

**Background:** Surveys consistently show that the top priority of people with mental illness is participation in the open labor market. Despite this finding, the employment outcome for people with psychotic illnesses is not good. At the onset of illness, unemployment rates of 40%–50% are commonly found. For those who develop schizophrenia, unemployment rises to 70%–95%. These figures are troubling to consumers, clinicians and politicians. Individual Placement and Support (IPS) is a vocational intervention, which has been developed and trailed successfully in populations with chronic serious mental illness in America. To date, there has been no published randomized trial of IPS in early mental illness. This study aimed to examine the efficacy of IPS in a randomized controlled trial with people with first-episode psychosis.

**Methods:** Clients of EPPIC at ORYGEN in Melbourne who wished to find work were randomized to treatment as usual (TAU) ( $n = 20$ ) or TAU + IPS ( $n = 20$ ). The IPS condition involved working with an employment consultant who was integrated with the mental health team.

**Results:** Results to be presented will show that clients in the IPS group achieved greater employment outcomes than those in the TAU-only group. Other results will be presented examining symptomatic and functioning factors.

**Conclusions:** There is an increasing recognition that the rehabilitation of people with mental illness needs to take into account functional as well as symptomatic domains. Although there are structural obstacles making this more difficult, the current project shows what is possible with minimal extra resources.

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## Diagnosing mild cognitive impairment – a data-driven approach

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**Background:** There has been increasing research interest in the concept of mild cognitive impairment (MCI) as a prodrome to Alzheimer's disease and other dementias. Several diagnostic schemas have been proposed with a central feature being the presence of cognitive impairment in one or more domains. But how should cognitive impairment be determined? Which tests, how many and what cut-offs should be used? The current study uses a data-driven approach to determine patterns of healthy cognitive functioning and impairment in a community sample of older adults.

**Methods:** Four hundred adults aged 70–90 years completed a comprehensive neuropsychological assessment as part of the Memory and Ageing Study, Sydney.

**Results:** Prevalence of cognitive impairment across the domains of memory, language, psychomotor speed, visuospatial and frontal-executive functions varied considerably when different sources of normative data, demographic corrections, cut-scores and clusters of tests were applied.

**Conclusions:** MCI is a very difficult construct to define at an individual and group level. This study provides much needed normative neuropsychological data in an Australian older adult sample. Longitudinal data will inform us about the most sensitive and specific neuropsychological profile that will predict those who progress to dementia.

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## The effects of adjunctive estradiol on cognitive performance in women with schizophrenia

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**Background:** Development of pharmacological strategies for improving cognitive impairment has recently become a key issue in the treatment of schizophrenia. The steroid hormone estrogen is hypothesized to be protective for women with schizophrenia and has been found to exert positive effects on specific cognitive domains in healthy postmenopausal women. We have previously reported a significant improvement in psychopathology ratings associated with adjunctive estrogen treatment. We additionally investigated the effects of adjunctive estrogen treatment on cognitive function in women with schizophrenia.

**Methods:** Fifty women of childbearing age with schizophrenia or schizoaffective disorder received 100 µg/day transdermal estradiol or placebo for 4 weeks, under double-blind conditions. The cognitive battery, assessing attention, verbal fluency, memory and executive function, was administered at baseline and at 4 weeks. Hormone assays were collected, and psychopathology was measured weekly.

**Results:** Results indicated no significant changes in cognition following 4 weeks of adjunctive estrogen treatment. While baseline endogenous estrogen levels were also not significantly related to cognitive function, there was a correlation found between LH and a measure of information processing.

**Conclusions:** Short-term estrogen treatment as an adjunct to antipsychotics does not significantly alter cognitive functioning, despite significant improvements in psychopathology ratings. It may be that estrogen treatment has selective effects on psychopathology;

however, further exploration of this area is needed before definitive conclusions can be drawn.

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## Tamoxifen – a potential treatment for women in the manic phase of bipolar affective disorder?

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**Background:** Bipolar affective disorder (BPAD) is an illness with high morbidity and mortality. Lithium and other anticonvulsant drugs are the main treatments for BPAD, despite little being known about their mechanisms of action. Recent attempts to elucidate the biochemical actions of these drugs have focused on the protein kinase C (PKC) pathways. Another PKC inhibitor hypothesized to be effective in the treatment of mania is tamoxifen, a synthetic nonsteroidal antiestrogen. The aim of the current study was to test and compare the effectiveness of two adjunctive antiestrogen agents (tamoxifen or progesterone) in the treatment of acute mania.

**Methods:** A 28-day, three-arm (40 mg/day oral tamoxifen or 20 mg/day oral progesterone or oral placebo), double-blind, placebo-controlled, adjunctive study of 34 women with mania was conducted. All patients also received a mood stabilizer as the baseline treatment. Manic symptoms and psychopathology were measured weekly using the CARS-M and Positive and Negative Syndrome Scale rating scales together with estrogen, progesterone and gonadotropin levels. Cognitive functioning (RBANS) was assessed in a subsample of five participants at baseline and repeated on day 28.

**Results:** Results indicated a decline in the symptoms of mania and psychopathology in the tamoxifen group, and to a lesser extent in the progesterone and control groups. The tamoxifen group also had significant changes in estrogen levels, as well as correlations between estrogen and mania ratings.

**Conclusion:** The results suggest that tamoxifen may be a useful adjunct in the treatment of acute manic symptoms in women with BPAD.

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## The use of selective estrogen receptor modulators in the treatment of menopausal women with schizophrenia

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**Background:** Estrogen modulates rat brain dopamine and serotonin systems in a way that mimics atypical antipsychotics. Our work indicates that adjunctive estrogen is a useful treatment in women of childbearing age with schizophrenia. We studied the use of a selective estrogen receptor modulator (SERM) in menopausal women with schizophrenia.

**Aim:** To test and compare the effects of adjunctive use of an SERM (raloxifene) and standard hormone therapy (HT) on psychotic symptoms in menopausal women with schizophrenia. To examine the effect of an SERM and HT on cognition in menopausal women with schizophrenia.

**Method:** A double-blind, 3-month, placebo-controlled, adjunctive study of raloxifene (60 mg/day) vs. HT (2 mg estradiol plus 10 mg dihydroprogesterone) vs. placebo was conducted. Participants received standardized doses of risperidone (or equivalent doses of similar antipsychotic medication). Psychopathology was measured fortnightly using the Positive and Negative Syndrome Scale rating scale. Cognitive testing and sex hormone assays were conducted monthly.

**Results:** Data collected from 23 participants indicated that while SERM or HT adjuncts did not result in an improvement in psychotic symptoms when compared with risperidone alone, the use of adjunctive SERM resulted in improved cognitive performance on working and verbal memory tasks when compared with the HT or risperidone alone.

**Conclusions:** The use of adjunctive SERM at 60 mg/day may induce a mild increase in cognitive performance in menopausal women with schizophrenia. Yaffe et al. (2005) show that 120 mg/day raloxifene was more effective in improving cognition in healthy postmenopausal women. We are undertaking a new study with this increased dose of raloxifene.

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## The estrogen 100

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**Aim:** To compare the efficacy of adjunctive transdermal estradiol with adjunctive placebo in the treatment of acute psychotic symptoms in 100 women with schizophrenia.

**Background:** Estrogen has been shown in animal studies to have dopamine downregulation effects and has also been shown to impact the serotonergic system. Additionally, there are clinical case reports of women whose schizophrenic symptomatology is exacerbated at low estrogen phases of the menstrual cycle. Similarly, there are clinical case reports of women with