

NOBLE

A New Study for People with Mild to Moderate Alzheimer's Disease

A special newsletter for participants in the Noble Research Study

Fall 2015

Letter from the Director



Dear NOBLE Study Participants,

By the time you receive this newsletter the NOBLE Study will be about 75% towards its goal of enrolling 450 people. Please know that we could

not have reached this important milestone without your willingness to volunteer and your contribution as a study participant. Indeed, you are the foundation and heart of our work.

Like all treatments the medical community cannot advance therapies without the generous volunteers who help test experimental treatments. It is the cornerstone of clinical research. You may not realize it, but you are part of a long history of testing potential treatments to help researchers determine if they are working. In this issue of the newsletter you'll find an article that discusses the history of the research in which you play an essential role.

I'm sure you've heard how important it is to stay and be your healthiest self. This holds true whether burdened with an illness or not. We take a look at what you can do to be your healthiest self, what steps you can take now that will help you live as healthy as possible as you contend with adversity. I encourage you to read the

article and if you are not already doing so apply the principles discussed.

One of the principles noted in the healthy living article is the necessity of incorporating exercise into daily life. But don't just take our word for it. Read the article about an exercise study conducted at the University of Kansas by Jeffrey Burns, M.D., professor of Neurology and co-director of the KU Alzheimer's Disease Center. He led a six-month study with a group of healthy seniors. The volunteers were split into groups of non-exercisers and exercisers who were further instructed in various amounts of weekly exercise. They found that everyone who exercised received benefit; and those who exercised the most saw the most benefit, especially in brain functioning. Take a look at the article; I think you will be surprised and encouraged at the results. I hope you enjoy this issue. Please send us any comments, questions or ideas for articles in future issues to brainlink@ucsd.edu. I look forward to communicating with you again later in the year.

Until next time,

Lon

Lon Schneider, M.D., M.S.,
Keck School of Medicine of USC

Playing a Part in History

Who doesn't secretly dream of playing an important role in the history of the world? Most people want to be remembered in some way. You may not realize this, but you are playing a historical role by participating in the NOBLE Study. How, you wonder? By volunteering for NOBLE, you are playing a role in the long history of clinical trials.

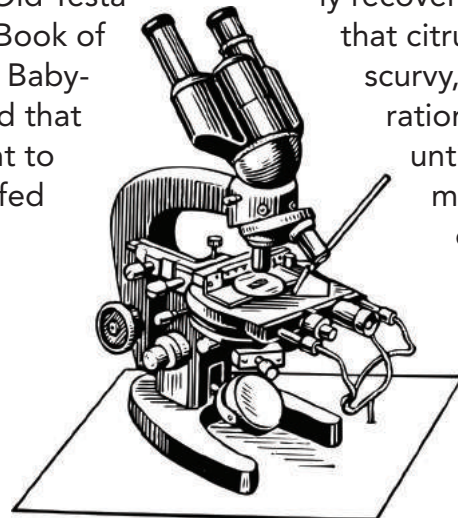
Many people think that clinical trials are a recent phenomenon; in fact they date back to ancient times. The earliest documented clinical trial is mentioned in the Old Testament. In the first chapter of the Book of Daniel, King Nebuchadnezzar of Babylon conquered Israel and ordered that several Jewish youths be brought to his palace where they would be fed and taught as though they were his own children. One of the youths, Daniel, did not want to disgrace himself by eating the king's meat and drinking his wine. He suggested to the king's head eunuch, Melzar, that instead they be allowed to eat a mixture of peas and beans called pulse and drink only water. Melzar feared the king's anger should the youths become sick on a diet of beans and water. So Daniel suggested an experiment – allow some of the youths to eat pulse and drink water for 10 days, while the others eat meat and drink wine and to watch them carefully. After 10 days, the children that ate pulse and drank water were healthier than those who ate the meat and drank the wine. Convinced, Melzar gave all of them only pulse and water at future meals.

In 1025 A.D. Avicenna, an early Persian physician, introduced the first rules for conducting what are now called clinical trials in The Canon

of Medicine. These rules and principles for testing the effectiveness of substances and medications formed the basis of modern clinical trials by providing a logical method for measuring and comparing effects.

One of the most famous clinical trials was James Lind's 1747 demonstration aboard the ship Salisbury that citrus fruits could cure scurvy, the bane of sailors. He fed various acidic substances to groups of afflicted sailors. The group that ingested oranges and lemons mostly recovered in six days. Although he proved that citrus fruit could cure and even prevent scurvy, the fruits were not included in ship rations due to their high cost. It was not until 50 years later that the British Navy made lemon juice an essential part of the Naval diet. Soon after that, lemon juice was replaced by lime juice because of its lower cost. It has been postulated that is the reason why British sailors, and later on all British citizens, were nicknamed "limeys" by Americans.

The next clinical trial of sorts occurred in 1789 with English physician Edward Jenner. Noting the common observation that milkmaids did not generally get smallpox, Jenner theorized that the fluid in the blisters which milkmaids received from cowpox (a disease similar to smallpox but much less virulent) protected the milkmaids from smallpox. On 14 May 1796, Jenner tested his theory by inoculating James Phipps, a neighbor's eight year old child. Jenner inoculated Phipps with the blister fluid from a milkmaid. This produced a fever and some uneasiness, but no great illness. Later, he injected Phipps with infectious material which surely would have caused smallpox. No disease



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followed. Jenner reported that later the boy was again challenged with material and again showed no sign of infection. He tested his theory on a series of 23 subjects, and proved vaccination could work in reducing the incidence of smallpox infection.

In 1884 French physician Louis Pasteur inoculated a nine year-old boy with a rabies antidote. The boy had been bitten by a rapid dog and several physicians were sure the boy would die without some kind of treatment. Although nervous about experimenting on the child he relented under pressure from the boy's mother. The boy survived.

The first placebos (non-active ingredient substances) were used in 1863 and in 1923. The word placebo, Latin for "I shall please", dates back to a Latin translation of the Bible by Jerome. It was first used in a medicinal context in the 18th century. In 1785 it was defined as a "commonplace method or medicine" and in 1811 it was defined as "any medicine adapted more to please than to benefit the patient." In 1948 the first trial using randomization, control groups and "double blinding" (where neither the doctor nor patient knows if the patient

is getting the study drug or placebo) was conducted by the Medical Research Council for using streptomycin to treat tuberculosis.

Unfortunately, there have also been abuses in the name of research. Unethical experiments conducted by the Nazis on concentration camp internees led to strict regulation of medical experiments on human beings: the Nuremberg Code and the Declaration of Helsinki. Sadly these declarations held little weight in the United States which is why the iniquitous Tuskegee experiment, an observational study of 400 African American men with syphilis continued for 40 years until it was brought to light in 1970 and closed down for not treating the men with penicillin, a known cure for the disease. That scandal led to the creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. In 1979 the commission issued The Belmont Report that stipulated ethical principles and requirements for clinical trials.

Fortunately there have been many more positive benefits from clinical research than abuses. There is not a drug on the market today that has not been studied extensively. Every time you take ibuprofen for a headache or strained muscle, an acid reducer for a stomach ache or use an inhaler for asthma, remember that you can use these drugs because someone else, someone like you, agreed to participate in a clinical research trial, much like the NOBLE Study. Your participation in this study is blazing the trail toward a possible treatment for Alzheimer's, just like Lind, Jenner and Pasteur were pioneers in their time to find treatments for diseases that plagued their communities. Feel proud of what you are doing. Indeed you are part of a historical effort to find a treatment for Alzheimer's.

Growing Your *Best* Older Self



Everyone knows that as we grow older our bodies go through a number of physical changes. While we may not like some of these changes there isn't much we can do about them as they are a natural part of aging. Fortunately you have lots of company and there are ways to age in such a way that you can live a healthier life, even with memory and cognition concerns. When you reach your golden years you can expect to see many physical changes, to varying degrees. Just remember that everyone is different and ages differently. So what can you do to live as healthy as possible in your golden years?

You've heard it before, but it is worth repeating: diet and exercise form the foundation of a healthy life for seniors, and pretty much everyone else. Regular exercise and a healthy diet that incorporates all the food groups can have a strong bearing on your health and your quality of life. Statistics show that seniors who exercise, follow a proper diet, modify lifestyle choices (such as smoking) can avoid or reduce their risk of developing conditions such as high cholesterol, hypertension, heart disease, arthritis, osteoporosis, diabetes and depression. Even some cancers can be prevented or more easily treated with a proper diet, exercise and

lifestyle choices. So, what kind of changes are we talking about?

- If you smoke, quit
- Moderate alcohol consumption, limit yourself to one drink a day
- Use sunscreen and hats for sun protection
- Take care of your teeth – brush, floss and see your dentist regularly
- Visit your primary doctor on a regular basis to review your health, medicines and discuss any side effects or drug interactions
- Be sure your doctor conducts an annual health care screening to ensure your overall health is optimal. This includes vaccinations and prevention strategies.
- Don't forget to also see your eye doctor and podiatrist if you have diabetes
- Make sure you fill out an Advance Directive so your family knows your wishes.
- Engage in social activities, go on vacations and volunteer for causes that interest you.
- And finally, be sure to get adequate sleep.

Now for the two biggest changes you should make if you're not yet doing them.

Diet

No one likes the "D" word yet we can't emphasize its importance enough. The benefits of a healthy diet go miles and miles in helping seniors live as healthy a life as possible. What you eat can affect your lungs, heart, blood vessels, cholesterol, blood pressure, whether you develop diabetes, skin condition, some cancers and even vision. How is this possible?

First off it's worth pointing out that the body's tissues comprise of proteins, carbohydrates, fats, vitamins, minerals and water, which is also what is in the food we eat. Therefore a balanced diet that comprises of fruit, vegetables, whole grains, vitamins, minerals, proteins, eggs, dairy and adequate fluids is essential to providing these important elements and keeping the body's tissues in prime shape.

Equally as important to what we eat is how much of it we consume. Your body needs roughly the same number of calories as your body's metabolic requirements. As we grow older our bodies need fewer calories so it's important not to overeat. Depending on height, weight and activity level the older body requires approximately 1,500 – 2,000 calories per day. A dietician can help you determine more specifically what your individual body needs. As you hone in on your individual dietary needs it's essential to avoid empty calories that provide no nutritional value such as donuts, cookies, pastries, cakes, soda, chips, etc. Such things can be consumed on a special occasion but should be avoided on a regular basis. Certain conditions such as diabetes and heart disease require additional limitations that should be followed for optimum health. Your doctor or dietician can best advise you on those requirements.



Exercise

If you already exercise you already know the benefits as well as the fact that nothing else can replace exercise, not a pill, not an online game, not even reading a good book. Regular physical activity can control certain conditions, prevent others and affect cholesterol, high blood pressure, heart disease, diabetes, thinning bones, muscle weakness and depression. More specifically regular exercise has been shown to be beneficial in burning excess calories and maintaining weight, building up muscle and physical endurance, reducing falls and injuries, delivering oxygen and nutrients to the body's tissues, and enhancing both mood and quality of sleep.

If you're just getting started with exercising, consider a membership at your local Y or health club where you can get started with a trainer to show you safe exercise tips. If you'd like to go it alone consider the following:

- Start out exercising 30 minutes at a time to increase your heart rate to 75% of it's maximum rate. Maximum heart rate is calculated by subtracting age from the number 220.

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Exercise can improve brain function in older adults

Courtesy of University of Kansas Medical Center

New research conducted at the University of Kansas Medical Center indicates that older adults can improve brain function by raising their fitness level.

Jeffrey Burns, M.D., professor of neurology and co-director of the KU Alzheimer's Disease Center, led a six-month trial conducted with healthy adults ages 65 and older who showed no signs of cognitive decline. The results of the study were published on July 9 in the journal PLOS ONE.

The randomized controlled trial attempted to determine the ideal amount of exercise necessary to achieve benefits to the brain. Trial participants were placed in a control group that did not have monitored exercise, or they were put into one of three other groups. One group moderately exercised for the recommended amount of 150 minutes per week, a second exercised for 75 minutes per week, and a third group exercised for 225 minutes per week.

All groups who exercised saw some benefit, and those who exercised more saw more benefits, particularly in improved visual-spatial processing — the ability to perceive where objects are in space and how far apart they are from each other. Participants who exercised also showed an increase in their overall attention levels and ability to focus.

"Basically, the more exercise you did, the more benefit to the brain you saw," Burns said. "Any aerobic exercise was good, and more is better."



The research indicated that the intensity of the exercise appeared to matter more than the duration.

"For improved brain function, the results suggest that it's not enough just to exercise more," said Eric Vidoni, PT, Ph.D., research associate professor of neurology at KU Medical Center and a lead author of the journal article. "You have to do it in a way that bumps up your overall fitness level."

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— Eric Vidoni, PT, Ph.D.

Marjorie Troeh, of Independence, Mo., participated in the trial. Troeh, 80, was placed in the lowest level of exercise group. She said she signed up for the study in part to motivate herself to exercise more.

"I love exercising my mind, but I hate exercising my body," she said, adding that the findings about the exercise being linked to better brain function were new to her. "I knew about the evidence that said exercise was good for endurance and agility, but I really didn't make any connection with that and brain health."

Troeh, who lives in an independent living facility, said she was glad to have the opportunity to contribute to the fight against Alzheimer's by participating in a trial, as she had a grandmother and an aunt who battled the disease.

"I'm surrounded by people who face memory problems," she said. "I'm really anxious to do anything I can to further knowledge in this area."

Scientists at the KU Alzheimer's Disease Center have focused on the relationship between exercise and brain metabolism for years and are conducting a number of research studies on how exercise may help prevent or delay the onset of Alzheimer's.

BRAIN GAME

Can you find these hybrid dog names?

N B E A G O M N N M R M Y H R P P R S B
 E O U Z Y R D O R P A N E A U A D E C A
 X S H A Q J I H E E Z L U A T S I Z H S
 E J E S S C P C L A I E T T G T I W N S
 B N B N A C I I G G F L E E T L G O E U
 I U G D R K H F O L L R G O A L E B A G
 T C O A X E Q F B E B A C A E G E B G G
 O B A V C Z D I S E C S B C E R L K L Z
 N I K N B H B R A M A L H B A B G E E D
 B O C K E R O G O B E O M B E O A R U T
 C A V A C H O N S B N L L U B A E B P M
 Q M O L O L G A E B D V G I U J M O W V
 J R F M O T R V A H S E V N W J O C I P
 R V K C U D M M Y V L F X U E G P C L V
 B E A G L E M A N X V Y C D L R B A Y Y
 A E L G G U P F O I C A D E U Y F S M T
 B O V Q E X D D U X P U Z Z N V S H A Y

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|------------|------------|-----------|
| BASCOTTIE | BASSUGG | BEABULL |
| BEACOL | BEAGLEMAN | BEAGLIER |
| BEAGLOLO | BEAGO | BITON |
| BOCKER | BODACION | BOGLE |
| BORDERNESE | BOWZER | CAVACHON |
| DOXLE | ENGACHON | FRENGLE |
| GLECHON | GRIFFICHON | KASHON |
| LABBE | MALTEAGLE | MEAGLE |
| PATTERBEA | PEAGLE | POMEAGLE |
| POOGLE | PUGGLE | SCHNEAGLE |



Growing Your Best Older Self

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For example a 65 year-old's target heart rate should be no higher than 132 beats per minute. When beginning an exercise program start at a lower target rate such as 78 beats per minute and work up to the max over time.

- The easiest way to achieve this goal is to pursue basic exercises such as swimming, walking, using exercise machines such as a treadmill or stair stepper. Though they won't raise your heart rate, balance, flexibility and weight lifting exercises can also be useful in building muscle, increasing balance and preventing falls.
- Keep tabs on how you feel while you are exercising. If you experience chest pains or tightness, shortness of breath, dizziness or fainting while during or after exercising, stop and notify your doctor immediately.

And that's about it, nothing terribly complicated, just good solid advice based on years of experience. If you have any questions about improving your diet or starting an exercise program talk with your doctor before you get started. Once you have your doctor's okay start your new lifestyle changes slowly to ensure your greatest chance of success. If you're not already eating a healthy diet or exercising, once you do and acclimate to your new lifestyle changes you will likely be so pleased with the changes that you won't want to go back to your previous way of life.



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