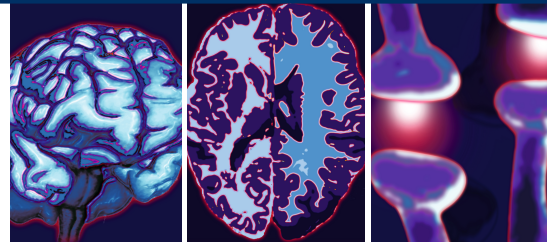


NEWS

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Antibiotic may be new weapon against schizophrenia

Observations in schizophrenic patients being treated with the antibiotic minocycline have revealed some interesting results that could potentially lead to a new treatment for the disease. A Japanese psychiatrist, Tsuyoshi Miyaoka, associate professor of psychiatry at Japan's Shimane University School of Medicine (Shimane, Japan), observed two cases in which treating bacterial infection with minocycline caused patients' schizophrenic symptoms to resolve. In one of these cases, minocycline was administered to a 61-year-old

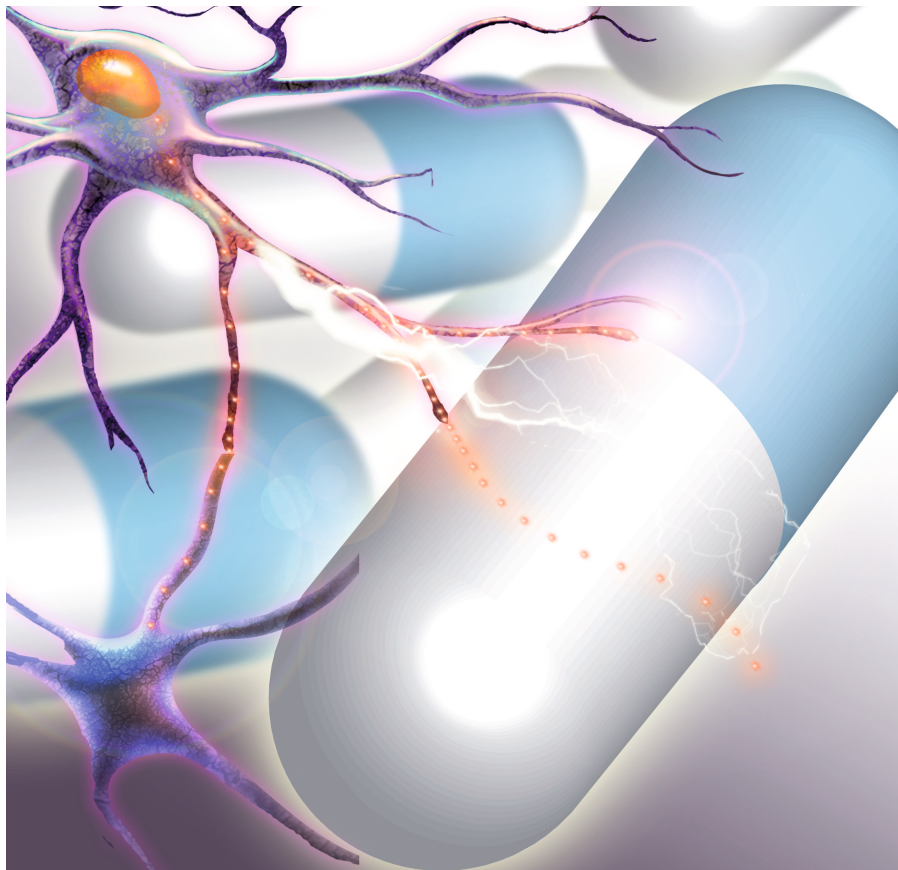
schizophrenic man for the treatment of a bedsore. Once this had healed, minocycline was discontinued and the patient's schizophrenia symptoms became worse. Doctors resumed minocycline and after 3 days the patient's schizophrenia symptoms improved.

As a result of this, Miyaoka and colleagues decided to conduct a small open-label study to examine the relationship between minocycline and schizophrenia. The drug was given, in addition to anti-psychotic medication, to 22 schizophrenic

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patients over a period of 4 weeks. A reduction of over 50% was seen in both positive and negative schizophrenia in these patients. These results, suggesting antipsychotic properties of minocycline, were all the more promising as the patients showed improvement in negative symptoms, which are usually difficult to resolve.

This led psychiatrists at the University of Maryland (MD, USA) to give minocycline to several patients with severe schizophrenia. They observed positive changes in these patients they had never seen before. In addition, results from a randomized, double-blind, placebo-controlled trial evaluating the relationship between minocycline and schizophrenia were published in the *Journal of Clinical Psychiatry*. In this study, a cohort of 54 patients with early phase schizophrenia were given an atypical antipsychotic plus either minocycline or placebo. As well as being beneficial

against negative symptoms, minocycline had a positive effect on cognitive deficits, which are notoriously hard to treat.

“The mechanism behind minocycline’s antipsychotic properties is still to be elucidated, although minocycline’s ability to cross the blood–brain barrier and to counter inflammation in the brain might be involved.”

The mechanism behind minocycline’s antipsychotic properties is still to be elucidated, although minocycline’s ability to cross the blood–brain barrier and to counter inflammation in the brain might be involved. This theory is supported by the growing amount of evidence that inflammation may play a role in the pathophysiology of schizophrenia.

Further research to establish whether minocycline is an effective medication

against schizophrenia is underway. A randomized, double-blind, placebo-controlled trial of 50 subjects with severe schizophrenia who have shown partial or no response to clozapine is being carried out, funded by the National Institute of Mental Health. Patients are being randomized to either minocycline plus clozapine or placebo plus clozapine for a period of 10 weeks. Similar trials are underway at the University of Texas Health Sciences Center (TX, USA) and in the UK.

There is hope among the scientific community that minocycline will prove to be an effective treatment for schizophrenia. “From our experience and clinical research, I believe that minocycline will turn out to be a truly revolutionary treatment for schizophrenia,” Miyaoka stated.

Source: Joan Arehart-Treichel. Will antibiotic fulfill its psychosis-fighting promise? <http://psychnews.psychiatryonline.org/newsArticle.aspx?articleid=1310500>

Gene variants involved in obsessive–compulsive disorder and Tourette’s syndrome identified

Two studies from Massachusetts General Hospital (MA, USA) may help in identifying gene variants predisposing people to a risk of developing obsessive–compulsive disorder (OCD) or Tourette’s syndrome. These investigations, which will appear in *Molecular Psychiatry*, are the first genome-wide association studies in individuals suffering from these conditions.

“...none of the SNPs identified in either study reached the threshold of genome-wide significance, which would suggest that the association represented a true risk factor.”

In both OCD and Tourette’s syndrome, close relatives of affected individuals have a high risk of developing the conditions. Although studies comparing affected and unaffected individuals have been carried

out previously, these were too small to identify specific genes contributing to risk.

In the current studies, investigators analyzed hundreds of thousands of single-nucleotide polymorphisms (SNPs) in thousands of individuals affected by either OCD or Tourette’s syndrome in order to try and identify the many gene variants which likely contribute to the conditions.

The OCD study, carried out by the International OCD Foundation Genetic Collaborative (MA, USA), involved the analysis of 480,000 SNPs in 1465 OCD sufferers and over 5000 controls, as well as 400 samples of an OCD patient and both parents.

The study found a possible association between OCD and areas of the genome close to *BTBD3*, which is closely related to a gene that has been linked with Tourette’s syndrome. An association was also found within *DLGAP1*, which is closely related to

a gene that causes OCD-like symptoms in mice when deleted.

The Tourette’s study, which was run by the Tourette Syndrome Association International Consortium for Genetics and the GWAS Consortium, analyzed 1500 cases and over 5200 controls and involved 484,000 SNPs.

“If future studies confirm that some of these variants do contribute to risk – either directly or by altering the function of other risk genes – that would suggest both novel mechanisms and might give us new treatment targets.”

The investigation revealed a possible association between Tourette’s and the gene *COL27A1*. It is thought that this gene might be expressed in the cerebellum during development and it has

variants involved in the regulation of gene expression in the frontal cortex.

However, none of the SNPs identified in either study reached the threshold of genome-wide significance, which would suggest that the association represented a true risk factor. The authors, therefore, stress the need for further, larger studies. “Although GWAS analysis allows much more comprehensive examination of the entire genome than do studies focused on particular families or candidate genes, these two studies are still underpowered and should be interpreted with caution,”

said David Pauls, co-senior author of both papers. “The current results are interesting and provide us with a starting point for analyzing future studies that must be done to replicate and extend these findings.”

In order to identify genes contributing to the risk of developing these disorders, Jeremiah Scharf of the Psychiatric and Neurodevelopmental Genetics Unit in the Massachusetts General Hospital Departments of Psychiatry and Neurology and co-lead author of both studies, said that SNPs identified by these studies should be tested in other groups and

patients and controls. He added that international collaborations should be expanded to increase the power of studies for OCD and Tourette’s syndrome. Scharf added that, “If future studies confirm that some of these variants do contribute to risk – either directly or by altering the function of other risk genes – that would suggest both novel mechanisms and might give us new treatment targets.”

Source: Gene variants that increase risk of obsessive-compulsive disorder and Tourette syndrome identified: www.sciencedaily.com/releases/2012/08/120814085535.htm

Paternal age increases risk of autism and schizophrenia in children

A large genetic sequencing project has shown that there is an increased risk of *de novo* mutations occurring in the sperm of older fathers and that when passed onto offspring, these mutations can increase a child’s risk of developing both schizophrenia and autism spectrum disorder (ASD).

The Icelandic study, published in *Nature*, showed that the probability of a 40-year-old man fathering a child with either schizophrenia or ASD is twice that of a 20-year-old man.

In contrast to women who can pass on only about 14 *de novo* mutations to their offspring due to the fact they are born with a finite number of eggs, men can form *de novo* mutations each time they generate sperm. This sequencing project found that, on average, men form an additional two mutations in sperm with each year of age at the time of conception. It was also found that there is a doubling of *de novo* mutations in sperm every 16.5 years. An investigator on the study, Kari Stefansson (deCODE Genetics, Reykjavik, Iceland), said these findings were ‘striking’.

Previous studies directly examined parent–offspring transmission and were largely limited to studying specific genes or regions. To gain further insight into the nature of these mutations, investigators sequenced 219 individuals comprising 78 trios to identify single-nucleotide polymorphism *de novo* mutations. Of the offspring, 44 had ASD, 21 were schizophrenic and 13 others were included for other reasons. All 78 trios were examined for the relationship between number of mutations and parents’ age. The number of mutations was found to increase with both paternal and maternal age. The results of a regression analysis, however, revealed that while paternal age remained highly significant, the mother’s age did not. Researchers on the study noted that the results “support the notion that the increase in mutations with parental age manifest itself mostly, maybe entirely, on the paternally inherited chromosome”.

There is substantial variation in paternal *de novo* mutations with one model used in the investigation revealing that “97.1% of all these variations could be explained by the father’s age and nothing else,” Stefansson said.

These findings place the focus of passing genetic mutations onto offspring on paternal rather than maternal age.

Source: Pam Harrison. Paternal age ups autism, schizophrenia risk in offspring: www.medscape.com/viewarticle/769531

Common parasite might lead to suicidal behavior

Evidence is growing that individuals infected with *Toxoplasma gondii* are at significant risk for later suicide attempts. A recent study from Sweden, due to be

published in the August issue of the *Journal of Clinical Psychiatry* has shown that individuals infected with *T. gondii* were seven-times more likely to carry out

nonfatal, self-directed violence than those who were not infected.

This builds on previous research linking *T. gondii* and suicidality in various

populations. However, co-senior author Lena Brundin, associate professor of experimental psychiatry in the Department of Translational Science and Molecular Medicine at Michigan State University College of Human Medicine (MI, USA), stressed that not all infected individuals will go on to attempt suicide, saying that some people may be more susceptible to developing symptoms than others.

“Participants who tested positive for *T. gondii* ... demonstrated a mean suicide assessment scale score 13 units higher than uninfected participants.”

T. gondii is present in approximately 10–20% of people in the USA and was thought to lie dormant. It now appears that

over time the parasite causes inflammation leading to the production of harmful metabolites that can damage brain cells.

This study by Brundin *et al.* is the first to use a suicide assessment scale in those infected with *T. gondii*. Participants who tested positive for *T. gondii* (IgG level of >22 IU/ml) demonstrated a mean suicide assessment scale score 13 units higher than uninfected participants. The relationship was, however, only significant for the entire group and not for those who attempted suicide only.

Historically, selective serotonin reuptake inhibitors have been the treatment of choice for depression. This class of drugs increase the levels of serotonin in the brain but are effective in only half of patients suffering from depression. However, Brundin’s research suggest that rather than

a cause, a reduction in serotonin levels in the brain may be a symptom of depression and that inflammation caused by an infection or parasite could alter brain chemistry, leading to depression and suicidal behavior.

“The consistency of *T. gondii*’s association with nonfatal suicidal self-directed violence across studies, regardless of the patient sample and ... diagnostic category, is noteworthy, as it lends further credence to the hypothesis that the link is independent of mental illness specificity of severity,” write the researchers.

Source: Deborah Brauser. More evidence links common parasite to suicidal behaviour: www.medscape.com/viewarticle/769498

– All news stories written by Sarah Jones

About the News

The News highlights some of the most important events and research.

If you have newsworthy information, please contact: Adam Williams, Head of Commissioning, *Neuropsychiatry*

Future Medicine Ltd, Unitec House,

2 Albert Place, London, N3 1QB, UK

Tel.: +44 (0)20 8371 6090;

Fax: +44 (0)20 8343 2313;

a.williams@futuremedicine.com