NeuroImage: Clinical 11 (2016) 20–29

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Verbal memory impairments in schizophrenia associated with cortical thinning

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ARTICLE INFO

Article history:
Received 3 November 2015
Received in revised form 11 December 2015
Accepted 20 December 2015
Available online 23 December 2015

Keywords:
Schizophrenia
Cortical thickness
Verbal memory
Frontal lobes
Parahippocampal gyrus

ABSTRACT

Verbal memory (VM) represents one of the most affected cognitive domains in schizophrenia. Multiple studies have shown that schizophrenia is associated with cortical abnormalities, but it remains unclear whether these are related to VM impairments. Considering the vast literature demonstrating the role of the frontal cortex, the parahippocampal cortex, and the hippocampus in VM, we examined the cortical thickness/volume of these regions. We used a categorical approach whereby 27 schizophrenia patients with 'moderate to severe' VM impairments were compared to 23 patients with 'low to mild' VM impairments and 23 healthy controls. A series of between-group vertex-wise GLM on cortical thickness were performed for specific regions of interest defining the parahippocampal gyrus and the frontal cortex. When compared to healthy controls, patients with 'moderate to severe' VM impairments revealed significantly thinner cortex in the left frontal lobe, and the parahippocampal gyri. When compared to patients with 'low to mild' VM impairments, patients with 'moderate to severe' VM impairments showed a trend of thinner cortex in similar regions. Virtually no differences were observed in the frontal area of patients with 'low to mild' VM impairments relative to controls. No significant group differences were observed in the hippocampus. Our results indicate that patients with greater VM impairments demonstrate significant cortical thinning in regions known to be important in VM performance. Treating VM deficits in schizophrenia could have a positive effect on the brain; thus, subgroups of patients with more severe VM deficits should be a prioritized target in the development of new cognitive treatments.

1. Introduction

Schizophrenia patients consistently display lower brain volumes and reduced cortical thickness when compared to healthy controls (Edgar et al., 2012; Kuperberg et al., 2003; Olabi et al., 2011; Shenton et al., 2001; van Haren et al., 2011; Venkatasubramanian et al., 2008). However, there is growing evidence of heterogeneity of brain structural patterns in schizophrenia patients. That is, different subgroups of patients seem to show different degrees and extent of structural alterations depending on their clinical or cognitive profile (Cobia et al., 2011; Nenadic et al., 2012, 2015). While verbal memory (VM) is considered a core cognitive domain affected in schizophrenia (Aleman et al., 1999; Cirillo and Seidman, 2003; Dickinson, et al., 2008; Keefe et al., 2005; Lewis and Gonzalez-Burgos, 2006), some studies have also revealed different subgroups of patients with a close to normal VM profile (Brazo et al., 2013; Bruder et al., 2004; Kremen et al., 2004; Turetsky et al., 2002). Yet, little is known about how cortical thickness is associated with the level of VM capacity in schizophrenia.

A large number of functional neuroimaging studies investigating VM impairments in schizophrenia have linked lower performance to abnormal brain activity in the medial temporal lobes (i.e. the hippocampus and the parahippocampal gyrus (PHG)) and frontal lobes (Achim and Lepage, 2005a; Francis et al., 2015; Haut et al., 2015; Hawco et al., 2015; Hutcheson et al., 2015; Ragland et al., 2004, 2009; Weiss et al., 2003). Nonetheless, it remains unclear whether VM impairments in schizophrenia are related to cortical thinning in these regions. One correlational study reported a similar positive and significant relationship between cortical thickness and VM capacity in these regions in schizophrenia, and in healthy controls (Hartberg et al., 2010). A more recent study failed to show any association between cortical thickness and VM performance in schizophrenia, nor in healthy controls (Ehrlich et al., 2012). The only positive relationship with VM observed by the authors pinpointed hippocampal volume in schizophrenia patients, but not in healthy controls.

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http://dx.doi.org/10.1016/j.nicl.2015.12.010

Table 1
Demographic, clinical and neuropsychological data.

	Controls (N = 23)			'Low to mild' VM impairments (N = 23)			'Moderate to severe' VM impairments (N = 27)			*p-value*
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	
Age	33.26	8.17	22:50	34.57	8.7	24:50	35.85	8.66	21:50	0.49
IQ	112.50	14.21	80:133	99.43	12.53	75:116	90.19	12.80	70:120	<0.001
ISLT										
Learning recall	27.27	3.13	20:31	24.67	2.96	21:33	16.75	4.02	7:24	
Delayed recall	9.14	2.03	5:12	9.00	1.55	6:11	4.61	2.00	1:8	
z-scores	0.00	0.92	−1.93:1.14	−0.47	0.75	−1.30:1.37	−2.85	1.00	−5.24 :− 1.44	<0.001
		N	%		N	%		N	%	
Gender										0.16
Male		15	65		13	57		22	81	
Female		8	35		10	43		5	19	
Parental socioeconomic status										0.15
Lower		1	4		4	20		3	14	
Lower-middle		6	26		5	25		4	19	
Middle		8	35		8	40		12	57	
Upper-middle		4	17		1	5		2	10	
Upper		4	17		2	10		0	0	
Handeness category										0.28
Right		15	65		14	61		11	40	
Moderately right		3	13		4	17		8	30	
Ambidextrous		2	9		2	9		3	11	
Moderately left		2	9		2	9		4	15	
Left		1	4		1	4		1	4	
		Mean	SD	Range	Mean	SD	Range			
SANS (without attention total)		19.13	8.7	4:34	25.52	9.93	6:51			0.03
SAPS		17.13	18.05	0:60	20.15	15.85	1:53			0.63
Age of onset		21.74	4.56	15:33	24.22	7.69	14:43			0.19
Duration of illness		12.83	7.41	4:28	11.63	7.61	3:33			0.48
Medication (mg chlorpromazine)		632.63	472.13	45:1774	480.83	456.32	11:2179			0.26

Note: VM = verbal memory, ISLT = International Shopping List Task, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms. Post-hoc Bonferroni correction (with a criteria of $p < .05$) was applied for IQ (each group differed from each other) and ISLT (a significant difference existed between the patient subgroups). Due to incomplete records, 3 patients with 'low to mild' VM impairments and 6 with 'moderate to severe' VM impairments having missing datapoints for parental socioeconomic status.

One possible explanation for the discrepancy in these results is that VM performance may not be linearly related to cortical thickness; thus using a regression approach may not be optimal. Considering the inconsistency of previous findings, further investigation of VM impairments in schizophrenia and cortical thickness are warranted, and using a categorical approach based on a clinical threshold of VM

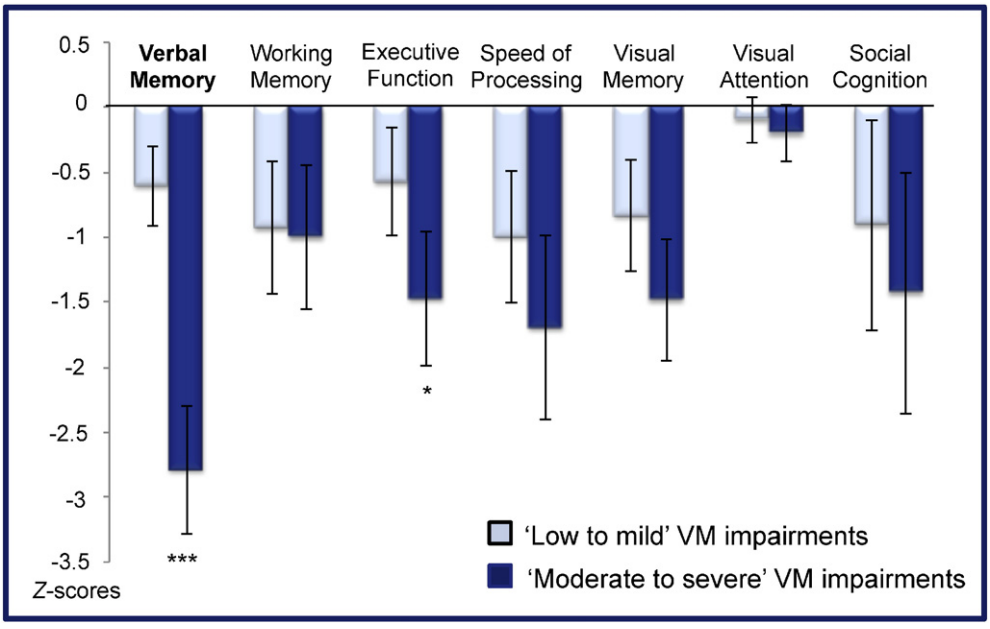

Fig. 1. Mean z-scores for cognitive domain evaluated by the Cogstate battery in the 'moderate to severe' verbal memory (VM) impairments group compared to the group with 'low to mild' VM impairments.