



Is Exposure to Herpes Simplex Virus, Type 1 Associated with Skills of Daily Living in Schizophrenia?

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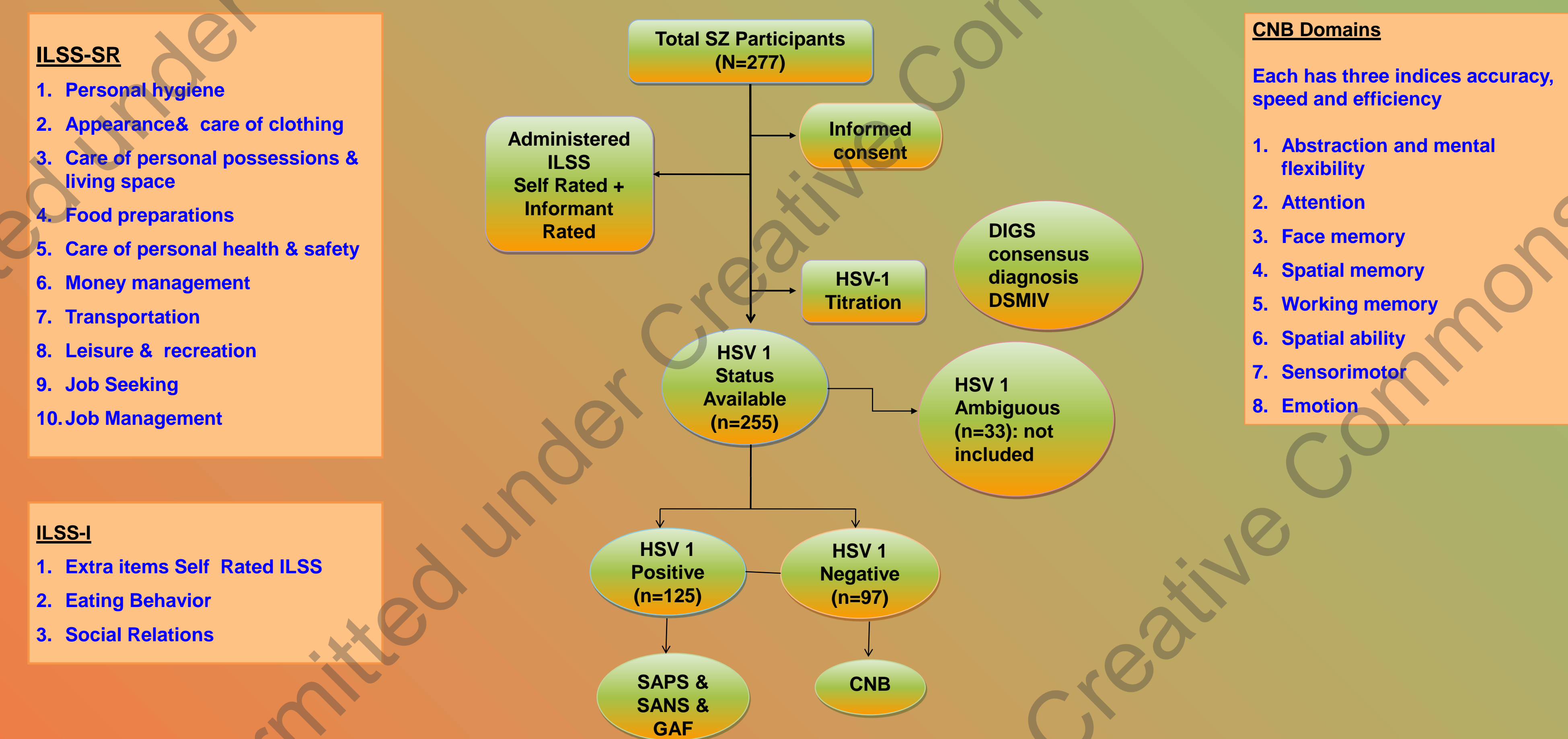
INTRODUCTION:

- Herpes Simplex virus, type 1 (HSV-1) causes lifelong latent infection in sensory ganglia (~60% of adults), with periodic lytic recurrences in mucosal membranes. Post-mortem studies suggest that latent infection also occurs in the brain, with severe encephalitis in immune-compromised individuals. Exposure to HSV-1 is not a proven risk factor for schizophrenia (SZ), but it has been replicably associated with cognitive dysfunction among SZ patients.
- Functional capacity deficits are associated with level of residential independence (Mausbach et al., 2007, Mausbach et al., 2010).
- Activities of daily living which are impaired include washing, dressing, cooking, shopping, self care and independent living especially in schizophrenia.
- As cognitive impairments adversely affect skills of daily living, we explored cognition and daily living skills in relation to daily living skills. We also explored functional impairments in relation to HSV-1 exposure.

METHODOLOGY:

- As part of the project 'The impact of yoga supplementation on cognitive function among Indian outpatients with schizophrenia' funded by FIC-NIH, SZ patients above 18 years were recruited after written informed consent. Daily functioning of the participants was evaluated by Independent Living Skills Survey (ILSS).
- Diagnostic Interview for Genetic Studies (DIGS) was administered to ascertain diagnosis on DSM IV criteria (Bhatia et al. 2014).
- Independent Living Skills Survey (ILSS) (Wallace et al. 2008) (Hindi version- Bhatia et al. 2014), a comprehensive survey to assess daily functioning of SZ was used in two versions: Self rated (SR) and Informant rated (I). The SR has 103 items divided in 10 areas. Items are scored as no-0, yes-1 and summed and averaged per functional area, and a third option 'does not apply' which has no scores. The informant version has similar areas with some extra items plus two more areas eating behaviors (9 items) and social interactions (9 items). These are rated as never, sometimes, often, usually, and always and scored from 0-4 respectively. Items which do not apply are ignored and average of each functional area is calculated.
- University of Pennsylvania Computerized Neurocognitive Battery (CNB)(Gur et al. 2001) has ten cognitive domains (each assessed on three indices: accuracy, speed, efficiency). We used eight non-verbal domains (Bhatia et al. 2012).
- Scale for Assessment of Positive Symptoms (SAPS) (Andreasen 1984), Scale for Assessment of Negative Symptoms (SANS) (Andreasen 1984) and Global Assessment of Functioning (GAF) (Endicott et al. 1976) were used to evaluate current psychopathology.
- HSV-1 status was determined for consenting participants as part of the project 'A Follow up Study of Cognitive Function and Herpes Simplex Infection in Schizophrenia Patients and Normal Controls' (funded by Govt. of India). Immunoglobulin (IgG) antibodies to HSV-1 were tested in a certified commercial laboratory Quest Diagnostics.

FLOWCHART: Showing Study Procedures



KEY RESULTS

- There were significant differences in total self-rated ILSS scores between patients exposed to HSV-1 and those not exposed, after correcting for age and gender ($F(2, 251)=8.164, p=0.005$).
- There was no significant difference between HSV-1 exposed and HSV-1 not exposed on age and gender.
- The money management domains in both the ILSS-SR and ILSS-I versions was associated with HSV-1 exposure, following correction for SAPS, SANS and CNB variables.
- In ILSS-I, HSV-1 exposure was also associated with job seeking functional area following correction for SANS, SAPS and CNB.
- There were significant associations between functional skills assessed in the ILSS and cognitive domains, including spatial ability, attention, abstraction & mental flexibility and spatial memory.
- ILSS scores were associated with scores for symptom severity estimated using the SANS and SAPS.
- Total SANS scores were associated with total ILSS scores, as well as other functional domains.
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- Associations with GAF scores (past month), as well as SAPS scores were noted, particularly bizarre behavior.
- Job maintenance was compatible with delusions and hallucinations in SAPS.

Figure: Comparison of HSV Positive and Negative Subjects on ILSS-SR Total Score

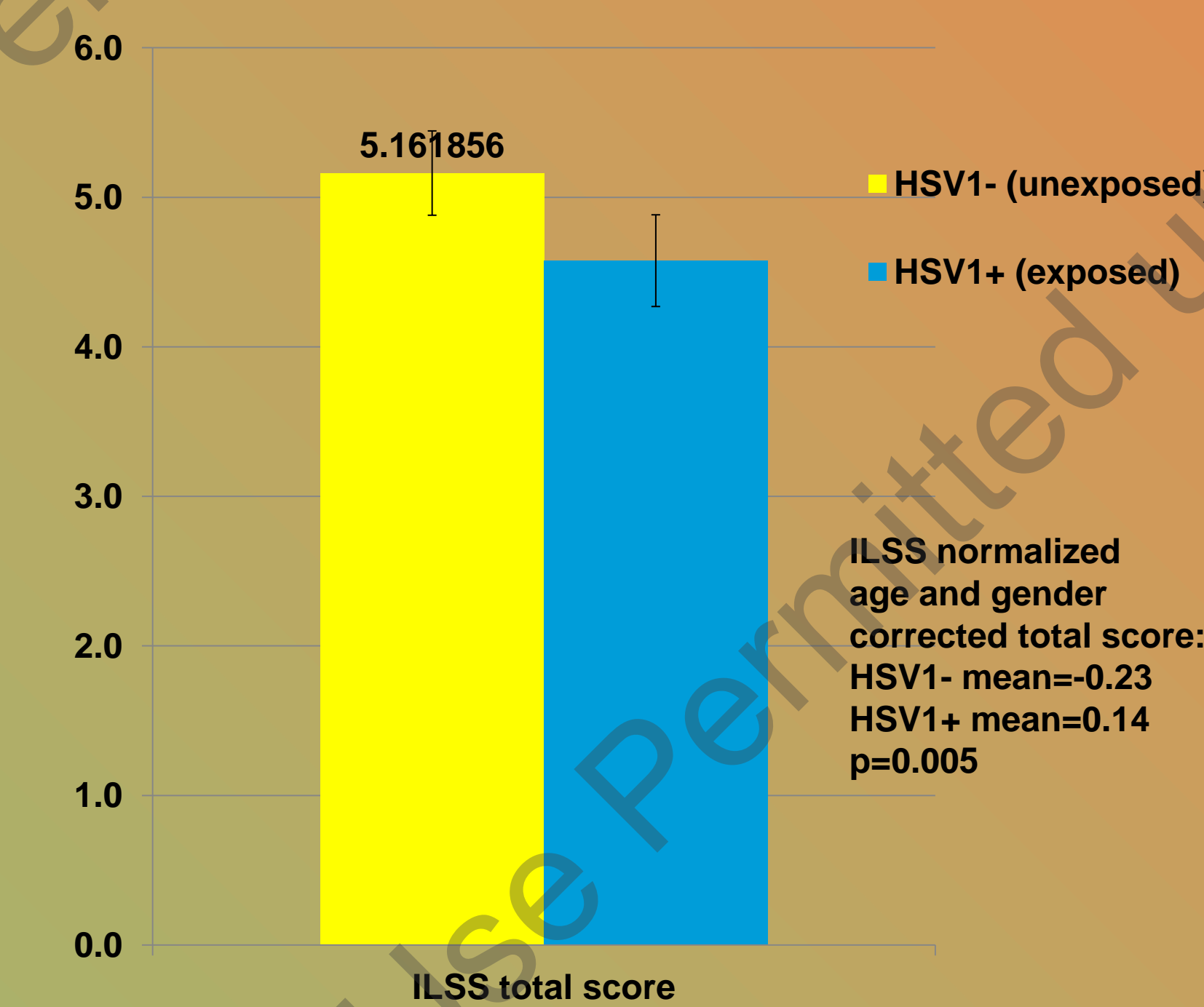


Table1: Comparison of HSV Positive and Negative Subjects on ILSS Functional Areas (ANOVA)

Functional Areas	Self rated p-value	Informant rated p-value
Personal hygiene	0.009	NS
Money management	0.008	0.016
Leisure and recreational activities	0.019	NS
Job seeking	NS	0.011
Total ILSS score	0.005	NS

Table 2: Effect of HSV-1 status, cognitive domains (CNB), clinical variables (SANS and SAPS) and demographic variables on areas of daily functioning (ILSS: SR (left) ILSS -I (Right) (significant linear regression results)

ILSS: Self rated version			ILSS: Informant rated version		
Dependent Variables*	Independent variables**	β (p-value)	Dependent Variables*	Independent variables**	B (p-value)
Appearance and clothing	Total SANS scores	-0.50 (0.00003)	Appearance and clothing	Total SANS Scores	-0.22(0.01)
	Alogia	0.37(0.0017)		Avolition	-0.28(0.0006)
	Bizarre behaviour	-0.20(0.02)	Spatial ability: accuracy	0.22(0.01)	
Personal hygiene	Attention: speed**	0.19(0.02)	Avolition	-0.39(0.00001)	
	Total SANS scores	-0.57(1.26E-06)	Care of personal possessions and living space	Attention: accuracy***	0.17(0.04)
Care of personal possessions and living space	Alogia	0.34(0.0028)	Face memory: speed***	0.18(0.04)	
	Spatial memory: Accuracy***	-0.18(0.02)	Past month GAF	0.22(0.01)	
Food preparation	Total SANS scores	-0.20(0.01)	School years	-0.16(0.03)	
	Attention: accuracy***	0.21(0.01)	Emotion: accuracy***	0.28(0.0002)	
Care of personal health and safety	Abstraction and mental flexibility: speed***	0.20(0.02)	Affective flattening	-0.15(0.05)	
	Total SANS	-0.37(0.009)	Food preparation	Past month GAF	0.20(0.01)
Money management	HSV status	-0.25(0.01)	Emotion: accuracy***	0.23(0.0002)	
	Attention: accuracy***	0.38(0.0081)	Total SANS	-0.28(0.0002)	
	Working memory: accuracy***	-0.24(0.03)	Delusions	-0.16(0.02)	
Transportation	Face memory: speed***	0.31(0.0021)	HSV-1 status	-0.19(0.03)	
	Working memory: speed***	0.19(0.01)	Attention: accuracy***	0.26(0.01)	
	Total SANS	0.25(0.05)	Abstraction and mental flexibility: speed***	0.25(0.006)	
Leisure and recreational activities	Affective flattening	-0.33(0.0012)	Past month GAF	0.31(0.0005)	
	Duration of illness	0.18(0.03)	School Years	0.15(0.04)	
Job seeking	Total SANS scores	-0.61(8.71E-07)	Transportation	Spatial memory: accuracy***	0.20(0.01)
	Alogia	0.28(0.02)	Leisure and recreational activities	Spatial memory: accuracy***	0.17(0.01)
Job maintenance	Total SANS scores	-0.27(0.00257)	Anhedonia	-0.19(0.01)	
	Delusions	-0.39(0.01)	Job seeking	Anhedonia	-0.28(0.0002)
Average ILSS Scores	Bizarre behavior	0.34(0.02)	Job maintenance	HSV-1 Status	-0.21(0.01)
	Face memory: speed***	0.016(0.02)	Job maintenance	Total SANS scores	Not significant
	Total SANS scores	0.006(0.05)	Eating behavior	Total SANS scores	-0.25(0.003)
			Working memory: accuracy***	0.25(0.03)	
			School years	0.17(0.04)	
			Affective flattening	-0.22(0.02)	
			Social Relations	Anhedonia	-0.26(0.01)
			Most responsible occupation	-0.22(0.02)	
			Total SANS scores	-0.48(3.04E-06)	
			Average ILSS Scores	Delusions	-0.21(0.03)

* All ILSS scores were age and gender adjusted.
 ** Significant variables from separate regression analyses with CNB and clinical variables were selected.
 *** CNB scores were age adjusted.

CONCLUSION:

- Cognition is important factor in determining daily living skills in schizophrenia as widely reported.
- Negative symptoms affect daily functioning of SZ patients but some positive symptoms are also associated.
- HSV-1 exposure is associated with impairment in daily living skills in SZ (Total ILSS score).
- After removing cognitive and clinical variables also some skills (money management and job seeking) are associated with HSV-1. As exposure is common, the associations have substantial public health significance.

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