

INTRODUCTION

Antipsychotics (AP) are often used among individuals with clinical high risk (CHR) for psychosis and affect cortical thickness (CT) in the short term. How to associate the effect of antipsychotics on CT with long-term clinical outcomes among CHR populations remains largely unknown. We conducted a two-month MRI scan and 2 year clinical follow up to investigate the CT alterations induced by initial AP exposure, and explore how these changes influence the clinical trajectory of CHRs.

METHODS

138 CHR individuals and 65 healthy controls (HC) were enrolled. Based on 2-month AP response, CHRs were further categorized as responders (CHR_R, n = 59) and non-responders (CHR_NR, n = 79). CHRs were also subdivided into converter (CHR_C, n=29) and no-converter (CHR_NC, n=109) groups according to 2 year follow up. The relationships among short-term CT changes, AP effects and long-term outcomes were explored using survival analysis, and random forest prediction model.

RESULTS

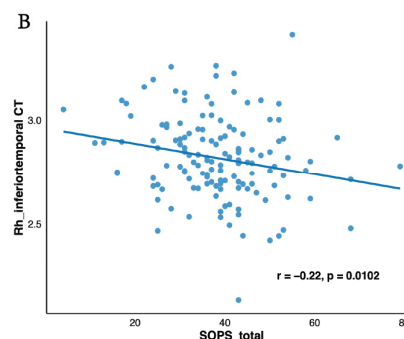
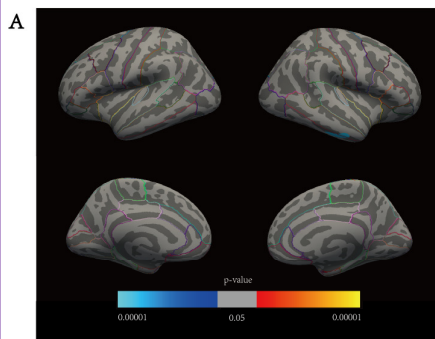


Figure 1. CHRs had CT reduction in right inferior temporal cortex with a correlation with clinical symptoms at baseline.

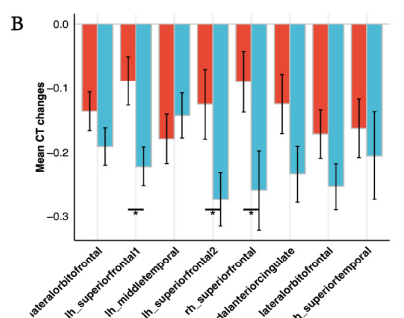
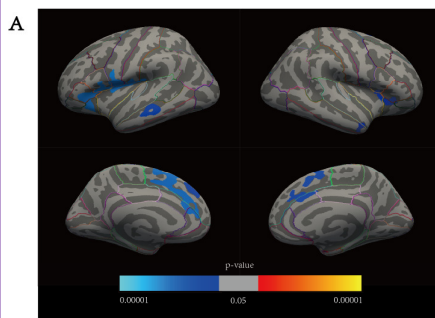


Figure 2. CHRs showed a steeper rate of gray matter loss in bilateral frontotemporal and right caudal anterior cingulate areas than HC. Non-responders showed more pronounced CT reduction than responders in bilateral superior frontal cortex.

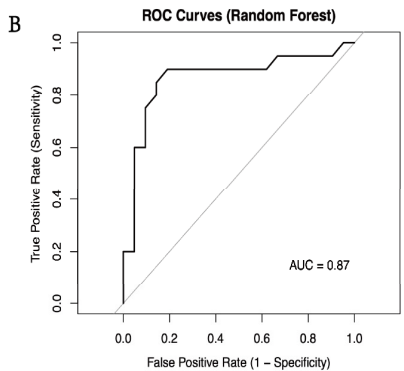
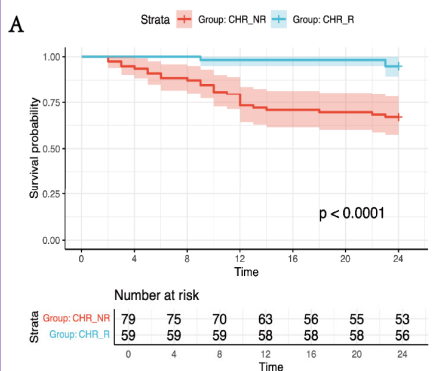


Figure 3. 2-year psychosis conversion rate was significantly higher in non-responders than in responders (5.1% vs 32.9%). A random forest model based on baseline and longitudinal CT changes classified CHR-C and CHR-NC with an accuracy of 0.83.

CONCLUSIONS

Among CHR populations, cortical thickness reduction occurs before initial AP exposure, which induce further cortical thickness reduction. However, its effects on long-term psychosis conversion are differentiated by short-term clinical response. Our findings emphasizes the need for personalized treatment approaches in managing CHR populations.

KEY REFERENCES:

Cannon TD, Chung Y, He G, et al. Progressive reduction in cortical thickness as psychosis develops: a multisite longitudinal neuroimaging study of youth at elevated clinical risk. *Biol Psychiatry*. 2015;77(2):147-157.
Collins MA, Ji JL, Chung Y, et al. Accelerated cortical thinning precedes and predicts conversion to psychosis: The NAPLS3 longitudinal study of youth at clinical high-risk. *Mol Psychiatry*. 2023;28(3):1182-1189.