Seizure Presentation Varies by Age, Related Injury

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SAN JUAN, P.R. — Seizures in older adults have a different presentation than they do in younger patients, with these events resembling many other conditions and making diagnosis difficult, but there are a few keys that can help make the right diagnosis, said one expert speaking at the annual meeting of the American Association for Geriatric Psychiatry.

Seizures in older adults often are a by-product of stroke and/or hemorrhage, said Dr. Joseph I. Sirven, of the department of neurology at the Mayo Clinic in Phoenix, Arizona, who spoke from anecdotal experience. In addition, neurodegenerative conditions, such as dementia, also cause problems that lead to seizures.

In general, partial seizures are most commonly seen in older adults because there is a specific area of injury or damage involved, said Dr. Sirven. In older adults, the foci of seizures usually occur in the frontal or parietal lobes.

"We also know that simple partial seizures, in which there is not a loss of consciousness, tend to have more focal and/or sensory symptoms [such as] tremor or a sense of numbness," said Dr. Sirven. Auras—primarily dizziness—may also be present. Complex partial seizures often present with altered mental activity, staring, blackouts, and confusion.

The key to seizure recognition is episodic frequency of symptoms that are stereotypic. In particular, episodes may present with loss of consciousness, dizziness, confusion, or language change. "If you see transient episodes of certain behaviors that are stereotypic, the first test really is the EEG," said Dr. Sirven. Other diagnostic tests to consider include MRI, laboratory tests, cardiovascular testing, ambulatory EKG, and tilt table testing.

Seizure medication should be considered only if the seizures are truly impacting the patient's quality of life. "Why I'm making a big deal about it is that the moment you start someone on seizure medication … you've branded that person and no one down the road is going to stop that medication," said Dr. Sirven.

He listed three points to consider in choosing a seizure drug for an older patient:

▶ **Efficacy.** Try to use monotherapy whenever possible. Choose a medication that is appropriate for the seizure type. If the seizure type is unspecified, choose a broad-spectrum agent.

▶ **Safety and tolerability.** First, minimize drug interactions. In addition, choose a drug with a favorable safety profile that minimizes the inhibition of cognitive function and has a minimal effect on gait, balance, and orthostatic blood pressure.

▶ **Simplification.** Once-daily dosing helps with patient compliance. Choose a drug with a quick onset of action. Reduce interacting drugs, especially psychoactive ones. ■

Metabolic Dx Predicts Frailty In the Elderly

SAN FRANCISCO — Elderly individuals who have metabolic syndrome are about twice as likely to become frail as those who are healthy, Dr. Joshua I. Barzilay reported in a poster presentation at the Third World Congress on Insulin Resistance Syndrome.

The study involved 2,376 individuals aged 69-74 who were followed prospectively for 7-9 years. At baseline none of the participants were frail, nor did they have other illnesses that increase inflammation markers or mimic frailty, reported Dr. Barzilay, of Emory University, Atlanta, and his colleagues.

At the end of follow-up, 169 participants qualified as frail and another 1,082 qualified as prefrail. The three most commonly seen components of frailty were diminished walking speed, diminished strength, and diminished activity, all of which are consistent with sarcopenia.

Participants who developed frailty or prefrailty had significantly higher fasting insulin levels, higher white blood cell counts, higher C-reactive protein levels, and higher factor VII levels than those who didn't.

Participants were 30%-100% more likely to have metabolic syndrome at baseline, compared with those who did not develop frailty or prefrailty.

—Robert Finn

4. An addictive substance causes physical dependence, as evidenced by withdrawal and relapse

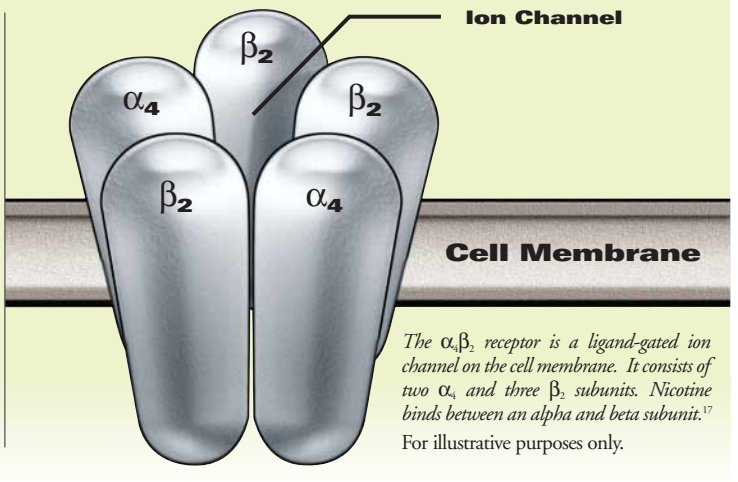
The symptoms of nicotine withdrawal have been clearly identified and confirmed. For most smokers, these symptoms include at least one, if not several, of the following: craving, irritability, insomnia, headache, anxiety, depression, and impaired concentration.[11,14] These withdrawal symptoms have been identified as key contributors to relapse, as the smoker often "self-medicates" with nicotine to return to a perceived state of normalcy.[12]

Additionally, chronic stimulation at the receptor site is believed to be responsible for upregulation (an increase) in the number of receptors expressed at the cell surface.[8,10,12] This is likely a result of the brain compensating for the desensitization of existing receptors, as described earlier. As nicotine leaves the system, however, desensitized receptors can return to an "open" state in which they are once again susceptible to stimulation.[10,11] The combination of these factors—ie, a greater number of available, sensitized receptors—may create "an excess excitability of the nicotinic cholinergic systems of smokers."[12] This hyperexcitable state is believed to contribute to the smoker's motivation to smoke another cigarette (craving).[9,12]

Hyperexcitably may also explain why the first cigarette smoked following a period of abstinence provides a more intense pleasure response for the smoker.[11,12] Note, for example, that most smokers derive the greatest pleasure from their first cigarette of the day.[10,12] **In fact, smoking a single cigarette following a cessation attempt often prompts a complete relapse to heavy smoking.**[10,11]

The $\alpha_4\beta_2$ receptor

Recent evidence suggests that scientists have identified a specific nAChR in the brain that is believed to act as **a primary mediator of the addictive properties of nicotine**—the $\alpha_4\beta_2$ receptor.[15-17] The isolation and characterization of this receptor is a significant advancement in the understanding of the neurobiology of smoking addiction.



The $\alpha_4\beta_2$ receptor is a ligand-gated ion channel on the cell membrane. It consists of two α_4 and three β_2 subunits. Nicotine binds between an alpha and beta subunit.[17]
For illustrative purposes only.

Conclusion

Smoking is a chronic, relapsing condition. For most smokers, the compounding effects of behavioral, psychological, and physical triggers make overcoming their addiction extremely difficult. However, given the high morbidity and mortality related to smoking,[3,8] getting smokers to quit is important. Proactive medical intervention for smokers may be beneficial.[1] Recent advancements in the study of nAChRs—specifically the identification and characterization of the $\alpha_4\beta_2$ receptor—represent a significant advancement in the understanding of the nature of nicotine addiction.

References: 1. Fiore MC, Bailey WC, Cohen SJ, et al. *Clinical Practice Guideline: Treating Tobacco Use and Dependence.* Rockville, Md: US Dept of Health and Human Services, Public Health Service; 2000. **2.** US Department of Health and Human Services. *The Health Consequences of Smoking: Nicotine Addiction: a Report of the Surgeon General.* Rockville, Md: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1988. Available at: http://www.cdc.gov/tobacco/sgr/sgr_1988/index.htm. Accessed October 25, 2005. **3.** US Department of Health and Human Services. *Sustaining State Programs for Tobacco Control: Data Highlights 2004.* Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2004. Available at: http://www.cdc.gov/tobacco/datahighlights/. Accessed October 19, 2005. **4.** Foulds J, Burke M, Steinberg M, Williams JM, Ziedonis DM. Advances in pharmacotherapy for tobacco dependence. *Expert Opin Emerg Drugs.* 2004;9:39-53. **5.** US Department of Health and Human Services. *Women and Smoking: a Report of the Surgeon General.* Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2001. Available at: http://www.cdc.gov/tobacco/sgr/sgr_forwomen/sgr_women_chapters.htm. Accessed October 26, 2005. **6.** Benowitz NL. Nicotine pharmacology and addiction. In: Benowitz NL, ed. *Nicotine Safety and Toxicity.* New York, NY: Oxford University Press; 1998:3-16. **7.** Carper K, Machlin SR. Variations in smoking by selected demographic, socioeconomic, insurance, and health characteristics, United States, 2003. October 2005. Available at: http://www.meps.ahrq.gov/papers/st101/stat101.pdf. Accessed February 15, 2006. **8.** Fagerström K. The epidemiology of smoking: health consequences and benefits of cessation. *Drugs.* 2002;62(suppl 2):1-9. **9.** Anthenelli RM. Recent advances in the treatment of tobacco dependence. *Clin Neurosci Res.* 2005;5:175-183. **10.** Watkins SS, Koob GF, Markou A. Neural mechanisms underlying nicotine addiction: acute positive reinforcement and withdrawal. *Nicotine Tob Res.* 2000;2:19-37. **11.** DiFranza JR, Wellman RJ. A sensitization–homeostasis model of nicotine craving, withdrawal, and tolerance: integrating the clinical and basic science literature. *Nicotine Tob Res.* 2005;7:9-26. **12.** Dani JA, De Biasi M. Cellular mechanisms of nicotine addiction. *Pharmacol Biochem Behav.* 2001;70:439-446. **13.** Cordero-Erausquin M, Marubio LM, Klink R, Changeux JP. Nicotinic receptor function: new perspectives from knockout mice. *Trends Pharmacol Sci.* 2000;21:211-217. **14.** American Psychiatric Association. Substance-related disorders. In: *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. Washington, DC: American Psychiatric Association; 1994. **15.** Tapper AR, McKinney SL, Nashmi R, et al. Nicotine activation of α4* receptors: sufficient for reward, tolerance, and sensitization. *Science.* 2004;306:1029-1032. **16.** Picciotto MR, Zoli M, Rimondini R, et al. Acetylcholine receptors containing the β2 subunit are involved in the reinforcing properties of nicotine. *Nature.* 1998;391:173-177. **17.** Coe JW, Vetelino MG, Bashore CG, et al. In pursuit of α4β2 nicotinic receptor partial agonists for smoking cessation: carbon analogs of (–)-cytisine. *Bioorg Med Chem Lett.* 2005;15:2974-2979.