

# THE RECOLLECTION CONNECTION



## MEMORY WELLNESS PROGRAM UNIVERSITY OF WASHINGTON VA PUGET SOUND HEALTH CARE SYSTEM

### *The Memory Wellness Program: Clinical Research and You*

The Memory Wellness Program is on a mission! We are busy studying why memory changes as we get older, and what can be done about it. In particular, our interest focuses on the link between glucose (sugar), insulin, and memory. We want to know

how memory is affected when the body's metabolism involving glucose and insulin, changes. Such metabolism changes are a natural consequence of aging, at least to some degree. However, a large proportion of adults over 50 years of age are experiencing even greater metabolism changes, a situation that could potentially have serious consequences for memory and thinking abilities down the road.

How do we study this link between aging memory, glucose and insulin? We approach the task with two different goals in mind. One approach is to understand

**WHY** changes in metabolism affect memory they way they do. Our second approach is to find out **HOW** memory can be improved. Using this second approach, we can evaluate whether specific treatments improve memory for older adults.



The **WHY** studies help us learn valuable information such as *why* does memory change with age, and *why* are metabolism changes linked to memory impairments? This information will ultimately be used to

design new beneficial treatments for memory. One such study currently in progress is our **TRIM** study. In this study, we raise blood levels of insulin and triglycerides for a short period of time (few hours) to examine the effects on memory. The purpose of the **TRIM** study is to learn not only about the influence of insulin and triglycerides on memory, but also to evaluate what

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## Supporting Memory Wellness Research: The Role of Volunteering

People often ask the question...how can I help find a treatment for Alzheimer's disease? One answer is to volunteer as a research participant with the Memory Wellness Program. We have a variety of studies that are enrolling people with or without memory problems, all of which have the goal of finding new ways to treat Alzheimer's disease and memory loss.

Some studies focus on *mechanisms* that might help to explain why certain biological processes contribute to memory impairment. These mechanism studies provide the

framework where we come to understand the biologic process in the development of memory impairment and enable us to develop exciting new *treatments* for Alzheimer's disease. Studies of this sort are typically of short duration, involving 3-7 visits with 2-6 weeks in between visits and a lot of flexibility in scheduling

We then take what we have learned from the mechanism studies to develop and test new treatments for people with memory impairment. These treatment studies enable

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## Supporting Memory Wellness Research: The Role of Philanthropy

Not able to help with time and effort but would love to make a difference? Philanthropic contributions can go a long way to making the reality of finding treatments for Alzheimer's disease a reality. Although the UW Memory Wellness Program successfully competes for research grants from organizations like the National Institutes of Health, it also seeks private funding from grateful patients and other members of the community. The reason is straightforward: the NIH and other public entities simply cannot support all worthy research efforts. They're also less likely to support ideas that — though novel and promising — have not yet been tested. Private funding, in short, fuels research innovation.

Gifts from individuals, corporations, and foundations allow the UW Memory Wellness Program to expand its clinical and training programs, pilot new scientific research, and retain and attract the best faculty leadership and scholarship. If you are interested in supporting the UW Memory Wellness Program in this way, please contact Steve Hettinga,

associate director of development at UW Medicine, at 206-897-1887.

If you prefer to mail your donation, please address your envelope, as follows:

UW Medicine  
Office of Development  
1325 4th Ave, Suite 2000  
Seattle, WA 98101

Make the check payable to "University of Washington Foundation" and indicate that you wish to support the UW Memory Wellness Program on the check

If you are interested in making a gift by credit card, please contact Donna Calliri, UW Medicine development office, at 206-543-6347.

Donations are 100% tax-deductible and will be used 100% to support UW Memory Wellness research and education. We greatly appreciate your interest and support.✿

## *An Update on Research: Past, Present, and Future*

### *G. Stennis Watson, PhD, Brian VanFossen, PhD*

Research is our lifeblood at the Memory Wellness Program (MWP), our primary way of contributing to the human well-being. We are excited about the progress that we've made over the past decade and continue to make today. As some of you know, the MWP studies the relationship among insulin and other hormones, blood sugar regulation, and memory as people age. Our work includes both treatment studies and more basic clinical studies. Our treatment studies seek to identify potential therapeutic strategies to prevent or slow the progression of Alzheimer's disease. Equally important, our more basic clinical studies seek to explain the mechanisms through which Alzheimer's disease and memory loss occur and determine how successful treatments work. Most studies take two to three years to complete, and we are continually designing and adding new studies to further our ability to understand and treat memory disorders. The next few paragraphs describe our findings in three recently completed studies (SNIFF-21, Diabetes, PACE), our progress in two ongoing studies (SNIFF-120, TRIM), and our plans for two new studies (MEAL, WIN).

#### *A Sniff of Nasal Insulin to Fight Forgetfulness (SNIFF-21 and SNIFF-120)*

We are excited that the results of our SNIFF-21 study are being published in the prestigious medical journal *Neurology*. SNIFF-21 was designed to determine the effects of intranasal insulin administration on memory in persons with progressive memory loss. Participants in SNIFF-21 received a daily dose

of intranasal insulin or saline for 21 days and took memory tests before they started taking insulin and again after 21 days of insulin administration. As we predicted, participants in the insulin group showed improvement in memory, attention, and basic living skills. Insulin also appeared to have a beneficial effect on blood levels of beta-amyloid, a protein closely identified with Alzheimer's disease. Insulin increased levels of the non-toxic form of beta-amyloid, but did not affect levels of toxic form of beta-amyloid. Recently, other scientists have proposed that increasing the non-toxic form of beta-amyloid relative to the toxic form may be protective against Alzheimer's disease.



SNIFF-21 led us directly into our current study, SNIFF-120, a four month intranasal insulin treatment trial. SNIFF-120 extends our previous research in several ways. It is a longer trial with a larger number of participants, and we are measuring biomarkers that we did not measure in earlier intranasal insulin studies. For example, some participants in SNIFF-120 will undergo a PET scan to characterize brain function before and after insulin treatment. Other participants will undergo a spinal tap to collect fluid made in the brain and transported down the spinal column. Our enrollment has been very good but we're still recruiting participants with memory loss for this study.

#### *Treating Diabetes Improves Memory (Diabetes)*

Many of you may be surprised to learn that older adults with diabetes have an increased risk for poor memory and poor attention. In

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## What is “MCI?”

*Brenna Renn and Lauren Smith*

Ever walk into a room and forget what you were looking for? Have you set your keys down and minutes later forgotten where you placed them? Do you sometimes get that “tip-of-the-tongue” feeling when you’re searching for a certain word or a person’s name, but you just can’t think of it?

Little memory glitches such as these are often just a part of getting older, or what we call “normal aging.” When this occasional forgetfulness becomes more routine or bothersome, or when you start to forget things that you wouldn’t usually forget, such as a weekly book club meeting or a doctor’s appointment, there might be something more serious going on.

Mild cognitive impairment, or MCI, is a term that is used to describe problems with memory or other thinking abilities that are worse than

other people in the same age group, but that don’t seriously affect a person’s ability to do their daily activities, such as driving and managing finances. Clinics (such as the Memory Wellness Program) determine what’s normal and what’s not by performing a variety of tests and asking a series of questions about memory concerns and medical history



People with MCI may be at higher risk for Alzheimer’s disease or other dementias; however, the good news is that not everyone with MCI goes on to develop more severe memory problems, and taking certain measures may help to slow or

even halt the progression. One important precaution is controlling cardiovascular risk factors. If your blood pressure or cholesterol levels are high, speak with your primary

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## Hyper tension and Memory Wellness

*Laura Bonner, PhD*

Hypertension, or high blood pressure, is a very common medical disorder, especially among older adults. Unfortunately, it may be tempting to ignore the diagnosis, especially because it may not cause noticeable symptoms. If you feel fine, you may not see the point of taking medications. However, if it is not treated, hypertension can cause serious problems such as stroke, and may contribute to cognitive impairment and dementia.

Recent research studies have found that hypertension is related to memory disorders such as mild cognitive impairment and

dementia. Patients with Alzheimer’s disease may experience a more rapid decline in cognitive abilities if they also have hypertension. Also, the combination of hypertension with diabetes has a negative impact on memory wellness. Hypertension is a serious health risk, but the good news is that we can do something about it!

So, what can you do to maintain a healthy blood pressure? Not surprisingly, the well-known advice to eat a healthy diet, get some exercise and reduce stress levels is important for healthy blood pressure.

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## Karen's Korner

### Karen Hyde, RN



Karen Hyde, RN

**Question:** My husband has gotten more irritable as his memory gets worse. He gets angry if I remind him or correct something he says. How do I handle these situations?

**Answer:** Your husband is trying to protect his independence and personal dignity. He is very aware of his losses. I know it can be difficult, but with lots of love and patience you can form a stronger bond with your husband.

Try to avoid correcting his misstatements or repetitive questions. He is not deliberately trying to annoy or frustrate you, and your "corrections" simply remind him over and over again that he has a memory impairment. He will feel better about himself if he is given choices and allowed to make decisions.

When you sense that your husband is angry and the situation is escalating, change the subject or redirect the conversation away from the sore point. Often just restating the topic in a nonjudgmental, nonconfrontational way can calm the situation.

Supporting your husband by enabling him to do as much as possible on his own is paramount in order to protect his sense of dignity. However safety is always a concern and if this is an issue, use your best judgment.

Take very good care of yourself and don't be afraid to ask family and friends for help so that you can have time for yourself. Joining a support group will allow you to share with others who are dealing with similar types of issues.

Finally, if you feel your husband's irritability possibly reflects *depression*, it is important that you discuss this with his physician. Sometimes treatment for the depression can improve how he feels about himself - thereby improving the quality of both your lives.✿

#### *Volunteer (Continued from page 2)*

us to evaluate novel interventions for Alzheimer's disease with the ultimate goal of helping to improve quality of life for those suffering from memory problems. The treatment studies are typically of longer duration, involving multiple visits over a two to eighteen month period.

However, as with all research, not all interested people are eligible to participate as research study participants. If you are not eligible to participate, there are other ways that you can help to make a difference in understanding and treating Alzheimer's disease and memory loss. In particular, you

can volunteer to assist with the myriad of tasks that go into making a research group like the Memory Wellness Program function. If you have computer/office skills, a medical background, or can provide transportation for some of our research participants, and have a few hours a week to commit to a regular schedule of volunteering, we can use your services.

For more information on volunteering as a research subject or in another capacity, please call Donna Davis, RN in Seattle at 206-764-2809 or Jaime Iliff in Tacoma at 253-583-2011.✿

*Clinical Research (Continued from page 1)*

influence elevated insulin and elevated triglycerides have on proteins that have been linked to blood sugar control, inflammation, and yes – Alzheimer's disease! Understanding *why* high insulin and high triglycerides impact memory can help us identify new treatments aimed at reducing the negative effects.

The **HOW** studies help us learn *how* to effectively treat memory problems and diseases, such as Alzheimer's. Once we understand *why* memory impairments develop and *why* they get worse over time, we can design a placebo-controlled, randomized study to identify beneficial treatments. **SNIFF**, **PACE**, and **RECALL** are three examples of placebo-controlled, randomized clinical trials conducted by the Memory Wellness Program. In these studies, participants are randomly chosen to receive the "active" treatment or to be part of a control group. The active treatment can be a medication, or another intervention such as exercise, that researchers believe will have a beneficial effect. For example, in **SNIFF**, some participants received insulin (the active treatment group), and other participants received saline (the control group). In **PACE**, some adults participated in a high intensity exercise program (the active treatment), while others participated in a stretching program (the control).

Participants often wonder why we include a control group in our studies, and they may be disappointed if they do not receive the active treatment. There are two important reasons to include a control group in any treatment study. First, we include a placebo control group, receiving no treatment, to serve as a comparison when we don't know whether a new treatment will have an impact. For example, most believe that exercise is good for memory; however, this has not yet been scientifically proven. Once we are certain that exercise

improves memory, we will no longer need to include a placebo control group in our exercise studies. Rather, we may include groups that engage in different levels of exercise, or we may include groups that engage in exercise with or without a healthy diet. Control groups are also important because they help us tease apart influences that are related to the study and those that are not. For example, when given the opportunity to complete a memory task now and in 3 months, your score will likely be a little higher in 3 months because you are more familiar with the task and you are more familiar with your surroundings in the clinic. As a consequence, you may feel more relaxed the second time around. Without a control group, we have no way of knowing if what appears to be a benefit in performance can be attributed to the active treatment or, simply to practice. When we include the control group, since everyone is likely to benefit from practice equally, any remaining differences between the groups can be attributed to the effects of the intervention. So, without the comparison that the control group provides, you can never know whether the intervention is actually working.

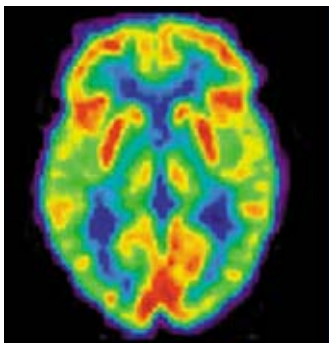
To continue our mission to understand **WHY** memory impairments develop and **HOW** to effectively treat this problem, we need your help. At this time are looking for participants for **SNIFF**, **RECALL**, **TRIM**, and now **MEAL** (see pg. 8). Please give us a call to find out more information about any of these ongoing studies.

In closing, I want to express my thanks to the many participants who have joined in our efforts to explore the complex and important relationships between insulin, glucose, memory, and aging. Your willingness to volunteer is vital to our research, so that we may work together to provide help for the present and hope for the future.\*

*Update (Continued from page 3)*

our diabetes study, we posed the research question: Will treating people with pre-diabetes or diabetes improve their memory? We also asked whether inefficient insulin activity contributes to memory impairments. Participants received either a drug that decreases blood sugar levels by increasing insulin levels, or a drug that improves the ability of existing insulin to promote the body's use of sugar as fuel, or a placebo pill. They took memory tests before they started taking the drug, and two and four months after they started taking the drug. As we predicted, both active drugs had improved memory; however, the drug that improves insulin efficiency had a much stronger effect than did the other drug. Thus, both improving insulin efficiency and reducing blood sugar levels are important facets of treating memory loss in diabetes. We also looked at the effects of these drugs on beta-amyloid, a protein that plays an important role in Alzheimer's disease. Only the drug that improves insulin efficiency decreased blood levels of the toxic form of beta-amyloid, relative to the non-toxic form. This finding raises the intriguing possibility that improving insulin efficiency may influence the fundamental disease process.

Some participants in the study also had PET scans—a form of brain imaging—to detect whether diabetes is associated with changes in brain functioning. We found that persons



Above is an example of a PET scan. The blue and green areas show lower brain activity, while the red and yellow areas show higher brain activity.

with diabetes had several brain regions with reduced brain activity, relative to healthy older adults. Thus, insulin appears to play a crucial role in memory, beta amyloid regulation, and brain functioning.

### *Triglycerides, Insulin, and Memory (TRIM)*

We all know that high-fat diets can increase our risk for heart disease, high cholesterol, and diabetes, and research with animals shows that diets rich in fat can impair memory. We designed two studies to look at how increased fat affects memory in humans. One study (MEAL) will examine how high-fat diets contribute to memory loss. The other study (TRIM) explores how elevated triglyceride levels relate to memory disorders in older adults.

Raising triglyceride levels even briefly can impair the ability of insulin to use glucose as fuel (insulin resistance). TRIM participants undergo four treatment conditions (increased insulin, increased triglycerides, increased insulin and triglycerides, placebo), and they take memory tests during each condition. We predicted that increasing insulin will improve memory, increasing triglycerides will impair memory, and simultaneously increasing insulin and increasing triglycerides will reverse triglyceride-induced memory deficits. Some participants are also receiving spinal taps. Since spinal fluid is made in the brain, identifying changes in spinal fluid allows us to infer changes in the brain when we increase insulin or triglycerides. Furthermore, we want to know whether these metabolic changes have different effects on older adults with or without memory disorders.

We have been very pleased with the number of persons who want to participate in this study, and we have almost reached our recruitment target for older adults without a memory disorder; however, we are still seeking

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participants with memory loss for the study. Soon, we will analyze the initial data from this study, which we plan to present at the annual meeting of the Society for Neuroscience this fall.

### Macronutrient Effects on Alzheimer's Disease (MEAL)

By now, many of you have read or heard about the MEAL study. The MEAL study is an exciting new line of research examining the effect of nutrition on memory. Participants in this study will eat one of two special diets and will have their memory tested to really determine if "you are what you eat." We are very pleased to announce that we have recently joined forces with one of the nation's foremost metabolic kitchens at the Fred Hutch Cancer Research Center in order to prepare the food for participants according to our very rigorous standards. With this new collaboration, we anticipate screening new participants for the study very soon!

Some of you who have already expressed interest in the study will be contacted to re-assess your commitment to this new line of research that has been chosen as a study of special merit by the National Institutes of Health and the National Institute on Aging. As with all of our research, it is our wonderful



volunteers that make all the difference. We need people with normal memory, mild memory problems, as well as those with diagnosed memory disorders like AD, to carry out this work.

### Working Memory, Insulin, and Norepinephrine (WIN)

Do you ever worry about your ability to do math in your head...or your ability to compute change the grocery store...or your ability to keep up with two things at once? These tasks are examples of a mental process called "working memory." Working memory requires that we hold bits of information in our minds and perform some mental operation on that information. Most of the time we take working memory for granted; however, without adequate working memory, we would have difficulty performing many of our daily tasks. For example, we need adequate working memory to do two things at once, to drive an automobile, and to formulate a response while you're listening to someone speak. Just like memory for a news story or a grocery list, working memory declines as we age and declines even more rapidly when a person has a progressive memory disorder such as Alzheimer's disease.

We want to introduce you to one of our upcoming studies, the WIN study. In the WIN study, we will explore pharmacologic strategies for improving working memory in older adults with mild cognitive impairment or Alzheimer's disease, as well as in older adults with normal memory. An extensive body of research demonstrates that working memory relies upon a brain chemical called norepinephrine. Our research at the Memory Wellness Program suggests that insulin influences norepinephrine and thus influences working memory. Therefore, age-related changes in working memory may be related to age-related changes in insulin and norepinephrine. Drugs that affect

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*Update (Continued from page 8)*

norepinephrine or insulin in the brain may affect working memory skills. In WIN, we will test hypotheses that insulin and guanfacine (a drug that stimulates norepinephrine activity) will improve working memory and that yohimbine (a drug that inhibits norepinephrine activity) will impair working memory. Participants will make six study visits to the VA Medical Center, receive a different infusion at each visit, and take tests of working memory. We predict that three of the infusion conditions will improve working memory, one condition will impair working memory, and one condition will not change working memory, relative to the control condition.

The WIN study has implications for understanding how working memory functions and for designing novel treatment strategies for working memory impairments in older adults. Results of this study have the potential to confirm that working memory relies on insulin and norepinephrine and that impairments in working memory may be due, in part, to age-related changes in insulin and norepinephrine. WIN findings may also suggest that guanfacine or a similar medication can be effective in treating working memory loss. You will be hearing more about this exciting study in the near future. ✨

*Hypertension (Continued from page 4)*

What is a healthy diet? A low-fat diet with lots of fruits and vegetables is always a good place to start, but when thinking about blood pressure, we also need to think about sodium. Sodium can increase blood pressure, and unfortunately, many of us eat a lot more sodium than we realize. Pre-packaged “convenience” foods often have 25% or more of our daily sodium allowance in just one serving. Try reading the labels on packaged foods you buy and choosing low-sodium options whenever possible. If you are used to having a lot of sodium in your diet, you may find that lower-sodium foods might taste bland. You might want to add more spices to enhance the flavor.

Another step you can take is to talk to your healthcare provider about blood pressure. If your blood pressure is too high, your provider might recommend one or more medications. In some cases, more than one medication will be necessary. Be sure to talk to your provider about any side effects you are experiencing that are discouraging you from taking the medication. It will work only if you take it! Your provider might also suggest that you monitor your own blood pressure in between medical appointments.

Don't ignore high blood pressure. Be proactive about blood pressure for overall good health. ✨

*MCI (Continued from page 4)*

care physician about getting them controlled with a medication or with diet and exercise. Also, keeping physically, mentally, and socially active are great recommendations for all older adults, regardless of memory impairment. Research participation is one way to maintain an active lifestyle, while contributing to our future understanding of MCI.

If you are concerned about your memory and are interested in taking part in research studies here at the Memory Wellness Program, please call our American Lake clinic at (253) 583-2011 or the Seattle clinic at (206) 764-2809. ✨

## Staff Highlights

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### American Lake:

#### *Julie Moorer, RN Community Liaison*

Julie has practiced as a Registered Nurse in Washington State for over 22 years. Her first years as charge nurse on a Geriatric medical floor planted the seeds of interest in providing healthcare services to elders. Her ensuing years as a daughter and granddaughter caring for her mother and grandmother at home, fueled the passion that she carries today in helping other families access care for their loved ones.



As an insurance case manager and hospice liaison nurse, Julie has traveled extensively in Pierce and King Counties and brings to her position a strong connection to the vast network of senior services and providers available throughout the community.

Julie's goal is to be the link between the community and the research and educational opportunities that are available for families through the Memory Wellness Program. From providing information about memory loss and Alzheimer's disease, to educating the public about the need for their participation in research, Julie is committed to connecting people to services and our community to its elders.

Julie describes herself as a good friend with a kind heart. She is passionate about her family, friends and animals. Her favorite times are spent with her husband Nathan, out on a good long walk with her dogs, or cooking a huge meal in the favorite room of her house – the kitchen.\*

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### Seattle:

#### *Debbie Burges, RN*

One of our newest members to The Memory Wellness Program is our study nurse, Debbie Burges, BSN. She is a graduate from the Boston University School of Nursing with 25 years of nursing experience, specializing in cardiac and rehab clinical care.

Debbie has been a VA employee since 2002, and recently joined The Memory Wellness program here at the Seattle VA Hospital. Look for Debbie's cheery personality on the 6<sup>th</sup> floor of the hospital, meeting participants for study visits!



Debbie says that she loves working at the VA and being involved in a research program that provides treatment and discovery. Her comments were "I love working with the participants and sharing in their passion for making a difference. The staff is great and we all have fun doing our jobs!"

Debbie spends her free time with her husband Chris, and their three daughters, two of whom are college bound, and one who is in high school. She enjoys music and painting and playing with her two dogs.\*

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## Staff Updates: Farewell, Welcome!, and Congratulations!

### Farewell...

*This last year we had to say a very reluctant good-bye to some of our staff:*

Joy Nelson, RN, is working with another research program at the University of Washington.

Kristoffer Rhoads, PhD is working at Virginia Mason as a Neuropsychologist.

Molly Mullen is going to school to get her nursing degree.

Meabh Carter is working in private health care.

Tracia Clark is working at the American Lake VA in the Dept of Mental Health.

Laura Fisher is in the Peace Corps in South America.

Kathleen Reilly has retired after many years of service at the VA Hospital.

Alice Fong has gone back to school to pursue her Masters.

*We wish them all the best.*

### Welcome!

*We are very happy to welcome some wonderful new members to our team:*

Julie Moorer, RN, is our new community liaison.

Jane Judd joins us as a recruitment coordinator and research technologist.

Lauren Smith and Brenna Renn join us as research technologists at American Lake.

Laura Bonner, PhD is a neuropsychologist who will be working at American Lake and Seattle.

Debbie Burges, RN is a research nurse in Seattle.

Jen Bayer, a nutrition student at Bastyr, is working on our MEAL study.

Tracey Poirrier joins us as a psychology technician, and will work in both American Lake and Seattle.

### Congratulations! New Arrivals

Michael Dennis Chapman was born to Darla and Tom Chapman on July 9 at 6:57PM. Michael weighed in at 8 lbs.



Michael enjoying his first encounter with snow.

Preston Andrew Dembiczak~ DOB 11/21/07. Staff member, Jane Judd, a first-time grandma, couldn't be more thrilled!



Preston Andrew

### Weddings

Jaime Iliff (now Jaime Tidwell) married Brian Tidwell on June 23, 2007.



Jaime and Brian

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Please visit our new and improved website at  
<http://www.memorywellness.org>  
for information on community resources, upcoming lectures,  
our researchers, and studies.

For information about having a Memory  
Wellness Program representative or speaker at  
your event, please contact Julie Moorer at  
253-583-2008.