Structural MRI studies investigating basal ganglia in patients with schizophrenia and normal controls.

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| Study | Schizophrenia Patients Males/Females (Tot)  Age (Mean±S.D.) | Normal Controls  Males/Females (Tot)  Age (Mean±S.D.) | Length Of Illness (Years ) | Neuroleptic Therapy  (chronic treatment; naive-never been treated-; not treated now) | Methods | Findings in Schizophrenia |
| Jernigan et al, 1991 | 28/14 (43)  32.2±6.4 | 19/5 (24)  30.0±7.9 | 12.8 | chronic treatment | MRI 1.5 T lentiform nucleus | - ↑ lentiform nucleus  - earlier onset associated with larger lentiform nucleus |
| Gordon et al, 1994 | 14/8 (22)  14.4±2 | (37) | 4 | chronic treatment | MRI 1.5 T caudate | larger left caudate |
| Chakos et al, 1994 | 17/12 (29)  25.2±6.3 | 8/2 (10)  30.5±4.9 | 0.8  (FE) | - 21 naive  - 8 treated fewer than 12 weeks | MRI 1.5 T caudate (no accumbens), at the baseline and after 18 months of neuroleptic treatment | - caudate volumes ↑ 5.7% after treatment  - greater amounts of antipsychotic medication before the scan and younger age associated with larger increase in caudate volume |
| Hokama et al, 1995 | 15 males  22.3±2.8 | 15 males  aged between 20 and 55 years | 15.7±8.8 | chronic treatment | - Hebb’s Recurring Digits  - MRI 1.5 T caudate, putamen, GP | - ↑ BG volumes  - ↑ volumes associated with poorer neuropsychological test performance |
| Stratta et al, 1997 | 26/9 (35)  34.06±7.54 | 17/7 (24)  32±4.96 | 11.97±6.58 | chronic treatment | - WCST  - MRI 0.25 T caudate, putamen, accumbens | poor WCST performers have ↓ left caudate, left putamen and right total striatum compared to healthy controls |
| Shihabuddin et al, 1998 | 12/6 (18)  38.5±14.8 | 15/9 (24)  37±13.1 | 15.7 | - 7 naive  - 11 not treated now | - AIMS  - MRI of striatum | caudate smaller in naive patients than in controls and larger in previously medicated patients |
| Keshavan et al, 1998 | - 11/5 (16) SCZ  aged 27.18±8.93;  - 4/5 (9) other psychotic  aged 23.22±0.67 | 12/5(17)  22.94±5.10 | - newly diagnosed SCZ 301.35±  269.14 weeks  - others 155.06±  159.04 weeks | naive | MRI 1.5 T caudate (accumbens included) and putamen | - volumes not correlated with age or length of illness  - ↓ caudate volume |
| Gur et al, 1998 | 50/46 (96)  - naive 28.9±11.3  - not treated now 30.9±8.7 | 60/68 (128)  27.6±8.6 | - 4.3 naive  - 8.4 not treated now | - 21 naive  - 75 not treated now | - SAPS, SANS  - MRI 1.5 T caudate (accumbens included), lentiform nucleus | - naive: BG volumes not differ from healthy; positive correlation putamen-SAPS  - not treated now: ↑ putamen and GP; higher dose of typical neuroleptic associated with higher caudate and putamen |
| Corson et al, 1999 | 25/11 (36)  28.86±7.8 | 29/13 (43)  26.53±8.14 | 5.75 | naive | MRI 1.5 T caudate measured with ANN (no accumbens) | ↓ volumes |
| Corson et al, 1999 | 23 males  25.57±6.19 |  | 3.33 | - 19 not treated now  - 4 naive | MRI 1.5 T caudate and lentiform nucleus at admission and after 2 years of treatment | - volume ↑ in patients treated with typical neuroleptics  - volume ↓ with atypical |
| Kumra et al, 2000 | - 25/19 (44) SCZ; aged 14.4±2.3  - 22/5 (27) other psychotic disorders; aged 12.3±2.9 | - 38/25 (64); aged 13.7±2.2  - 35/7 (42); aged 11.7±3.3 |  | chronic treatment | MRI 1.5 T caudate, putamen, GP | - ↑ volumes of BG in all patients  - patients have left putamen larger than right and right caudate larger than left |
| Scheepers et al, 2001 | 22  35±10 |  |  | treated typical | - MRI 1.5 T caudate during treatment with typical antipsychotics and after 24 and 52 weeks of clozapine treatment  - PANSS before clozapine and after a month | - clozapine resulted in reduction of left caudate volume in patients who respond, not in others  - the degree of reduction in left caudate volume related to improvement in positive and general symptoms |
| Scheepers et al, 2001 | 18/8 (26)  35.23±10.34 |  | 159.5±  114.1 months | treated typical | - MRI 1.5 T caudate and TD evaluation (Sympson Scale) during treatment with typical antipsychotics and after 24 weeks of clozapine treatment  - PANSS in drug free period and once a month after | - ↓ caudate volume after clozapine treatment  - no differences in caudate volumes between responders and non-responders |
| Lang et al, 2001 | - FE 21/9 (30); aged 22.9±6.4  - chronic 7/5 (12); aged 38.4±11.6 | 12/11 (23)  27.7±7.2 | - 30 FE  - 12 chronic | - FE naive (24 of them then treated with risperidone for 1 year)  - chronic treated | MRI 1.5 T: caudate (accumbens included), putamen, GP | - ↑ in chronic patients  - same volumes for first episode patients and controls  - risperidone do not alter volumes |
| Shihabuddin et al, 2001 | - SPD 15/1 (16)  43.3±12.7  - SCZ 30/12 (42) 37.8±12.4 | 35/12 (47) 38.3±12.6 |  | - SPD: 10 naive, 6 not treated now  - SCZ: 10 naive, 32 not treated now | - BPRS  - MRI  - California verbal learning test | - SPD have smaller putamen than controls  - SCZ have larger putamen than controls  - size of caudate is similar in all 3 groups |
| Tauscher-Wisniewsky et al, 2002 | 10/5 (15)  23±6.2  (4 affected by schizoaffective disorder) | 7/3 (10)  29.4±8.6 | FE | - 8 naive  - 7 chronic treatment | MRI 1.5 T caudate at baseline and after 5 years of treatment with atypical or low doses of typical antipsychotics | - no differences at baseline  - decrease volumes in both patients and controls after 5 years |
| McCreadle et al, 2002 | - 18/13 (31) with dyskinesia; aged 43±16  - 18/13 (31) without dyskinesia; aged 44±15 | 18/13 (31)  43±16 | - 11 with dyskinesia  -9 without dyskinesia | naive  (India) | - MRI 1.5 T caudate and lentiform nucleus  - PANSS  - AIMS  - Simpson and Angus Scale | - lentiform nucleus larger in patients with dyskinesia compared with controls  - in controls negative correlation between age and volumes of caudate and lentiform nucleus |
| Gunduz et al, 2002 | 37/14 (51)  24.5±5.0 | 17/11 (28)  25.8±6.7 | FE (94.4±157 weeks) | - 36 naive  - 15 treated (minimal exposure) | MRI 1.5 T caudate, accumbens, putamen | - volumes of BG not differ between groups  - age negative correlated with caudate and putamen volumes bilaterally in healthy comparison group, not among patients |
| Buchsbaum et al, 2003 | 27/10 (37)  43±11.9 | 23/14 (37)  44.1±13.7 | 22 | chronic treatment | - PANSS score  - MRI: caudate and putamen | - ↑ volumes putamen and caudate  - positive correlation between good outcome and putamen size  - volumes not related with type or neuroleptic treatment |
| Heitmiller et al, 2004 | 7/7 (14)  23.6±6.8 | 7/7(14)  26.7±11.3 | 46±50.34 months | naive | MRI caudate at baseline and after atypical neuroleptics exposure  (30.2 months±13.3) | - no difference between patients and controls in amount of change over the time  - female patients have a negative correlation between drug exposure and volume change, males have a positive correlation |
| Takase et al, 2004 | 11/14 (25)  32.9±7.1 | 13/8 (21)  33±6.8 | 2445.4±  513.2 days | - 20 chronic treatment  - 1 not treated now  - 4 treatment unknown | MRI 1.5 T caudate  (no accumbens) | - smaller white matter in caudate  - negative correlation between age and volumes of white matter in healthy subjects, not in patients  - correlation between dosage of neuroleptics and volumes of white and grey matter |
| Lang et al, 2004 | - 7/3 (10)  35.3±8.8  - 10/4 (14)  23.7±3.3  - 10/3 (13)  25.6±8.2 | 12/11 (23)  23.3±7.4 |  | - 10 treated typical neuroleptics then switch to olanzapine  - 14 treated risperidone  - 13 treated risperidone then switch to olanzapine | - MRI 1.5 T caudate, putamen, GP  - ESRS | - in group treated with typical antipsychotics: BG greater than in controls and after switch to olanzapine putamen and GP volumes decreased  - in group treated with risperidone and switch to olanzapine BG volumes no change |
| Massana et al, 2005 | 8/3 (11)  23±4 |  | FE | naive | MRI 1.5 T caudate and accumbens at baseline and after 3 months of treatment with risperidone | ↑ gray matter volume for caudate nuclei and for the left accumbens after treatment |
| Spinks et al, 2005 | 26 M  24.58±5.95 | 26 M  24.65±5.51 | 3.02 | naive | - SAPS e SANS  - MRI 1.5 T GP trimodal image (T1, T2, PD) and measurement with software BRAINS2 | - the volume for GP, GPi, GPe do not differ  - larger volume of GP on the right compared to left in both group  - volume of GPe inversely correlated with the severity of global symptoms |
| Taylor et al, 2005 | 11  34.7±12.4 | 11  26.8±6.6 | 6 | - 5 naive  - 6 not treated now | - SAPS  - MRI 1.5 T striatum at baseline and after 4 weeks of treatment | - no different volumes at baseline  - ↑ after treatment  - ↑ left striatum associated with ↓ of positive symptoms |
| Tamagaki et al, 2005 | 36/22 (58)  40±7.3 | 34/22 (56)  38.2±8 | 14 | chronic treatment | - MRI 1.5 T caudate, putamen and accumbens.  - volumes divided in grey matter, white matter, CSF, non class, venous blood tissue class | - striatal white matter/gray matter ratios ↓  - ↓ white matter in caudate and accumbens e ↑ gray matter in putamen  - negative correlation between white matter volumes and increasing age  - typical neuroleptic consumption positively correlated with right gray matter volume of putamen in male patients |
| Jayakumar et al, 2006 | 10/2 (12)  28.7±8.8 | 6/7 (13)  29.6±9.4 | 3.94±3.45 | naive | MRI 1.5 T caudate | - ↓ caudate volume  - age at onset has negative correlation with caudate volumes bilaterally |
| Lawyer et al, 2006 | 54/14 (71)  40.8±7.6 | 39/26 (65)  44.1±7.7 | 16.4±8.3 | - 64 chronic treatment  - 7 not treated now | - MRI 1.5 T caudate and putamen  - cognitive tests covering 6 functional domains | - caudate and putamen larger gray matter volumes  - verbal learning and vigilance associated with putamen volume  - working memory associated with caudate volume |
| McClure et al, 2006 | 1) 9/2 (11)  33±7.3  2) 5/3 (8) 33.6±9.8 |  | 1) 11±7  2) 9±8 | 1) not treated now (placebo)  2) chronic treatment | MRI 1.5 T caudate and putamen at baseline and after 4 weeks of treatment | - no effect on putamen and caudate  - ↑ in patients treated with typical and ↓ in patients treated with atypical antipsychotics |
| Hoptman et al, 2006 | 43/6 (49)  41.5±8.2 |  | 18.6 | chronic treatment | - aggression measured: OAS and log (TAS score); PANSS  Hostility; PANSS Poor Impulse Control  - MRI 1.5 T: head of caudate segmenteted in axial view | - larger caudate associated with greater level of aggression  - left caudate volumes inversely correlated with age |
| Crespo-Facorro et al, 2007 | 53/23 (76)  27.7±6.8 | 30/15 (45)  26.2±5.4 | FE  11.1 months | naive | - MRI 1.5 T caudate  - SAPS, SANS  - ESRS  - cognitive tests | - no changes in caudate volume  - longer duration of untreated psychosis associated with  smaller caudate  - no association between caudate volume and cognitive functioning |
| O'Daly et al, 2007 | 25/3 (28)  33±10 | 28/4 (32)  34±8 | 8±8 | - 26 chronic treatment  - 2 not treated now | - MRI 1.5 T caudate  - BPRS (scored 4 or more on items related to hallucinatory behavior) | - ↑ gray matter in right caudate nucleus |
| Chua et al, 2007 | 26  32±10 | 38  33±8.1 | FE  120 days | naive | MRI 1.5 T caudate | - ↓ caudate volumes  - less gray matter volume in caudate bilaterally |
| Mamah et al, 2007 | 32/22 (54)  37.6±12.3 | 35/35 (70)  39.1±14.3 | 12.9±12.5 | all chronic treatment (except 1) | - MRI caudate, accumbens, putamen, GP  - SAPS, SANS  - ESRS  - cognitive tests | - ↑ caudate, putamen and GP volumes  - positive correlation between attention/vigilance and volume of caudate and putamen  - no correlation volumes - ESRS |
| Glenthoj et al, 2007 | 14/5(19)  25.9±5.1 | 11/8(19)  27.5±5.3 | first episode | naive | - patients randomly assigned to treatment with either low doses of typical antipsychotic or atypical for 12 weeks  - MRI 1.5 T caudate, putamen and accumbens, before and after medication | - no total volume differences between naive patients and controls  - the two medication group do not differ with respect to volume changes  - ↑ volume of putamen in risperidone group  - altered asymmetry in caudate volume |
| McClure et al, 2008 | 9/1 (10)  36.7±7.7 |  | 10.6±9.7 | not treated now | MRI 1.5 T caudate at baseline and after 12 weeks of atypical antipsychotics treatment | no change in caudate volume after treatment |
| Haukvik et al, 2010 | 37/17 (54)  41.9±1.1 | 33/21 (54)  41.5±1.2 | 15.93±9.5 | - 3 not treated now  - 25 treated typical  - 26 treated atyipical | MRI 1.5 T | -↑ globus pallidus  - no differences in putamen and caudate volumes |
| Horga et al, 2011 | 47/17 (64)  33.7±17.4 | 35/21 (56)  36.8±11.9 | 19.1±16 | naive or not treated now | MRI 1.5 T | - ↓ caudate volumes  - no differences in putamen volumes |
| Li et al, 2012 | 17/23 (40)  24.05±7.75 | 9/14 (23)  22.48±5.48 | 9.33±12.72 | naive | - MRI 3 T at baseline and after 6 weeks antipsychotic treatment  - PANSS and GAF | - ↑ volume of putamen after treatment  - volume of putamen positively correlated with the reduction of ratio of positive symptoms |
| Fischer et al, 2012 | - deficit schizophrenia 17/3 (20)  23-51  - non deficit schizophrenia 31/5 (36)  21-50 | 23/5 (28)  26-48 | - deficit schizophrenia  18±1.9  - non deficit schizophrenia  19.3±1.4 | chronic treatment (clozapine, typical, atypical) | MRI 1.5 T | no differences in caudate volume between deficit schizophrenia, non deficit schizophrenia and control subjects |
| Oertel-Knochel et al, 2012 | 16/15(31)  38±11.24 | - REL  14/15(29)  40.38±15.84  - CON  17/20(37)  39.36±9.97 | 13.71±6.87 | chronic treatment (27 atypical, 4 atypical + typical) | MRI 3 T  VBM | - larger volumes in caudate and lentiform nucleus in patients compared to controls  - larger volume in caudate in patients relatives compared to controls |
| Juuhl-Langseth et al, 2012 | EOS patients  10/8 (18)  16.1±1.6 | 16/17 (33)  15.8±1.8 | 1.4±0.8 | - 13 chronic treatment (all atypical and 2 atypical + typical)  - 5 not treated now | MRI 1.5 T | - ↑ volume of caudate  - no differences in putamen and globus pallidus volumes |
| Roiz-Santiañez et al, 2013 | 66/43 (109)  29.5±8.2 | 47/29 (76)  27.8±7.7 | FE  11 months | naive  At 3 years: all on atypical but 4 individuals | MRI 1.5 T  BRAINS  Longitudinal at 3 years | A lower progressive decrease in the  volume of caudate nucleus in  patients  than in control subjects |

MRI: Magnetic Resonance Imaging

T: Tesla

Lentiform nucleus: putamen + globus pallidus

FE: first episode patients

GP: Globus Pallidus

BG: basal ganglia

WCST: Wisconsin Card Sorting Test

Striatum: caudate + putamen

AIMS: Abnormal Involuntary Movement Scale

SCZ: Schizophrenia patients

SAPS e SANS: Scale for the Assessment of Positive Symptoms; Scale for the Assessment of Negative Symptoms

ANN: Artificial Neural Network

PANSS: Positive and Negative Syndrome Scale

TD: Tardive Diskinesia

SPD: Schizotypal Personality Disorder

BPRS: Brief Psychiatric Rating Scale; Overall e Gorham, 1962

ESRS: Extrapyramidal Symptoms Rating Scale

Gpe: external segment of Globus Pallidus

Gpi: internal segment of Globus Pallidus

CSF: Cerebral Spinal Fluid

OAS: Overt Aggression Scale

TAS: Total Aggression Severity score

GAF: Global Assessment of Functioning

REL: first-degree relatives

CON: controls

VBM: Voxel-Based Morphometry

EOS patients: Early Onset Schizophrenia patients