Schizotypy and neurological soft signs in schizophrenic subjects and unaffected relatives: a study of functional magnetic resonance

Galindo L.[1,2,3], Pastoriza F.[1,2,3], Roé N.[1,3], Bergé D.[1,2,3], Picado M.[1,3], Mané A.[1,2,3], Bulbena A.[1,2,3], Vilarroya O.[1,3]

[1]GREEN, Grup de Recerca en Neuroimatge, Fundació IMIM, Barcelona, Spain. [2]Unitat de Recerca en Neurociència Cognitiva, Departament de Psiquiatria i Medicina Legal, UAB, Barcelona, Spain.
[3]Institut de Neuropsiquiatria i Addiccions, Parc de Salut Mar, Barcelona, Spain

Background

Neurological soft signs have been proposed as a component of a schizophrenia endophenotype. In this sense, neurological soft signs have been found to be correlated with schizotypal personality traits in healthy schizophrenic relatives. Mainly, alterations in motor coordination and integration of stimuli, are positively correlated with total scores and the cognitive perceptive aspect of schizotypy scales [3,4,5] Several functional neuroimaging studies of resting state, have suggested changes in connectivity patterns in patients with schizophrenia compared with healthy controls.[7] However, there are no studies investigating resting state abnormalities of schizophrenic patients and healthy relatives and the association of neurological soft signs with schyzotipy traits in the same population.

Aim

a) To explore resting state abnormalities in the Default Mode Network (DMN) and schizotypy-related areas in patients with schizophrenia and first-degree relatives in relation to control subjects.
b) To study the association of neurological soft signs with the schizotipy traits.

Material and methods

Participants
19 Patients with schizophrenia
12 Healthy siblings of patients not included in the present study
20 Healthy Controls

Standard

	Age	Studies	Gender
Mean	37,79	12,6	1:1
Deviation	9,241	1,597	,504

Neuropsicological Studies:
-Schizotypical Personality Questionnarie
-Neurological Soft Signs (NES)

Images were acquired with a Phillips Achieva de 3T scanner. Reference anatomical scans were obtained with a FSPGR T1-weighted sequence (TR: 8 ms; TE: 4ms; FA: 8º; FOV: 240mm; matrix size 256x256x180, voxel size 0,94x0,94x1mm, gap 0.0 mm). Functional images were generated with an EPI-T2* sequence (TR: 2 ms; TE: 25 ms; FA: 90; FOV: 230mm, Matrix size 128x128, each volume consisting of 30 slices with a GAP of 0,5mm).

Image analysis: Functional images were reoriented to the first scann and normalized to the MNI EPI template and smoothed with an **8 mm** kernel, with SPM.
The CONN- FMRI Tollbox v1.2 was used to create individual subject seed-to-voxel connectivity maps, corresponding the following seed ROIs (table 2)

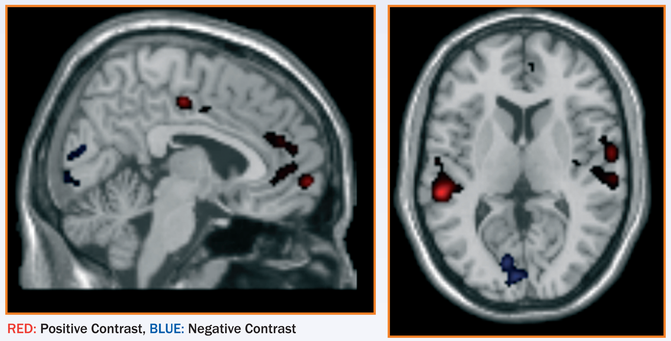
Results

Table 1: Pearson Correlation in subscales of Schizotipy traits and Neurological Soft Signs

	Total SPQ	Cognitive P	Interpersonal	Desorganitation
NSS Total	,402**	,283*	,500**	,285*
Sensorial Integration	0,262	0,159	,341*	0,212
Motor Coordination	,402**	,295*	,486**	,290*

**. P< 0,01 (bilateral). *. P<I 0,05 (bilateral).

Figure 1: Resting State Functional differences with respect to controls shared by patients with schizophrenia and non-phycotic relatives. The ROIs are explain on Table 2.



RED: Positive Contrast, BLUE: Negative Contrast

Table 2: Resting-State network alterations

	Pacients vs control			*Familiar vs Control*		
Default network		**MNI(x,y,z)**	**t**		**MNI (x,y,z)**	**t**
Superior temporal gyrus (BA22)	R	(-4,-88,+12)	3.33	R	(+2,-88,+12)	3.39
Middle temporal gyrus (BA21)		*NSD*		L	(-16,+54,-22)	3.39
Precentral Gyrus		*NSD*			*NSD*	
Middle frontal gyrus (BA6)	L	(-18,-96,+12)	3.33	L	(-20,+4,+50)	3.39
Somatosensorial Cortex (BA7)	L	(-02,-75,+36)	3.33		*NSD*	
Schyzotipy and Schizophrenia Spectrum						
Inferior temporal gyrus (B20)	L	(-52,-14,+16)	3.33	L	(-56,-20,-02)	3.39
Fusiform Gyrus (BA 37)	R	(-06,+80,-04)	3.33	L	(-10,+32,-28)	3.39
Visual primary cortex (BA17)	L	(+54,-32,-08)	3.33	L	(+42,+40,+08)	3.39
Visual primary cortex (BA17)	R	(+32,-06,-10)	3.33	R	(+42,-140,+26)	3.39
Cuneus	L	(02,-76,+46)	3.33	L	(+40,+40,+26)	3.39

Abreviations: BA: Brodmann´s Area, L: Left, R: Right, *NSD: No significant diferences founded. FWE correction was applied for the obtention of these clusters*

Conclusions

- We found changes in patterns of brain connectivity in the DMN and schizotypy-related areas in patients and in healthy relatives.
- The engagement of the right superior temporal gyri during baseline cerebral activity may have be explained by schizotipy auditory-related abnormalities.
- The primary visual cortex connectivity increased in patients and non phycotic relatives could be related to schizotipy visual-related activity. [7]
- There are other regions that are activated during baseline cerebral activity in patients but not in healthy relatives
- There is a positive correlation between the presence of minor neurological symptoms and the presence of schizotypal personality traits in the three groups.
- It is necessary to replicate the study in a larger sample. The drug therapy may be an important confounder in our study.

References

1. Thomann PA, Roebel M, Dos Santos V, et al. Cerebellar substructures and neurological soft signs in first-episode schizophrenia. Psychiatry Res. 2009;173 (2):83-87.
2. Mechri A, Gassab L, Slama H, et al. Neurological soft signs and schizotypal dimensions in unaffected siblings of patients with schizophrenia. Psychiatry Res. 2010;175(1-2):22-26.
3. Chan RCK, Wang Y, Zhao Q, et al. Neurological soft signs in individuals with schizotypal personality features. Aust N Z J Psychiatry. 2010;44(9):800-804.
4. Kaczorowski JA, Barrantes-Vidal N, Kwapil TR. Neurological soft signs in psychometrically identified schizotypy. Schizophr. Res. 2009;115(2-3):293-302.
5. Takahashi T, Suzuki M, Zhou S, et al. A follow-up MRI study of the superior temporal subregions in schizotypal disorder and first-episode schizophrenia. Schizophr. Res. 2010;119(1-3):65-74.
6. Woodward ND, Rogers B, Heckers S Functional resting-state networks are differentially affected in schizophrenia. Schizophr Res. 2011 Aug;130(1-3):86-93. Epub 2011 Mar 31.
7. Annalaura Lagioia, Dimitri Van De Ville, Martin Debbané. Adolescent resting state networks and their associations with schizotypal trait expression. Frontiersin 2010;4(35).

Universitat Autònoma de Barcelona · CRC Diagnòstic per la imatge · INAD Institut de Neuropsiquiatria i Addiccions · Parc de Salut MAR Barcelona