

# White Matter Lesions May Affect Alzheimer's Tx

BY AMY ROTHMAN  
SCHONFELD  
Contributing Writer

ATLANTA — Fast fluid-attenuated inversion-recovery MR images reveal that the brains of patients with Alzheimer's disease show more extensive areas of focal white matter hyperintensities than do those of normal con-



**'We still don't know the exact pathology underlying leukoaraiosis as seen on' MRI.**

DR. DEVOUS

trols, and the extent of pathology is inversely correlated with cognitive performance, said Michael D. Devous, Ph.D., of the University of Texas Southwestern Medical Center at Dallas.

This new evidence strengthens the link between Alzheimer's disease and cerebrovascular pathology, he said in a poster presentation at the annual meeting of the Society for Neuroscience.

The white matter hyperintensities, also known as leukoaraiosis, are thought to be a consequence of cerebral small vessel disease.

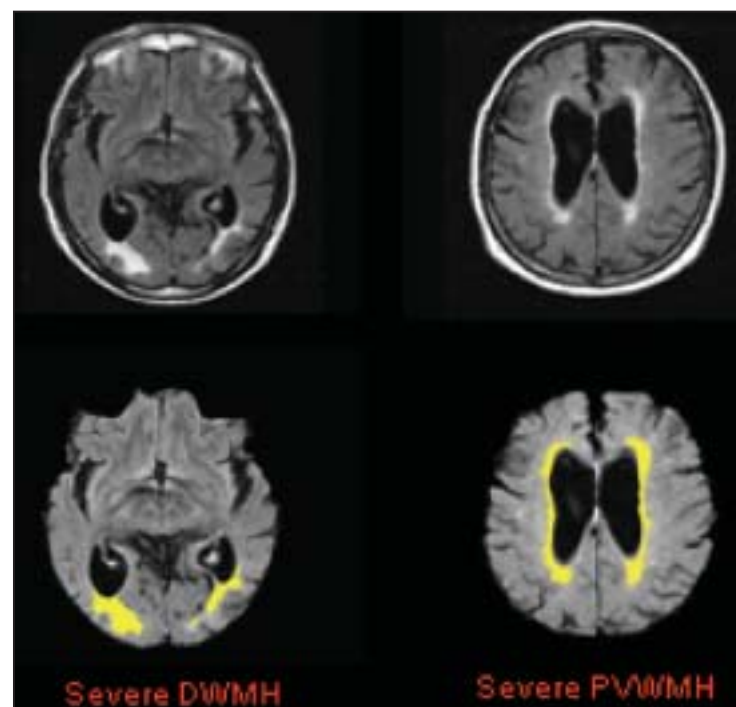
By calculating the ratio of the volume of the white matter hyperintensities to whole brain volume (the leukoaraiosis index), physicians may be able to identify Alzheimer's patients at higher risk of rapid progression or those who are unlikely to respond well to treatment, Mitali Bose, a graduate student at the University of Texas at Dallas and a coauthor, said in an interview.

The mean leukoaraiosis index was almost twice as high in the Alzheimer's group (n = 30) than in the normal control group (n = 40) ( $1 \pm 0.9$  vs.  $0.6 \pm 0.7$ ,  $P = .01$ ). Total leukoaraiosis volume was also significantly higher in the Alzheimer's group than in controls ( $14 \pm 11$  vs.  $6 \pm 9$ ,  $P = .01$ ) while whole brain volume was significantly lower in patients than in controls ( $1,100 \pm 107$  vs.  $1,164 \pm 112$ ,  $P = .01$ ).

Alzheimer's patients with higher leukoaraiosis index scores were

more likely to have poorer cognition, as measured with the Mini Mental State Examination ( $r = -0.28$ ,  $P$  less than .05). "While this correlation was modest, it suggests an impact of leukoaraiosis on a coarse measure of general cognitive status. It is possible that correlating the specific neuroanatomical sites of leukoaraiosis with a more refined neuropsychological variable may provide additional insight into the effect of this abnormality on patient cognition," said Dr. Devous, director of the Neuroimaging Core of the Alzheimer's Disease Center, UT Southwestern Medical Center.

The researchers also compared leukoaraiosis index scores to creatinine levels, another marker of vascular risk, and found a significant positive correlation between the two indicators ( $r = 0.35$ ,  $P$  less than .01). "We still don't know the exact pathology underlying leukoaraiosis as seen on FLAIR MRI, but if [ongoing work finds that] there is correlation with pathological findings on postmortem brain, it may help us relate the leukoaraiosis to other vascular risk factors. Of



Subcortical and periventricular areas of hyperintensities are seen in this fluid-attenuated inversion-recovery MR image.

course, a main goal of this work is to understand this and other risk factors as predictors of symptom severity, disease progression, and response to therapy," Dr. Devous said in an interview.

"This is semiautomated software so it is at the first level of

application. It should have clinical application once the tool is totally automated," said Ms. Bose. The group is now exploring whether hyperintensities in the periventricular or deep subcortical areas have differential prognostic value. ■

## Moderate Daily Wine Intake Improves Cognition

BY BARBARA J. RUTLEDGE  
Contributing Writer

MENDOZA, ARGENTINA — Many studies show that light to moderate drinkers have better cognitive function than do abstainers—particularly in old age—Dr. Roger Pinder reported at the Sixth World Congress on Depressive Disorders.

In addition, moderate daily consumption of wine appears to reduce the risk for dementia and improve cognitive function, with a greater beneficial effect for women than for men.

The association between alcohol consumption and cognitive function often is illustrated as a J-shaped curve, because heavy alcohol consumption, or binge drinking, is associated with worse cognitive functioning and increased risk of dementia, said Dr. Pinder, an independent consultant in Dublin.

The association between alcohol consumption and risk of dementia has been investigated in several large cohort studies and in case-control studies analyzing a subset of subjects from within a larger community-based cohort.

A 3-year study of elderly subjects (older than 65 years) in the Bordeaux area of France and a similar 6-year study of subjects older than 55 years in Rotterdam, the Netherlands, showed beneficial effects of moderate alcohol consumption in lowering the risk of dementia.

A case-control study from a U.S. community-based cohort of older subjects compared more than 300 pairs of subjects with incident dementia to controls and found sig-

nificantly lower risk for dementia associated with light to moderate alcohol consumption.

The Bordeaux study focused on wine consumption. In the U.S. study, wine consumption had a greater benefit than did consumption of beer or spirits. The Rotterdam study showed no significant differences based on type of alcohol consumed.

Three major population-based studies with long-term follow-up have demonstrated an association between moderate alcohol consumption and improved cognition: The Whitehall Study of British Civil Servants, the U.S. Nurse's Health Study, and the Women's Health Initiative Memory Study.

The Whitehall Study, conducted in the United Kingdom, was a cohort study of 4,272 male and 1,761 female civil servants, with a median follow-up of 11 years. Assessment of cognitive function was performed when the subjects were aged 46-68 years. Cognitive function was significantly better in drinkers, compared with nondrinkers, even in those who drank more than 240 g alcohol per week (*Am. J. Epidemiol.* 2004;160:240-7). The benefit was greater in women than in men.

In the long-term, U.S.-based Nurse's Health Study, cognitive function was evaluated in 12,480 female nurses, aged 70-81 years. Subjects were reevaluated after 2 years. Compared with nondrinkers, moderate drinkers had higher mean cognitive scores and showed reduced risks of cognitive decline (*N. Engl. J. Med.* 2005;352:245-53).

The Women's Health Initiative Memory Study examined cognitive function and alcohol consumption in more than 4,000

women aged 65-79 years, with an average follow-up of 4 years. Relative to no alcohol consumption, moderate consumption of alcohol was associated with better cognition and reduced risk of cognitive decline (*Am. J. Epidemiol.* 2005;161:228-38).

One caveat when it comes to assessing the beneficial effects of wine is the presence of potential confounding factors in the studies. Alcohol consumption in many studies is not limited to wine but also includes beer or spirits. Compared with those who drink beer or spirits, wine drinkers tend to have healthier lifestyles. In addition, wine drinkers are more likely to be women, college graduates, and nonsmokers, Dr. Pinder said.

Finally, heavy drinkers often underestimate—or lie about—their alcohol consumption, which can distort results by lowering the apparent threshold for harmful effects. Nonetheless, in several studies, wine consumption appeared to be better than consumption of beer or spirits at improving cognitive function.

Consumption of red wine seems to have a stronger beneficial effect than consumption of white wine or rosé, Dr. Pinder reported. The beneficial effects of red wine may largely be attributable to antioxidants derived from grape skins. "Unlike beer and distilled spirits, wine contains not only alcohol, but also has a lot of polyphenolic antioxidant compounds extracted when the grapes are vinified," Dr. Pinder said. "Red wine contains more polyphenols than white or rosé, simply because of the greater extraction from the grape skins. And they use grape varieties that are rich in polyphenols." ■

## Hypersexuality Resolves With Oxcarbazepine

MADRID — Oxcarbazepine appears to significantly decrease hypersexual behavior in patients with Alzheimer's disease, Dr. Joshua Shua-Haim reported in a poster presented at the 10th International Conference on Alzheimer's Disease and Related Disorders.

All 11 men in the small pilot study showed improvement in the behavior after 2 weeks of treatment, noted Dr. Shua-Haim, who is with the Jersey Shore University Medical Center in Neptune, N.J.

All of the patients lived in a special care unit in an assisted living facility.

Treatment began with 150 mg oxcarbazepine daily. The dose was titrated by 150 mg/day, given in two divided doses, until the behavior ceased or a maximum of 900 mg/day was reached, Dr. Shua-Haim wrote.

Hypersexual behavior resolved in all 11 patients after they received an average dose of 600-750 mg/day, given in two doses. No adverse events were reported, and there were no changes in blood chemistry.

—Michele G. Sullivan