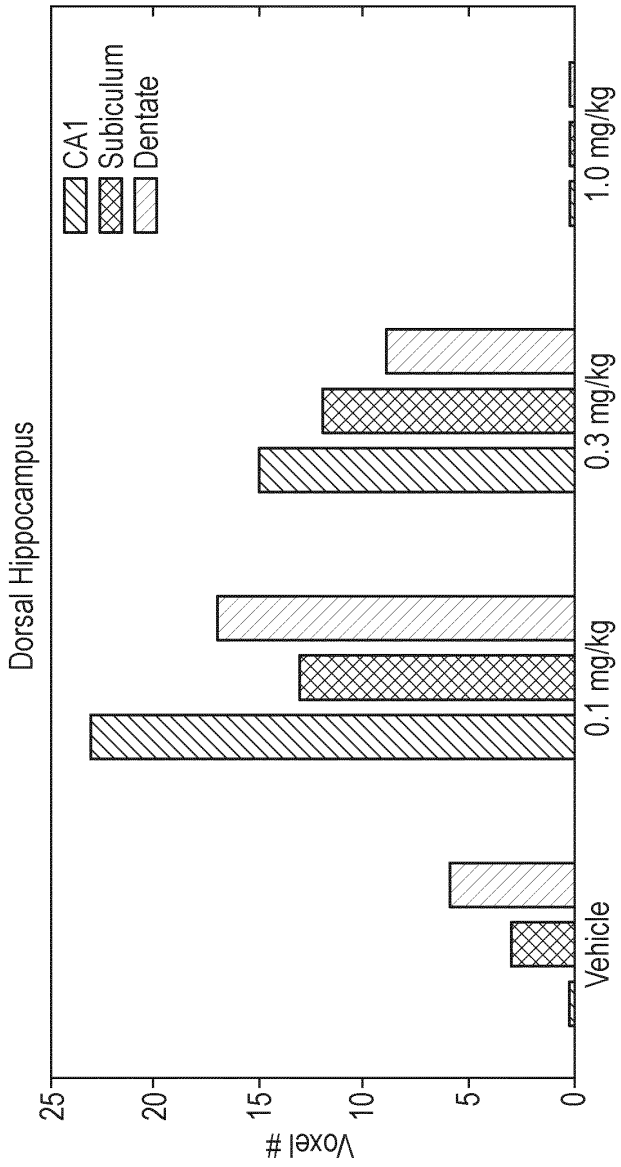

Dorsal Hippocampus
CA1
Subiculum
Dentate
Voxel #
0
5
10
15
20
25
Vehicle
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg

Fig. 3

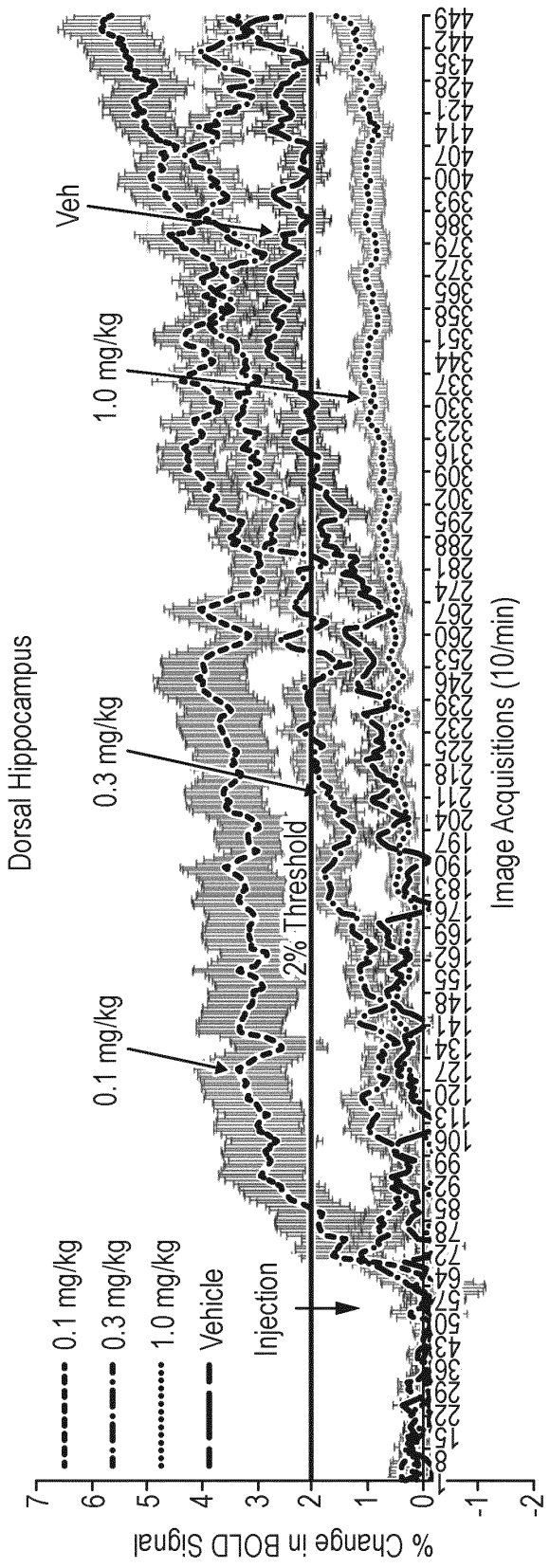

Dorsal Hippocampus
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg
Veh
2% Threshold
Injection
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg
Vehicle
% Change in BOLD Signal
Image Acquisitions (10/min)

Fig. 4

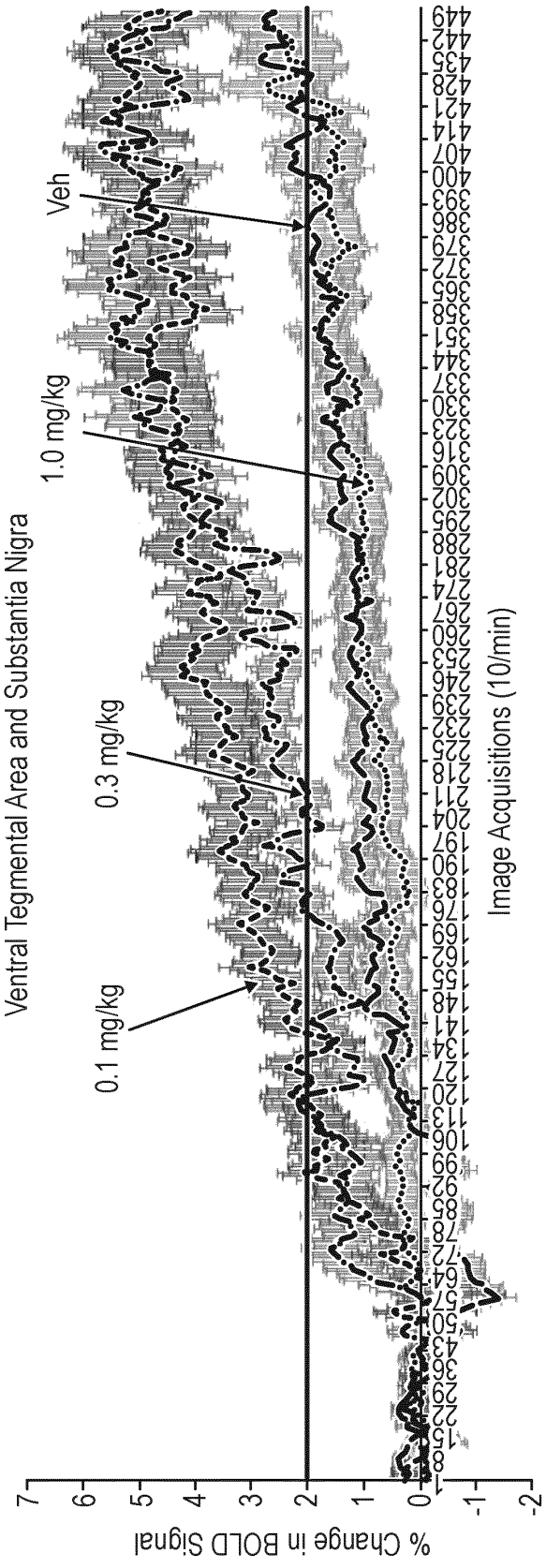

Ventral Tegmental Area and Substantia Nigra
Veh
1.0 mg/kg
0.3 mg/kg
0.1 mg/kg
% Change in BOLD Signal
Image Acquisitions (10/min)

Fig. 5

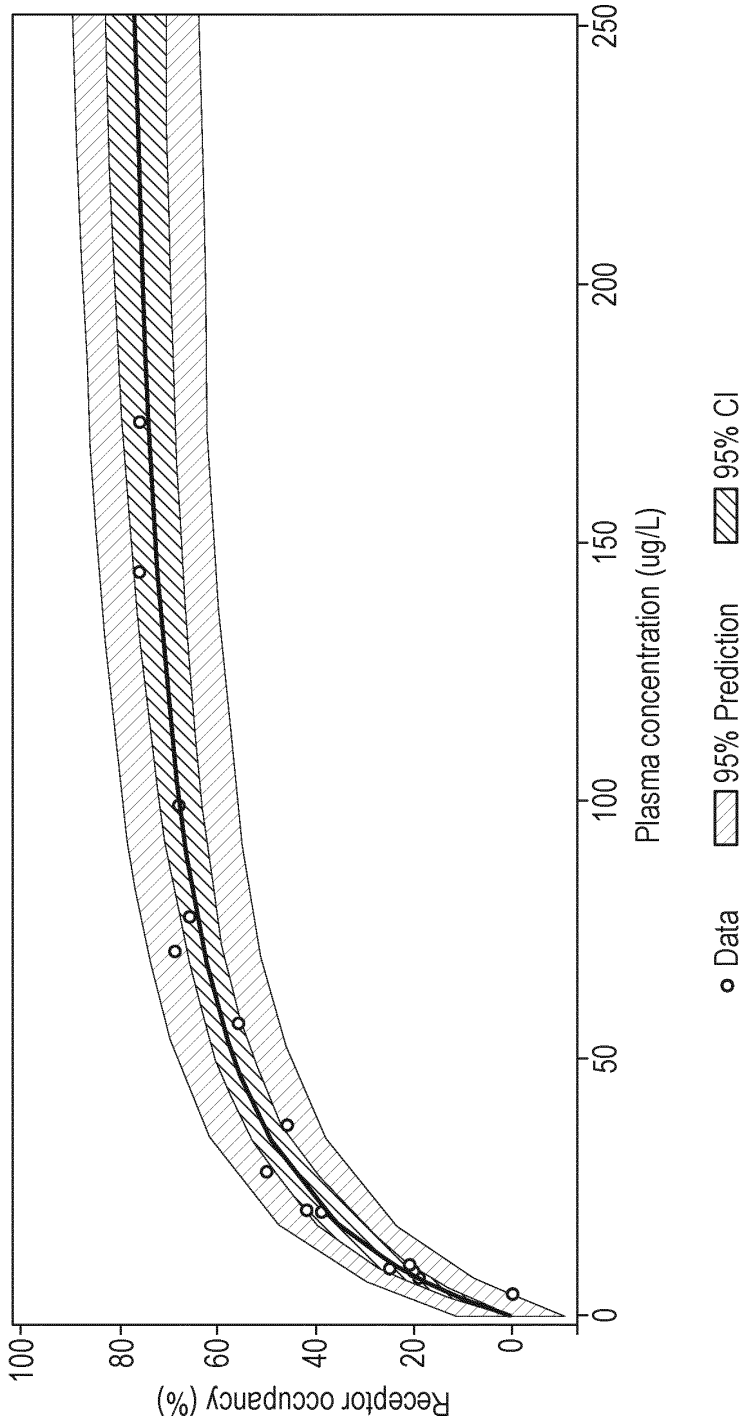

Receptor occupancy (%)
100
80
60
40
20
0
0
50
100
150
200
250
Plasma concentration (ug/L)
Data
95% Prediction
95% CI

Fig. 6

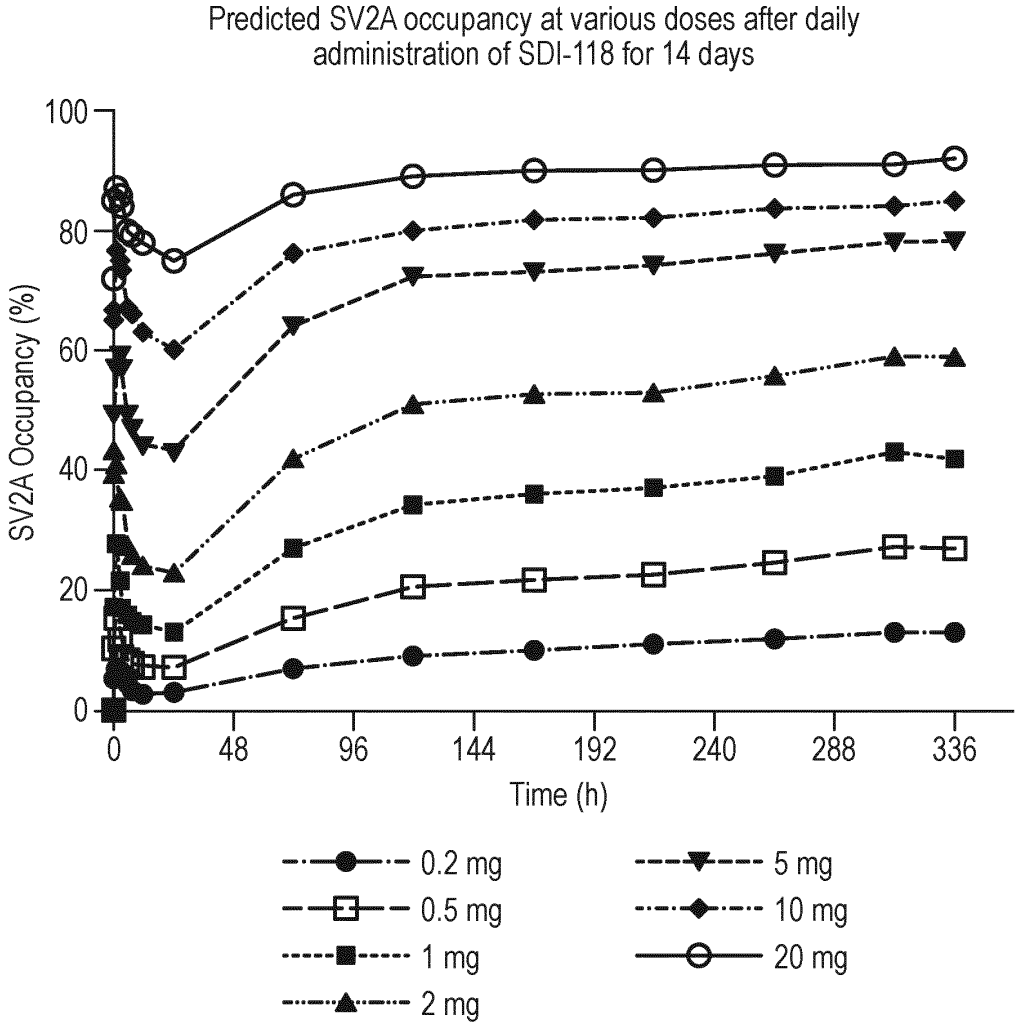
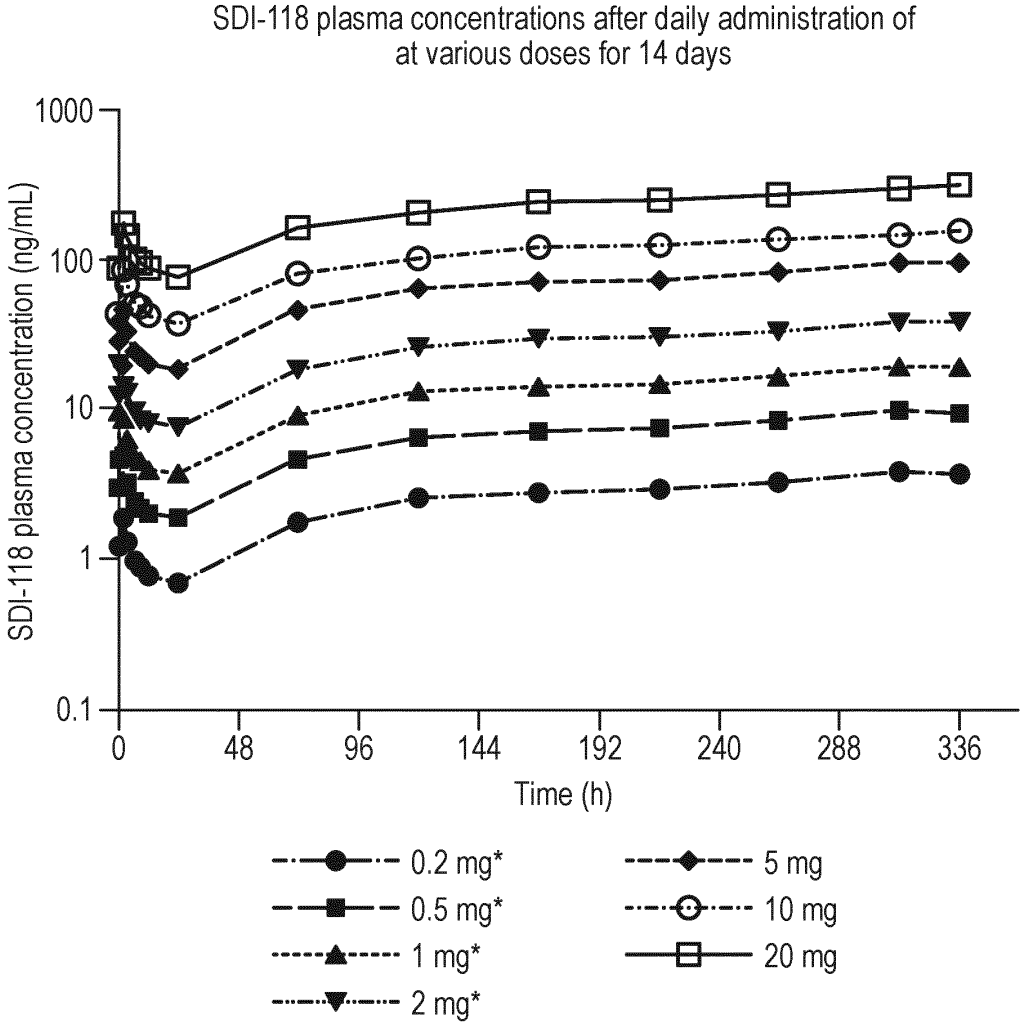

Predicted SV2A occupancy at various doses after daily administration of SDI-118 for 14 days
SV2A Occupancy (%)
100
80
60
40
20
0
0
48
96
144
192
240
288
336
Time (h)
0.2 mg
0.5 mg
1 mg
2 mg
5 mg
10 mg
20 mg

Fig. 7



*Values extrapolated from 5 mg MAD PK data.
PK parameters linear both in SAD and MAD

Fig. 8

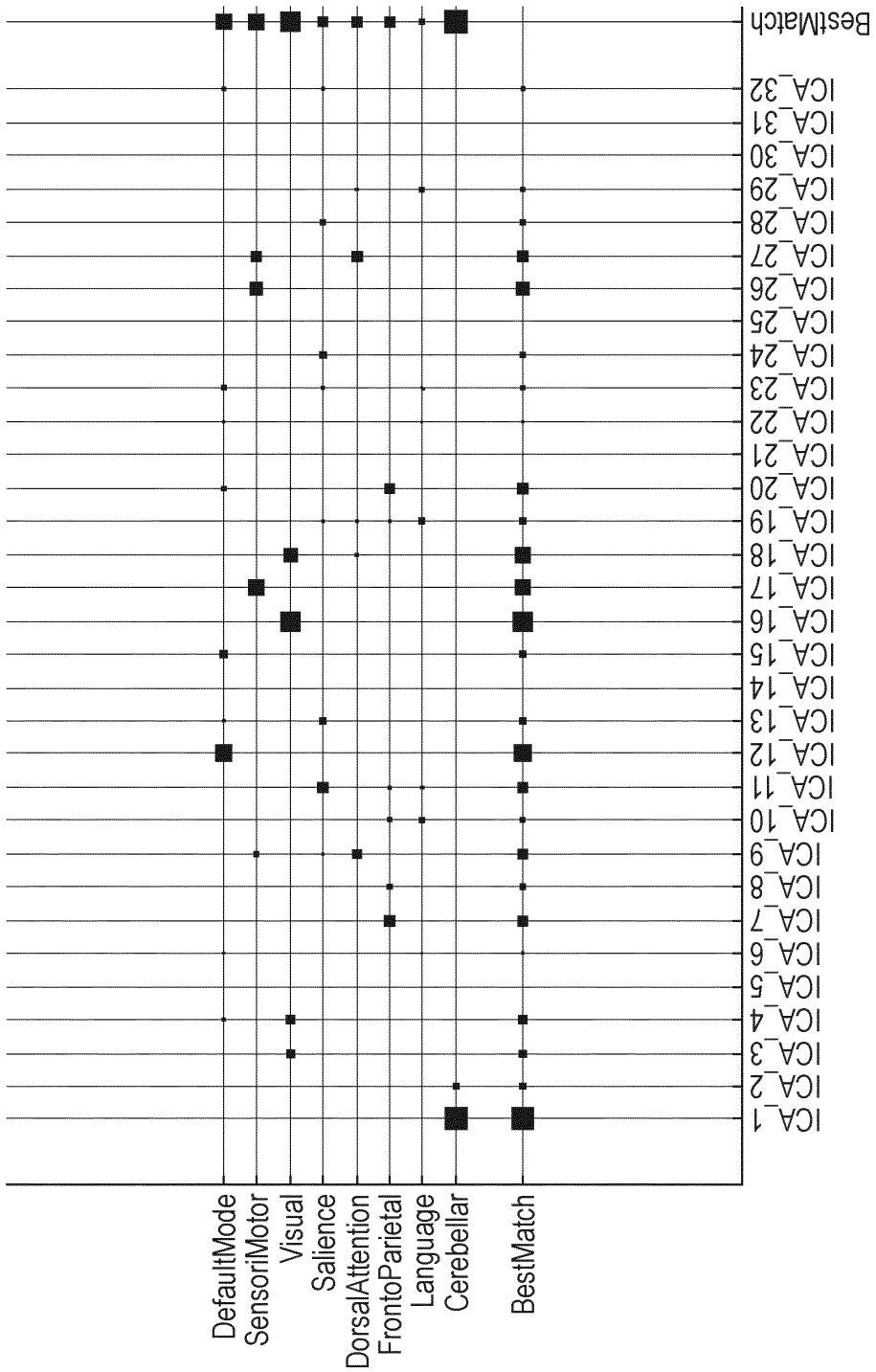
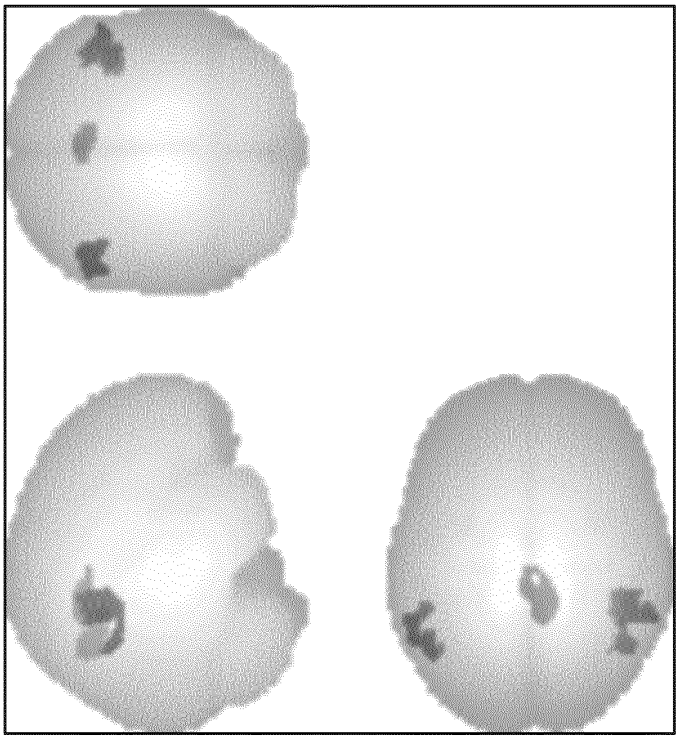
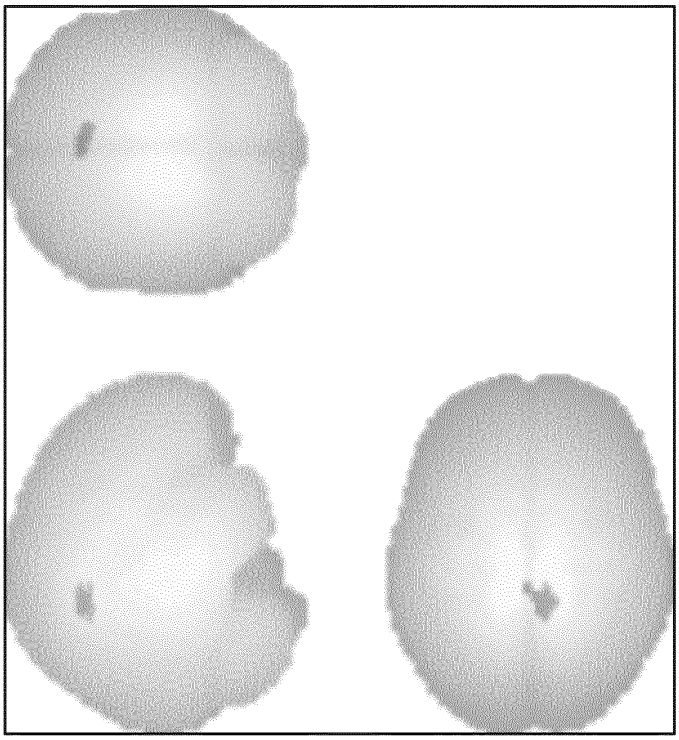

DefaultMode
SensoriMotor
Visual
Salience
DorsalAttention
FrontoParietal
Language
Cerebellar
BestMatch
ICA_1
ICA_2
ICA_3
ICA_4
ICA_5
ICA_6
ICA_7
ICA_8
ICA_9
ICA_10
ICA_11
ICA_12
ICA_13
ICA_14
ICA_15
ICA_16
ICA_17
ICA_18
ICA_19
ICA_20
ICA_21
ICA_22
ICA_23
ICA_24
ICA_25
ICA_26
ICA_27
ICA_28
ICA_29
ICA_30
ICA_31
ICA_32
BestMatch

Fig. 9



Cluster threshold: $p < 0.005$ p-uncorrected
voxel threshold: $p < 0.005$ p-uncorrected



Cluster threshold: $p < 0.05$ cluster size p-FDR
corrected / voxel threshold: $p < 0.001$ p-uncorrected

Fig. 10

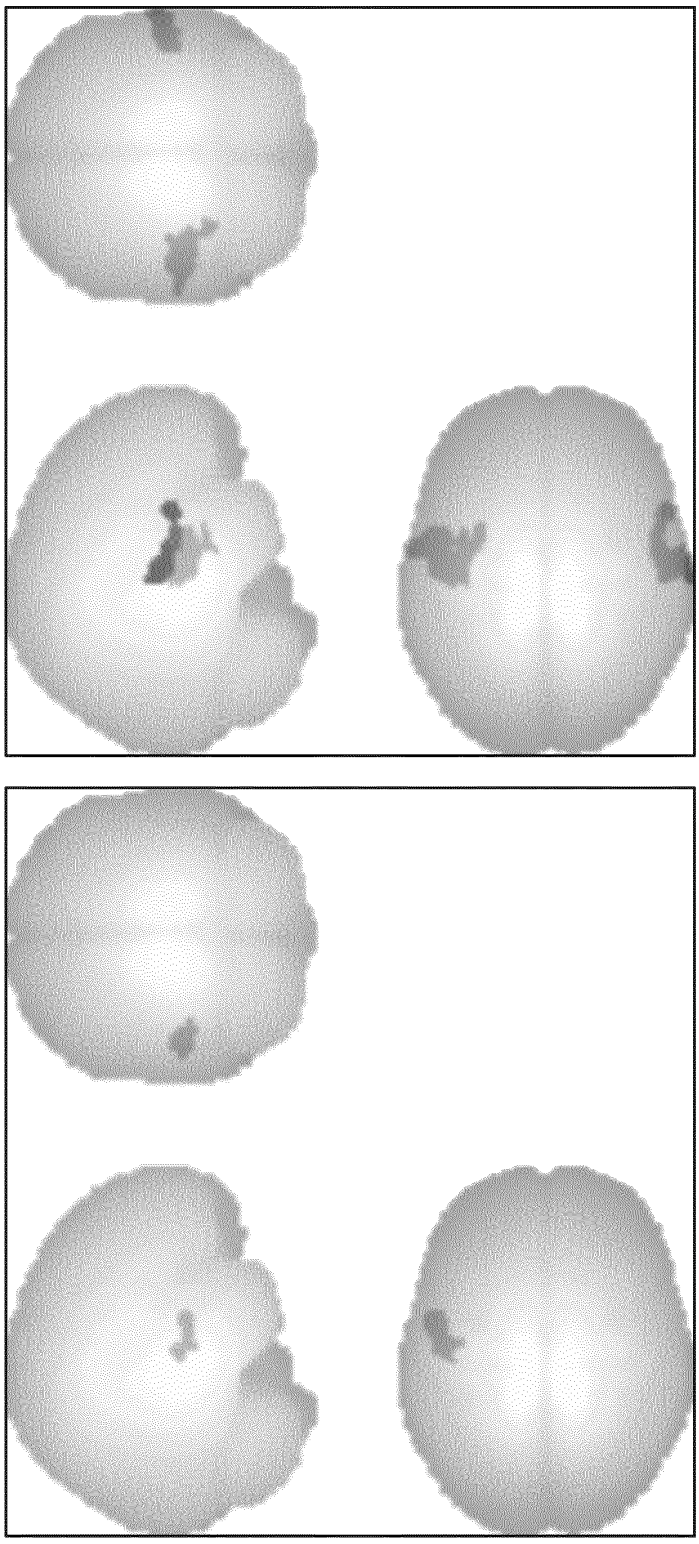
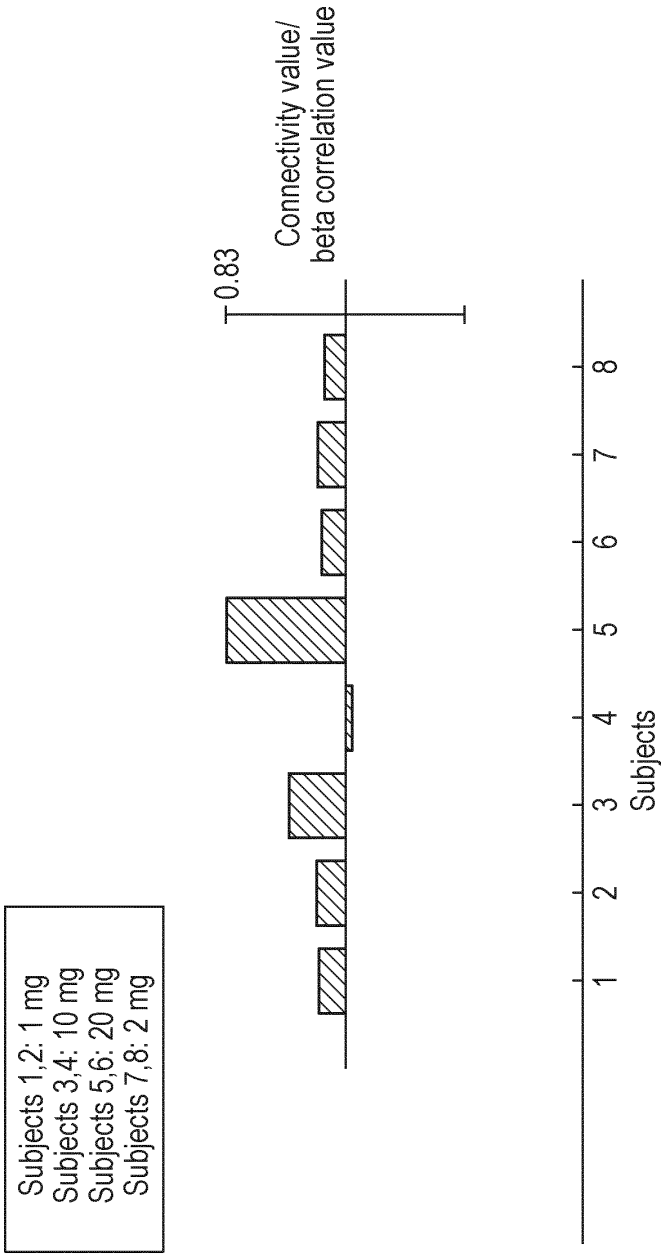

Cluster threshold: p < 0.05 cluster size p-FDR
corrected / voxel threshold: p < 0.001 p-uncorrected
Cluster threshold: p < 0.005 p-uncorrected
voxel threshold: p < 0.005 p-uncorrected

Fig. 11


Subjects 1,2: 1 mg
Subjects 3,4: 10 mg
Subjects 5,6: 20 mg
Subjects 7,8: 2 mg
0.83
Connectivity value/
beta correlation value
1
2
3
4
5
6
7
8
Subjects