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Differences between cumulative effects of first and second generation antipsychotics on the cortical thickness: Mega-analysis of 214 patients with schizophrenia from São Paulo, Brazil

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Schizophrenia is a severe mental disorder that impact individual social functioning and defy recent developments and treatment strategies. One fundamental problem to face schizophrenia is to balance the benefits and side effects of Antipsychotics (AP), including their effects on the cerebral cortex. Generally, morphometric studies on schizophrenia suffer from limited sample size. Consequently, they are unable to distinguish many confounding effects of illness-related factors from AP effects. Multi-centric transversal studies are reliable alternatives to evade these limitations. The present study is a conjunction analysis of two studies conducted in the State of São Paulo (5 samples) using data from 214 patients with schizophrenia by DSM-IV. Image quality control and analysis was conducted following ENIGMA consortium standards for surface measures. Brain thickness was taken as response variable, AP class was taken as fixed factor, life cumulative doses of AP and other variables as explain variables. Positive correlations with brain thickness were found bilaterally on the insula and left cingulate ($p < 0.001$, corrected), among other regions. Smaller mean thickness for first generation AP were found on the right pre-central, fusiform supramarginal girus, left cingulate and insula ($p < 0.001$, corrected). Smaller mean thickness for cumulative doses of first AP relative to the second generation were found, predominantly, on the lateral surfaces of both hemispheres. These findings were located in the right precentral, supramarginal, rostral middle frontal, post-central, supramarginal, fusiform and inferior temporal girus, as well as, in the left lateral occipital, superior temporal, inferior parietal, superior parietal, fusiform, supramarginal, caudal middle frontal, pars opercularis and precentral gyri ($p < 0.001$, GLM, corrected by Monte Carlo simulations). Other tested correlations/covariations did not survive the correction for multiple comparisons. The findings obtained expand previous results obtained for volumetry and introduce novel findings of protective effects of second generation in the treatment of schizophrenia compared to first generation AP.

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