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Authors

Koethe, D
Giuffrida, A
Schreiber, D
[et al.](#)

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P.3.f Psychotic disorders and antipsychotics – Other (basic)

P.3.f.001 Does anandamide elevation in cerebrospinal fluid protect against transition into frank psychosis?

D. Koethe^{1*}, A. Giuffrida², D. Schreiber¹, M. Hellmich³, F. Schultze-Lutter¹, S. Ruhrmann¹, J. Klosterkoetter¹, D. Piomelli⁴, F.M. Leweke¹. ¹University of Cologne, Psychiatry and Psychotherapy, Cologne, Germany; ²University of Texas Health Science Center, Department of Pharmacology, San Antonio, USA; ³University of Cologne, Institute of Medical Statistics Informatics and Epidemiology, Cologne, Germany; ⁴University of California, Department of Pharmacology, Irvine, USA

Endocannabinoids are a family of bioactive lipids that bind to cannabinoid receptors in the brain. As in schizophrenic psychosis a homeostatic role for the endocannabinoid lipid Anandamide (AEA) was suggested, we investigated patients suffering of initial prodromal stage (IPS) of schizophrenic psychosis, which is defined as an early disease stage prior to the onset of frank psychosis (for review see [1]).

We measured the levels of the endogenous cannabinoid AEA, and its structural analog oleoylethanolamide (OEA) in cerebrospinal fluid (CSF) and serum of IPS (n=27) patients alongside healthy volunteers (HC; n=81) by HPLC/MS [2]. An IPS was assumed if any of ten cognitive-perceptive basic symptoms or any attenuated or any transient psychotic symptom was present. Lumbar puncture took place shortly after the first visit in the Cologne Early Recognition and Intervention Centre for mental crises. All IPS and HC showed a negative urine drug screening for illicit drugs, for cannabis use demographic details see Table 1.

Eleven of the IPS subjects (40.7%) developed manifest schizophrenic psychosis since examination. Skewed empirical distributions of continuous variables were summarized by median and interquartile range (25th to 75th percentile). Independent groups were compared by exact Wilcoxon rank sum test (corrected for ties). The cumulative probability of no transition into frank psychosis was estimated by the Kaplan-Meier method and compared overall by the log rank test (hazard ratio). We found that AEA levels in CSF of IPS patients were significantly elevated, while neither AEA in serum nor OEA in both body fluids were altered. In HC, the median concentration of AEA was <0.001 (25th to 75th percentile: <0.001 to 0.005) pmol/ml in CSF and <0.001 (<0.001 to 0.700) pmol/ml in serum. Median AEA levels in CSF of IPS patients were 0.006 (<0.001 to 0.073, p=0.004) pmol/ml and 0.216 (<0.001 to 0.515, p=0.838) pmol/ml in serum. In IPS patients we found a trend for the elevation of AEA in CSF to be associated with extended time of transition into frank psychosis (p=0.095) during an observational period of at least 45 months after initial investigation, calculated by splitting patients at the median CSF AEA value (0.006 pmol/ml) into low and high groups. The relative risk of transition of the high vs low group was 0.33 (95% confidence interval 0.09 to 1.29).

Our data provide further support for the hypothesis of an adaptive or potentially protective role for the endocannabinoid system in early schizophrenia. The AEA elevation was comparable to that found by Giuffrida et al. [3] in first-onset, antipsychotic-naive schizophrenia. AEA increase was found in CSF exclusively, making its central origin most likely. The longer transition time

into frank psychosis in IPS patients showing an AEA elevation is in line with our hypothesis of an adaptive role of the endocannabinoid system in psychosis. As the anandamidergic dysregulation is already manifest in the prodromal course of the disease it emphasizes the importance of longitudinal studies to improve our understanding of endocannabinoid function in early schizophrenia and may lead to new pharmacological treatment strategies.

Table 1: Demographic and clinical characteristics of participants

	Initial prodromal stage (n=27)	Healthy controls (n=81)
Age, years; median (25th to 75th percentile)	24.3 (19.9 to 29.1)	27.3 (23.9 to 29.9)
Sex, male; n (%)	19 (70.4)	45 (55.6)
Body mass index; mean (SD)	22.70 (± 2.55)	23.13 (± 3.29)
Nicotine use; n (%)	7 (70%)	35 (43.8)
Cannabis use; n (%)		
never	9 (33.3)	28 (34.6)
<20 lifetime	7 (25.9)	28 (34.6)
>20 but <50 lifetime	3 (11.1)	25 (30.9)
>50 but <100 lifetime	1 (3.7)	–
>100 but <500 lifetime	7 (25.9)	–

References

- [1] Piomelli, D., 2003, The molecular logic of endocannabinoid signalling. *Nat Rev Neurosci* 4(11), 873–884.
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P.3.f.002 CNS infections during childhood and risk for schizophrenia: a case control study

D. Halperin^{1*}, M. Davidson¹, N. Werbeloff¹, R. Yoffe², A. Levine³, G. Livni⁴, M. Weiser⁵. ¹Chaim Sheba Medical Center, Psychiatry, Tel Hashomer, Israel; ²Israeli Ministry of Health, Ministry of Health, Jerusalem, Israel; ³Wolfson Medical Center, Psychiatry, Holon, Israel; ⁴Schneider Children's Medical Center, Pediatrics, Petah Tikva, Israel; ⁵Sheba Medical Center, Psychiatry, Tel Hashomer, Israel

Purpose of the study: The aim of this study was to assess the risk for schizophrenia after a viral or bacterial CNS infection during childhood, through a large case control study.

Introduction: Some studies found a positive association between viral or bacterial CNS infections during childhood and risk for later schizophrenia, psychotic disorder or mood disorder with psychotic symptoms [1,2]. A study conducted to evaluate the influence of viral CNS infection on later risk for schizophrenia could not confirm these results [3]. A large, recently published Swedish study found a slightly increased risk for nonaffective psychotic illness and schizophrenia with previous viral CNS infections, but no increased risk with bacterial infections [2].