

Aspirin shown to benefit schizophrenia treatment

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Berlin, 20 October 2014 A new study shows that some anti-inflammatory medicines, such as aspirin, estrogen, and Fluimucil, can improve the efficacy of existing schizophrenia treatments. This work is being presented at the European College of Neuropsychopharmacology conference in Berlin.

For some time, doctors have believed that helping the immune system may benefit the treatment of schizophrenia, but until now there has been no conclusive evidence that this would be effective. Now a group of researchers at the University of Utrecht in the Netherlands has carried out a comprehensive meta-analysis of all robust studies on the effects of adding anti-inflammatories to antipsychotic medication. This has allowed them to conclude that anti-inflammatory medicines, such as aspirin, can add to the effective treatment of schizophrenia.

Research has shown that the immune system is linked to certain psychiatric disorders, such as schizophrenia and bipolar disorder. Schizophrenia in particular is linked to the HLA gene system, which is found on chromosome 6 in humans. The HLA system controls many of the characteristics of the immune system.

According to lead researcher, Professor Iris Sommer (Psychiatry Department, University Medical Centre, Utrecht, Netherlands):

“The picture on anti-inflammatory agents in schizophrenia has been mixed, but this analysis pulls together the data from 26 double-blind randomised controlled trials, and provides significant evidence that some (but not all) anti-inflammatory agents can improve symptoms of patients with schizophrenia. In particular, aspirin, estrogens (in women) and the common antioxidant N-acetylcysteine (fluimucil) show promising results. Other anti-inflammatory agents, including celecoxib, minocycline, davunetide, and fatty acids showed no significant effect”.

In spite the fact that schizophrenia affects around 24 million people worldwide¹, treatment has not changed much in over 50 years, and largely relies on correcting the regulation of dopamine in the brain of schizophrenia sufferers. This has been shown to help symptoms such as hallucinations and delusions, but has been unable to help many other symptoms such as decreased energy, lack of motivation and poor concentration. In addition, around 20

to 30% of all patients don't respond to antipsychotic treatment. Co-treatment with anti-inflammatory agents holds the possibility of improving patient's response to treatment.

Professor Sommer continued:

"The study makes us realise that we need to be selective about which anti-inflammatory we use. Now that we know that some effects are replicated, we need to refine our methods to see if we can turn it into a real treatment. We have just started a multicenter trial using simvastatine to reduce inflammation in the brain of patients with schizophrenia. Studies like these will provide the proof-of-concept for targeting the immune system in schizophrenia".

Commenting for the ECNP, Professor Celso Arango (Hospital General Universitario Gregorio Marañón, Madrid) said:

"Inflammation and oxidative stress seem to be important factors in different mental disorders. Patients with different mental conditions, including schizophrenia, have been shown to have reduced antioxidants in the brain as well as excess inflammatory markers. Animal models and clinical trials have shown that antioxidants and anti-inflammatory drugs could not only reduce symptoms associated with the disorders but also prevent the appearance of neurobiological abnormalities and transition to psychosis if given early during brain development. This work is a step towards the possibility of better treatment, but we need more research in this area, especially with younger subjects where we might expect more brain plasticity".

Ends

Notes for editors

Please mention the European College of Neuropsychopharmacology Berlin Congress in any story resulting from this press release

Contacts

Professor Iris Sommer can be reached via I.Sommer@umcutrecht.nl

Professor Celso Arango can be reached via: carango@hggm.es

ECNP Press Officer, Tom Parkhill, can be reached at press@ecnp.eu or on phone number +39 349 238 8191.

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The annual ECNP Congress 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. Website: www.ecnp.eu

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Note 1 http://www.who.int/mental_health/management/schizophrenia/en/

Abstract – presented 15.10, Monday 20th October

S.18.02 Anti-inflammatory strategies in the treatment of schizophrenia

I. Sommer¹*, L.D. De Witte¹, R. Van Westrhenen¹, M. Begemann¹, R.S. Kahn¹ *¹University Medical Center Utrecht, Psychiatry Department, Utrecht, The Netherlands*

Background: The inflammatory hypothesis of schizophrenia is not new, but recently it has regained interest as more data suggest a role of the immune system in the pathogenesis of schizophrenia. If increased inflammation of the brain contributes to the symptoms of schizophrenia, reduction of the inflammatory status could improve the clinical picture. Lately, several trials have been conducted investigating the potential of anti-inflammatory agents to improve symptoms of schizophrenia. This study provides an update regarding the efficacy of anti-inflammatory agents on schizophrenic symptoms in clinical studies performed so far.

Methods: An electronic search was performed using PubMed, Embase, the national institutes of Health Web site clinicaltrials.gov, Cochrane Schizophrenia Group entries in Psitri <http://psitri.stakes.fi/EN/psitri.htm>, and the Cochrane Database of systematic reviews. Only randomized, double-blind, placebocontrolled studies that investigated clinical outcome (PANSS) were included.

Results: Our search yielded 26 double blind RCTs that provided information on the efficacy on symptom severity of the following components: aspirin, celecoxib, davunetide, EPA/DHA fatty-acids, estrogens, minocycline and N-acetylcysteine (NAC). Of these components aspirin [mean weighted effect size (ES) 0.3, 95% CI 0.06–0.537, $I^2 = 0$], estrogens (ES 0.51, 95% CI 0.043–0.972, $I^2 = 69\%$) and NAC (0.45, 95% CI 0.112–0.779) showed significant effects. Celecoxib, minocycline, davunetide and fatty acids showed no significant effect.

Conclusion: The results of aspirin addition to antipsychotic treatment seem promising, as does the addition of NAC and estrogens. These three agents are all very broadly active substances and it has to be investigated if the beneficial effects on symptom severity are indeed mediated by their anti-inflammatory aspects.

References

[1] Sommer IE, de Witte L, Begemann M, Kahn RS. Nonsteroidal anti-inflammatory drugs in schizophrenia: ready for practice or a good start? A meta-analysis. *J Clin Psychiatry*, 2012 73(4):414–419. [2] Sommer IE, van Westrhenen R, Begemann MJ, de Witte LD, Leucht S, Kahn RS. Efficacy of Anti-inflammatory Agents to Improve Symptoms in Patients With Schizophrenia: An Update. *Schizophr Bull*. 2014 Jan;40(1):181–91.