Introduction: Although several studies have demonstrated the presence of brain structural alterations in schizophrenia [Am J Psychiatry 2005;162:2233], to the best of our knowledge only one study, using a Region of Interest approach, has assessed structural correlates of treatment-resistant schizophrenia [Prog Neuropsychopharmacol Biol Psychiatry 2008;32:257], suggesting lower GM volume in frontal and occipital regions in Non Responder (NR-SC) schizophrenia patients compared to Responders (R-SC).

We designed a pilot study to explore, by mean of voxel-based analysis of segmented MR studies, structural cerebral differences between R-SC and NR-SC.

Subjects: 19 NR-SC and 16 R-SC (classified according to Kane et Al. [Arch Gen Psychiatry 1988;45:789] and matched in terms of disease duration and age at onset), and 16 normal volunteers (NV) were enrolled. All subjects were male and right-handed, the three groups were age-matched. All patients were under antipsychotic treatment, the protocol was approved by the ethical committees of participating Institutions and written consent was obtained.

Morphometric analysis: T1-weighted volumes were acquired at 1.5 Tesla (Achieva, Philips Medical Systems, NL) using a magnetization-prepared 3D fast Gradient-Echo sequence (TR/TE/TI 11/2/600ms, voxel size 0.98x0.98x1.2mm, 124 contiguous axial slices), and segmented by the unified segmentation approach [NeuroImage 2005;26:839] implemented in SPM5 (Wellcome Department of Cognitive Neurology, London, UK). GM volumes were normalized to the MNI space, modulated [Neuroimage 2000;11:805], and smoothed (5mm FWHM).

Local differences in gray matter volume between the three groups were assessed using permutation tests [IEEE Trans Med Imaging 1999;18:32] [Hum Brain Mapp 2004;22:193] implemented in the CamBA software (http://www-bmu.psychiatry.cam.ac.uk/software).

Results: Clusters of significant GM differences among the three groups emerged mainly in bilateral frontal cortices and right insula and medial temporal lobe. Post-hoc analysis disclosed that differences were mainly due to a reduced GM volume of these structures in NR-SC, as compared to both NV and R-SC (see figure).

Discussion and Conclusion: Our results suggest that differences between NV an SC may be mainly driven by NR-SC patients.

Results of this pilot study need to be confirmed in larger patient populations and in longitudinal studies in drug-naïve patients, to assess a potential predictive value of these alterations and/or the relationship between TRS and putative neurodegenerative phenomena which may play a role in SC.