

# Is the Insula a Final Common Neuroanatomical Pathway for Schizophrenia, associated with its Major Clinical Domains?

Susanna Gebhardt, Henry Nasrallah, M.D.  
University of Cincinnati, College of Medicine

## Background:

Insular dysfunction plays a vital role in the neurobiology and clinical phenomenology of Schizophrenia (SZ). The insula is central to interoception, cognitive, social-emotional, and sensorimotor tasks, and participates in several significant brain networks.

## Objective:

Examine research on insular structural and functional abnormalities in the domain of SZ in clinical trials from 2011-2021 to identify common findings or major divergences related to the insula's contribution to SZ.

## Methods:

Used PubMed to identify controlled trials that examined association between structure and function of insula with SZ. 49 reports met inclusion/exclusion criteria.

## Results:

These studies reported that insular abnormalities are associated with the three major domains of positive, negative, and cognitive symptoms of SZ.

The studies correlate these symptoms to morphological changes to the unilateral and bilateral insulae, as well as specific areas within the insula. Insular abnormalities in SZ included:

- 1) reduced gray matter volume
- 2) cortical thinning
- 3) loss of white matter connectivity
- 4) hypo-gyrification

Evidence of hyper- and hypoactivation and functional connectivity defects were similarly found.

Studies found statistically significant ( $p < .05$ ) correlations between structural abnormalities or functional disconnection and positive and negative symptoms, cognition, awareness of illness/insight into illness, interoception, and Quality of Life.

Structural changes to the insula also served as markers for illness duration and as potential markers of symptomatic improvement.

Anatomical Finding	Number of Studies ( $p < .05$ )
Reduced GMV, bilateral insula	12
Reduced GMV, right insula	3
Reduced GMV, left insula	4
Cortical thinning, right insula	3
Loss of connectivity (Functional and Structural)	11
Hypogyrfication	2
Reduced surface area	1
Other changes to GM	1

Prognostic Marker	Number of Studies ( $p < .05$ )
Illness duration	5
Age of onset	2
Marker of symptom improvement/Response to treatment	2
Premorbid functioning	1

Functional Deficit	Number of Studies ( $p < .05$ )
Cognitive performance; Processing speed; Memory	4
Positive symptoms, including hostility, "bizarre" behavior	7
Negative symptoms	8
Empathy; Social agreeableness/Alienation; Emotion	4
Gesture deficits	1
Awareness of illness; Insight	3
Quality of Life (subjective, objective)	2
Salience	1

## Conclusion and Future Directions:

Abnormalities of the insula structures and functions appear to have a central role in generating most of the clinical symptoms of SZ. Several studies posit that insular changes occurring during fetal neurodevelopment may produce the psychotic and non-psychotic features of SZ. The extensive connections between the insula and brain areas implicated in SZ may position it as a final common neuroanatomical pathway in the SZ syndrome. Various measurable abnormalities of the insula in children and adolescents may serve as potential biomarkers for susceptibility to developing SZ and the negative and positive symptomatology. Further research into the insula as a core clinico-anatomical structure is warranted.

