

Media Release: European College of Neuropsychopharmacology (ECNP)

“For the science and treatment of disorders of the brain”

[“But doctor, I’m not ill”: research finds relation between marker of brain cell dysfunction and awareness of illness in psychotic patients](#)

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How do you convince someone with schizophrenia or other psychotic disorders that they are ill if they don’t want to believe it? If you don’t recognize that you are ill, you may resist treatment, but is there something which causes this lack of awareness? Awareness of illness, also known as ‘insight’, is a serious problem in the treatment of psychotic patients. Now work being presented at the ECNP Congress in Amsterdam investigated whether concentrations of a marker of brain cell dysfunction are associated with impaired insight.

Past studies have indicated that an area at the front of the brain called the prefrontal cortex may be associated with poor insight. In addition, numerous studies found reduced levels of a neurometabolite called N-acetylaspartate (NAA) in the prefrontal cortex of patients with a psychotic disorder. Reduced NAA is thought to reflect impaired functioning, damage or loss of brain cells.

A group of researchers from Groningen in the Netherlands worked with 80 patients with psychotic disorders. They measured their levels of insight using standard questionnaires (the Birchwood Insight Scale, and one item of the Positive and Negative Syndrome Scale), and then measured the concentrations of various neurometabolites in the dorsolateral prefrontal cortex, using a technique called ¹H-MRS (Proton Magnetic Resonance Spectroscopy, an image processing which shows the local chemical environment rather than anatomical structures).

They found that patients with poorer insight had a significantly lower level of NAA in the prefrontal cortex, while no significant relation was found between levels of other neurometabolites in the prefrontal cortex and insight.

As presenting author, Daouia Larabi said:

“NAA is seen as a marker for brain cell density and viability. What we found is a specific association between decreased NAA concentrations and impaired insight: basically, the lower the levels of NAA in the prefrontal cortex, the worse patients’ insight is. It should be noted that our study was correlational. Therefore, we cannot draw conclusions about whether one causes the other”.

“It’s important to understand what causes lack of insight. People with poor insight tend to drop out of treatment, have poorer functioning in general and have worse prognosis. If you are convinced that you are not ill, you won’t want to be treated. We hope our findings will help in a better understanding of the neurobiology of impaired insight. This may help in the development of new treatment options such that insight, and consequently patients’ likely course of their condition, can be improved”.

Commenting, Dr Andreas Meyer-Lindenberg, Editor-in-chief of European Neuropsychopharmacology and member of the ENP executive board, said:

“Biological research in recent years has moved beyond diagnoses towards trying to understand clinical features of the illness that are important to patients and their families, and this work on insight is a good example. Insight is highly relevant for the prognosis of people with schizophrenia and psychosis, and linking it to dysfunction in a specific brain system, if replicated, may point to new therapeutic or diagnostic approaches in the future”

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Notes for Editors

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The European College of Neuropsychopharmacology

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe. Website: www.ecnp.eu

The annual ECNP Congress takes place from 29th August to 1st September in Amsterdam. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting between 5,000 and 8,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: <http://www.ecnp-congress.eu/>

Abstract

P.3.b.020 The association between dorsolateral prefrontal N-acetylaspartate and insight in psychotic disorders

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Introduction: Awareness of illness, also called insight, is impaired in most individuals with a psychotic disorder.

Impaired insight has been associated with poorer outcome of the disease, making it an important target for treatment. The etiology of poor insight remains unknown, but pathology of the dorsolateral prefrontal cortex (DLPFC) may play a part. Several proton magnetic resonance spectroscopy (¹H-MRS) studies found reduced N-acetylaspartate (NAA) concentrations in the DLPFC of patients with a psychotic disorder [1], which is assumed to reflect neuronal pathology. In this study, we examined the association between insight and NAA concentrations in the white matter (WM) of the DLPFC. We hypothesized that NAA levels would correlate positively with levels of insight.

Methods: Insight was measured with the Birchwood Insight Scale (BIS) [2] and item G12 of the Positive and Negative Syndrome Scale (PANSS) [3] in 80 patients with a psychotic disorder. The BIS is an 8-item self-rating questionnaire with a higher total score indicating better insight. Item G12 of the PANSS is scored by a trained interviewer and measures lack of judgment and insight from 1 (no impairment) to 7 (severe impairment). ¹H-MRS was used to assess absolute concentrations of neurometabolites and ratios of these compounds to creatine (Cre) in the WM of the DLPFC. Partial correlational analyses between insight scores and NAA concentrations were conducted using illness duration, antipsychotic

use, gray matter content and cerebrospinal fluid content as covariates. Exploratory correlational analyses between insight scores and concentrations of other neurometabolites, such as glutamate, creatine, choline-containing compounds and myoinositol, were also conducted.

Results: We found a significant negative correlation between NAA concentrations and PANSS item G12 scores ($r = -0.231$, $p = 0.045$, $n = 80$). We also found a significant positive correlation between NAA/Cre ratios and BIS scores ($r = 0.338$, $p = 0.004$, $n = 76$). In either case, reduced NAA concentrations were associated with poorer insight. Additional partial correlational analyses revealed significant correlations between NAA/Cre ratios and the BIS subscale Awareness of illness ($r = 0.358$, $p_{FDR} = 0.006$, $n = 76$) and NAA/Cre ratios and the BIS subscale Awareness of need for treatment ($r = 0.256$, $p_{FDR} = 0.045$, $n = 76$).

Conclusions: This is the first study showing an association between insight and concentrations of a marker of neuronal integrity in the DLPFC. Our results provide further support for the involvement of the DLPFC in impaired insight in psychotic disorders. This involvement may be explained by the role of the DLPFC in executive functions such as self-monitoring and cognitive flexibility [4]. Since poor insight may lead to treatment non-adherence, worse prognosis and more hospitalizations, a better understanding of the neurobiology of impaired insight is important. This may help in the development of new treatment options such that insight, and ultimately patients' prognosis, can be improved.

References [1] Schwerk, A., Alves, F.D.S., Pouwels, P.J.W., van Amelsvoort, T., 2014. Metabolic alterations associated with schizophrenia: a critical evaluation of proton magnetic resonance spectroscopy studies. *Journal of Neurochemistry* 128(1), 1–87. [2] Birchwood, M., Smith, J., Drury, V., Healy, J., Macmillan, F., Slade, M., 1994. A self-report Insight Scale for psychosis: reliability, validity and sensitivity to change. *Acta Psychiatrica Scandinavica* 89(1), 62–67. [3] Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* 13(2), 261–276. [4] Shad, M.U., Tamminga, C.A., Cullum, M., Haas, G.L., Keshavan, M.S., 2006. Insight and frontal cortical function