Voxel – based morphometry in chronic schizophrenia

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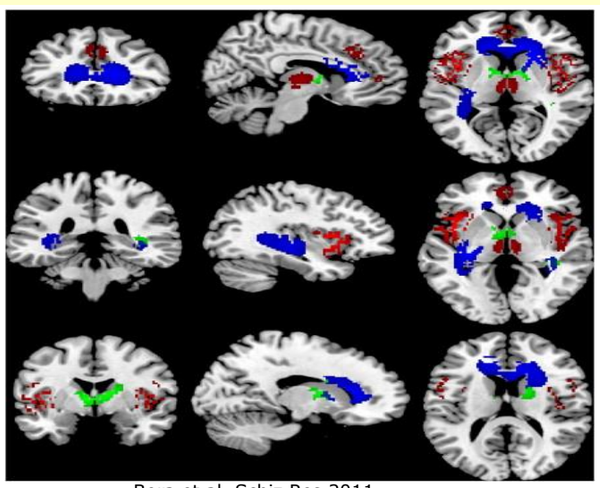
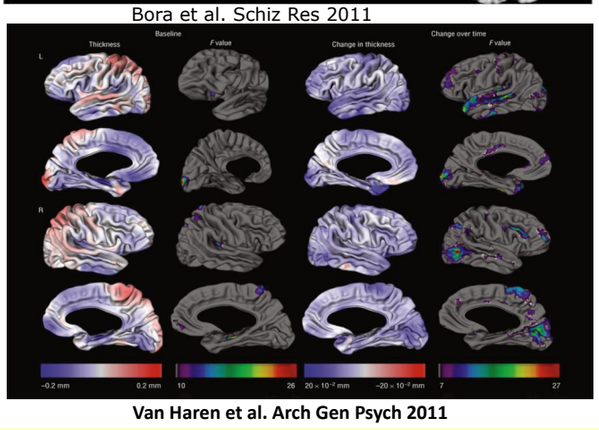
Introduction: Schizophrenia (SCH) is considered as a great mental disorder without clearly explained mechanisms of ethiology. New hypothesis about ethiology of SCH consider numeruos molecular mechanisms . Some of them selected abnormalities in membrane phospholipides and cytokines influencing oxydative and antoxydative processes in SCH . Changes in membrane phospholipides are associated with intensity of symptoms and with speciphic clinical manifestations in SCH. Second hypothesis suggests abnormalities (decrease) in syntesis of proteins in SCH (CPSR hypothesyis) . CPSR hypothesyis explains 96,7% major findings in SCH, reveals links between previously unrelated findings, and is able to integrate several important hypothesis. Central to CPSR hypothesis is the assumption of deficient protein synthesis rate, especially in cortical and lymbic systems. Analyses of existing theories of schizophrenia showed discrepancy of well proved facts and hypotheses (dopamine, neural development, synaptic plasticity, glutamate and viruses as etiologic entities) in the development of schizophrenia.

The neurotoxic hypothesis of schizophrenia is based on idea that psychosis is biologically toxic. Number of psychotic episodes in patients with chronic schizophrenia varies; some patients have one or few psychotic episodes, while other have numerous. If we consider a psychotic episode as neurotoxic insult we can expect severe brain abnormalities in patients with multiple episodes of schizophrenia. Voxel-based morphometry helps us detect brain regions that are affected by neurotoxic process. Voxel-based morphometry (VBM) involves a voxel-wise comparison of the local concentration of gray matter between two groups of subjects..



Bora et al. Schiz Res 2011



Van Haren et al. Arch Gen Psych 2011

Objectives: To investigate gray matter volume (GMV) differences between patients with chronic schizophrenia according to number of psychotic episodes and normal controls (NC), using voxel-based morphometry (VBM).

Patients and Methods: Patients were diagnosed according to DSM-IVTR. Control group (NC) consisted of healthy individuals. All patients and NC were from the same region Croatian.The study included 76 schizophrenia patients with disease duration longer than 8 years, grouped according the number of psychotic episodes (31 patients with up to 3 episodes (SCH-1) and 45 patients with at least 4 episodes (SCH-2) and 63 NC. Voxel-based morphometry (VBM) is an adaption of the statistical parametric mapping technique that allows investigation of quantitative brain structural changes.VBM involves a voxel-wise comparison of the local concentration of gray matter between two groups of subjects. Voxel-wise parametric statistical tests which compare the smoothed gray-matter images from the two groups are performed

Group name	No of participants	No of episodes	Disease duration
NC	63	~	~
SCH-1	31	≤3	>8 years
SCH-2	45	≥4	>8 years

Group			
Characteristic	NC	SCH-1	SCH-2
Age, years, mean (SD)	35.5 (9.6)*	37.7 (10.4)*	43.2 (10.6)*
Sex, male/female	32/31	18/13	28/17
Handedness, R/L/A	59/2/2	28/2/1	44/1/0
No of episodes, Mean (SD)	~	2.1 (0.8)*	8.6 (4.9)*
Age at onset, (M±SD)	~	24.2 (6.4)*	26.2 (6.9)*
Duration of illness, (M±SD)	~	13.7 (6.3)*	16.8 (4.9)*

Statistically significant differences ($p<0.05$) between groups using MANOVA

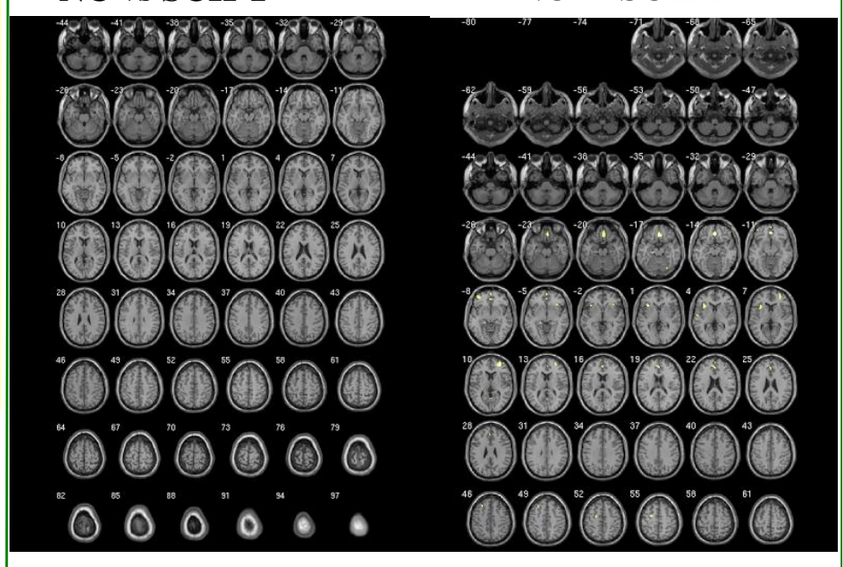
Results: Patients with up to 3 psychotic episodes compared to NC had reduced GMV in the inferior frontal gyrus and prefrontal gyrus. Patients with at least 4 episodes compared to NC revealed GMV reduction in cingulate bilaterally, middle frontal gyrus bilaterally, right medial frontal gyrus, left parahippocampalgyrus, left superior temporal gyrus, insula bilaterally, frontal sub-gyral gray matter, right posterior cingulate gray matter and right culmen.

Region Brodmann area (BD)	k	t	x	y	z
Frontal Left Inferior frontal gyrus, BD 44	19	5,32	-53,93	4,65	17,32
Frontal Right Precentral gyrus, BD 6	17	5,34	46,15	-7,69	5,23

Region - Brodmann area (BD)	k	t	x	y	z
Limbic Right Anterior cingulate, BD 32	753	6,22	1,07	36,53	-3,05
Limbic Right Anterior cingulate, BD 32	235	5,66	-1,14	37,57	24,93
Frontal Right Medial frontal gyrus, BD 10	90	5,74	1,06	52,95	2,11
Frontal Left Inferior frontal gyrus, BD 10	358	5,93	28,61	50,31	18,54
Frontal Right Middle frontal gyrus, BD 46	31	5,23	40,63	47,45	18,47
Frontal Left Middle frontal gyrus, BD 8	48	5,79	-25.59	21,11	49,99
Frontal Right Culmen	20	5,10	21,21	-48,35	-10,75
Frontal Left Middle frontal gyrus, BD 6	87	5,65	-21,11	-10,18	52,50

Region - Brodmann area (BD)	k	t	x	y	z
Frontal Left Sub-gyral	129	5,40	-36,90	45,70	0,78
Temporal Left Superior temporal gyrus, BD 22	36	5,41	-51,06	-11,17	5,96
Sub-lobar Left Insula, BD 13	292	5,47	-32,44	19,74	6,50
Sub-lobar Right Insula	84	5,41	32,39	20,68	4,08
Limbic Right Posterior cingulate, BD 30	39	5,34	1,47	-58,72	9,55
Limbic Left Parahippocampal, BD 30	37	5,33	-17,69	-32,83	-4,54
Limbic Left Parahippocampal, BD 35	41	5,49	-15,70	-20,88	-11,48

NC vs SCH-1 **NC vs SCH-2**



References:

1.Perkins, Lieberman et al. 2004; 2.Vanderzeypen, Bier et al. 2003; 3.McClellan, Susser et al. 2007; 4.Arolt, Rothermundt et al. 2000; 5.Arvindakshan, Ghate et al. 2003; 6.Nadalin, Rubesa et al. 2008; 7.Lander, Linton et al. 2001, 8.Moises, Zoega et al. 2002; 9.Kasper and Papadimitriou 2009; 10.Pantelis, Yucel et al. 2003; 11.Keshavan 1999; 12.Keshavan 1999; 13. Bota, Sagduyu et al. 2005; 14.Lander, Linton et al. 2001; 15. Moises, Zoega et al. 2002; 16. Rubesa, Gudelj et al. 2011; 17.Lander, Linton et al. 2001; 18.Moises, Zoega et al. 2002; 19. Tamminga and Holcomb 2005; 20.Andreasen, Nopoulos et al. 1999; 21.Selten, Veen et al. 2001; 22. Honea, Meyer-Lindenberg et al. 2008; 23.Kasper and Papadimitriou 2009; 24. Honea, Crow et al. 2005; 25.Hietala, Cannon et al. 2003; 26.van Haren, Hulshoff Pol et al. 2007; 27.Chan, Chia et al. 2009; 28. McGlashan 2006; 29.Mason, Harrison et al. 1996; 30. Arango, Kirkpatrick et al. 2001; 31. Kasper and Papadimitriou 2009; 32. Van Haren et al. Arch Gen Psych 2011; 33. Bora et al. Schiz Res 2011

Conclusion:GMV reduction in schizophrenia varies depending on the number of psychotic episodes. The affection of multiple regions in patients with multiple episodes, opposed to patients with less episodes indicates the existence of a neurotoxic effect induced by the psychotic state.

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Introduction: Schizophrenia (SCH) is a serious mental disorder without a clear etiology. Numerous molecular mechanisms are being examined in relation to the etiology of SCH. Some hypotheses reason that abnormalities in membrane phospholipids and cytokines affect oxidative and antioxidative processes in SCH, as changes in membrane phospholipids are associated with the intensity of symptoms and with specific clinical manifestations in SCH. Another hypothesis suggests that a decrease in the rate of cerebral protein synthesis is at the root of SCH (cerebral prothesis rate [CPSR] hypothesis). The CPSR hypothesis explains 96.7% of the major findings in SCH, reveals links between previously unrelated findings, and is able to integrate several important hypotheses. Central to the CPSR hypothesis is the assumption of a deficient protein synthesis rate, especially in the cortical and lymbic systems. Analyses of existing theories of schizophrenia showed discrepancies between well-proved facts and hypotheses (dopamine, neural development, synaptic plasticity, glutamate and viruses as etiologic entities) in the development of schizophrenia.

The neurotoxic hypothesis of schizophrenia is based on the idea that psychosis is biologically toxic. The number of psychotic episodes in patients with chronic schizophrenia varies; some patients have one or few psychotic episodes, while others have many. If we consider a psychotic episode a neurotoxic insult we should find severe brain abnormalities in patients with multiple episodes of schizophrenia. Voxel-based morphometry helps us detect brain regions that are affected by neurotoxic processes.

Objectives: To investigate differences in gray matter volume (GMV) between patients with chronic schizophrenia and different numbers of psychotic episodes as well as non-schizophrenic controls (NC), using voxel-based morphometry (VBM).

Patients and Methods: Patients were diagnosed according to DSM-IV-TR. The control group (NC) consisted of healthy individuals. All participants were from the same Croatian region. The study included 76 schizophrenic patients with disease duration longer than 8 years, grouped according the number of psychotic episodes (31 patients with up to 3 episodes and 45 patients with at least 4 episodes) and 63 NC.

Voxel-based morphometry (VBM) is an adaption of the statistical parametric mapping technique that allows investigation of quantitative brain structural changes. VBM involves a voxel-wise comparison of the local concentration of gray matter between two groups of subjects. Voxel-wise parametric statistical tests which compare the smoothed gray-matter images from the two groups are performed.

Results: Patients with up to 3 psychotic episodes, when compared to NC, had reduced GMV in the inferior frontal gyrus and prefrontal gyrus. Patients with at least 4 episodes, when compared to NC, revealed GMV reduction in cingulate bilaterally, middle frontal gyrus bilaterally, right medial frontal gyrus, left parahippocampal gyrus, left superior temporal gyrus, insula bilaterally, frontal sub-gyral gray matter, right posterior cingulate gray matter and right culmen.

Conclusion: GMV reduction in schizophrenia varies depending on the number of psychotic episodes. The involvement of many more brain regions in patients with multiple episodes than in patients with less episodes indicates the existence of a neurotoxic effect induced by the psychotic state.

1. Gordana Rubesa, Lea Gudelj and Natalija Kubinska: Etiology of Schizophrenia and Therapeutic options. Psychiatria Danubina 23, No. 3: 308–315; 2011.

2. Buretic-Tomljanovic A., Giacometti J., Nadalin S., Rubesa G., Vulin M:, Tomljanovic D: Phospholipid membrane abnormalities and reduced niacin skin flush response in schizophrenia. Psych. Danubina 20 No. 3; 372–383; 2008.

3. Ruzic-Barsic A, Antulov R, Lerga J, Rubesa G, Miletic D: Gray matter changes in patients with schizophrenia: a voxel-based morphometry study. 5. Congres of Croatian Society of Radiology with international participation. Rijeka/Opatija, Croatia; 2010. Abstract book 002.

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Keywords

Schizophrenia: basic

Neuroimaging: structural

Neuroanatomy