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Abstract Topic:- Complex traits and polygenic disorders

Abstract Title:- Runs of Homozygosity (ROH) analysis in Indian aging cohorts: Contrasting homozygosity patterns in rural and urban populations and their genetic implications

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Aims:-Runs of Homozygosity (ROH) are continuous, homozygous DNA segments inherited from recent ancestors and are common in human populations. ROH is linked to inbreeding in family trees. ROH length and quantity provide insights into demographic history and can help to explore the genetic basis of complex diseases. Mexican, American, African, and European population studies have linked ROH to diseases like diabetes, heart disease, cancer, intellectual disabilities, and neurodegenerative diseases. Stature and cognition-related quantitative traits have shown a robust association with ROH burden, suggesting recessive variants play a role in their genetic makeup. Investigating ROH levels in unique genetic populations, like those in India with high endogamy and consanguinity, is crucial, as findings may differ from those in other worldwide populations.

Methods:- The Srinivaspura Aging Neuro Senescence and Cognition (CBR-SANSCOG) and TATA Longitudinal Study of Aging (CBR-TLSA) are the cohort studies at the Centre for Brain Research (CBR), focusing on the study of brain aging for respectively rural (n = 10,000) and urban (n = 1000) populations aged 45 and above. We conducted ROH analyses for both the CBR-SANSCOG array and CBR-TLSA sequencing datasets and evaluated various ROH parameters such as average length, frequency, number of segments, and the total length of ROH segments in individuals and compared them with the 1000 genome South Asian population (SAS) dataset. Furthermore, we are currently conducting an association analysis of these ROH parameters with metabolic traits and cognitive parameters to understand the relevance of ROH for complex diseases.

Results:- We observed distinct levels of homozygosity in the rural and urban datasets. Comparing our findings with the SAS dataset, we found an increased number of ROH segments with shorter lengths in the CBR-TLSA dataset. However, in the CBR-SANSCOG dataset, we found higher levels of homozygosity, characterized by longer ROH segments with elevated average length in individuals.

Conclusions:- Previous studies have shown larger populations have fewer ROH segments with shorter lengths, while isolated populations have more, longer ROH segments. Admixed groups have the fewest ROH, and consanguineous communities have very long ROH segments. The findings of CBR_SANSCOG and CBR-TLSA cohort datasets emphasize increased endogamy and consanguinity in the rural population compared to the urban population in India. The association analysis may shed light on the population-level impact of homozygosity in complex diseases.

Keywords:- Runs of Homozygosity (ROH), cohort studies, consanguinity, population, complex diseases