## Title

Five negative symptom domains are differentially associated with resting state amplitude of low frequency fluctuations in Schizophrenia.



## Authors

Cheon, Eun-Jin
Male, Alie
Gao, Bingchen
et al.

## Publication Date

2023-03-01

## DOI

10.1016/j.pscychresns.2023.111597

Peer reviewed

HHS Public Access

Author manuscript

*Psychiatry Res Neuroimaging*. Author manuscript; available in PMC 2024 June 06.

Published in final edited form as:

*Psychiatry Res Neuroimaging*. 2023 March ; 329: 111597. doi:10.1016/j.pscychresns.2023.111597.

# Five Negative Symptom Domains are Differentially Associated with Resting State Amplitude of Low Frequency Fluctuations in Schizophrenia

**Eun-jin Cheon, MD, PhD**[*,1,2], **Alie G. Male, PhD**[*,1], **Bingchen Gao, MS**[1], **Bhim M. Adhikari, PhD**[3], **Jesse T. Edmond, MA**[4], **Stephanie M. Hare**[3], **Aysenil Belger, PhD**[5], **Steven G. Potkin, MD**[6], **Juan R. Bustillo, MD**[7], **Daniel H. Mathalon, PhD, MD**[8,9], **Judith M. Ford, PhD**[8,9], **Kelvin O. Lim, MD**[10], **Bryon A. Mueller, PhD**[10], **Adrian Preda, MD**[6], **Daniel O'Leary, PhD**[11], **Gregory P. Strauss, PhD**[12], **Anthony O. Ahmed, PhD**[13], **Paul M. Thompson, PhD**[14], **Neda Jahanshad, PhD**[14], **Peter Kochunov**[3], **Vince D. Calhoun, PhD**[4], **Jessica A. Turner, PhD**[15], **Theo G. M. van Erp, PhD**[1,16]

[1.]Clinical Translational Neuroscience Laboratory, Department of Psychiatry and Human Behavior, School of Medicine, University of California, Irvine, CA, USA

[2.]Department of Psychiatry, Yeungnam University College of Medicine, Daegu, South Korea

[3.]Maryland Psychiatric Research Center, Catonsville, MD

[4.]Center for Translational Research in Neuroimaging and Data Science (TReNDS), GSU/GATech/Emory, Atlanta, GA

[5.]Department of Psychiatry, University of North Carolina, Chapel Hill, USA

[6.]Department of Psychiatry and Human Behavior, School of Medicine, University of California, Irvine, CA, USA

[7.]Departments of Psychiatry & Neuroscience, University of New Mexico, Albuquerque, NM, USA

[8.]Department of Psychiatry, Weill Institute for Neurosciences, University of California, San Francisco, San Francisco, CA, USA

[9.]Veterans Affairs San Francisco Healthcare System, San Francisco, CA, USA

[10.]Department of Psychiatry and Behavioral Sciences, University of Minnesota, Minneapolis, MN, USA

[11.]Department of Psychiatry, University of Iowa, IA, USA

[12.]Department of Psychology, University of Georgia, Athens, GA, USA

Corresponding Author: Theo G.M. van Erp, Clinical and Translational Neuroscience Laboratory, Department of Psychiatry and Human Behavior, School of Medicine, University of California Irvine, Irvine Hall, room 109, Irvine, CA, 92697-3950, tvanerp@uci.edu.

[*]shared first author

Contributors

EJC, AGM, and TGMvE created the first draft of the manuscript. BG, BMA and TGMvE conducted the imaging and statistical analyses. All other co-authors critically reviewed the manuscript and provided comments.

Conflict of interest

Dr. Daniel H. Mathalon consulted for Neurocrine Biosciences, Gilgamesh Pharmaceuticals, and Recognify Life Sciences, and served on a data safety monitoring/advisory board for Neurocrine Biosciences. The other authors have no conflict of interest to report.

[13]Department of Psychiatry, Weill Cornell Medicine, White Plains, NY, USA

[14]Imaging Genetics Center, University of Southern California, Marina del Rey, CA, USA

[15]Department of Psychiatry, Ohio State University, OH, USA

[16]Center for the Neurobiology of Learning and Memory, University of California Irvine, Irvine, CA, USA

## Abstract

This study examined associations between resting-state amplitude of low frequency fluctuations (ALFF) and negative symptoms represented by total scores, second-order dimension (motivation and pleasure, expressivity), and first-order domain (anhedonia, avolition, asociality, alogia, blunted affect) factor scores in schizophrenia (n=57). Total negative symptom scores showed positive associations with ALFF in temporal and frontal brain regions. Negative symptom domain scores showed predominantly stronger associations with regional ALFF compared to total scores, suggesting domain scores may better map to neural signatures than total scores. Improving our understanding of the neuropathology underlying negative symptoms may aid in addressing this unmet therapeutic need in schizophrenia.

### Keywords

ALFF; Negative Symptoms; Avolition

## 1. Introduction

The clinical course, prognosis, and quality of life of individuals with schizophrenia are associated with the severity of negative symptoms which are defined as deficiencies in the areas of motivation, emotion, and communication (Green et al., 2012). An improved understanding of the underlying neuropathology of negative symptoms may aid in developing better treatments for this unmet therapeutic need (Rabinowitz et al., 2012; Robertson et al., 2014).

Studies of the pathophysiology underlying the broad construct of negative symptoms have failed to show consistent findings, ostensibly due to heterogeneity between different negative symptom constructs (Galderisi et al., 2018). Negative symptoms form a hierarchical structure with two second-order dimensions [motivation and pleasure (MAP), diminished expression (EXP)] and five first-order domains (anhedonia, avolition, and asociality, blunted affect and alogia) (Strauss et al., 2019a, 2019b, 2018). We assert that examining associations between these negative symptom dimensions and domains and brain imaging measures will be informative regarding their pathophysiology, advancing efforts to develop more refined treatments targeting specific symptom domains.

Abnormalities in resting-state brain activity are robust in schizophrenia. Amplitude of low frequency fluctuations (ALFF)—a resting-state brain activity measure obtained from functional magnetic resonance imaging (fMRI) data—is computed as the average square root of the power spectrum within a frequency band at each brain voxel, yielding a measure

of the average amplitude of blood oxygen level dependent (BOLD) signal fluctuations over time. It can also be normalized by the power of the entire frequency range resulting in fractional ALFF (fALFF). ALFF is sensitive to baseline cerebral blood flow and reflects spontaneous and intrinsic neural activity (Zhou et al., 2010).

A meta-analysis found that ALFF is lower in somatosensory cortex, posterior parietal cortex, and occipital cortex, and is higher in bilateral striatum, medial temporal cortex, and medial prefrontal cortex in schizophrenia compared to controls (Xu et al., 2015). There is also evidence of associations between ALFF and hallucinations (Hare et al., 2018, 2017). However, associations between regional ALFF and negative symptoms remain to be determined.

One study found that deficit schizophrenia (DS), characterized by primary and persistent negative symptoms, compared to non-deficit schizophrenia (NDS) exhibited lower fALFF in the left insula and frontotemporal cortex, bilateral insula, and anterior cingulate gyrus, and greater fALFF in the bilateral visual cortex (Zhou et al., 2019). Another found a positive association between right putamen ALFF and a negative association between left cerebellum ALFF and total negative symptom severity in DS but not NDS (Li et al., 2017). However, these studies did not examine associations between ALFF and negative symptom subdomains. This study examined, to our knowledge for the first time, the associations between ALFF and dimensions and domains of negative symptoms.

## 2. Methods

Eyes-closed rsfMRI data (echo planar imaging with TE/TR/FA/slices/frames/voxel size/gap = 30 ms/2 s/77°/32/162/3.4×3.4×4 mm/1 mm) was obtained from 57 individuals with schizophrenia (44 males, 32.7±11.0 age in years, 20.7±6.9 age at onset, 12.1±9.0 duration of illness in years, and CPZ dose equivalent of 378±339), who participated in the Function Biomedical Informatics Research Network (FBIRN), using an rsfMRI analysis pipeline developed by the Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) consortium (Adhikari et al., 2019, 2018).

Mean±SD scores for clinical measures were 56.5±13.7 for PANSS (Positive and Negative Syndrome Scale) Total, 14.9±4.9 for PANSS Positive, 13.6±5.3 for PANSS Negative, 15.9±15.4 for SAPS (Scale for the Assessment of Positive Symptoms) Total, and 18.4±12.5 for SANS (Scale for the Assessment of Negative Symptoms) Total. We extracted mean ALFF from 68 (34 left/34 right hemisphere) Desikan-Killiany atlas cortical regions obtained using FreeSurfer (Fischl, 2012). Exploratory regression analyses examined associations (partial Pearson's $r$) between regional ALFF and total negative symptom, MAP and EXP dimension (Khan et al., 2017; Strauss et al., 2018), and anhedonia, asociality, avolition, blunted affect, and alogia domain scores derived from the SANS (Strauss et al., 2018) and the PANSS (Khan et al., 2017), while statistically controlling for age, gender and scanner/site (R's *lm*). We considered all $|r\text{-values}| > 0.266$ (critical $r$-value, $df$=55, $p$<0.05, two-tailed), without correction for multiple comparison, as regions of interest (ROIs) for exploration in future work on larger multicenter samples. We conducted spin-tests (n=1,000

permutations) to determine similarities of correlation patterns between ALFF and symptoms (Alexander-Bloch et al., 2018).

## 3. Results

ALFF in bilateral entorhinal and inferior temporal, left lateral orbital, and right fusiform, insula, medial orbitofrontal, middle temporal, pars triangularis, postcentral, and precentral gyri were significantly correlated with SANS Total (Table 1). Among these 12 regions, nine showed significant associations with MAP and two with the EXP. Among the nine regions associated with MAP, three, four, and eight were significantly associated with anhedonia, asociality, and avolition, respectively. Of the two regions associated with EXP, one was associated with alogia, and both were associated with blunted affect (Table 1, underlined correlations).

Nine of the 12 regions that showed positive associations with SANS Total also showed positive associations with PANSS Negative. Four of the nine regions that showed positive associations with SANS MAP also showed positive associations with PANSS MAP, and both regions that showed positive associations with SANS EXP also showed positive associations with PANSS EXP (Table 1, underlined correlations).

Importantly, most of the correlations with first-order domains (e.g., SANS avolition), were higher than the broader second-order dimensions (e.g., SANS MAP), which were higher than global total scores (e.g., SANS Total).

Finally, the relationships between correlation patterns of ALFF and symptoms were: r(PANSS TOT, SANS TOT)=0.84, r(PANSS EXP, SANS EXP)=0.96, r(PANSS MAP, SANS MAP)=0.97, r(PANSS EXP, PANSS MAP)=0.62, and r(SANS EXP, SANS MAP)=0.55; all p-spin < 0.001.

## 4. Discussion

This study explored associations between ALFF and negative symptom second-order dimensions and first-order domains. We found significant associations between frontal and temporal lobe ALFF and negative symptom severity. For the SANS, we found a larger number of significant associations between ALFF and MAP than between ALFF and EXP. For the PANSS, we found a larger number of significant associations between ALFF and EXP than between ALFF and MAP. The relationships between correlation patterns of ALFF and symptoms were higher within (EXP or MAP between PANSS/SANS) than between domains (EXP and MAP within PANSS/SANS) suggestive of different regional mapping between ALFF and EXP/MAP. While future studies should corroborate these findings, they suggest that SANS items may better reflect the MAP dimension, while PANSS items better reflect the EXP dimension.

Among the MAP subdomains, avolition exhibited the strongest association with ALFF. Moreover, most of the associations with first-order domains (e.g., avolition), were stronger than for second-order dimensions (e.g., MAP), which were stronger than for total scores, suggesting that refined symptom domain scores may better map onto some imaging

phenotypes than total negative symptom scores. Notably, a recent study showed that the MAP dimension and its subdomains (avolition, anhedonia, asociality) had similar associations with ventral striatum activation during reward anticipation (Kaliuzhna et al., 2021). While these findings may suggest limited added value of deconstructing the MAP dimension into its subdomains when examining relationships with brain imaging measures, they may also support the hypothesis that the ventral striatum is involved in all three subdomains (Strauss et al., 2019a). This study represents a first step in advancing our understanding of the pathophysiology of negative symptoms using ALFF, and we plan to generate more robust and replicable findings by conducting ENIGMA schizophrenia working group resting-state meta-analysis employing Collaborative Informatics and Neuroimaging Suite Toolkit for Anonymous Computation (COINSTAC; http://coinstac.trendscenter.org) framework (Ming et al., 2017).

## 5. Conclusion

The severity of negative symptoms is positively associated with larger amplitude spontaneous BOLD signal fluctuations in frontal and temporal lobe regions. The SANS may be more sensitive to measuring MAP, while the PANSS may be more sensitive to measuring EXP. MAP associations appear predominantly driven by avolition as compared to anhedonia and asociality. Finally, the strongest, observed associations for first-order domain scores suggest that they may represent more homogeneous constructs, that better map onto imaging phenotypes than total negative symptom scores, and may serve as separate treatment targets.

## Acknowledgement

This study was supported by was supported by the National Center for Research Resources at the National Institutes of Health [grant numbers: NIH 1 U24 RR021992 (Function Biomedical Informatics Research Network), NIH 1 U24 RR025736 (Biomedical Informatics Research Network Coordinating Center)], National Institutes of Health [grant numbers: 1R01MH121246 (ENIGMA-COINSTAC: Advanced Worldwide Transdiagnostic Analysis of Valence System Brain Circuits to JAT, TGMvE, and VDC, and R01MH118695 to VDC), and the National Science Foundation [grant number: NSF 2112455 to VDC]. The funding sources had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

## References

Adhikari BM, Jahanshad N, Shukla D, Glahn DC, Blangero J, Reynolds RC, Cox RW, Fieremans E, Veraart J, Novikov DS, Nichols TE, Hong LE, Thompson PM, Kochunov P, 2018. Heritability estimates on resting state fMRI data using ENIGMA analysis pipeline. Pac. Symp. Biocomput. 23, 307–318. [PubMed: 29218892]

Adhikari BM, Jahanshad N, Shukla D, Turner J, Grotegerd D, Dannlowski U, Kugel H, Engelen J, Dietsche B, Krug A, Kircher T, Fieremans E, Veraart J, Novikov DS, Boedhoe PSW, van der Werf YD, van den Heuvel OA, Ipser J, Uhlmann A, Stein DJ, Dickie E, Voineskos AN, Malhotra AK, Pizzagalli F, Calhoun VD, Waller L, Veer IM, Walter H, Buchanan RW, Glahn DC, Hong LE, Thompson PM, Kochunov P, 2019. A resting state fMRI analysis pipeline for pooling inference across diverse cohorts: an ENIGMA rs-fMRI protocol. Brain Imaging Behav. 13, 1453–1467. [PubMed: 30191514]

Alexander-Bloch AF, Shou H, Liu S, Satterthwaite TD, Glahn DC, Shinohara RT, Vandekar SN, Raznahan A, 2018. On testing for spatial correspondence between maps of human brain structure and function. Neuroimage 178, 540–551. [PubMed: 29860082]

Fischl B, 2012. FreeSurfer. Neuroimage 62, 774–781. [PubMed: 22248573]

Galderisi S, Mucci A, Buchanan RW, Arango C, 2018. Negative symptoms of schizophrenia: new developments and unanswered research questions. Lancet Psychiatry 5, 664–677. [PubMed: 29602739]

Green MF, Hellemann G, Horan WP, Lee J, Wynn JK, 2012. From perception to functional outcome in schizophrenia: modeling the role of ability and motivation. Arch. Gen. Psychiatry 69, 1216–1224. [PubMed: 23026889]

Hare SM, Ford JM, Ahmadi A, Damaraju E, Belger A, Bustillo J, Lee HJ, Mathalon DH, Mueller BA, Preda A, van Erp TGM, Potkin SG, Calhoun VD, Turner JA, Functional Imaging Biomedical Informatics Research Network, 2017. Modality-Dependent Impact of Hallucinations on Low-Frequency Fluctuations in Schizophrenia. Schizophr. Bull. 43, 389–396.

Hare SM, Law AS, Ford JM, Mathalon DH, Ahmadi A, Damaraju E, Bustillo J, Belger A, Lee HJ, Mueller BA, Lim KO, Brown GG, Preda A, van Erp TGM, Potkin SG, Calhoun VD, Turner JA, 2018. Disrupted network cross talk, hippocampal dysfunction and hallucinations in schizophrenia. Schizophr. Res. 199, 226–234. [PubMed: 29571753]

Kaliuzhna M, Kirschner M, Carruzzo F, Hartmann-Riemer MN, Bischof M, Seifritz E, Tobler PN, Kaiser S, 2021. How far to go in deconstructing negative symptoms? Behavioural and neural level evidence for the amotivation domain. Schizophr. Res. 236, 41–47. [PubMed: 34390980]

Khan A, Liharska L, Harvey PD, Atkins A, Ulshen D, Keefe RSE, 2017. Negative Symptom Dimensions of the Positive and Negative Syndrome Scale Across Geographical Regions: Implications for Social, Linguistic, and Cultural Consistency. Innov. Clin. Neurosci. 14, 30–40.

Li Z, Lei W, Deng W, Zheng Z, Li M, Ma X, Wang Q, Huang C, Li N, Collier DA, Gong Q, Li T, 2017. Aberrant spontaneous neural activity and correlation with evoked-brain potentials in first-episode, treatment-naïve patients with deficit and non-deficit schizophrenia. Psychiatry Res Neuroimaging 261, 9–19. [PubMed: 28092779]

Ming J, Verner E, Sarwate A, Kelly R, Reed C, Kahleck T, Silva R, Panta S, Turner J, Plis S, Calhoun V, 2017. COINSTAC: Decentralizing the future of brain imaging analysis. F1000Res. 6, 1512. [PubMed: 29123643]

Rabinowitz J, Levine SZ, Garibaldi G, Bugarski-Kirola D, Berardo CG, Kapur S, 2012. Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia: analysis of CATIE data. Schizophr. Res. 137, 147–150. [PubMed: 22316568]

Robertson BR, Prestia D, Twamley EW, Patterson TL, Bowie CR, Harvey PD, 2014. Social competence versus negative symptoms as predictors of real world social functioning in schizophrenia. Schizophrenia Research. 10.1016/j.schres.2014.10.037

Strauss GP, Ahmed AO, Young JW, Kirkpatrick B, 2019a. Reconsidering the Latent Structure of Negative Symptoms in Schizophrenia: A Review of Evidence Supporting the 5 Consensus Domains. Schizophrenia Bulletin. 10.1093/schbul/sby169

Strauss GP, Esfahlani FZ, Galderisi S, Mucci A, Rossi A, Bucci P, Rocca P, Maj M, Kirkpatrick B, Ruiz I, Sayama H, 2019b. Network Analysis Reveals the Latent Structure of Negative Symptoms in Schizophrenia. Schizophrenia Bulletin. 10.1093/schbul/sby133

Strauss GP, Nuñez A, Ahmed AO, Barchard KA, Granholm E, Kirkpatrick B, Gold JM, Allen DN, 2018. The Latent Structure of Negative Symptoms in Schizophrenia. JAMA Psychiatry. 10.1001/jamapsychiatry.2018.2475

Xu Y, Zhuo C, Qin W, Zhu J, Yu C, 2015. Altered Spontaneous Brain Activity in Schizophrenia: A Meta-Analysis and a Large-Sample Study. Biomed Res. Int. 2015, 204628.

Zhou C, Tang X, You W, Wang X, Zhang X, Zhang X, Yu M, 2019. Altered Patterns of the Fractional Amplitude of Low-Frequency Fluctuation and Functional Connectivity Between Deficit and Non-Deficit Schizophrenia. Front. Psychiatry 10, 680. [PubMed: 31572248]

Zhou Y, Wang K, Liu Y, Song M, Song SW, Jiang T, 2010. Spontaneous brain activity observed with functional magnetic resonance imaging as a potential biomarker in neuropsychiatric disorders. Cogn. Neurodyn. 4, 275–294. [PubMed: 22132039]

*Psychiatry Res Neuroimaging*. Author manuscript; available in PMC 2024 June 06.

**Table 1.**

Significant associations between amplitude of low frequency fluctuations (ALFF) and symptom domain factor scores based on the scale for the assessment of negative symptoms (SANS) and positive and negative syndrome scale (PANSS).

| | SANS Total | | SANS MAP | | SANS EXP | | SANS Anhedonia | | SANS Asociality | | SANS Avolition | | SANS Alogia | | SANS Blunted Affect | | PANSS Negative | | PANSS MAP | | PANSS EXP | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| Left entorhinal | 0.294 | 0.043 | | | | | | | | | 0.286 | 0.049 | | | | | | | | | | |
| Left frontal pole | | | −0.288 | 0.047 | | | −0.327 | 0.023 | | | | | | | | | | | | | | |
| Left fusiform | | | 0.298 | 0.040 | | | | | | | 0.348 | 0.015 | | | | | | | | | | |
| Left inferior temporal | 0.413 | 0.004 | 0.531 | <0.001 | | | 0.451 | 0.001 | 0.380 | 0.008 | 0.597 | <0.001 | | | | | 0.326 | 0.024 | 0.424 | 0.003 | | |
| Left insula | | | | | | | | | | | 0.373 | 0.009 | | | | | | | | | | |
| Left lateral orbitofrontal | 0.302 | 0.037 | 0.334 | 0.020 | | | | | 0.305 | 0.035 | 0.316 | 0.029 | | | | | | | | | | |
| Left rostral anterior cingulate | | | | | | | | | | | | | | | | | 0.307 | 0.034 | | | 0.295 | 0.042 |
| Left temporal pole | | | | | 0.297 | 0.041 | | | | | | | | | 0.293 | 0.043 | | | | | 0.310 | 0.032 |
| Right entorhinal | 0.304 | 0.036 | | | 0.307 | 0.034 | | | | | | | | | 0.334 | 0.020 | 0.290 | 0.045 | | | 0.305 | 0.035 |
| Right fusiform | 0.355 | 0.013 | 0.391 | 0.006 | | | | | 0.294 | 0.043 | 0.460 | 0.001 | | | | | 0.293 | 0.043 | 0.297 | 0.040 | | |
| Right inferior parietal | | | | | | | | | | | | | | | | | | | | | | |
| Right inferior temporal | 0.322 | 0.026 | 0.471 | 0.001 | | | 0.374 | 0.009 | 0.358 | 0.012 | 0.510 | <0.001 | | | | | | | 0.350 | 0.015 | | |
| Right insula | 0.318 | 0.028 | 0.343 | 0.017 | | | | | | | 0.407 | 0.004 | | | | | 0.293 | 0.043 | | | | |
| Right isthmus cingulate | | | | | 0.295 | 0.042 | | | | | | | 0.306 | 0.035 | | | | | | | | |
| Right lateral occipital | | | | | | | | | | | 0.309 | 0.033 | | | | | | | | | | |

| | SANS Total | | SANS MAP | | SANS EXP | | SANS Anhedonia | | SANS Asociality | | SANS Avolition | | SANS Alogia | | SANS Blunted Affect | | PANSS Negative | | PANSS MAP | | PANSS EXP | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** | ***r*** | ***p*** |
| Right medial orbitofrontal | 0.301 | 0.037 | | | | | | | | | | | | | | | 0.290 | 0.046 | | | 0.306 | 0.034 |
| Right middle temporal | 0.295 | 0.042 | 0.299 | 0.039 | | | | | | | | | | | | | 0.316 | 0.028 | | | | |
| Right pars triangularis | 0.401 | 0.005 | 0.325 | 0.024 | 0.325 | 0.024 | | | | | 0.383 | 0.007 | 0.285 | 0.050 | 0.311 | 0.031 | 0.428 | 0.002 | 0.305 | 0.035 | 0.363 | 0.011 |
| Right postcentral | 0.352 | 0.014 | 0.332 | 0.021 | | | 0.347 | 0.016 | | | 0.290 | 0.045 | | | | | 0.355 | 0.013 | | | 0.349 | 0.015 |
| Right precentral | 0.329 | 0.022 | 0.320 | 0.027 | | | | | | | 0.356 | 0.013 | | | | | 0.320 | 0.027 | | | | |
| Right superior temporal | | | | | 0.294 | 0.043 | | | | | | | | | | | | | | | 0.336 | 0.019 |
| Right temporal pole | | | | | | | | | | | | | | | | | | | | | 0.297 | 0.040 |
| Right transverse temporal | | | | | | | | | | | | | | | | | | | | | 0.293 | 0.043 |

Underlined correlations indicate consistency of PANSS Negative ratings, and second order and first order factor scores with SANS Total ratings.