Lamination abnormalities in the neocortex of patients with schizophrenia *Schmitz C\*/\*\**, de Zeeuw L\*, Kreczmanski P\*/\*\*, Heinsen H\*\*\*, Steinbusch HWM\*/\*\*, Casanova MF\*\*\*\*

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It has been postulated that the prefrontal cortices of schizophrenic patients have less interneuronal space than controls, specifically in areas 9 and 46. This is thought to reflect an alteration in the neural circuitry of these areas and is a possible component of the pathology of schizophrenia. However, the corresponding studies were based on measures of neuronal density. The present study re-examined this finding based on the distribution of interneuronal space in regards to the morphology of the cell minicolumn. Material comprised brains from 13 schizophrenic patients (DSM-IV criteria) and 13 age-matched controls. Photomicrographs of Brodmann areas 9, 4, 3/1/2 and 17 were analyzed with computerized image analysis to measure minicolumnar width (CW), mean interneuronal distance (MCS), columnarity index (CI), and standard deviation in columnar width (Vcw). Diagnosis, cortical area, hemisphere, and lamina were included as effects in a full factorial model. All four dependent variables CW, MCS, CI, and Vcw were analyzed simultaneously. The multivariate likelihood ratio statistics supported a relationship between the dependent variables and cortical area (p < p0.001), lamina (p < 0.001), and the diagnosis by cortical area interaction (p = 0.048). Each of the four measurements taken individually varied significantly with cortical area (p < 0.001). MCS was the only measurement with a significant dependence on the diagnosis by cortical area interaction term (p = 0.022). This study supports the hypothesis that interneuronal spacing (MCS) is reduced in the prefrontal cortex (area 9) of schizophrenic patients. The lack of variation in the columnarity index and the lamina specificity of the changes argue in favor of a defect postdating the formation the cell minicolumn. Another implication is that the source of pathology may lie outside of the prefrontal cortex and only affect its innervation. Supported by The Stanley Medical Research Institute

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