ATYPICAL NEUROLEPTIC MEDICATION EFFECTS ON THE DORSAL AND VENTRAL STRIATUM IN CHRONIC SCHIZOPHRENIA: AN MRI STUDY

BACKGROUND

• The striatum is the largest component of the basal ganglia and is made up of the caudate, putamen, and nucleus accumbens (NA). The striatum may be delineated into the ventral striatum (VS), primarily made up of the NA, and the dorsal striatum (DS) made of the caudate and putamen. The caudate and putamen may be further segmented into anterior and posterior regions at the level of the anterior commissure-posterior commissures (AC-PC) line.

• The striatum involved in reward pathways and motor control. Volumetric abnormalities of the striatum, particularly increased putamen volume, have been observed in schizophrenia patients medicated with typical neuroleptics when compared to healthy controls (2, 3).

• The striatum is also implicated in the expression of neuropsychiatric disorders which accounts for the effects of antipsychotics achieved at dopamine (DA) D2 receptors in the striatum.

• Furthermore, there may be a difference in the way that typical and atypical antipsychotics effect striatal DA receptors and DA release. This is supported by findings that while basal ganglia volume increased following exposure to typical neuroleptics, the volume decreased following atypical neuroleptics (1).

• Lang et al. (2004) found that patients treated with typical antipsychotics exhibited increased striatal volumes compared to healthy controls. Some patients were then switched to Olanzapine (an atypical medication) and at a two year follow-up, striatal volumes of patients on Olanzapine had decreased and did not differ from volumes of healthy controls (4).

METHODS

Subjects:

• Fifteen male patients diagnosed with chronic schizophrenia (mean age=43.533) and nineteen male healthy controls (mean age=43.158) matched for age (p=0.013), parental socio-economic status (p=0.525), and handedness (all right handed).

• To mitigate the confound of medication only patients taking atypical neuroleptics at the time of the scan were included in the study. Atypicals were further broken into type 1 and type 2 type 1 having a higher affinity for D2 receptors than type 2); eight patients were taking type 1 and seven were taking type 2.

Image Acquisition and Processing:

• Images were acquired on a 3T GE-shortbore magnet; scan parameters: TR 7.48ms, TE 3ms, FOV 256mm, 1 mm slice thickness, 176 axial slices.

• The plane through the anterior and posterior commissures (AC-PC line) (a) is defined axially. A line was drawn crossing the top of the putamen and the caudate (b) and then bisected with a line drawn up the medial edge of the putamen (c). The voxel at this crossing point was defined as the most superior point of the putamen and from here a line was dropped down to the ventral-lateral boundary of the putamen (d). This was done moving in the anterior direction until the line dropped down not cross the AC-PC line.

• The midline of the striatum was defined at the level of the AC-PC (a) by taking the average of two voxels placed at the lateral (e) and medial (f) borders of the putamen.

• An oblique line was drawn from the ventral-lateral border through the mid-rostal border of the striatum (g). All striatal tissue below the oblique line was defined as VS and traced and shaded in the coronal view (h).

• The caudate and putamen were traced and shaded primarily in the axial view and corrected in the coronal and sagittal views then divided into anterior and posterior regions yielding a total of ten regions for each subject (Figure 3).

RESULTS

• No significant differences were found between the striatal volumes of schizophrenic patients and healthy controls (Table 1).

• Collective caudate and putamen volumes of patients were negatively correlated with the amount of medication (CPZ equivalent) they were taking (r=-0.473, p=0.002; r=-0.599 respectively) while VS volumes tended to increase with the amount of medication (r=0.295, r=0.290) though not significantly.

• A differential effect was found in the DS and VS based on atypical medication type. While VS volumes were significantly larger in patients taking Type 1 meds (r=0.913, r=0.815). DS volumes were significantly larger in those taking Type 2 meds (p=0.017, r=0.272).

DISCUSSION

• We found a differential effect, not previously reported to our knowledge, of atypical neuroleptics on DS vs. VS structures. Relative volumes of the DS structures were significantly inversely correlated with atypical neuroleptic CPZ equivalent dosages whereas there was a non-significant positive correlation between atypical CPZ equivalent dosages and VS volume.

• Furthermore, when we subdivided atypical neuroleptics into type 1 (high D2 receptor affinity) and type 2 (low D2 receptor affinity) we found a similar differential effect between DS and VS structures with the DS being significantly larger in patients on type 2 medications and VS volumes being significantly larger in patients on type 1 medications.

• The above findings support the usefulness of only looking at patients on atypical neuroleptics as a way to mitigate the confounding enlarging effect of typical neuroleptic medications in measuring basal ganglia volumes in SZs as well as the importance of subdividing the basal ganglia into DS and VS sub-regions for volumetric analysis, as we have done.

• The above findings suggest that there is a complex interaction between neuroleptic medication and basal ganglia volume and that one-dimensional explanations for enlargement, such as D2 receptor affinity/blockade, may require refinement.

SELECTED REFERENCES


Figure 1: 3D rendering of the striatum segmented into the 10 regions we used, the left striatum is labeled.

Figure 2: The segmentation process of the ventral striatum.

Table 1. We performed independent samples T-tests for all 10 regions as well as total structure volumes from both hemispheres (all relative to ICC). There were no significant differences between any regions in the schizophrenic patients (n=15) and healthy controls (n=19).