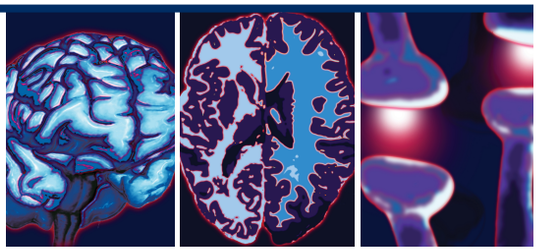

Late-life depression and dementia link explored in cohort study

Elderly patients with depression and mild cognitive impairment (MCI) may be at greater risk of eventually developing dementia suggests a recent study published in *Archives of Neurology*.

Many studies have looked at the relationship between dementia and depression; however, results have been far from conclusive, with different studies indicating that between 3 and 63% of patients with MCI demonstrate depressive symptoms. It is thought that several mechanisms underlie the complex relationship between cognitive decline and this psychiatric disorder. It has also been suggested that those who suffer from depression have an increased risk of developing dementia later in life. Indeed, a study published in the May issue of *Archives of Neurology* revealed that MCI and dementia were more common among elderly women.

In an attempt to better clarify and evaluate the link between late-life depression and MCI and dementia, the researchers, led by Edo Richard from University of Amsterdam (Amsterdam, The Netherlands), enrolled 2160 community-dwelling Medicare® (MD, USA) recipients aged 65 years or older in a multiethnic community cohort. MCI, dementia and progression from MCI to dementia were the main outcome measures. MCI was subcategorized into amnestic and nonamnestic MCI. The researchers assessed depression using the ten-item version of the Center for Epidemiological Studies Depression scale (CES-D) and defined by a CES-D score of 4 or more.

"We found that depression was related to a higher risk of prevalent MCI and dementia, incident dementia and progression from prevalent MCI to dementia, but not to incident MCI," said Richard. These results suggest that depression accompanies cognitive impairment but does not precede it.

Baseline depression was linked to prevalent MCI and dementia, as well as a greater risk of incident dementia. Individuals with MCI and depression at baseline were found to have an increased risk of developing certain forms of dementia later in life, particularly vascular depression but not Alzheimer's disease.

– Written by Sarah Freeston

Source: Richard E, Reitz C, Honig LH *et al.* Late-life depression, mild cognitive impairment, and dementia. *Arch. Neurol.* doi:10.1001/jamaneurol.2013.603 (2012) (Epub ahead of print).

About the News

The News highlights some of the most important events and research. If you have newsworthy information, please contact: Adam Williams, Commissioning Editor, *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

"Individuals with mild cognitive impairment and depression at baseline were found to have an increased risk of developing certain forms of dementia later in life..."

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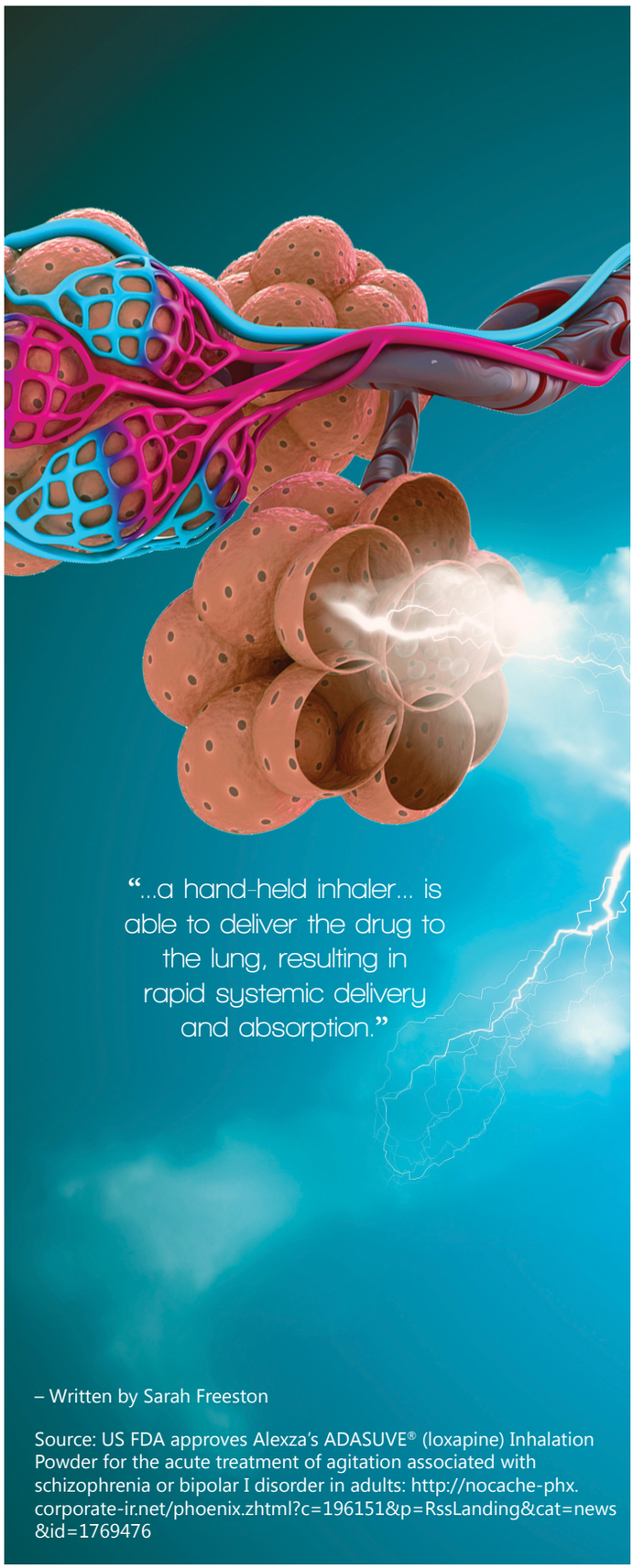

US FDA approves new treatment for schizophrenia and bipolar-related agitation

Alexza Pharmaceuticals, Inc. (CA, USA) has announced that ADASUVE® (loxapine) Inhalation Powder 10 mg has been approved by the US FDA for the treatment of acute agitation experienced by adults with schizophrenia or bipolar I disorder.

Agitation, including irritability and hostility, is a severe symptom evident in both schizophrenia and bipolar disorder. It is thought that nine out of every ten of these patients experience agitation at some point throughout the disease course.

Described as a 'unique product', ADASUVE combines the antipsychotic drug, loxapine, with Alexza's Staccato® delivery system, a hand-held inhaler that is able to deliver the drug to the lung, resulting in rapid systemic delivery and absorption.

"We believe that the ability to deliver medications rapidly and noninvasively will be important for patients and the professionals who care for them," said Thomas King, President and CEO of Alexza, who continued, "We project that ADASUVE will be available for commercial launch early in the third quarter of 2013." This will be the first approved noninjectable therapy for agitation in these patients.

The results from Phase III trials of the inhalant in schizophrenia and bipolar I patients were described as "compelling" by a principal investigator in the ADASUVE clinical trials, Michael Lesem, Executive Medical Director of Claghorn–Lesem Research Clinic (TX, USA). "I believe that ADASUVE represents an important new and much needed therapeutic option in treating agitation patients who will benefit from a noncoercive therapeutic intervention that works quickly to relieve their symptoms," explained Lesem.

The FDA's decision was based on a clinical data package involving over 1600 subjects. In two Phase III trials, ADASUVE 10 mg was deemed efficacious following statistically significant reductions in agitation compared with placebo 2 h after administration (the primary end point). In some cases, agitation was reduced as quickly as 10 min following administration.

Alexza identified a risk of bronchospasm in certain asthma and chronic obstructive pulmonary disease patients following ADASUVE administration and, therefore, is only available in enrolled healthcare facilities under a restricted program.

– Written by Sarah Freeston

Source: US FDA approves Alexza's ADASUVE® (loxapine) Inhalation Powder for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults: http://nocache-phx.corporate-ir.net/phoenix.zhtml?c=196151&p=RssLanding&cat=news&id=1769476

Functional MRI could predict onset of bipolar disorder in at-risk individuals

A recent functional MRI (fMRI) study from Australian researchers has revealed that individuals with an increased genetic risk of bipolar disorder actually have clear and quantifiable differences in brain activity compared with controls before clinical signs of the condition are detectable.

Dysfunctional neural mechanisms involved in the cognitive control of emotion have been previously associated with genetic risk of bipolar disorder but the triggers are not yet understood. Bipolar disorder has the highest suicide rate of all psychiatric disorders.

"This study is important for two reasons: first, any differences (such as those we identified in our recent study) may indicate endophenotypes (trait abnormalities) that are indicative of a vulnerability to bipolar disorder and not a consequence of developing this condition," explained study leader Philip Mitchell from the Black Dog Institute (Sydney, Australia) and University of New South Wales (Sydney, Australia), two institutions involved in this recent study, when speaking to *Neuropsychiatry*. "Second, demonstration of biological differences in those at increased risk will be important in the development of prevention and early intervention programs for those at heightened risk of this condition."

In this recent study, fMRI was used to monitor functional brain activity during a facial-emotion go/no-go task, in which participants were shown images of happy, fearful or calm (neutral) human faces. There were 47 study participants aged 18–30 years with a high genetic risk of developing bipolar disorder and 47 control subjects of the same age without a family history of bipolar or other severe mental illness.

Whole-brain corrected fMRI analyses revealed significantly reduced brain activity in response to the facial emotions in individuals with a high risk of bipolar disorder compared with the control group. Researchers observed an impaired inhibitory function of the inferior frontal cortex in response to fearful faces in at-risk individuals. This brain area is known to regulate emotional responses and the study authors suggest that this may be a trait marker of bipolar vulnerability.

"A number of our subjects (at-risk or controls) were either currently depressed or on psychotropic medications, both of which could potentially confound our findings," explained Mitchell when discussing the challenges faced in this recent study. "After we removed those subjects from the analyses, the results persisted; giving us increased confidence in the validity of the findings."

In addition to providing evidence that those at a high risk of bipolar disorder could have pre-existing functional disturbances, the recent study also suggests that fMRI could be used in the future as a tool for improving the lives of young people at future risk of the condition by allowing early detection, leading to improved outcomes and even prevention of onset.

The researchers are also analyzing other imaging data in this same clinical population and are following participants annually to determine predictors (neuroimaging, genetic, neuropsychological and clinical) for subjects that eventually go on to develop bipolar disorder.

Mitchell explained to *Neuropsychiatry* that his group has a long-standing interest in identifying biological and psychological mechanisms in bipolar disorder: "We commenced the current study over 3 years ago, and will be commencing our fourth year of follow-up of this clinical sample later this year. We have found the families very interested in this study as they are all concerned with the risk of their children developing the illness and wish to assist research which aims to eventually reduce this."

"...functional MRI could be used in the future as a tool for improving the lives of young people at future risk of the condition by allowing early detection, leading to improved outcomes and even prevention of onset."

– Written by Sarah Miller

Sources: Roberts G, Green MJ, Breakspear M *et al.* Reduced inferior frontal gyrus activation during response inhibition to emotional stimuli in youth at high risk of bipolar disorder. *Biol. Psychiatry* doi:10.1016/j.biopsych.2012.11.004 (2012) (Epub ahead of print); University of New South Wales. Brain imaging identifies bipolar risk: http://newsroom.unsw.edu.au/news/health/brain-imaging-identifies-bipolar-risk

Workplace bullying linked to psychotropic medication prescriptions

A Finnish study, published in *BMJ Open*, has found that workplace bullying has the potential to cause mental health problems and increased psychotropic medication usage. The authors call for the problem to be tackled to help prevent mental problems among employees.

Workplace bullying can take many forms, such as intimidating, undermining or punishing an employee unreasonably. It can be verbal, physical or psychological abuse and it may be overt or covert as it takes place within established corporate policies.

> "...workplace bullying and also observing bullying was found to be associated with subsequent psychotropic medication..."

The investigators set out to longitudinally assess whether workplace bullying was associated with subsequent psychotropic medication use among women and men. This was the first study to differentiate between witnessing bullying or being the subject of bullying, and a link to psychotropic drug prescriptions. "Previous studies have been mainly cross-sectional or used self-reported data on mental health outcomes. This study was prospective and we examined register-based data on psychotropic medication," explained Tea Lallukka, lead author of the study from the Department of Public Health, University of Helsinki (Helsinki, Finland) in correspondence with *Neuropsychiatry*.

A cohort of 6606 participants aged between 40 and 60 years were enrolled at baseline.

Being the subject of current or earlier bullying, or observing workplace bullying, was assessed through a survey. This information was linked with data on purchases of prescribed reimbursed psychotropic medication from the Finnish Social Insurance Institution's register. Medication taken 3 years before and up to 5 years after the baseline survey was included. Covariates included age, previous psychotropic use, bullying during childhood, occupational class and BMI.

"Our study confirmed the earlier (cross-sectional and self-reported) evidence as those who reported that they were victims of bullying or observed bullying at work were more likely to have psychotropic medication over follow-up," clarified Lallukka.

After adjusting for age and prior medication use, workplace bullying and also observing bullying was found to be associated with subsequent psychotropic medication in both men and women. However, the associations only modestly attenuated after full adjustment.

"One might find it surprising that the associations tended to be stronger among men than women. This was seen regarding victims of bullying," said Lallukka.

A total of 5% of employees stated that they were current victims of bullying while 18% of females and 12% of males reported being bullied at some point during their careers. In both genders, bullying was linked to being prescribed psychoactive drugs; indeed, females who suffered bullying at work were 50% more likely to be prescribed medication. In addition, approximately half of employees admitted to occasionally witnessing workplace bullying and this was linked to a similar number of psychotropic medication prescriptions.

These findings highlight the significance of workplace bullying to subsequent psychotropic medication, reflecting medically confirmed mental problems.

> "In both genders, bullying was linked to being prescribed psychoactive drugs..."

"Workplace bullying bears significance for subsequent mental-health problems and thus bullying should be tackled in the workplace in efforts to prevent mental-health problems among employees," said Lallukka, who concluded, "Perhaps better guidelines could be developed not only for occupational healthcare but also for supervisors to better detect bullying and handle the situations at early phase and promote employee (mental) health."

– Written by Sarah Freeston

Source: Lallukka T, Haukka J, Partonen T, Rahkonen O, Lahelma E. Workplace bullying and subsequent psychotropic medication: a cohort study with register linkages. *BMJ Open* 2(6), e001660 (2012).