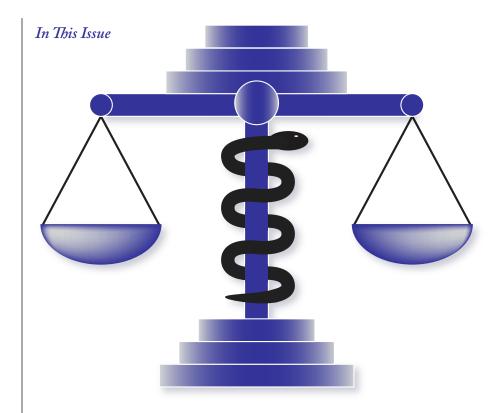


June 2013 Volume 8 Issue 6

Inside

- 2 Advancing to the Next Phase Monifa Seawell, M.D.
- 3 Duties to Warn and Protect in Current Psychiatric Practice Jacob M. Appel, M.D., J.D.
- 5 Psychopathy in Women: A Clinical and Diagnostic Update Alexis Mermigas, M.D. Jacqueline Landess, M.D.
- 7 Incorporating ACGME Core Competencies in Educational Curricula Deepak Prabhakar, M.D., M.P.H.
- 8 Traditional and Herbal Medications in the Treatment of Alzheimer's Disease John C. Wilson, M.D., Ph.D.
- 1 Mental Illness and Stigma: How Far Have We Come? Parnika P. Saxena, M.D.
- 12 A Different Theory of Relativity: Jungian Synchronicity Shannon L. Delaney, M.D.
- 14 Author Information
- 14 Upcoming Themes



This issue of the *Residents' Journal* features a section theme on forensic psychiatry. Jacob Appel, M.D., J.D., provides enlightening information on the duty to warn and protect in current psychiatric practice. Alexis Mermigas, M.D., and Jacqueline Landess, M.D., discuss the poorly understood concept of psychopathy in women, including clinical manifestations and comorbidities.

Editor-in-Chief Monifa Seawell, M.D. Senior Editor Sarah M. Fayad, M.D. Associate Editor

Arshya Vahabzadeh, M.D.

Guest Section Editor **Megan Testa, M.D.**

Editors Emeriti
Sarah B. Johnson, M.D.
Molly McVoy, M.D.
Joseph M. Cerimele, M.D.
Staff Editor
Angela Moore

Advancing to the Next Phase

Monifa Seawell, M.D. Editor-in-Chief

As this academic year comes to a close, many of us will be advancing on to the next level of training, while others will be concluding the journey as trainees and entering the workforce as early-career psychiatrists. On behalf of the *Residents' Journal* editorial staff, I wish you well as you move on to the next phase of your career path and hope you continue to use the *Residents' Journal* as one of your trusted educational resources.

For those of you who will be continuing your training, I strongly encourage you to become further involved with the *Residents' Journal* over the next academic year. The *Journal* remains strongly committed to the educational development of trainees and provides close guidance to trainees in order to maximize their individual potential as authors, editors, and peer reviewers. My coeditors and I can each personally attest to the *Journal's*

strong commitment to trainee development, as we each began our career at the *Journal* in the same position many of you are in: as readers of the *Journal*! We have many opportunities available and can assist you in identifying a way to become involved that is in line with your interests and professional goals.

We also regularly seek feedback from our readers in order to identify opportunities to further develop the *Journal*. In response to your comments and suggestions, we implemented the following changes over the past academic year:

- The Journal obtained a permanent webpage, which can be accessed through the American Journal of Psychiatry homepage (http://ajp.psychiatryonline. org/journal.aspx?journalid=13);
- We created a third editorial position on our editorial staff in order to meet

- the expanding needs of the *Journal* and the needs of the *Journals*' readership;
- The Journal established the annual Editor's Choice Award in order to recognize the trainee whose manuscript represents the most significant contribution to the Journal over the academic year; and
- We established a Facebook page, which serves as an additional means for trainees to access the *Journal* and engage in dialogue with other readers.

If you have questions on how you can become involved, or if you have further ideas on how the *Journal* can evolve, please contact us at ajp@psych.org.

It has been my pleasure serving as Editor-in-Chief, and I wish each of you much continued success.

Correction

In the article "Talking to Our Patients About DSM," by Monifa Seawell, M.D. (Am J Psychiatry Res J 2013; 5:2–3), it states that histrionic personality disorder is not included in DSM-5; however, histrionic personality disorder is included in DSM-5, Section II.

A corrected version of the article is posted online (in the May 2013 issue).

Duties to Warn and Protect in Current Psychiatric Practice

Jacob M. Appel, M.D., J.D.

Few areas of practice generate more confusion for psychiatric residents than do the rules governing duties toward third parties (1). Ever since the California Supreme Court decision in Tarasoff vs. Regents of the University of California (1974, reheard in 1976) established obligations for providers in that state, mental health practitioners have grappled with the extent of similar duties in their own jurisdictions either "to warn" or "to protect" potential victims from harm by violent patients (2). One significant impediment to understanding is the vast difference in the approaches adopted by various states through both judicial and legislative action over the past three and one-half decades; a review of these policies reveals several general principles that may prove helpful in guiding practice.

During the pre-Tarasoff era, the common law liability of outpatient physicians generally did not extend beyond patients and the close associates of patients with whom they had a special relationship. The California Supreme Court, widely regarded as a "progressive court" that "wanted to expand theories of law," radically broadened the duties of mental health providers in Tarasoff, a ruling whose name has come to be synonymous with obligations to third parties (3).

In 1969, Prosenjit Poddar, a 25-year-old East Indian graduate student, informed psychologist Lawrence Moore of plans to murder an unnamed woman, who Dr. Moore could easily identify as college student Tatiana Tarasoff. Dr. Moore reported the case to the police, recommending that his patient be detained under a 72-hour emergency hold, but the authorities released Poddar with only a warning. Poddar subsequently stabbed Tarasoff to death. Her survivors sued Moore and his employer, the University of California, under the then novel theory

that providers had a duty to warn third parties of potential dangers from patients under their care.

In a highly unusual turn of events, the California Supreme Court heard the Tarasoff case twice. In his initial opinion (Tarasoff I), Associate Justice Matthew Tobriner established a duty of mental health providers to warn identifiable third parties of dangerous patients. According to Tobriner, "If in the exercise of reasonable care the therapist can warn the endangered party or those who can reasonably be expected to notify him, we see no sufficient societal interest that would protect and justify concealment" (4). The importance of Tarasoff I lays in the court's conclusion that the need for therapistpatient confidentiality did not trump the public policy benefits of a legal duty toward potential victims. A wide swath of professionals in both mental health and law enforcement soon denounced the implications of the ruling, particularly its reliance on the premise that dangerousness was reasonably foreseeable (5). In response, the California Supreme Court reheard the case 2 years later. Rather than speaking solely of a duty to warn, in Tarasoff II, Tobriner established a duty to protect third parties: "The discharge of this duty may require the therapist to take one or more of various steps, depending upon the nature of the case. Thus it may call for him to warn the intended victim or others likely to apprise the victim of the danger, to notify the police, or to take whatever other steps are reasonably necessary under the circumstances" (6). In other words, warning was permissible, but neither always necessary nor always sufficient.

Following *Tarasoff*, a majority of states have adopted provisions requiring certain providers to either protect or warn third parties. However, individual state

statutes and court rulings differ in many respects, and thus providers need to ask (at a minimum) the following questions to determine their specific obligations: 1) Which providers are encompassed by a third-party duty? For instance, some states apply Tarasoff-like language only to mental health professionals, while others include all physicians. 2) What level of threat triggers the obligation? Most states specify a threat of violence to persons, but only some qualify that threat as "imminent." At least one state, New Hampshire, also requires protection of real property (see reference 7). 3) What class of individuals must be warned or protected? While some states require that a specific victim be easily identifiable, a federal district court in Connecticut in Almonte v. New York Medical College (1994) extended a duty to protect to all potential victims of a confessed pedophile (see reference 8). 4) Is the duty spelled out by state law mandatory, or is it merely permissive, shielding providers who do breach confidentiality from liability for doing so? Each jurisdiction answers these questions distinctively. This variation in state laws is of particular importance to trainees and early-career psychiatrists, whose career paths may require relocation across jurisdictional lines. Of note, in 1989, the American Psychiatric Association Council on Psychiatry and Law proposed a model "duty to protect" statute, but it has not been widely followed (9).

Residents should also be aware that multiple jurisdictions have rejected duties to third parties in various ways. At one extreme, the Supreme Court of Virginia in *Nasser v. Parker* (1995) embraced the principle that there is "no duty to control the conduct of third persons in order to prevent harm to another," barring the existence of a "special relationship" that the court found does not exist between ther-

apists and third-party victims (10). Left open is whether psychiatrists in Virginia who do breach confidentiality to warn or protect potential victims can then be sued by their patients for such a breach. At present, at least six other states (Arkansas, Kansas, Maine, Nevada, New Mexico, North Dakota) have no law overtly protecting such disclosures, while the rules in several other jurisdictions are not yet entirely clear (11). In addition, Louisiana treats cases in which failure to protect leads to injury as matters of general negligence, rather than professional negligence, because the provider is not deemed to have a fiduciary relationship with the third party. As a result, psychiatrists in these cases are not shielded by the protections of Louisiana's Medical Malpractice Act (3).

Of particular interest to trainees are "Tarasoff-limiting statutes" that protect providers from liability if they meet specific thresholds of care. Slovenko has dismissed such laws as "formalistic" and "not likely to be helpful" as mechanisms for reducing harm (3). Nonetheless, residents should be aware of any such limiting statutes applicable in their jurisdictions.

Walcott et al. (11) offer several suggestions to providers who confront cases involving duties to third parties. The authors emphasize the importance of treating third-party obligations "as primarily a clinical rather than a legal issue" and, when possible, of both informing the

patient of one's duties to third parties and involving the patient in the actual process of warning. They also emphasize the importance of revealing as little confidential information as necessary to achieve safety goals. For trainees concerned that breaches of confidentiality may jeopardize the therapeutic process, a survey of residents by Binder and McNeil (12) demonstrated that few trainees who issued Tarasoff-like warnings in Michigan saw a significant impact on provider-patient dynamics. At the same time, little evidence exists to demonstrate that the enactment of Tarasoff-like duties has in fact reduced danger to third parties. What remains beyond dispute is that the most fundamental protection available to residents is to familiarize themselves with the specific duties and limitations that apply in their own states.

Dr. Appel is a fourth-year resident in the Department of Psychiatry, Mount Sinai School of Medicine, New York.

References

- Kelso JD: No duty to warn of threats of violence: dispelling the myth in Texas jurisprudence. http://www.law.uh.edu/health law/perspectives/Tort/990917Thapar. html
- Tarasoff v Regents of University of California, 529 P2d 553 (Cal 1974); Tarasoff v Regents of University of California, 551 P2d 334 (Cal 1976)

- Slovenko R: Psychiatry in Law/Law in Psychiatry. New York, Routledge, 2009, pp, 691
- Tarasoff v. Regents of the University of California, 17 Cal 3d 425, 551 P2d 334, 131 Cal Rptr 14 (Cal 1976)
- 5. Hager P: Death threat warnings: some fear more harm than good: required warnings by therapists protested. Los Angeles Times, Dec 29, 1974, p 1
- 6. Herbert PB, Young KA: Tarasoff at twenty-five. Focus 2003; 1(4)
- 7. McCullough Lynda: A training analyst's dilemma: the limits of confidentiality. Psychiatric News, September 4, 1998
- 8. Reed DB: Therapist's duty to protect third parties: balancing public safety and patient confidentiality. Comm Health Report 2001; 1(5)
- 9. Nasser v Parker, 249 Va 172, March 3, 1995
- 10. Edwards GS: Doing Their Duty: An Empirical Analysis of the Unintended Effect of Tarasoff v Regents on Homicidal Activity (Emory Law and Economics Research Paper No. 10-61). http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1544574
- Walcott DM, Cerundolo P, Beck JC: Current analysis of the Tarasoff duty: an evolution towards the limitation of the duty to protect. Behav Sci Law 2001; 19:325–343
- 12. Binder RL, McNiel DE: Application of the Tarasoff ruling and its effect on the victim and the therapeutic relationship. Psychiatr Serv 1996; 47:1212–1215



If you will be completing your residency this year, we would like your help in recruiting new subscribers by encouraging an incoming resident or fellow to subscribe to our monthly e-publication. Also, if you'd like to continue receiving e-mail notification alerts when each issue of the AJP Residents' Journal is published, send your new e-mail address to ajp@psych.org with the subject line "New e-mail address post-residency."

Psychopathy in Women: A Clinical and Diagnostic Update

Alexis Mermigas, M.D. Jacqueline Landess, M.D.

Despite being frequently referenced by modern culture, psychopathy remains an often poorly understood concept. Diagnostically, it is frequently mistaken with antisocial personality disorder because of considerable symptom cross-over between the two; antisocial personality disorder does not account for the dysregulated interpersonal and affective components commonly found in individuals with psychopathy (Table 1). The difficulty of the diagnosis is compounded in female populations because this clinical phenomenon has primarily been studied in male populations (1). Nevertheless, disruptive and parasitic interpersonal behavior in women severely affects many aspects of their lives, including personal relationships and work-environment relationships. This article highlights the clinical manifestations of psychopathy and comorbid diagnosis across gender and the inherent challenges in the assessment of psychopathy in women, focusing specifically on the Psychopathy Checklist-Revised (PCL-R) as a diagnostic tool (2).

Clinical Manifestations and Comorbidities

Gender differences among individuals with psychopathy are apparent in childhood. While boys present with the classic symptoms of conduct disorder (1), girls tend to manifest with adolescent-onset conduct problems, including diverse antisocial behaviors, callousness, lack of emotionality, and dysregulated impulse control, which includes self-harm (3). Compared with boys, girls are less likely to engage physically and more likely to manifest verbal and relational aggression in the form of gossip and ostracism (1). Females with psychopathy are less likely to display glibness, superficial charm, and grandiosity and are more likely to be flirtatious and commit frauds and thefts more than violent crimes (4). Because psychopathy is classified as a personality disorder, predictably, the most common comorbid diagnoses among individuals of both genders with psychopathy tend to be other personality disorders, par-

ticularly antisocial personality disorder (5). However, women are frequently diagnosed with a myriad of cluster A and B disorders as well (6). While the prevalence of axis I diagnoses among women in a correctional setting is higher than that of the general population (7, 8), the precise prevalence of axis I disorders among women with psychopathy is unclear, although this population is thought to abuse substances at a higher rate than women who do not have psychopathy (5). In a therapeutic setting, women with psychopathy are more disruptive and nonadherent and have poorer response to treatment interventions (9).

In forensic settings, the diagnosis of psychopathy is used to predict the risk of criminal recidivism and institutional and societal violence. Future violence and recidivism are positively correlated with psychopathy, and the PCL-R has been used as a predictive instrument in male populations (1). Weizmann-Henelius et al. (10) found that among violent women, those who were recidivist were more likely to have been violent at a younger age and have personality disorders, psychopathy, or substance abuse, and their victims were less likely to be family members or friends, mirroring the pattern found in violent, recidivistic men. However, Salekin et al. (5) found that women with psychopathy were less likely to recidivate after release from incarceration compared with men, and the diagnosis of psychopathy was at best a modest predictor of recidivism. Women with psychopathy were only at slightly greater risk of recidivism compared with female offenders without psychopathy, barring the time period immediately after release from incarceration. Currently, the data indicate that violent female recidivists are more likely to display characteristics similar to those seen in their male counterparts, but the risk of recidivism and future violence is uncertain in less criminal populations.

TABLE 1. Diagnostic Criteria of Psychopathy Compared With Antisocial Personality Disorder

Psychopathy ^a	Antisocial Personality Disorderb	
Superficial charm	Failure to conform to social norms	
Grandiosity	Reckless disregard for safety of self and/or other	
Pathological lying	Pathological lying	
Manipulative	Impulsivity	
Lack of guilt/remorse	Lack of guilt/remorse	
Shallow affect	Irritability/aggression	
Lack of empathy	Consistent irresponsibility	
Failure to accept responsibility for actions	Conduct disorder before age 15	
Thrill seeking		
Parasitic lifestyle		
Lack of realistic goals		
Impulsivity		
Irresponsibleness		
Lack of behavioral control		
Early disregard for societal norms		
Criminal versatility		
Sexual promiscuity		
Multiple brief romantic relationships		

^a Data are from the Psychopathy Checklist–Revised (see reference 2).

^b Data are from DSM-IV-TR.

Assessment of Psychopathy

The PCL-R is considered the diagnostic gold standard for assessing psychopathy in forensic research settings. The 20-item checklist is scored on a 3-point scale and is subdivided into two factors. Factor 1 screens for dysfunctional affective and interpersonal experiences of an individual, such as guilt and/or remorse, callousness and/or lack of empathy, and shallow affect. Factor 2 screens for antisocial behaviors, such as juvenile delinquency and criminal versatility. The evaluation is based on a semistructured interview and file review. Scores greater than 30 (out of 40) indicate psychopathy. Often used to diagnose psychopathy in women, its use is somewhat controversial, especially for predictive purposes, since it has been validated primarily in white, male forensic populations (11).

Interestingly, the base rates of psychopathy among women are generally lower than the rates among men. Studies have found rates ranging from 11% to 23% in forensic populations, with higher rates in maximum-security settings (12). Few studies have examined rates within the community, but overall low rates, around 1%, have been reported for both men and women, with women routinely scoring lower than men on the PCL-R (11). These data beg the question, Are there simply fewer women with psychopathy, or are we failing to adequately detect them given the nature of our diagnostic instruments and conceptual understanding? Some theorize that "true" gender differences exist, making women less likely to express psychopathic traits (13). Alternatively, women may express antisocial behavior differently than their male counterparts and thus may not screen positive on the PCL-R or similar instruments. If women with psychopathy tend to engage in less violent or overt criminal behavior than their male counterparts, sampling bias can occur, since research and screening of psychopathy is typically done in a forensic setting. For example, Salekin et al. (14) found characteristic differences in expression of PCL-R items among women. The authors reported that factor 1 is "characterized by lack of empathy or guilt, interpersonal deception, proneness to boredom and sensation seeking," and factor 2 is characterized by "early behavioral problems, promiscuity, and adult antisocial behavior." These findings may necessitate a different approach to screening. For instance, an extensive history of physical violence would typically correspond with callousness on the PCL-R. In women, it would be important to look for alternative markers of callousness, including aberrant parenting, fraud, and deception, since these acts may occur more frequently than violence (15). As mentioned above, women may also display impulsivity differently than men, engaging in self-harm more frequently than harm toward others. Awareness of the differential gender expression of psychopathy is important in both screening and diagnosis.

While neuroradiology holds promise, no "smoking gun" has been produced regarding the neurobiological origins of psychopathy in general. Most studies have been performed in male or mixed populations and have found structural abnormalities in the superior temporal cortex, insula, and orbitofrontal cortex (16). Functional imaging has shown reduced amygdala and orbitofrontal cortex responses to reinforcement-based decision making tasks. This corresponds with the general difficulties persons with psychopathy have in aversive conditioning, instrumental learning, and processing fearfulness and sadness in others (16).

Conclusions

Despite advancements, psychopathy in women remains an under-researched concept. Given the divergent gender response patterns on the PCL-R, such tools should be used cautiously while diagnosing psychopathy and assessing recidivism and violence risk in women, particularly in less criminal populations.

Dr. Mermigas is a forensic psychiatry fellow at Northwestern Memorial Hospital, Chicago. Dr. Landess is a third-year resident at Northwestern Memorial Hospital, Chicago.

References

- 1. Patrick C: Handbook of Psychopathy. New York, Guilford Press, 2006
- Hare RD: Manual for the Hare Psychopathy Checklist–Revised, 2nd ed. Toronto, Multi-Health System, 2003
- 3. Silverthorn P, Frick PJ, Reynolds R: Timing

- of onset and correlates of severe problems in adjudicated girls and boys. J Psychopathol Behav Assess 2001; 23:171–181
- Forouzan E, Cooke DJ: Figuring out la femme fatale: conceptual and assessment issues concerning psychopathy in females. Behav Sci Law 2005; 23:765–778
- Salekin RT, Rogers R, Ustad KL, Sewell KW: Psychopathy and recidivism among female inmates. Law Hum Behav 1998; 33: 109–128
- Sprague J, Javdani S, Sadeh N, Newman JP, Verona E: Borderline personality disorder as a female phenotypic expression of psychopathy? Personal Disord 2012; 3:127–139
- 7. Daniel AE, Robins AJ, Reid JC, Wilfley DE: Lifetime and six-month prevalence of psychiatric disorders among sentenced female offenders. Bull Am Acad Psychiatry Law 1988; 16:333–342
- 8. Diamond P, Wang EW, Holzer CE 3rd, Thomas C, des Anges Cruser: The prevalence of mental illness in prison. Admin Policy Ment Health 2001; 29:21–40
- Richards H, Casey J, Lucent S: Psychopathy and treatment response in incarcerated female substance abusers. Crim Justice Behav 2003; 30: 251–276
- Weizmann-Henelius G, Viemero V, Eronen M: Psychological risk markers in violent female behavior. Int J Foren Ment Health 2004; 3:185–196
- 11. Nicholls TL, Ogloff JR, Brink J, Spidel A: Psychopathy in women: a review of its clinical usefulness for assessing risk for aggression and criminality. Behav Sci Law 2005; 23:779–802
- 12. Vitale JE, Newman JP: Using the Psychopathy Checklist–Revised with female samples: reliability, validity, and implications for clinical utility. Clin Psychol Sci Pract 2001; 8:117–132
- Rutter M, Caspi A, Moffitt TE: Using sex differences in psychopathology to study causal mechanisms: unifying issues and research strategies. J Child Psychol Psychiatry 2003; 44:1092–1115
- 14. Salekin RT, Rogers R, Sewell KW: Construct validity of psychopathy in a female offender sample: a multitrait-multimethod evaluation. J Abnorm Psychol 1997; 106: 576–585
- 15. Dolan M, Völlm B: Antisocial personality disorder and psychopathy in women: a literature review on the reliability and validity of assessment instruments. Int J Law Psychiatry 2009; 32: 2–9
- Blair J: Neuroimaging of psychopathy and antisocial behavior: a targeted review. Curr Psychiatry Rep 2010; 12:76–82

Incorporating ACGME Core Competencies in Educational Curricula

Deepak Prabhakar, M.D., M.P.H.

With the introduction of the Outcome Project, the Accreditation Council for Graduate Medical Education (ACGME) emphasized six core competencies for the purpose of continued evaluation and accreditation of training programs in the United States (1, 2). Educational modules, such as the use of clinical vignettes, to teach ACGME competencies can effectively teach residents core educational principles while conveying important aspects of how to deliver high-quality patient care. The following is an example of an ACGME competency-based alternative learning exercise for education in psychiatry.

Clinical Vignette

An on-call resident is consulted to evaluate a patient who is a graduate student

at the same institution. The patient presents with a depressed mood and recurrent thoughts of suicide. The resident checks the patient's chart and finds that there are no laboratory results or past medical records to review. A routine physical examination reveals no abnormalities. The patient states that he is receiving fluoxetine, as prescribed by his primary care provider. The resident does not believe that it is necessary to further explore the patient's psychiatric history and assumes that because the patient is a high-functioning graduate student, he would know to reveal any pertinent information about his background. Without obtaining a further history, the resident prescribes the patient bupropion and admits him to the inpatient psychiatry unit. The next day, the patient begins actively hallucinating. Further history provided by the patient's family reveals that he has a long history of regular and heavy alcohol use.

Using Clinical Vignettes to Teach ACGME Educational Competencies

Vignettes such as the one above can be used to help teach residents ACGME core competencies. The complexity of these case scenarios can be modified according to the educational needs of the intended audience. Table 1 illustrates how the above vignette could be paired with focused questions to help residents further their understanding of the ACGME core competencies.

Conclusions

Vignettes such as the one above can be used to help residents understand ACGME core competencies. By dissecting the vignettes and having residents critically analyze them, residents will be able to develop the skills necessary to apply the competencies to their practice of medicine, as well as to attain competency.

Dr. Prabhakar is a second-year child and adolescent psychiatry fellow in the Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit.

TABLE 1. Questions to Further Residents' Understanding of ACGME Core Competencies

ACGME Core Competency #1: Patient Care

Was appropriate patient care provided in this scenario?

How did the resident's preconceived notions about the patient affect the care the patient received?

ACGME Core Competency #2: Medical Knowledge

What types of mental health issues are frequently seen among college students?

What may have caused the patient's psychosis?

ACGME Core Competency #3: Interpersonal and Communication Skills

Comment on the necessity of obtaining collateral information in this case.

How would you communicate with ancillary services to ensure appropriate level of care?

ACGME Core Competency #4: Professionalism

The resident assumed that the patient's high level of education meant that he would reveal all the necessary information. How might this bias affect how others perceive the resident's level of professionalism?

Acgme Core Competency #5: System-Based Practice

Would you recommend that this patient be admitted to a medical floor with psychiatric follow-up? Do students at your institution have access to campus-based psychiatric services?

ACGME Core Competency #6: Practice-Based Learning And Improvement

What have you learned from this case?

Are there any different steps or additional steps that you would take in managing this patient or similar types of patients in the future?

References

- Swing SR, Clyman SG, Holmboe ES, Williams RG: Advancing resident assessment in graduate medical education. J Grad Med Educ 2009; 1:278–286
- 2. Batalden P, Leach D, Swing S, Dreyfus H, Dreyfus S: General competencies and accreditation in graduate medical education. Health Affairs 2002; 21:103–11

Traditional and Herbal Medications in the Treatment of Alzheimer's Disease

John C. Wilson, M.D., Ph.D.

Alzheimer's disease is the most common form of dementia, accounting for approximately 60%–80% of all cases of dementia (1). An estimated 5.4 million individuals in the United States live with Alzheimer's disease (as of 2011), with 45% of these persons being 85 years old or above. With the current increases in life expectancy and the ageing of the baby-boomer generation, it is anticipated that there will be a substantial increase in the number of people affected by Alzheimer's disease in the decades to come.

Alzheimer's disease is manifested by irreversible, progressive cognitive and functional decline, with memory loss as one of the primary cognitive complaints. Unfortunately, no disease-modifying therapies capable of halting the progression of Alzheimer's disease are yet available in clinical practice. Currently, there are five medications approved by the Food and Drug Administration (FDA) to treat Alzheimer's disease; four of these are cholinesterase inhibitors (donepezil, galantamine, rivastigmine, and tacrine), and one is an N-methyl-D-aspartic acidreceptor antagonist (memantine). In clinical studies, these drugs have been shown to have a small, temporary benefit on cognition, although they do not have a significant effect on disease progression

With this limited effect of pharmaceutical treatments, Alzheimer's disease remains a chronic, progressive disease. As in many other such illnesses, patients frequently use complementary and alternative therapies to improve their health (3, 4). Although there are a variety of complementary and alternative therapies under study for treatment of Alzheimer's disease, the vast majority of the research literature is concerned with the use of herbal medicines and foods. This appears to reflect the usage patterns of patients (3,

4), although there is little published data to directly support this issue.

The number of traditional and herbal therapies used to treat Alzheimer's disease are too great to be discussed here. A PubMed search of Alzheimer's and traditional or herbal returns more than 1,000 citations. However, three therapies curcumin, Ginkgo biloba, and huperzine A—account for more than one-half of these published studies. Therefore, the present review focuses on these three therapies. Studies related to these specific therapies are reviewed, and key aspects of current knowledge related to biological mechanisms, clinical effects, and concerns over potential adverse effects are summarized.

Curcumin

Curcumin is the principal pigment of turmeric and responsible for both the yellow color and medicinal properties of the spice. It has long played a role in not only Asian cooking but also Ayurvedic medicine. First isolated from natural sources in the early 19th century, curcumin has been the subject of scientific research for 200 years (5). It is known to have several dozen molecular targets and functions both as an antioxidant and as an inducer of a large number of genes, including cellular enzymes and transcription factors (5). With this wide array of actions, curcumin has been studied as a potential therapy for many diseases. The initial consideration of curcumin as a potential protective agent against Alzheimer's disease was based on epidemiological data that showed a lower rate of the disease in India, where turmeric is a common cooking ingredient, compared with the rates in the United States (6). Preclinical studies have demonstrated that dietary curcumin is able to reduce inflammation and oxidative

brain damage and accelerate clearance of beta-amyloid deposits (7). Only a limited number of clinical trials using curcumin have been conducted in humans, and relatively few patients have been enrolled in these studies (8). However, to date, completed clinical studies have not found that curcumin provides any cognitive benefit in patients with Alzheimer's disease (7, 8). There is some disagreement about the clinical significance of adverse effects reported in clinical trials (7,8), but these are mostly benign gastrointestinal symptoms, particularly diarrhea (Table 1). It is also noted that curcumin is an inhibitor of CYP3A4, which can alter serum levels of medications metabolized by this enzyme; two key drugs in this group are donepezil and galantamine, both used for the treatment of Alzheimer's disease.

Ginkgo Biloba

Ginkgo biloba is a "living fossil" found in central China. Extracts from Ginkgo biloba include a large number of bioactive compounds, most importantly flavonolglycosides and terpene-lactones. Like curcumin, Ginkgo biloba extracts are able to inhibit aggregation of Alzheimer's disease and function as antioxidants. These extracts are some of the most commonly used among all herbal remedies for dementia (9). Despite this, there remains considerable controversy over whether Ginkgo biloba is of benefit (7, 9). A metaanalysis showed that there were moderate benefits from the use of Ginkgo biloba in cognitive domains and in maintenance of activities of daily living among patients with Alzheimer's disease (9). This is in contradiction to a Cochrane review, which reported that the evidence supporting the use of Ginkgo biloba in the treatment of dementia and cognitive impairment is "inconsistent and unreliable" (10). Weinmann et al. (9) reported that

TABLE 1. Biological Mechanisms and Clinical Effects of Complementary and Alternative Therapies for Alzheimer's Disease

Therapy	Mechanism of Action	Adverse Effects	Drug Interactions	Level of Evidence to Support Use
Curcumin	Decreased inflammation; increased clearance beta-amyloid	Mild gastrointestinal effects	Many, through CYP3A4 inhibition; donepezil and galantamine are no- table for use in Alzheimer's disease	Level D ^a
Ginkgo biloba	Decreased inflammation; increased clearance beta-amyloid	Increased risk of seizures	Warfarin and aspirin, resulting in potential for clinically significant bleeding; may also decrease effect of certain antihypertensives	Level I ^b
Huperzine A	Acetylcholinesterase inhibitor	Dizziness	Little known, although presumed additive effects with other cholinesterase inhibitors	Level I ^b

^a The U.S. Preventive Services Task Force recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits (16).

this contradiction relates to their own analysis of dementia only, compared with the Cochrane review, which included studies of cognitive impairment not meeting criteria for dementia. Ginkgo biloba is generally safe when taken at daily doses used in these clinical trials (10), but it does have a significant number of drugdrug interactions. The most significant of these interactions is with warfarin (in particular) and aspirin. The Ginkgo biloba extracts used clinically have antiplatelet activity of their own and may also exert a pharmacokinetic effect through CYP enzyme activity modulation (Table 1). A number of reports of clinically significant bleeding events associated with the use of Ginkgo biloba have been published (11). Alterations in CYP enzyme activity are also thought to be responsible for Ginkgo biloba's reported interaction with antihypertensives; it has been reported that use of this herbal medication has decreased the effectiveness of both thiazides and nicardipine (11). In addition, Ginkgo biloba has the potential to increase the risk of seizures and is therefore considered dangerous in combination with other medications known to lower the seizure threshold (11).

Huperzine A

Huperzine A is a sesquiterpene alkaloid isolated from *Huperzia serrata*. It is a traditional medicine in China and is currently approved in China for the treatment of Alzheimer's disease (12).

Its primary mechanism of action is believed to be as a cholinesterase inhibitor. Interestingly, huperzine A has greater specificity for inhibition of acetylcholinesterase (found in mammalian brains) than the related enzyme butyrylcholinesterase (which is found peripherally) (12). In fact, it appears that huperzine A is both more potent a cholinesterase inhibitor and associated with fewer adverse effects than current FDA-approved medications for treatment of Alzheimer's disease (13). Clinical trials of huperzine A, however, have yielded mixed results. A Cochrane review on the benefits of huperzine A in treating Alzheimer's disease found that "huperzine A significantly improves global cognitive function" as measured by the Mini-Mental Status Examination and the Alzheimer's Disease Assessment Scale-Cognitive subscale, but the review also noted that this conclusion is based on studies that had significant methodological limitations (14). Additionally, all of the clinical trials that met inclusion criteria for the Cochrane review were conducted in China, and the authors of the review noted that this limited the generalizability of their conclusions. Additionally, a phase II clinical trial conducted in the United States, subsequent to the above reviews, found that a routine dosage of huperzine A (200 µg/twice daily) did not show significant benefit in patients with Alzheimer's disease as measured by scores on the Alzheimer's Disease Assessment Scale-Cognitive subscale after 16 weeks of treatment (15). A secondary

analysis found that a higher dosage (400 µg/twice daily) did provide some benefit after 11 and 16 weeks of treatment, but no further dose dependence of benefit was established. Most studies reported either no significant adverse effects or mild and transient effects, although there were some reports of dizziness (13). There is little published data on known interactions between huperzine and other medications. However, given its anticholinesterase activity, it is presumed that it may interact with other medications that modulate cholinergic signaling (Table 1).

Conclusions

While a large number of traditional and herbal medicines are used in the treatment of cognitive decline in general, and in Alzheimer's disease in particular, there remains relatively little research in this area. Many of these treatments show some promise, especially since early scientific studies have found biological activities that can be plausibly linked to the development or progression of Alzheimer's disease. However, clinical trials have frequently been criticized for poor methodology, making it difficult to draw definitive conclusions from available data. While there is some hope that these therapies make a positive impact, it is not yet appropriate to generally recommend them in the clinical setting. What is appropriate is to inquire about what traditional and herbal therapies patients are taking. Although it is widely believed that

b The U.S. Preventive Services Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined (16).

these treatments are generally benign, there are important adverse effects, about which patients and their caregivers must be cautioned. Particularly important are interactions with other common medications patients may be taking. Given the limited benefit that FDA-approved medications provide to patients with Alzheimer's disease, it is tempting to pursue other therapies in search of a better response. While this may be reasonable in some cases, clinicians should be aware of the general lack of scientific data on these therapies.

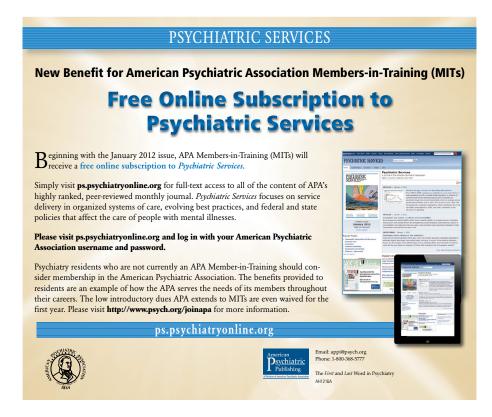
Dr. Wilson is a third-year psychiatry resident, in the Department of Psychiatry, Oregon Health and Science University, Portland, Ore.

References

- Alzheimer's Association: 2012 Alzheimer's disease facts and figures. Alzheimers Dement 2012; 8:131–168
- Hansen RA, Gartlehner G, Lohr KN, Kaufer DI: Functional outcomes of drug treatment in Alzheimer's disease. Drugs Aging 2007; 24:155–167
- 3. Dhikav V, Anand KS: Complementary and alternative medicine usage among Al-

- zheimer's disease patients. Int Psychogeriatr 2012; 24:1361–1362
- Coleman LM, Fowler LL, Williams ME: Use of unproven therapies by people with Alzheimer's disease. J Am Geriatr Soc 1995; 43:747–750
- Grynkiewicz G, Ślifirski P: Curcumin and curcuminoids in quest for medicinal status. Acta Biochim Pol 2012; 59:201–212
- Ganguli M, Chandra V, Kamboh MI, Johnston JM, Dodge HH, Thelma BK, Juyal RC, Pandav R, Belle SH, DeKosky ST: Apolipoprotein E polymorphism and Alzheimer disease: the Indo-US Cross-National Dementia Study. Arch Neurol 2000; 57:824–830
- Mancuso C, Siciliano R, Barone E, Preziosi P: Natural substances and Alzheimer's disease: from preclinical studies to evidence based medicine. Biochim Biophys Acta2012; 1822:616–624
- 8. Hamaguchi T, Ono K, Yamada M: Curcumin and Alzheimer's disease. CNS Neurosci Ther 2010; 16:285–297
- Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN: Effects of Gingko biloba in dementia: systematic review and meta-analysis. BMC Geriatr 2010; 10:14
- 10. Birks J, Grimley-Evans J: Ginkgo biloba for cognitive impairment and dementia.

- Cochrane Database Syst Rev 2009; 1:CD003120
- 11. Hu Z, Yang X, Ho PCL, Chan SY, Heng PWS, Chan E, Duan W, Koh HL, Zhou S: Herb-drug interactions. Drugs 2005; 65:1239–1282
- 12. Ha GT, Wong RK, Zhang Y: Huperzine A as a potential treatment of Alzheimer's disease: an assessment on chemistry, pharmacology, and clinical studies. Chem Biodivers; 8:836–842
- 13. Desilets AR, Gickas JJ, Dunican KC: Role of hyperzine A in the treatment of Alzheimer's disease. Ann Pharmacother 2009; 43:514–518
- Li J, Wu HM, Zhou RL, Liu GJ, Dong BR: Huperzine A for Alzheimer's disease. Cochrane Database Syst Rev 2008; 2:CD005592
- 15. Rafii MS, Walsh S, Little JT, Behan K, Reynolds B, Ward C, Jin S, Thomas R, Aisen PS, for the Alzheimer's Disease Cooperative Study: A phase II trial of huperzine A in mild to moderate Alzheimer disease. Neurology 2011; 76:1389–1394
- 16. US Preventive Services Task Force: US Preventive Services Task Force Grade Definitions. Rockville, Md, US Preventive Services Task Force, 2008 http://www.us-preventiveservicestaskforce.org/uspstf/grades.htm (Accessed March 2013)



Introspection

Mental Illness and Stigma: How Far Have We Come?

Parnika P. Saxena, M.D.

Mental illness has fascinated and frightened human beings since time immemorial, and patients with such illnesses are usually shunned and marginalized. While significant progress has been made in the diagnosis and treatment of mental illnesses, the deeply etched bias and stigma continue to remain. Fear of stigma can worsen the condition of such patients, leading to isolation, which is dehumanizing. As an international medical graduate, I have found that stigma crosses boundaries, cultures, and religions.

As a medical student in India, when I expressed my wish to specialize in psychiatry, my family and friends were apprehensive. They were concerned that I might be entering a field that is "a lost cause" and nonscientific. It was even relegated to quackery by some who believed that I would be an embarrassment to my family. I was astonished by how unaware even most nonpsychiatric physicians were about the treatment opportunities and prognoses for patients with psychiatric illness. However, I assumed that I was experiencing the environmental and cultural ignorance of mental illness.

I am now a resident in a psychiatry program in an inner city hospital in the

United States, and I am surprised to meet patients who have been abandoned by their families because of the fear of being stigmatized by society. This reinforces the fact that stigma is not topographical. As someone who has experienced societal concerns about my choice of specialty, I can appreciate how stigma can affect a human being. That said, even I am not immune to having biases. For example, when I evaluate a patient in the emergency department who is much larger than me and has a history of a psychotic illness, I automatically keep my distance from the patient when interviewing because I have a "gut" fear about my safety.

I have also realized that stigma is universal and may be prevalent even among health care professionals. I have observed that when patients with mental illness are medically hospitalized (for nonpsychiatric reasons), they are often assigned to a one-to-one observation without regard for the current severity of illness or lack of necessity of this level of care. This different approach is exclusive to psychiatric illness. Such attitudes need to be remedied.

I believe that communication with our patients' families, as well as with our fel-

low health care providers, is necessary to address these beliefs and concerns and may hold the key to changing the biased attitudes toward and stigma against those with mental illness. In the few instances that I've been able to convey this to the patient's family, I have witnessed remarkable improvement in the prognosis of the patient.

As mental health providers, we are in a unique role to advocate for our patients and to help stamp out the stigma that unfortunately continues to surround mental illness

Dr. Saxena is a first-year resident in the Department of Psychiatry, St Elizabeth's Medical Center, Brighton, Mass.

The author thanks Dr. Chitra Malur, Chair, Department of Psychiatry, St. Elizabeth's Medical Center, Brighton, Mass.

For further information related to the topic of stigma in mental illness, see the following articles recently published in Psychiatric Services: "Workplace Antistigma Initiatives: A Scoping Study," "Challenging the Public Stigma of Mental Illness: A Meta-Analysis of Outcome Studies," and "Empirical Studies of Self-Stigma Reduction Strategies: A Critical Review of the Literature."

Perspective

A Different Theory of Relativity: Jungian Synchronicity

Shannon L. Delaney, M.D.

My morning begins with my long-term therapy patient—a bright and smiling 19-year-old man who recently had his first episode of severe psychosis early last spring during his freshman year of college. Our conversation reverberates with similar themes, and I do my weekly check-in about his "superconnections, a term that he first coined to describe what happens when his thinking becomes riddled with too many connections. For example, during his first inpatient psychiatric hospitalization, he felt that every time he watched ESPN, the broadcasters were referencing him when giving the sports report. Since being maintained on olanzapine, my young patient no longer has difficulty watching ESPN and reports no current superconnections.

The next hour begins with a new therapy patient—a pleasant and intelligent 50-year-old high-functioning woman who carries the diagnosis of schizoaffective disorder—discussing some of her more subtle experiences in the past with psychotic thinking, for which she describes as "noticing coincidences." As she is talking, my mind meanders to my own predilection for observing coincidence and to one of my favorite subject matters: Jung's psychology of synchronicity.

Carl Jung originally coined synchronicity to describe meaningful coincidences of events separated in space and/or time and the meanings of patterns. Jung believed that life is not a random collection of events, but rather that life is governed by a deeper order and meaning. Jung was thinking about the nature of synchronicity around the time that Einstein was developing his theory of relativity and

believed that synchronicity serves a role similar to that of dreams, to shift a person's egocentric conscious thinking to greater wholeness.

I fondly recall one of my medical school experiences with synchronicity. I was sitting in my yard taking a break from studying and contemplating going to get my camera to take pictures of the trees that were filled with cherry blossoms. Moments after having that thought, I received a package in the mail from a friend, who had sent me a framed picture of cherry blossoms! I stood in awe and wondered whether this was just a chance occurrence or a representation of Jungian synchronicity. Did it prove that neutrinos were faster than the U.S. postal service? Did my friend and I just dance with intellectual intuition, or even scarier, for a brief second, did we tap into the abyss of the collective unconscious?

The truly rational mind may argue that my experience demonstrates a self-created idea of significance and exemplifies the principle of confirmation bias, pointing out the fact that I have thought about cherry blossoms hundreds of times in my life, and only once did this correspond with receiving my thought "framed," a mere coincidence and nothing more. Or maybe this was merely a reflection of Littlewood's Law, a law formulated by Cambridge University mathematics professor Littlewood to describe his theory that based on probability and the number of experiences we encounter on a daily basis, we are bound to experience a miracle (deemed something of special significance that occurs one in a million times) about every 35 days.

Mental illness represents a brain biology gone awry, but why does it frequently infuse the psyche with superconnections and notions of greater meaning? So frequently do we see religious and governmental delusions in disorders, such as schizophrenia and bipolar disorder, with grandiosity exemplifying the more positive amplifications of meaning and paranoia representing the more negative representations. Some could argue that religion itself is a collective example of superconnections: the Mormon tablets, the cross, the crescent moon, all important religious symbols representing ideas that give us a greater sense of connectedness. Whatever the nature of human experience, it is clear that human beings are "meaning makers."

Although we frequently see the negative and heart-wrenching effects of mental illness, we also cannot deny the moments of truth that sing true or the increased creativity that accompanies so many plagued by illness. As neurobiology advances, we likely can expect science to give us more answers about our illnesses, but also about our humanity. However, it is likely that even as we learn more about the neurobiological underpinnings of synchronicity and superconnections, our psychological selves will still largely remain a mystery, and maybe that is best for our making of meaning.

Dr. Delaney is a first-year fellow in the Department of Psychiatry, New York-Presbyterian University Hospital of Columbia and Cornell, New York.



In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions. (answers will appear in the next issue)

In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions (answers will appear in the next issue).

This month's questions are courtesy of Venkata B. Kolli, M.D., a third-year resident at Creighton-Nebraska Psychiatry Residency Training Program, Nebraska Medical Center, Omaha, Neb.

Question 1.

A 25-year-old male patient with posttraumatic stress disorder (PTSD) is treated with sertraline. His PTSD symptoms improve, but he reports new-onset loss of motivation and interest in activity. He denies low mood or feelings of hopelessness or worthlessness. What is the likely explanation?

- A. Antidepressant-induced apathy
- B. Residual depressive symptoms
- C. Dysthymia over PTSD
- D. Relapse of a depressive episode

Question 2.

Which of the following antidepressants has the least propensity to cause hyperprolactinemia?

- A. Citalopram
- B. Clomipramine
- C. Mirtazapine
- D. Venlafaxine

ANSWERS TO MAY QUESTIONS

Question #1.

Answer: D. DSM-III

The American Psychiatric Association first added posttraumatic stress disorder (PTSD) to the third edition of DSM in 1980 (1). Revisions to the diagnostic criteria were made in DSM-III-R (in 1987), DSM-IV (in 1994), and DSM-IV-TR (in 2000). DSM-II did not contain PTSD as a diagnosis.

Reference

1. Turnbull G: A review of post-traumatic stress disorder, part I: historical development and classification. Injury 1998; 29:87-91

Question #2.

Answer: B. Ataque de nervios

Ataque de nervios, an idiom of distress, is recognized among many Latin American, Latin Mediterranean, and Latin Caribbean groups. In addition to uncontrollable shouting, attacks of crying, trembling, sensations of heat, and verbal or physical aggression, this syndrome may also be associated with dissociative experiences, seizure-like or fainting episodes, suicidal gestures, amnesia of an event, and a rapid return to normal functioning. This syndrome is distinguished from panic disorder by the absence of acute fear or apprehension and by the association of most ataques with a defined precipitant.

Reference

2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Washington, DC, American Psychiatric Publishing, 2000

We are currently seeking residents who are interested in submitting Board-style questions to appear in the Test Your Knowledge feature. Selected residents will receive acknowledgment in the issue in which their questions are featured. Submissions should include the following:

1. Two to three Board review-style questions with four to five answer choices.

2. Answers should be complete and include detailed explanations with references from pertinent peer-reviewed journals, textbooks, or reference manuals. *Please direct all inquiries and submissions to Dr. Vahabzadeh: arshya.vahabzadeh@emory.edu.

Author Information for The Residents' Journal Submissions

The Residents' Journal accepts manuscripts authored by medical students, resident physicians, and fellows; manuscripts authored by members of faculty cannot be accepted. To submit a manuscript, please visit http://mc.manuscriptcentral.com/appi-ajp, and select "Residents" in the manuscript type field.

- 1. **Commentary:** Generally includes descriptions of recent events, opinion pieces, or narratives. Limited to 500 words and five references.
- 2. Treatment in Psychiatry: This article type begins with a brief, common clinical vignette and involves a description of the evaluation and management of a clinical scenario that house officers frequently encounter. This article type should also include 2-4 multiple choice questions based on the article's content. Limited to 1,500 words, 15 references, and one figure.
- **3. Clinical Case Conference:** A presentation and discussion of an unusual clinical event. Limited to 1,250 words, 10 references, and one figure.
- **4. Original Research:** Reports of novel observations and research. Limited to 1,250 words, 10 references, and two figures.
- **5. Review Article:** A clinically relevant review focused on educating the resident physician. Limited to 1,500 words, 20 references, and one figure.
- **6. Letters to the Editor:** Limited to 250 words (including 3 references) and three authors. Comments on articles published in *The Residents' Journal* will be considered for publication if received within 1 month of publication of the original article.
- **7. Book Review:** Limited to 500 words and 3 references.

Abstracts: Articles should not include an abstract.

Upcoming Themes

Please note that we will consider articles outside of the theme.

Geriatric Psychiatry

If you have a submission related to this theme, contact the Section Editor
David Hsu, M.D. (david.hsu@ucdmc.ucdavis.edu).

Global Psychiatry

If you have a submission related to this theme, contact the Section Editor
Misty Richards, M.D., M.S.
(mcrichards@mednet.ucla.edu).

The end of your psychiatric residency is coming up are you ready to land that perfect job?

Are you a 3rd year resident who wants to get started early?

Let APA JobCentral help!

APA JobCentral, the job board for the American Psychiatric Association can help you ready yourself for the most important search of your career—that FIRST job. Whether it be a group practice, private practice, or hospital-based work environment you seek, JobCentral has over 1,200 open positions. You can search our jobs by location, position type, keyword, and work setting.



How do I get started?

Simply visit **Jobs.psychiatry.org** and take control of your future.

Registration is free.

With a job-seeker account you can create a career profile, upload your resume, and search particular employers' open positions. If you are planning on attending the 2013 APA Annual Meeting, you will have the ability to flag your resume for meeting attendees to view. On-site interviews can be arranged.

Have a specific location/specialty you're searching for?

Set up a job alert and be notified immediately when a position is posted with your desired criteria.

Keep your resume on top of the others!

Use our free resume upgrade code FREERES100, while logged into your job-seeker profile to push your resume to the top of the screen.

For more information please contact:

Eamon Wood • 212-904-0363 • Ewood@pminy.com



