Moderate Alcohol Intake Is Associated With Nearly 40% Lower Risk of Dementia

Moderate alcohol intake, especially wine, has been associated with reduced risk of dementia in middle aged adults. It is not known whether this association is also true for older adults or those with mild cognitive impairment (MCI).

Researchers sought to determine the relationship between alcohol intake and incident dementia in 3,069 community-living adults aged 75 years and older without dementia who were enrolled in the Ginkgo Evaluation of Memory Study (GEMS), an NIH-sponsored study of ginkgo biloba for prevention of dementia. At the beginning of the study, 2,587 of the participants were assessed to be cognitively normal and 482 had MCI.

Alcohol consumption was self-reported by study participants and categorized by the researchers as none, 1-7 drinks/week (light), 8-14 drinks/week (moderate), and more than 14 drinks/week (heavy). All types of alcohol were counted.

Moderate alcohol intake (1-2 drinks per day) was associated with a 37% lower risk of dementia in participants with normal cognition at baseline.

(Cont’d on Page 3)

Does Caffeine Help Decrease Beta-Amyloid in Alzheimer’s Disease?

Back-to-back studies published in the Journal of Alzheimer’s Disease, show caffeine significantly decreased abnormal levels of beta-amyloid, the protein linked to Alzheimer’s disease, both in the brains and in the blood of mice exhibiting symptoms of the disease. Both studies build upon previous research by the Florida ADRC group showing that caffeine in early adulthood prevented the onset of memory problems in mice bred to develop Alzheimer’s symptoms in old age.

The just-published Florida ADRC study included 55 mice genetically altered to develop memory problems mimicking Alzheimer’s disease as they aged. After behavioral tests confirmed the mice were exhibiting signs of memory impairment at age 18 to 19 months – about age 70 in human years – the

(Cont’d on Page 3)

Good Morning.
Dear HBA Participants,

As you have probably heard we completed our enrollment for this study. We are very grateful to everyone who agreed to participate in this important study.

Although we hope it doesn't happen we know that from time to time you might experience issues with your equipment. If you encounter any problems at all please notify your research site immediately. They are ready to help you resolve the problems as quickly as possible. We have a team in place that stands ready to assist with the equipment.

We recognize that there are many other projects and interests pressing for your time, from health to family to the turn in our economy that may affect your home or lifestyle. We truly hope that none of the difficulties facing the country will affect you individually but if they do please let your research site staff know so they can assist you in staying connected in the study as long as is feasible.

I want you to know that your efforts in helping us with this project are truly innovative. You should feel proud of being part of this pioneering work. As you may know the HBA Study is the first of its kind on this level to collect cognitive and functional evaluations in the home utilizing these new methods. What we learn from your participation will help future generations for years to come.

It is a pleasure to work with such a committed group of volunteers and I look forward to our continued success.

Mary Sano, Ph.D
HBA Principal Investigator
Director, Mount Sinai Alzheimer’s Disease Research Center
Moderate Alcohol Intake is Associated With Nearly 40% Lower Risk of Dementia (Cont’d From Page 1)

The distribution of alcohol consumption per week was 0=42.6%; 1-7=38.2%; 8-14=9.4%; more than 14= 9.8%.

Participants were examined every six months for up to six years for changes in their memory or thinking abilities. If someone was suspected of having developed Alzheimer’s or another dementia, they were thoroughly evaluated. There were 523 news cases of dementia during the follow up period of the study.

After adjustment for demographics, smoking, co-morbidities, depression, social activity, and baseline cognition, moderate alcohol intake (1-2 drinks per day) was associated with a 37% lower risk of dementia in participants with normal cognition at baseline, but not in those with MCI.

For older adults who started the study with MCI, consumption of alcohol at any amount was associated with faster rates of cognitive decline; and those who were classified in the heavy drinker category (more than 14 drinks per week) were almost twice as likely to develop dementia during the study, compared to non-drinkers with mild cognitive impairment.

Does Caffeine Help Decrease Beta-Amyloid in Alzheimer’s Disease? (Cont’d From Page 1)

Researchers gave half the mice caffeine in their drinking water. The other half got plain water. The Alzheimer’s mice received the equivalent of five 8-oz. cups of regular coffee a day. That’s the same amount of caffeine – 500 milligrams -- as contained in two cups of specialty coffees like Starbucks, or 14 cups of tea, or 20 soft drinks.

At the end of the two-month study, the caffeinated mice performed much better on tests measuring their memory and thinking skills. In fact, their memories were identical to normal aged mice without dementia. The Alzheimer’s mice drinking plain water continued to do poorly on the tests.

In addition, the brains of the caffeinated mice showed nearly a 50-percent reduction in levels of beta amyloid, the substance forming the sticky clumps of plaques that are a hallmark of Alzheimer’s disease. Other experiments by the same investigators indicate that caffeine appears to restore memory by reducing both enzymes needed to produce beta amyloid. The researchers also suggest that caffeine suppresses inflammatory changes in the brain that lead to an overabundance of beta amyloid.

If larger, more rigorous clinical studies confirm that caffeine staves off Alzheimer’s in humans, as it does in mice, this benefit would be substantial.
Can You Trust What You Read?

If you read the newspaper, watch television or surf the internet, you know the overwhelming amount of medical information available. Some is scientifically sound, some based on opinion, and some is incomplete or even misrepresented.

Evaluating the credibility of reports is very challenging for the unprepared consumer. Do you have the necessary tools to make sense of what you read and hear? Are you ‘information literate’?

Asking the following questions can help you decide what to believe.

1. WHERE DOES THE INFORMATION COME FROM?

PEER-REVIEWED JOURNALS: Articles published in reputable peer-reviewed journals are the most respected source of information, as the work has been reviewed by other qualified members of the profession. If you have difficulty obtaining or interpreting findings from these primary source articles, turn to professionals skilled in explaining such data to help you understand the results and conclusions.

THE INTERNET: The internet is a rich source of information but because it is unregulated, you should check the sponsorship of a website to establish its reputability. Some reliable websites providing health information include:

- Government agencies (ending in .gov)
- National nonprofit organizations (ending in .org)
- Medical specialty groups, and university medical centers (ending in .edu)

Web addresses ending in .com may have valuable information, but many are commercial sites designed to sell you something.

SOME REPUTABLE WEBSITES FOR INFORMATION ABOUT ALZHEIMER’S DISEASE INCLUDE:

- WWW.ALZ.ORG - Alzheimer’s Association website
- WWW.NIA.NIH.GOV/ALZHEIMERS - Alzheimer’s Disease Education and Referral Center of the National Institute on Aging
- WWW.CLINICALTRIALS.GOV - National Institutes of Health website providing information about federally and privately supported clinical research, including information about specific trials and news about recent results
- WWW.MEDLINEPLUS.GOV - a service of the US National Library of Medicine, this website archives health news from the last 30 days, drug information for both prescription and nonprescription medications, a medical encyclopedia and a link list of health libraries, databases and resources

TV AND PRINT: Look carefully at information published in newspapers and magazines or reported on television. Most reporters are journalists rather than experts in the medical field. Very preliminary medical findings may be released in the news prematurely and with sensational impact. If your interest is sparked by something you hear or read in the news, go to a professional website to evaluate further.
Always be especially cautious about information that is based solely on opinion or personal experience. Phrases such as “miraculous treatment” and “cure”, and claims that a product treats a wide range of ailments, is available from only one source, or is available only for a limited time are generally aimed at selling you something.

Knowing something about the type or phase of a research study can help you determine the certainty of conclusions being drawn from its findings. The size and duration of the study are also important, as is the repeatability of a finding. A positive result from a single study is exciting. The same positive result across multiple studies is convincing!

The gold standard for scientific research has traditionally been a type of experimental study in which participants are randomly assigned to either an experimental or a control group. Neither the participants nor the researchers who evaluate them know which person is in which group until the study is completed. Known as a double-blind, placebo-controlled, randomized clinical trial, this type of study is rigorous and is able to establish with the greatest degree of certainty whether a given factor likely caused a specific outcome.

Treatment studies known as human clinical trials, are experimental studies specifically focused on treatments that appear promising in preliminary laboratory and animal studies. Clinical trials are usually conducted in distinct phases, each designed to answer specific questions and each being a necessary step toward FDA approval of the treatment option. In evaluating information from results of clinical trials, consider from which phase of investigation the finding comes. It will give you some idea of how much is known about the treatment being studied and whether it will likely be submitted for FDA approval in the near future.

<table>
<thead>
<tr>
<th>Phase I Clinical Trials</th>
<th>Is the treatment SAFE?</th>
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<tr>
<td>Phase II Clinical Trials</td>
<td>Does it WORK?</td>
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<tr>
<td>Phase III Clinical Trials</td>
<td>Is it BETTER than what’s already available?</td>
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Television and newspaper are media forms geared toward time-sensitive reporting, so the currency of information is generally not in question. When gathering information on the internet, however, be sure to check whether the web page you are viewing has been updated recently because outdated information can remain on the internet for a very long time.

Consider who participated in the study of interest and how they were recruited. If, for example, individuals with specific health problems were excluded from participating in a study, then the findings from this study may be limited to those who do not have the excluded health conditions. Those unaware of this limitation may place themselves in danger if they use such a treatment.

Staying well-informed about medical developments is to be applauded, but it is vitally important to remember that medical information you gather through public media sources is not a substitute for professional health care! Gather information freely but cautiously, and always discuss any questions or thoughts you may have about treatment options with your personal physician. After all, if diagnosing and treating disease were simply a matter of reading the newspaper or surfing the web, we’d be living in a disease-free society!
Statistically Speaking
A Brief Guide To Clinical Trial Terminology

Researchers use statistical methods to develop clinical trials and interpret the results. It is not always immediately obvious if an effect observed in a clinical trial is real (statistically significant) or caused by chance (not statistically significant). Presented here are a number of essential terms and concepts to help broaden your understanding of the clinical trials process.

**Endpoint:** A measurable outcome that indicates an intervention’s effectiveness. Endpoints differ depending on the phase and type of trial. For instance, an Alzheimer’s disease treatment trial endpoint could be improvement in short term memory ability or participant survival. Quality-of-life or supportive care trial endpoints could include participants’ welfare and control of symptoms such as agitation.

**Randomization:** In phase 3 trials (and some phase 2 trials) this means that participants are assigned to either the investigational drug or control (placebo) group by chance, via a computer program or table of random numbers. This process gives each person the same chance of being assigned to either group. Randomization ensures that unknown factors do not influence the trial results.

**Placebo:** An identical but inactive pill.

**Blinded:** A term used to describe the fact that the subjects are not aware whether they are receiving the experimental treatment being studied versus placebo. Double-blinded means that both the subjects and the researchers providing the drug are unaware of who is receiving drug or placebo, and only a central overseeing group of researchers know the true identity of the drug.

**P-values:** These reflect the likelihood that the results of a clinical trial are because of chance rather than due to a real difference between the tested treatments. The smaller the value of p, the greater the likelihood that the results are not because of chance. A p-value of 0.05 (that is, 1 in 20) or smaller is widely accepted as an indication that the results are statistically significant.

**Confidence intervals:** These reflect a range of values of the true value that would be obtained if everyone with a particular disease were treated with the treatment under study. The wider the interval, the more variable the result and the less likely it is to be close to the true value. Confidence intervals are typically thought of as the approximate bounds or limits of the true value. Researchers frequently use either a 95 or a 99 percent confidence interval.

**Sample size:** The number of people participating in a trial.

**Statistical power:** This refers to the chance of finding a statistically significant result when there is one. Ideally, statistical power should be 0.80 or 0.90, reflecting an 80 to 90 percent chance of detecting that the true difference in treatment effectiveness is the smallest size considered medically important to detect.

**Relative risk:** The likelihood that the disease will occur within a specific timeframe in one group versus another.

**Trial Phases:** There are 3 trial phases - During Phase I trials, treatment is given to a small number of participants and examines its action in the body and its safety. The main goals of Phase I trials are to establish the highest dose of a new drug that people can tolerate and to define the dose at which people may begin to experience harmful side effects. These trials generally last only a few months.

If results show that the treatment appears to be safe, it will go on to **Phase II** trials. Phase II trials involve larger numbers of people studied over longer periods of time than Phase I trials. In these trials, the study team wants to know whether the treatment is safe and effective at changing the course of the disease. Phase II trials occasionally also involve the use of a placebo (an inactive substance that looks like the study drug). Results from Phase II trials give study staff an indication of the effective dose to take into Phase III trials. **Phase III** trials are large studies that compare an experimental treatment with a placebo or standard treatment to determine safety and efficacy (whether the treatment has the power to produce an effect).
Exercise is a general recommendation for maintaining health across the lifespan. There is increasing evidence that physical exercise is not only good for the body, but is good for the brain. Evidence comes from animal models as well as research with humans. For example, rodents housed in enriched environments with access to a running wheel and other interesting objects to play and interact with, have been shown to have enhanced brain systems involved in learning and memory. In humans, evidence suggests that older adults who participate in physical exercise have improved thinking skills compared to more sedentary individuals. Exercise appears to be particularly beneficial to “higher order” or more complex thinking skills such as planning and multi-tasking. Physical activity may also prevent cognitive decline and may delay the onset of dementia. There is also emerging evidence that physical activity may contribute to maintenance of brain volume over time. These positive changes in the brain have been noted most prominently in the frontal lobes of the brain, a region generally associated with higher order mental skills.

Nonetheless, many questions remain regarding the link between exercise, brain volume, and thinking. How is exercise actually exerting its positive impact? What specific brain structures might be most positively impacted by physical activity? How much exercise is enough to reap the positive benefits? At what point in life does one need to begin physical activity to gain cognitive benefits? These are just some of the questions that I am interested in answering in my studies of the effects of physical exercise on cognition and brain health in older adults.

Preliminary work from my research shows that older adults without dementia who self-reported higher levels of physical activity, had significantly better visuospatial skills (i.e., visual perception and spatial relationships among objects), memory, and executive functioning (i.e., higher level cognitive skills like problem solving and planning). Exercise also aided cognition and brain maintenance in individuals with Mild Cognitive Impairment (MCI). Individuals with MCI are at increased risk for developing Alzheimer’s or a related dementia. My preliminary work in this area suggests that persons with MCI who are more physically active appear to have slower hippocampal volume loss in the brain (the hippocampus is a brain structure essential to forming memories) and better maintenance of overall thinking abilities and executive functioning than those who are more sedentary.

In summary, regular physical exercise holds promise as an important non-pharmacologic strategy to delay onset or slow the rate of cognitive decline in older adults, however, the exact amount and duration of exercise needed to reap these cognitive benefits is still not clear. It is also particularly encouraging that even in individuals with MCI, physical activity may extend periods of normal cognition and slow brain volume changes over time. As such, physical exercise may be particularly important for those who have already evidenced some mild cognitive decline.
BRAIN EXERCISE

Mind Games are a really fun way to exercise the mind. Check out the mind games on the BrainBashers website — [http://www.brainbashers.com](http://www.brainbashers.com) — good for both caregivers who want to stay sharp and study participants with mild dementia.

**Answer quickly. Starting with an empty barrel, which happens first?**

- 2/3 full
- 1/4 empty
- 1/2 full
- 3/4 empty

Since 3/4 empty means 1/4 full.

**What is represented by this BrainBat?**

- Schubert's Symphony
- Unfinished
- Symphony
- Schubert's

**What four related words are merged here:**

- SWAS
- PURI
- UINM
- NTTU
- MGER
- MNER

**Winter, autumn and spring, summer,**