Semantic processing in relation to anatomical integrity of the ventral language stream in schizophrenia

Werner Surbeck [1], Jürgen Hänggi [2], Felix Scholtes [3], Petra Viher [4], André Schmidt [5], Katharina Stegmayer [4], Studerus E. [5], Lang, U.E. [5], Riecher-Rössler, A. [5] , Erich Seifritz [1], Stefan Borgwardt [5], Boris B. Quednow [1], Sebastian Walther [3]

[1)] Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital of the University of Zurich, Zurich, Switzerland
[2)] Division Neuropsychology, Department of Psychology, University of Zurich, Zurich, Switzerland
[3)] Department of Neurosurgery, University Hospital of Liège, Liège, Belgium
[4)] University Hospital of Psychiatry, University of Bern, Bern, Switzerland
[5)] Department of Psychiatry, University of Basel, Basel, Switzerland

Background

Semantic processing anomalies, clinically reflected by disorganized speech, are a core symptom of schizophrenia [1,2]. In the light of accumulating evidence on its prominent role in semantic processing, structural disintegrity of the ventral language stream, and here in particular the inferior fronto-occipital fasciculus [IFOF] [3], may contribute to semantic deficits in affected patients. In two independents studies, we therefore aimed at investigating the relationship between verbal semantic processing impairments and the integrity of the white matter connectivity underlying language function in patients with schizophrenia and first episode psychosis [FEP]. We hypothesized that the specifically integrity of the IFOF is generally disrupted in patients with schizophrenia spectrum disorders and that semantic abnormalities are correlated with the disintegrity of this structure.

Method

Comparison of structural integrity of the components of the ventral (IFOF (Figure 1), inferior longitudinal fasciculus and uncinate fasciculus) and dorsal (arcuate fasciculus [AF]) language stream between patients with schizophrenia/FEP and healthy control subjects using diffusion tensor imaging combined with probabilistic fiber tractography has been performed. Furthermore, the relationship between semantic processing impairments and specific measures of tract integrity in patients was analyzed separately. Clinical data with respect to verbal semantic performance was retrieved from respective items of the assessment of thought, language and communication inventory (semantic paraphrasia, incoherence, neologisms, word approximations and derailment) and the Bern Psychopathology scale (person identification, coherence of speech, interruptions, naming and apprehension of meaning) for the Berne sample, and from the California verbal learning test (Semantic Clustering Index) for the Basel sample. Three-dimensional tract reconstructions were performed in 45/44 schizophrenia patients/controls (Bern sample) and replicated in an independent sample of 24/24 FEP patients/controls (Basel sample).

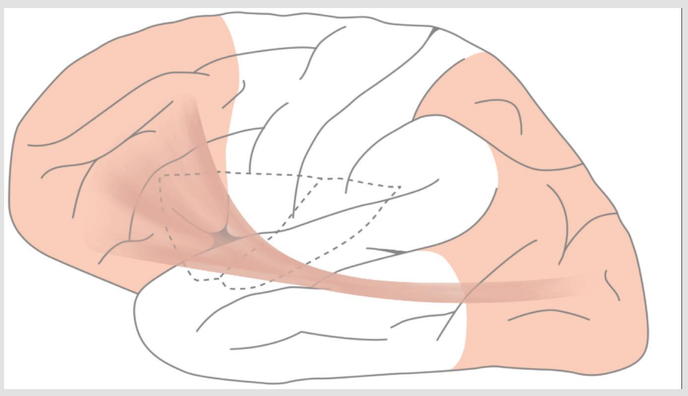

Figure 1: The inferior longitudinal fasciculus connecting the frontal lobe with the parietal, occipital and temporal lobes.

Results

Group comparisons of WM fiber pathways

Multivariate analyses of fractional anisotropy, mean, axial and radial diffusivity measures of the left IFOF indicated significant differences between patients and controls in both samples (Berne: $p < 0.001$, $\eta_p^2 = 0.23$; Basel: $p < 0.01$, $\eta_p^2 = 0.29$). FA was reduced, while other diffusivity measures were increased in patients. Additional group differences were found for the right AF in the Berne sample ($p < 0.01$, $\eta_p^2 = 0.19$) and for the left UF ($p < 0.01$, $\eta_p^2 = 0.26$) and for the right ILF ($p < 0.05$, $\eta_p^2 = 0.22$) in the Basel sample.

Association of tract integrity with impairments in semantic processing

In patients, axial diffusivity of the left IFOF was inversely correlated with semantic processing impairments in the Berne sample ($r = -0.579$, $p < 0.0001$) (Table 1 & Figure 2) and by trend also in the Basel sample ($r = -0.376$, $p = 0.09$). However, when correlating across FEP patients and healthy controls, a moderate but statistically significant inverse correlation has again been found between semantic impairments and AD of the left IFOF ($r = -0.317$, $p < 0.05$) (Figure 3) in the Basel sample.

		Fractional anisotropy	Axial diffusivity	Radial diffusivity	Mean diffusivity
IFOF left	Spearman's rho	-0.078	-0.564	-0.251	-0.388
	p-value	0.611	0.00006	0.096	0.008
IFOF right	Spearman's rho	-0.029	-0.321	-0.143	-0.204
	p-value	0.852	0.032	0.349	0.180

Table 1: Correlations between semantic processing impairments and measures of tract integrity within the schizophrenia patients of the Berne sample. Partial Spearman rank-ordered correlations corrected for global diffusivity measures and age. Significant correlations are printed in bold. Note that the explained variance of the left IFOF ($r^2 = 0.318$) is about three times in magnitude compared with that of the right IFOF ($r^2 = 0.103$).

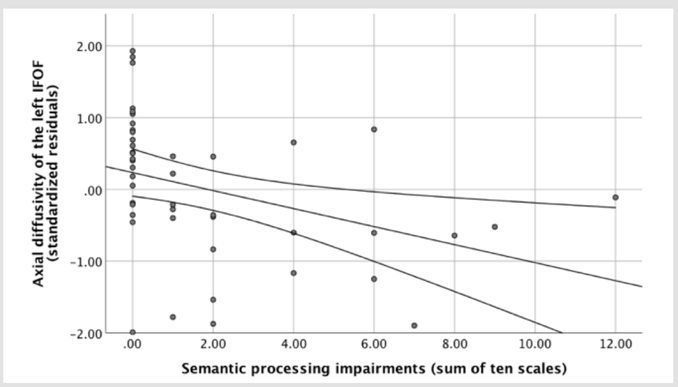

Figure 2: Associations between semantic processing impairments and axial diffusivity of the inferior fronto-occipital fasciculus (IFOF) - Berne sample. Scatterplot of the correlation between semantic processing impairments and the axial diffusivity standardized residuals (after regressing out global axial diffusivity and age) of the left IFOF ($r = -0.564$, $p = 0.00006$).

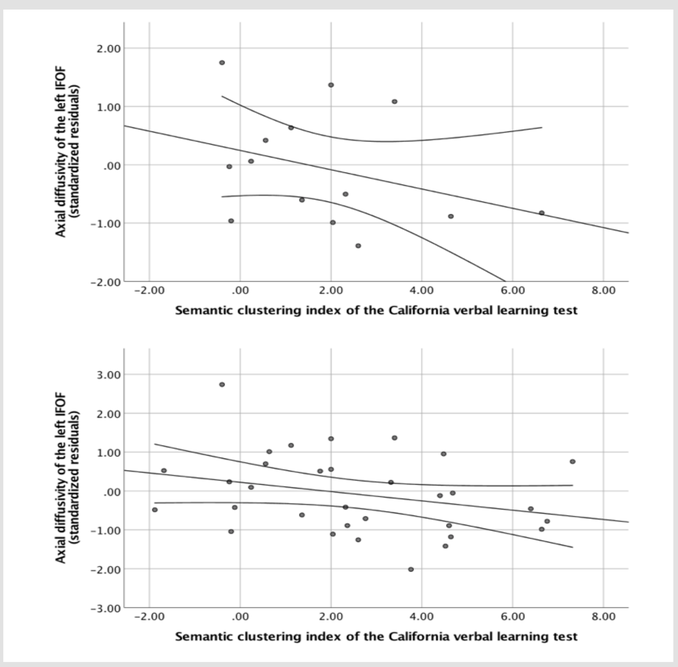

Figure 3: Associations between semantic processing impairments and axial diffusivity of the inferior fronto-occipital fasciculus (IFOF) - Basel sample. Shown are the scatterplots of the correlations between semantic processing impairments and the axial diffusivity standardized residuals (after regressing out global axial diffusivity) of the left IFOF. This correlation has been computed across 14 first episode psychosis (FEP) patients only (upper panel) as well as across 14 FEP patients and 18 healthy control subjects (lower panel). Shown are the fitted regression line and the 95% confidence intervals. Note that the there was only a trend towards significance in the upper panel ($r = -0.376$, $p = 0.0925$, one-tailed), whereas the correlation reached statistical significance in the lower panel ($r = -0.317$, $p = 0.0385$, one-tailed).

Conclusion

The present observation that structural alterations of the IFOF correlate with patients' semantic processing impairments provide first and direct evidence that disintegrity within the IFOF contributes to semantic processing deficit in schizophrenia spectrum patients. These results support the perspective that schizophrenia and related spectrum disorders are dysconnection syndromes, in which certain symptom clusters arise because of dysfunctional connectivity between brain regions that is likely driven by early neurodevelopmental changes.

Correspondence: werner.surbeck@puk.zh.ch

References

1. Bleuler E. Dementia Praecox or the Group of Schizophrenias. New York: International Universities Press; 1911.
2. Levy DL, et al. The Genetic Basis of Thought Disorder and Language and Communication Disturbances in Schizophrenia. J Neurolinguistics [Internet]. 2010 May 1 [cited 2018 May 26];23(3):176.
3. Duffau H, et al. A re-examination of neural basis of language processing: proposal of a dynamic hodotopical model from data provided by brain stimulation mapping during picture naming. Brain Lang. 2014 Apr;131:1–10.