Subspecialties Included

- Academic Psychiatry
- Addiction Psychiatry
- Child & Adolescent Psychiatry
- Forensic Psychiatry
- Geriatric Psychiatry
- Neuropsychiatry
- Psychosomatic Medicine
- Hospice and Palliative Medicine

Journals Included

- American Journal of Psychiatry
- American Journal of Geriatric Psychiatry
- Academic Psychiatry
- Current Psychiatry
- Psychosomatics
- Journal of the American Academy of Child & Adolescent Psychiatry
- JAMA Psychiatry
- New England Journal of Medicine

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CLASSICS IN PSYCHIATRY

Meredith Wylie, M.D.


Objectives: This study seeks to optimally derive temporal trends in the incidence of dementia among participants in the Framingham Heart Study by continuous monitoring for new cases in a longitudinal cohort study over three decades using consistent diagnostic criteria.

Methods: Four non-overlapping epochs were evaluated to determine the 5-year incidence of dementia during each of four epochs which included 5205 persons 60 years of age or older. The primary analysis used Cox proportional-hazards models adjusted for age at entry and sex to compare the incidence of dementia across the four epochs; separate analyses were performed for overall dementia, Alzheimer’s disease, and vascular dementia. Secondary analysis examined the effects of interactions between epoch and age, sex, Apo lipoprotein E ε4 status, and educational level, as well as the effects of vascular risk factors, stroke, atrial fibrillation, coronary heart disease and heart failure on temporal trends in dementia.

Results: 371 cases of dementia were observed with a trend toward an increasing mean age at diagnosis from 80 years during the first epoch to 85 years during the fourth epoch (P<0.001 for trend). The 5-year age- and sex-adjusted cumulative hazard rates for dementia declined over time from 3.6 per 100 persons during the first epoch (1977-1983), 2.8 per 100 persons during the second epoch (1986-1991), 2.2 per 100 persons during the third epoch (1992-1998), and 2.0 per 100 persons during the fourth epoch (2004-2008). Relative to the incidence during the first epoch, the incidence declined by 22%, 38%, and 44% during the second, third, and fourth epochs, respectively. There has been an average decline in the incidence of dementia of 20% per decade (hazard ratio, 0.80; 95% CI, 0.72 to 0.90) since 1977. There was no evidence to suggest that the interaction between epoch and age, sex, or APOE ε4 status had an effect on temporal trends in the incidence of dementia (P>0.10 for all comparisons), but the interaction between epoch and educational level had a significant effect (P=0.03). The decline in the incidence of dementia was observed only in the cohort of persons who had a high school diploma, with an average decline in risk of 23% per decade (hazard ratio, 0.77; 95% CI, 0.67 to 0.88); there was no decline in the cohort of persons who did not have a high school diploma.

Conclusions: Among participants in the Framingham Heart Study, the incidence of dementia has declined over the course of three decades, but the factors contributing to this decline have not been completely identified. The prevalence of most vascular risk factors (except obesity and diabetes) and the risk of dementia associated with stroke and heart disease have decreased over time, but none of these trends completely explain the decrease in the incidence of dementia. Earlier diagnosis and more effective treatment of stroke and heart disease might have contributed to a lower incidence of dementia, particularly vascular dementia, during more recent epochs. This benefit was more pronounced among persons who have a high school diploma.

Punchline: While an increase in the population of the elderly is expected to correspond to increase in the prevalence of dementia, the data from the Framingham Heart Study suggests that there is a decline in the incidence of dementia, with education being a possible protective factor.
**CHILD & ADOLESCENT PSYCHIATRY**

Ambreen Ghori, M.D.

**Study:** Thomas W. Frazier, PhD, Eric W. Klingemier, BA, Mary Beukemann, Leslie Speer, PhD, NCSP, Leslie Markowitz, PsyD, Sumit Parikh, MD, Steven Wexberg, MD, Kimberly Giuliano, MD, Elaine Schulte, MD, MPH, Carol Delahunty, MD, Veena Ahuja, MD, Charis Eng, MD, PhD, Michael J. Manos, PhD, Antonio Y. Hardan, MD, Eric A. Youngstrom, PhD, Mark S. Strauss, PhD

**Objectives:** To develop and replicate an objective, eye tracking–based autism risk index.

**Methods:** Participants were children varying in ages 3-8.11 years who were referred to a tertiary care multidisciplinary ASD specialty clinic following autism screening. Additional participants included those who did not go through an autism screen, but whose parents or teachers were concerned about social deficits.

The initial study was conducted from July 2014 to June 2015 followed by a replication study from August 2015 to November 2015. The research team was blinded to participant diagnosis. Eye tracking data was collected and recorded using an SMI remote eye tracker. Twelve healthy control children ages 2-15 years were recruited and their gaze data were viewed in SMI Be Gaze software to identify a priori social targets.

The stimuli in the initial study were selected to represent multiple distinct types previously used in the eye gaze literature, including static facial affect, biological versus non-biological pairing and dynamic/naturalistic scenes. The total experiment time was approximately 7 minutes for both studies. Replication study stimuli were chosen based on results from the initial study.

Children were seated approximately 65 cm from the LCD display and viewed stimuli subtending a visual angle of 18.8 degrees in a sparse room with visual barriers used to reduce distraction. Gaze needed to be detected on screen 40% or more of the time, and participants had to have at least 20 ROIs (range of interest) with available data to consider the eye tracking evaluation valid.

**Results:** Of the individuals who consented, 6 children from the initial study and 3 children from the replication study could not adequately attend to the stimuli at least 40% of the time. All individuals who could not achieve a valid administration had low language scores and/or severe autism symptoms levels, ADOS-2 calibrated severity score greater than or equal to 7. As expected the group with ASD had higher autism symptom severity scores on the ADOS-2 and lower language scores. The non-ASD group had a range of psychiatric diagnoses, with 1 non-ASD participant receiving no clinical diagnosis in each sample. There were no significant differences in SRS (social responsiveness scale) or CBCL (child behavioral checklist) total problem scores, and high scores did not discriminate cases of ASD and non-ASD cases in either sample. (SRS-2: AUC = 0.58 and 0.43, 95% CI= 0.39-0.77 and 0.22-0.66; CBCL: AUC= 0.36 and 0.41, 95% CIs = 0.18 - 0.54 and 0.19- 0.64). Importantly, the tracking ratio (total time-on-screen) did not significantly differ between patients with ASD and non-ASD patients.

**Conclusion:** The present investigation demonstrates the strong potential for remote eye tracking as an objective tool for quantifying autism risk and estimating autism symptom severity. The present data suggest that the ARI may have incremental validity for ASD identification when used in conjunction with other clinical measures. The relationship between the ARI and ADOS-2 overall severity scores were high but did not suggest redundancy. Future research is needed to establish precise estimates of stand-alone and incremental validity of the ARI for categorical ASD diagnosis.
Punchline: Autism Risk Index based on eye gaze to social and nonsocial information may be a useful and objective measure supplementing existing clinical observations among patients requiring evaluation for ASD diagnosis.

CONSULTATION-LIAISON/CLINICAL PSYCHIATRY

Katy LaLone, M.D.


Objectives: To provide a brief outline of the biological approaches to ‘treatment-resistant’ OCD in adults.

Methods: Authors summarize what literature is currently available to guide the clinician in management of OCD in patients who fail to respond adequately to first-line therapies.

Results: Authors note that the definition of treatment response in OCD is itself a source of debate, usually defined as a percentage reduction in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores. These authors define remission as a Y-BOCS scores <14, but caution that the Y-BOCS score alone may not reflect the full extent of the patient’s disability.

First-line treatment in OCD with SSRIs has been well established with an adequate trial of at least 12 weeks. Authors report it is generally accepted that higher doses of SSRIs are often needed in OCD (as compared to MDD) but warn that doses should not be escalated prematurely. Authors also suggest that all medications should be closely monitored for toxicity in addition to a baseline EKG and clear documentation when using higher-than-recommended doses.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Maximum doses used for OCD reported in the literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>escitalopram</td>
<td>60mg</td>
</tr>
<tr>
<td>fluoxetine</td>
<td>120mg</td>
</tr>
<tr>
<td>paroxetine</td>
<td>100mg</td>
</tr>
<tr>
<td>sertraline</td>
<td>400mg</td>
</tr>
<tr>
<td>clomipramine</td>
<td>300mg</td>
</tr>
</tbody>
</table>

In general, if some benefit has been obtained from the initial therapy, augmentation is recommended. If no benefit, switching to a new agent would be reasonable. There is no clear data that clomipramine is better than SSRIs. Most guidelines suggest two trials of high-dose SSRIs prior to switching to clomipramine. During augmentation, clinicians should be aware of potential drug-drug interactions, consider the increased risk of side effects, and add one agent at a time. Also with several newer agents, off-label usage may not be covered by insurers.

<table>
<thead>
<tr>
<th>Medications with evidence for use in OCD</th>
<th>Evidence for Mono-therapy</th>
<th>Evidence for Adjunctive Use with SSRIs</th>
<th>Routine Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td>Very good evidence</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>ago-melatine</td>
<td>Some evidence</td>
<td>None</td>
<td>Optimal dosing not yet established</td>
</tr>
<tr>
<td>vortioxetine</td>
<td>Theoretical efficacy for use</td>
<td>None</td>
<td>No studies to date</td>
</tr>
<tr>
<td>Medications for which no benefit has been found for treatment of OCD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNRIs</td>
<td>buspirone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAOIs</td>
<td>sumatriptan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lithium</td>
<td>naltrexone</td>
<td></td>
<td></td>
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<tr>
<td>pindolol</td>
<td>D-cycloserine</td>
<td></td>
<td></td>
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<tr>
<td>desipramine</td>
<td>inositol</td>
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</tbody>
</table>

Lastly, behavioral therapies especially CBT are certainly recommended in combination with pharmacologic therapy and have been shown to be more effective than SSRIs alone. A few studies suggest Transcranial magnetic stimulation (TMS) may be helpful in OCD. Surgical options including gamma ventral capsulotomy and deep brain stimulation have been shown effective for treatment-refractory cases.

Conclusions: There is limited evidence guiding OCD treatment for patients who have failed first-line therapy. The authors suggest a high-dose SSRI trial and consideration of adjunctive clomipramine as reasonable first steps with careful clinical and cardiac monitoring. While atypical antipsychotics are commonly used, the evidence supporting them is limited. While current data is limited, ondansetron and memantine are promising as they are both well tolerated.
Punchline: Residual symptoms in OCD are common and the use of augmentation strategies needs to be carefully weighed against the risks of additional side effects.

GERIATRIC PSYCHIATRY

Rajesh Tampi, M.D.


Objectives: The investigators wanted to evaluate the various predictors of outcome among older adults with delirium who are hospitalized.

Methods: The investigators conducted a literature review of MEDLINE, Embase and PsycINFO databases. They included studies that involved human subjects and were published in English language journals. These studies included individuals with delirium which was identified using a recognized and validated method. These studies also had quantifiable outcomes including death, institutionalization, length of stay and cognitive change. Additionally, these studies included patients from the general hospital setting, rehabilitation facilities or care homes but not from intensive care units or the community setting.

Results: A total of twenty seven studies met the inclusion criteria. All studies were found to have low risk of bias. The mean age ranged from 70 to 89 years and a majority of studies had more women than men. A total of thirteen studies were conducted in acute and general medical units. Six of the studies were conducted in hip fracture patients, four in post-acute and rehabilitation units, two in palliative care units and one study was conducted in the emergency department. Nineteen studies used Confusion Assessment Method (CAM) to diagnose delirium whereas eight studies used the DSM criteria.

The investigators identified eighteen main predictors of outcome. There were five delirium related predictors, two co-morbid psychiatric illness related predictors, eight patient related predictors and three biomarker related predictors. Among them the most frequently reported predictors for poor outcome were the increased duration of delirium, the hypoactive subtype, delirium severity and co-morbid dementia and depression. Other less frequently reported predictors of poor outcome were increased age, frailty, raised cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid (5-HIAA), reduced CSF acetylcholinesterase activity and reduced albumin levels.

Conclusions: The investigators found that longer duration of the episode of delirium, hypoactive subtype, greater severity of delirium episode and pre-existing comorbidity of dementia or depression are associated with worse outcomes in hospitalized older adults with delirium.

Punchline: Among the eighteen predictors that the investigators identified, duration of the delirium episode, a hypoactive subtype, greater delirium severity and pre-existing comorbidity with dementia or depression are predictors of poor outcome among older hospitalized individuals with delirium.

Rajesh Tampi, M.D.


Objectives: The investigators wanted to assess whether there is an increased incidence of antiparkinson drug prescription or the use of Parkinson disease (PD) diagnostic codes after
chronic lithium treatment when compared to chronic valproic acid or antidepressant use in older adults.

**Methods:** The investigators completed a retrospective cohort study where they evaluated the Ontario Drug Benefit database records data on all outpatient prescription claims that were paid for by the provincial drug benefit plan for all individuals ≥ 65 years in age. Diagnostic information was obtained from four databases including the Canadian Institute for Health Information Discharge Abstract Database, the National Ambulatory Care Reporting System, the Same-day Surgery database and the Ontario Health Insurance Plan physician billing database.

The investigators identified individuals who were ≥ 66 years in age who had been continuously treated for at least 1 year between April 1, 2002 and March 31, 2011 with one of the following drugs as a monotherapy: lithium, valproic acid or an antidepressant medication.

The outcomes were the start of a dopaminergic medication (levodopa or a dopamine agonist), the start of any antiparkinson drug (levodopa, dopamine agonists, anticholinergic medication, amantadine, monoamine oxidase B inhibitors), the start of any antiparkinson drug or a diagnostic code for PD and the start of any antiparkinson drug in the absence of a diagnostic code for PD.

The follow-up was continued until death, discontinuation of the medication, switching to or adding one of the other medications of interest, occurrence of the outcome of interest, new onset of seizures, start of palliative care, March 31, 2013 or 2 years after the start of follow-up, whichever came first.

**Results:** The investigators identified a total 1749 users of lithium, 1787 users of valproic acid and 285154 users of antidepressant. All these individuals had used the drug continuously in monotherapy for at least 1 year.

Among individuals with no previous antipsychotic use, individuals receiving lithium monotherapy had a higher incidence of dopaminergic drug use and a higher incidence of antiparkinson drug use or a parkinsonism diagnosis when compared to individuals receiving monotherapy with antidepressants.

There were no differences between the lithium monotherapy group when compared to the group receiving valproic acid monotherapy on the incidence of dopaminergic drug use, incidence of antiparkinson drug use or a parkinsonism diagnosis.

**Conclusions:** The investigators concluded that chronic lithium use is associated with an increased incidence of dopaminergic drug prescription, antiparkinson drug prescription and the use of PD diagnosis when compared with antidepressants among older adults.

**Punchline:** Increased prescription of dopaminergic or antiparkinson drugs may be an incorrect treatment of action tremors or the treatment of drug induced Parkinsonism.

**Rajesh Tampi, M.D.**


**Objectives:** The investigators wanted to study the rates of all-cause mortality among individuals with late life schizophrenia.
Methods:

The participants for this longitudinal study were individuals with a home address in the catchment area who were ≥ 60 years in age and had a DSM IV TR diagnosis of schizophrenia or schizoaffective disorder. The age at onset of the illness was defined as the youngest age at which in DSM-IV-TR criteria for the disorder were met. The level of education was dichotomized as the best primary education versus the least secondary education. The duration of illness, previous psychiatric admissions including compulsory admissions and the current prescription of antipsychotic medications were also noted. The investigators evaluated whether all the participants were alive or dead 5 years after study entry on January 1, 2013. The deaths were confirmed by death certificates and the cause of death was determined using the mental health organization database. When the data was indeterminate, the information was cross-checked with the general practitioners of the deceased participants. The causes of death were classified in accordance to the ICD 10 diagnostic criteria. The standardized mortality ratio (SMR) was calculated as the observed number of deaths divided by the expected number of deaths. The mortality rates of the general population in the catchment area were used as a comparator to the mortality rates in the study population.

Results: There were a total of 157 participants (44 men, 113 women) in the study sample. The mean age was 68.1 years. The mean age at onset of the disorder was 35.9 years. The mean duration of illness was 32.1 years. Approximately 81.4% of the participants had one or more psychiatric admissions. Antipsychotic medications were currently being prescribed to 76.4% of participants.

The census data indicated that 19.1% of the participants had died. The mean age at death was 73.0 years for men and 76.1 years for women. The participants had an all-cause SMR of 1.89. The SMR was 2.60 for men and 1.78 (95% CI: 1.02–2.90) for women. All the deaths were attributed to natural causes. The investigators found that the predictors for reduced survival were higher age, male gender and having had compulsory hospital admissions.

Conclusions: The investigators concluded that the all-cause mortality rates among individuals with late life schizophrenia are high especially among the men.

Punchline: This prospective study indicates that all-cause mortality rates among individuals with late life schizophrenia are high especially among men.
METROHEALTH EVIDENCE-BASED
PSYCHIATRY RESEARCH UPDATES

Department of Psychiatry
Resident Researchers
2015-2016

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