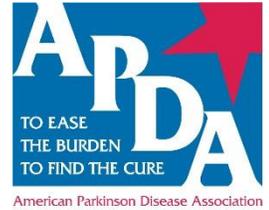




DEPARTMENT OF VETERAN AFFAIRS AND APDA



Winter 2015

PARKINSON PRESS NEWSLETTER

Consider the environment. Print newsletter as necessary.

John H Peacock, MD, PHD

USE OF ETHANOL WITH PARKINSON'S DISEASE, TO DRINK OR NOT TO DRINK

The medical note in this issue of the Parkinson Press explores the potential benefits of ethanol in Parkinson's disease with a focus on red wine. Red wine may provide a dual benefit for Parkinson's disease. First the ethanol in wine is capable of direct stimulation of dopamine-containing nerve cells (dopaminergic neurons) in the substantia nigra. Second, as some of you may know, red wine contains resveratrol a plant product with several potential neuroprotective effects. Note that other foods such as peanuts also contain resveratrol.

Looking first at the direct effects of ethanol. Laboratory studies on the direct effect of ethanol on dopaminergic neurons has been examined. In this research, injection of ethanol into the substantia nigra of anesthetized rats caused a dose-related increase in locomotor activity once the anesthetic was removed (1). Enzymes such as catalase were evaluated in this regulation of ethanol-induced motor activity. Previously Gessa, et al. (2) found that low doses of ethanol induced a 30-80% increase in firing rate of dopaminergic neurons in experimental animals.

Focusing next on the effects of resveratrol. It is an antioxidant (4, 5), modulates inflammation (6, 7), and stimulates growth factors (8). Each of these properties is presented below for those who want to review them. The science itself is complex, but hopefully the summary paragraphs are clear.

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What are the benefits of an antioxidant? By definition, “Antioxidants are man-made or natural substances that may prevent or delay some types of cell damage. Antioxidants are found in many foods, including fruits and vegetables” (3); many vitamins including Vitamin C are antioxidants.

Ono and Yamada (4) found a direct antioxidant effect of wine related phenols such as resveratrol on formation of alphasynuclein. You will recall that alphasynuclein is the protein that aggregates in dopaminergic neurons adversely affecting their function and ultimately their survival. The authors speculated that this group of molecules could play a key role in “the development of preventatives and therapeutics for LBD (Lewy Body disease) and MSA (Multiple System Atrophy) as well as Alzheimer's disease”.

Albani, et al. (5) studied the neuroprotective effects of SIRT1, a protein that can protect against oxidation when activated. Such activation occurs with resveratrol. In these experiments cells that were growing in culture provided the experimental model, not experimental animals. The oxidative challenge for these cells was exposure to weak solutions of hydrogen peroxide or 6-hydroxydopamine, a chemical that can kill dopaminergic neurons. Ensuing detrimental effects were blocked by resveratrol through the SIRT1 pathway. In the same experiments, SIRT1 itself was unblocked by its inhibitor, sirtinol.

Why is resveratrol an anti-inflammatory agent? The inflammatory response in Parkinson's disease is mediated by microglia. Glia are one of the non-neural cell types that are in the brain along with nerve cells. Proliferation of glial cells occurs after toxic insults to nerve cells in a way analogous to proliferation of scar forming cells outside of the brain following cuts and abrasions of the skin.

Zhang et al (6) examined the mechanisms underlying resveratrol-mediated neuroprotection in rat midbrain neuron-glia cultures. This region of the rat midbrain has dopamine neurons and provides a relevant model for Parkinson's disease. Using this model, his group exposed dopamine nerve cells in culture to lipopolysaccharide, a molecule that triggers microglial proliferation and an accompanying proinflammatory factor release. Resveratrol inhibited the microglial cell formation and blocked the toxic effects of lipopolysaccharide. Biochemical details of that inhibition are provided in the report and beyond the scope of this news article.

Additional experimental work on the modulation of microglial proliferation by resveratrol was reported by Gordon et al. (7). These scientists also examined the positive modulation of apoptosis, perhaps the topic of a subsequent newsletter, by resveratrol.

Additionally, resveratrol stimulates the production and release of growth factors. You may recall that neurotrophic factors such as glial cell line-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) are important for the development, maintenance and survival of neurons including dopaminergic neurons in the substantia nigra. Astroglia, another cell type in the brain are a source of neurotrophic factors. Zhang et al. (8) evaluated the possibility that resveratrol might stimulate the production and release of neurotrophic factors from astroglial enriched cultures. After cell cultures were exposed to low concentrations of resveratrol for 12–48 hours, BDNF and GDNF were measured in the culture medium. Following 24 hours of resveratrol exposure, the production of BDNF was increased five-fold over control levels and remained high 36 hours later. Meanwhile, the production of GDNF was initially increased by up to four-fold in 24 hours after resveratrol treatment and continued to increase to six-fold at 36 hours. The level remained high for 48 hours.

Ethanol and Multiple Sclerosis. It is notable that ethanol may be beneficial for other Neurological diseases such as MS. In January 2006, Hedstrom et al. (8) reported the results from their analysis

of two epidemiological studies. They found a dose-dependent, inverse association between alcohol consumption and risk of developing MS that was statistically significant in both sexes.

Conclusion. This report has briefly reviewed evidence for a direct stimulatory effect of ethanol on dopaminergic neurons as well as potential neuroprotective effects of resveratrol found in wine and other foods. These neuroprotective properties include antioxidation (4, 5), anti-inflammatory modulation (6, 7), and stimulation of production of growth factors (8). So enjoy a glass of red wine and don't let all this information about resveratrol spoil its magic for you. You may also purchase resveratrol in a capsule form at most health food stores.

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Disclaimer:

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Veteran Update



Veterans Crisis Line:

If you are in crisis, or know a veteran who is, telephone the Veterans Crisis Line toll-free 24/7/365 at 1-800-273-8255 and press 1, or text 838255, or visit the Veterans Crisis Line website at <http://veteranscrisisline.net> and chat with trained counselors (many of whom are veterans) anytime. This is also the National Suicide Prevention Lifeline for anyone in crisis.

Federal Benefits Book Updated:

The Federal Benefits for Veterans, Dependents & Survivors handbook was recently updated, adding 18 pages of new information. The book is available on the Department of Veterans Affairs (VA) website at http://www.va.gov/opa/publications/benefits_book.asp

New Veteran Care Options:

The new Veterans Access, Choice and Accountability Act give many veterans the option to receive non-VA health care rather than waiting for a VA appointment or traveling to a VA facility. Read about the new Veterans Choice Program and check your eligibility at VA's Veterans Choice Program webpage at: www.va.gov/opa/choiceact/.

RESEARCH OPPORTUNITIES

If you are interested in current research regarding Parkinson's disease, please visit one or all of the sites listed below.

Fox Trial Finder at www.foxtrialfinder.org

This is a website developed by the Michael J. Fox Foundation that helps people diagnosed with PD find personalized matches to clinical trials.

Clinical Trials at www.ClinicalTrials.gov

The U.S. National Institutes of Health developed this site to provide patients, family members and the public with current information about clinical research studies being funded by government and private industry. By searching for Parkinson's disease, you can get a listing of all clinical trials (including contact information) for Parkinson's disease being conducted in the U.S. and internationally. This site also provides information on the clinical trials process.

Center Watch at www.centerwatch.com

Center Watch is a listing service for clinical trials both industry and government funded. By searching for Parkinson's disease, you can get a listing of all clinical trials for Parkinson's disease being conducted in the U.S. and internationally. Contact information for each trial is included.

What's New???

Parkinson's disease can migrate from gut to brain, shows research: Parkinson's disease is strongly linked to the degeneration of the brain's movement center. In the past decade, the question of where disease begins has led researchers to a different part of the human anatomy. In 2003, the German neuropathologist Heiko Braak presented a theory suggesting that the disease begins in the gut and spreads to the brain. The idea has since, despite vocal critics, gained a lot of ground. Researchers at Lund University in Sweden now present the first direct evidence that the disease can actually migrate from the gut to the brain. To read more about this, go to the source: <http://link.springer.com/article/10.1007/s00401-014-1343-6>

Upcoming Educational Events

- **AD/PD 2015, Alzheimer's & Parkinson's Disease Congress, March 18-22, 2015, Nice, France.** For more information go to <http://www2.kenes.com/adpd/pages/home.aspx>
- **2015 PAN Forum. Join hundreds of Parkinson's advocates from around the country for the Parkinson's Action Network(PAN) Forum March 23-25, 2015.** Visit thepanforum.org to get more information about the agenda, hotel, and scholarships.
- **XXII World Congress of Neurology, October 31-November 5, 2015 in Santiago, Chile.**
- **Aces Reno Fundraiser. Join us for a day at the ballpark on August 30, 2015 at 1:00pm to support Parkinson's disease. Vouchers for tickets to the game are \$12.00. Please call us at 775-328-1715 to reserve your seat and help raise funds to support research for Parkinson's Disease.**

Northern Nevada Support Groups

Contact information: 775-328-1715 or 888-838-6256 ext. 1715

Website: www.reno.va.gov/parkinsons/parkinsons.asp

Spanish Springs	January 7	February 4	March 4
First Wednesday	Susan NeeleyRN	Caregiver Support Group	Kelly Cramond PhD
10:00 am	Lend-A-Hand	Caregivers●	Sleep, Hallucinations & Anxiety in PD
Cascades of the Sierra, 275 Neighborhood way			

Carson City	January 13	February 10	March 10
Second Tuesday	Valerie Williams	Susan Haas, Director	Cynthia Chorjel OTR
2:00 pm	Memory in PD	RSVP	Equipment for PD
Carson City Senior Center, 911 Beverly Drive			

Reno	January 9	February 13	March 13
Second Friday	Brian Terres Medtronic	Group Members	Tricia
2:00 pm	DBS & Duopa	Group Discussion	Right at Home
Atria at Summit Ridge, 4880 Summit Ridge Drive			

Reno	January 20	February 17	March 17
Third Tuesday	Dr. John Peacock	Melissa Gerdes PT	Dawn Curry D.Ph.
5:00pm	Update on Parkinson's Disease	LSVT "Big"	Medications & PD
Veterans Administration Medical Center, meet at 4:50pm in the Kirman Street Lobby			

Sparks	January 22	February 26	March 26
Fourth Thursday	Alison Shelton?	Sandy Wilson PT	Group Members
2:30 pm	ADT	LSVT "Big"	Group Discussion
Morning Star Senior Living, 2360 Wingfield Hills Drive, Sparks, NV			

Reno	January 15	February 19	March 19
Third Thursday	Melissa Gerdes PT	Tracie Pistone	Amanda Smith/Tiffany
2:00pm	LSVT “Big”	Interim HomeStyle	Eden Hospice Care
Five Star Premier Residences of Reno, 3201 Plumas Street, Reno, NV 89509			

Elko-Las Vegas- Reno	January 2	February 6	March 6
First Friday	Jacob Harmon	Brian Terres Medtronic	Don Vonerx
1:00 pm	What is Alzheimer’s?	DBS & Duopa	REMSA
University of Nevada Cooperative Extension, 4955 Energy Way. Reno, NV University of Nevada Elko, 701 Walnut Street, Elko, NV			

- **Please bring your family member with Parkinson’s disease to the February 4th 2015 meeting. Dick Stoddard will present information of interest on Parkinson’s disease to the patient group. Caregivers will meet in the conference room on the first floor.**