Clinical News … new Nature journal … gains in drug development … neurodegeneration versus neurodevelopment and brain changes … neurohistology and risk factors … peer support and recovery … social media and schizophrenia …

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Schizophrenia International Research Society (SIRS) Launches New Open-Access Schizophrenia Journal

SIRS, in collaboration with the Nature Publishing Group, has launched a new open-access, on-line, peer-reviewed journal dedicated to high-quality schizophrenia research. The inaugural editor is Dr. Jim Meador-Woodruff, an outstanding colleague and gifted schizophrenia researcher. We are delighted that this new journal will provide more opportunities to expand and disseminate research work in schizophrenia. Just as *Schizophrenia Research and Schizophrenia Bulletin* welcomed ***CS*** as a nascent journal to our field now several years ago, we wish Jim and *npj Schizophrenia* (www.nature.com/npjschz/) every success. Welcome aboard!

Drug Development Update

The U.S. Food and Drug Administration (FDA) recently approved the use of the once-monthly formulation of long-acting injectable paliperidone palmitate for the treatment of schizoaffective disorder. Additionally, the FDA just received a New Drug Application (NDA) from Janssen Pharmaceuticals, Inc. regarding a 3-month formulation of paliperidone palmitate, seeking approval for use in the treatment of schizophrenia. This NDA application is supported by results of a placebo-controlled trial of this 3-month formulation. The study was concluded early following an analysis that favored this putative antipsychotic significantly over placebo in reducing relapse in patients with schizophrenia.

The FDA also approved a new formulation, based upon a pre-filled dual-chamber syringe, of the once monthly long-acting injectable antipsychotic aripiprazole (Abilify Maintena). The FDA also received an NDA for another novel long-acting antipsychotic, Aripiprazole Lauroxil. This putative antipsychotic, developed by Alkermes plc, could enable both one- and two-month formulations since the prodrug in vivo becomes aripiprazole.

As mentioned in earlier issues of ***CS***, Alkermes also has another putative antipsychotic—ALKS3831; a combination of samidorphan (a mu-opioid antagonist) and olanzapine—under development. Results from a 12-week Phase 2 study are expected in 2015.

Actavis plc also announced the FDA's acceptance of a supplemental new drug application (sNDA) to extend the use of asenapine to treat pediatric bipolar disorder.

Finally, the FDA is also set to review the NDA jointly submitted by Otsuka Pharmaceutical Company and H. Lundbeck A/S for the putative new antipsychotic brexpiprazole for the treatment of schizophrenia. This agent has a partial agonist pharmacological profile of similar modulation of both serotonin and dopamine receptors, as well as histaminergic and adrenergic antagonist effects.

Long-Acting Injectable Antipsychotics (LAI) Study of 14 Years (1995–2009) in Danish Population

In recent issues of ***CS*** we have highlighted the (perhaps surprising) lack of differences between first- and second-generation (FGAs vs. SGAs) antipsychotic medications. Noteworthy studies that were previously described in ***CS*** include the meta-analysis of 15 antipsychotic drugs by Leucht and colleagues (2013) and the comparative study of paliperidone palmitate versus haloperidol decanoate that was reported by McEvoy and colleagues (2014). Using a Danish registry spanning some 14 years of treatment, Nielsen and colleagues report on relapse between patients receiving LAI risperidone and LAI FGAs (predominantly 2 drugs, zuclopenthixol decanoate and perphenazine decanoate). The outcome—in terms of several measures of relapse—was similar between the SGA- and FGA-treated groups.

Nielsen J, Jensen SO, Friis RB, Valentin JB, Correll CU. Comparative effectiveness of risperidone long-acting injectable vs first-generation antipsychotic long-acting injectables in schizophrenia: results from a nationwide, retrospective inception cohort study. Schizophr Bull 2014 Sep 1; doi:10.1093/schbul/sbu128. [Epub ahead of print]

Brain Imaging and Schizophrenia: Time Dependent Changes?

The University of Barcelona has conducted a large and systematic study of schizophrenia. Here, the team has collaborated with Dr. Arthur Toga's neuroimaging group at the

University of Southern California to look at brain changes over time in 51 patients with schizophrenia and 49 normal subjects (Pujol et al., 2014). Interestingly, they found accelerated age-related decrements in hippocampal volume in patients with schizophrenia. These findings add weight to the notion that some patients may have a neurodegenerative component to their illness.

Pujol N, Penadés R, Junqué C, Dinov I, Fu CH, Catalan R, et al. Hippocampal abnormalities and age in chronic schizophrenia: morphometric study across the adult lifespan. Br J Psychiatry 2014;205(5):369-375.

Another Study Shows Relationship Between Progressive Brain Loss and Antipsychotic Medications in Schizophrenia

This is a provocative study of 9-year follow-up MRI scans in patients with schizophrenia drawn from the Northern Finland Birth Cohort of 1966. The authors found mean annual brain loss of 0.69% in patients with schizophrenia (n=33) compared with 0.49% in control subjects (n=71). Surprisingly, brain atrophy was not associated with worsening of symptoms. This reduction was, however, associated with exposure to antipsychotic medications; actually, in a dose-dependent status. It is hard, nevertheless, to disentangle illness duration and illness severity effects as they pertain to use of antipsychotic medications. That said, this study is congruent with several other studies showing some association between antipsychotic exposure and brain tissue loss.

Veijola J, Guo JY, Moilanen JS, Jääskeläinen E, Miettunen J, Kyllönen M, et al. Longitudinal changes in total brain volume in schizophrenia: relation to symptom severity, cognition and antipsychotic medications. PLoS ONE 2014;9(7):e101689. doi: 10.1371/journal.pone.0101689.

Preventative Mortality in Schizophrenia

A recent Canadian study (Kredentser et al., 2014) reminds us of the markedly heightened risk of early death from schizophrenia, its consequences (suicide especially) and its physical comorbidities. Looking at a Canadian database, the authors found over twice the rate of (age-controlled) death among people with schizophrenia, contributed predominantly by suicide, accidental deaths, respiratory and circulatory conditions. Overall, the rate of cancer deaths was similar, except (not surprising given the smoking prevalence in schizophrenia) for lung cancer deaths which were markedly overrepresented in people with schizophrenia. These observations, coupled with current rates of metabolic syndrome that run about 50% among people with schizophrenia, are a clarion call for integrated care reform and service delivery.

Kredentser MS, Martens PJ, Chochinov HM, Prior HJ. Cause and rate of death in people with schizophrenia across the lifespan: a population-based study in Manitoba, Canada. J Clin Psychiatry 2014;75(2):154-161.

Emergency Room Visits Due to Side Effects of Antipsychotic Medications

Hampton and colleagues (2014) present interesting findings from an analysis of emergency room visits for psychotropic drug-related side effects as determined by the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance system (NEISS-CADES). They found, controlling for one number of prescriptions written for each drug class of psychotropic medications, that antipsychotic medications predominated (31.3%) among emergency room visits due to adverse effects, especially among adults under age 45 years. First-generation antipsychotic medications (FGAs) overall, FGAs (excluding haloperidol), and second-generation antipsychotics had much higher rates of emergency room visits due to adverse effects (6.2 times, 3.1 times, and 2.2 times, respectively) than either nonbenzodiazepine hypnotics or anxiolytics. Antidepressants were the second highest drug class represented in this important analysis.

Hampton LM, Daubresse M, Chang HY, Alexander GC, Budnitz DS. Emergency department visits by adults for psychiatric medication adverse events. JAMA Psychiatry 2014;71(9):1006-1014.

Immune Dysfunction in Schizophrenia Has Origin in Utero?

There is a confluence of evidence—from epidemiological through clinical studies—of immunological abnormalities in schizophrenia. Early epidemiological study that presaged the recent wave of immunological studies showed elevated exposure to in utero infections (viral, rubella, toxoplasmosis) associated with maternal pregnancies of people who later develop schizophrenia. Another recent study by Canetta and colleagues (2014) adds further emphasis to this by examination of C-reactive protein (CSP) in the Finnish Prenatal Study of Schizophrenia. This study—based upon maternal blood samples—showed a 1.31 higher risk of schizophrenia with higher CSP. While the finding is of itself "nonspecific," it is robust despite many confounding variables. This study also advances the (perhaps fanciful) notion of schizophrenia as an autoimmune disorder. Moreover, these findings—through the epidemiological lens—are complementary to the recent Schizophrenia Working Group of the Psychiatric Genomics Consortium (2014) *Nature* paper showing abnormalities of immunological genes in schizophrenia.

Canetta S, Sourander A, Surcel HM, Hinka-Yli-Salomaki S, Leiviskä J, Kellendonk C, et al. Elevated maternal C-reactive protein and increased risk of schizophrenia in a national birth cohort. Am J Psychiatry 2014;171(9):960-968.

Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature 2014;511(7510):421-427.

Impact of Peer Support Specialists is Recognized

There is a gradual evolution of the role of peer support specialists as core members of the multidisciplinary team who care and coordinate the care of people with schizophrenia. Peer support specialists bring unique and complementary skills to the treatment team, especially their "lived experience" with mental illness. This evidence-based report by Chinman and colleagues (2014) chronicles some 20 studies that evaluate the effectiveness of peer support services. As anticipated, the results are mixed, in part due to the varied roles (including "quasi case management") of peer support specialists. The article is a good read for those who are contemplating the involvement of peer support specialists in their care delivery system.

Chinman M, George P, Dougherty RH, Daniels AS, Ghose SS, Swift A, et al. Peer support services for individuals with serious mental illnesses: assessing the evidence. Psychiatr Serv 2014;65(4):429-441.

Patients in Recovery and Role in Research: Results of a British Survey

Patterson and colleagues (2014) report on an online survey of what the British health system (the National Health System [NHS]) calls "service users." Although they canvassed a large and diverse group of constituents, ultimately 166 service users contributed meaningful data on their perceptions and experiences in supporting clinical research within the NHS. Continued concerns of stigmatization and even exploitation during research was expressed. Most participants had been in voluntary or paid research positions rather than being actual study participants. The respondents also affirmed the merits of including service users in research. Indeed, the authors see opportunity in coming together between academic leaders and service users to enhance research.

Patterson S, Trite J, Weaver T. Activity and views of service users involved in mental health research: UK Survey. Br J Psychiatry 2014;205(1):68-75.

Social Media and Schizophrenia: "Twitter Psychosis?"

It is apparent that social media can—and is—being used by younger people who develop and suffer from schizophrenia. Whether this is "a blessing or a curse" remains to be determined. Kalbitzer and colleagues (2014) provide a salutary account of a 31-year-old female who had a rush of "tweets" that appeared related to sudden-onset psychotic experiences. Doubtless we will see more of this. On the other hand, social media also has the potential to mitigate the social isolation of people with schizophrenia. Social media and internet communications may also be harnessed to advance public awareness and primary prevention strategies, as well as to promote medication adherence and early detection of relapse as secondary prevention strategies. Time will tell.

Kalbitzer J, Mell T, Bermpohl F, Rapp MA, Heinz A. Twitter psychosis: a rare variation or a distinct syndrome? J Nerv Ment Dis 2014;202(8):623.

*Readers wishing to know more about the details of individual studies cited in **Clinical News** should consult directly the pharmaceutical company who sponsored the study and/or www.clinicaltrials.gov, or go directly to the journal that published this work.*