

Newsletter Glossary

Discordant: This refers to differences within a pair of twins. A twin pair “discordant for combat exposure” would be a pair where one brother was exposed to combat and the other brother was not.

Magnetic resonance imaging (MRI) produces detailed 3-dimensional pictures of the inside of the human body. Researchers use MRI to show the *size, appearance and form* of tissues and organs in the body. Functional MRI (fMRI) is a special type of MRI used to see how brain cells work.

Methylation: This is a type of chemical modification of DNA that can be inherited, but also changes during your life without changing the original DNA sequence. The modification can alter how your genes work during the course of your life. DNA methylation happens naturally over time and helps determine which genes get “switched on and off” as we age.

Positron emission tomography (PET) produces 3-dimensional pictures of the inside of the human body. Researchers use PET imaging to see *biologic processes* that occur within tissues and organs in the body.

Post Traumatic Stress Disorder (PTSD): This is a condition triggered by a traumatic event. PTSD can develop after experiencing or witnessing an event that causes intense fear, helplessness or horror.

News for Participants in the Vietnam Era Twin Registry

Researcher Spotlight: Dr. Roger Pitman

We would like to introduce you to Dr. Roger Pitman, who has made important discoveries about posttraumatic stress disorder (PTSD) working with VET Registry twins. Dr. Pitman is a Professor of Psychiatry at Harvard University and an



Dr. Roger Pitman, PTSD Researcher and Professor of Psychiatry at Harvard University

internationally known researcher, clinician, and teacher. Dr. Pitman recently received the Lifetime Achievement Award from the International Society for Traumatic Stress Studies for his path-breaking research on PTSD.

Many of Dr. Pitman’s studies involve VET Registry twins undergoing tests in his Boston research center. By studying twins he has been able to better understand the genetic and environmental factors related to the development of PTSD. Dr. Pitman enjoys working with Veterans and contributing to science. He has published more than 100 articles related to PTSD. Dr. Pitman stated that, “Without the members of the Registry, we wouldn’t know nearly as much as we do about PTSD.”

If you are interested in learning more about the work Dr. Pitman is doing, you can check out one of his recent publications: “Posttraumatic stress disorder and dementia: What is the origin of the association?” in the June 9, 2010 edition of the *JAMA*, the Journal of the American Medical Association.

You can help Veterans by participating

Have you been contacted regarding a VET Registry research study? If so, researchers are looking forward to hearing from you. Many research projects are ongoing and your participation will help Registry researchers answer important questions about the health of Veterans. You can read about the different studies now taking place in the *Study Updates* section of this Newsletter on page 3.

If you have been contacted about a study and have questions, please feel free to contact the VET Registry at our toll free 1-866-774-9647.

The researchers working with the VET Registry want to thank you for your continued participation and support of Registry research. It is only with your help that we can learn how to improve the health of Veterans.

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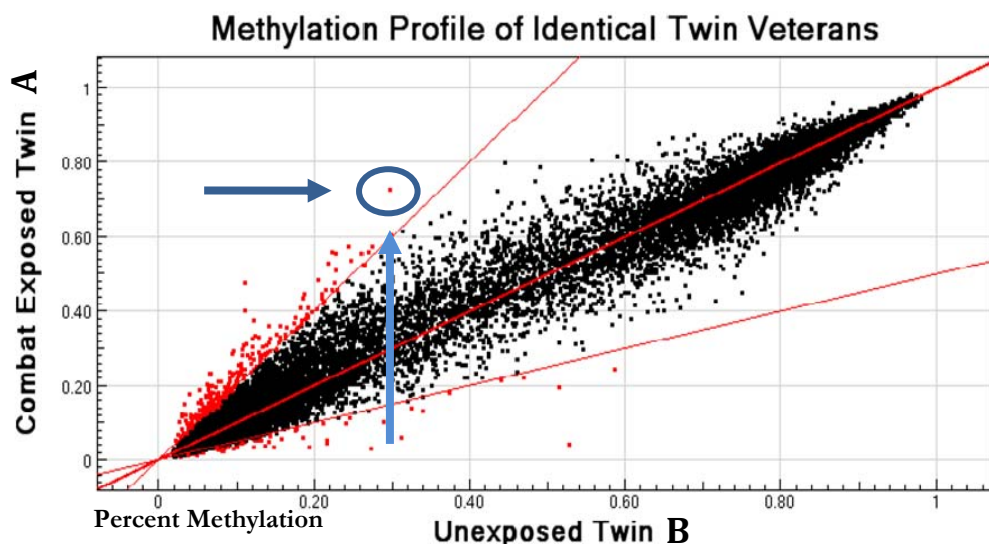


What are researchers doing now?

The Cooperative Studies Program (CSP) is a division of VA's Office of Research & Development and uses state-of-the-art research methods to study the health of Veterans. CSP is involved in the VA Genomic Medicine Program, whose goal is to improve Veterans' health through the study of the human genome. Genomic analyses can be used to learn how people's genes influence their susceptibility to diseases, the progression of diseases, and their response to drug therapy.

The VET Registry is now working with the VA Pharmacogenomics Analysis Laboratory (PAL) to learn how an individual's genes influence their health. The first VET Registry study completed by PAL was a pilot project to examine the long-term effects of stress on DNA. This pilot study involved 12 identical twin pairs where one twin had experienced traumatic events in their life and the other twin had not. We compared differences in DNA methylation (see glossary on page 1) between each twin to see if exposure to stress or trauma had an impact on methylation.

The second VET Registry pilot study with PAL is a project designed to discover common genes related to both emotional depression and inflammation. This pilot study proposes to identify differences between depressed Veterans and their twin brother. Researchers hope to find additional genetic links between major depression and inflammation.



Methylation profiles of 14,000 genes analyzed by microarray technology. DNA is from one pair of identical twin veterans—one who was exposed to combat stress and one who was not exposed to severe stress. The gene circled on this chart is an example of how one gene from the same DNA has had significantly different methylation between Twin A (75%) and Twin B (30%).

Figure provided by the Cooperative Studies Program

Summary: Genetic influences on the stability of mental ability

The VETSA investigators at Boston University and the University of San Diego recently published a paper based on Registry twin research and have summarized their article for us here:

“The way that genes and the environment influence mental ability may change over time. Despite remarkable long-term stability plus strong evidence for genetic influences, we haven't had a clear picture of the role of genes in maintaining the stability of mental ability. Members of VETSA were re-

administered a test of general mental ability (Armed Forces Qualification Test) that they had taken when they entered the military. We found that genetic influences are stronger in late middle age (around 55 years) than during young adulthood (around 20 years).

About 33% of the variation in intellectual ability during early adulthood is due to genetic factors, but by late middle age genetic influences were responsible for 58% of the variation among individuals. Although the strength of

genetic influences increased over time, it was the same genes operating at both ages. However, future research, including the ongoing VETSA study, may find that at later ages different genes may begin to operate.”

Lyons, M., York, T., Franz, C., Grant, M., Eaves, L., Jacobson, K., Panizzon, M., Boake, C., Xian, H., Toomey, R., Eisen, S., Kremen, W. *Genes determine stability and the environment determines change in cognitive ability during 35 years of adulthood.* *Psychological Science*, 2009, 20(9), 1146-1152.

VET Registry Study Updates

★Vietnam Era Twin Study of Aging (VETSA)

Principal Investigators: Dr. William Kremen, University of California, San Diego, CA, and Dr. Michael Lyons, Boston University, Boston, MA

The goal of VETSA is to follow twins throughout their lives, contacting them every 5 years to learn about genetic (nature) and environmental (nurture) factors that influence the aging process.

The VETSA magnetic resonance imaging (MRI) studies are linked to the main VETSA project and are studying the brain and how it changes as Veterans age.

Through these studies, researchers hope to learn about the influence genes have on the aging brain. Their studies include over 1,200 twins and follow-up research on these twins is now underway.

★Twin Study of Biological Markers for Post Traumatic Stress Disorder (PTSD)

Principal Investigator: Dr. Lisa Shin and Dr. Roger Pitman, Harvard School of Medicine, Boston, MA

This study is using functional magnetic resonance imaging (fMRI) to compare the brain function in identical twin pairs, where only one twin was exposed to combat during the Vietnam War.

The goal of this study is to determine if specific brain regions function differently in combat Veterans with PTSD compared with their identical twins who were exposed to combat and do not have PTSD.

★Memory and Hippocampus in Vietnam Veteran Twins with Post Traumatic Stress Disorder

Principal Investigator: Dr. J. Douglas Bremner, Emory University, GA,

The purpose of this study is to look at an area of the brain involved in learning and memory (called the hippocampus) over time and see how that relates to twins who were exposed to combat and have a diagnosis of PTSD.

The study includes an in-depth clinical evaluation involving interviews, paper and pencil questionnaires, tests of memory, laboratory testing, magnetic resonance imaging (MRI), and positron emission tomography (PET) imaging of the brain.

★Stress and Vascular Disease Evaluation in Twins (SAVE IT) and Twins Heart Study 2 (THS-2)

Principal Investigator: Dr. Viola Vaccarino, Emory University, GA

The goal of this research is to measure the influence of mental health on heart disease. The SAVE IT study involves participants traveling to Atlanta to undergo testing for early symptoms of heart disease.

The objective of the THS-2 study is to better describe the role of emotional depression on heart disease. Eighty pairs of twins who had already participated in an earlier phase of this study, have been invited to participate. This new study will look at how heart disease progresses and the relationship between the depression and heart disease.

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Introducing: The VET Registry team

Nicholas L. Smith, PhD, is the VET Registry Director. He provides overall leadership for the administrative and scientific goals of the Registry.

Jack Goldberg, PhD, is an epidemiologist with more than 25 years of experience in the management and analysis of complex epidemiological studies. He has intimate and unique knowledge of the VET Registry, having worked at the Registry since 1983.

Jen Sporleder, BS, is the VET Registry Program Manager. Her overall responsibilities include data management, data security, and human subjects' protections. Ms. Sporleder keeps the Registry running smoothly, ensuring it will remain successful in the future.

Alaina Mori, BA, is a VET Registry Research Coordinator. Ms. Mori helps with general Registry administration, coordinates the biospecimen repository, and works on several in-person assessment studies.

Casey Evans, BS, is a VET Registry Research Coordinator. She works with researchers interested in using Registry data and assists with human subjects protections.

Melyssa Tsai, BA, is a VET Registry Research Assistant for the Veteran Health Study. She coordinates data security matters for Registry studies and contractors.

Nicole Waiss, BS, is a VET Registry Research Assistant and assists with the coordination of family studies and in-person assessment studies.

Seattle ERIC Staff

Phil Terry, MHA, Assistant Director

Carrie Gehring, CPS/CAP, BSTM, Administrative Support Specialist

Kate Moore, PhD, Research Data Manager

Chris Forsberg, MS, Biostatistician

Vickie Blakey, BA, Program Assistant

About VET Registry

Update: VET Registry consent

The VET Registry consent process was updated to make it simpler and easier for you. In the 2008 edition of *Twin Times* we told you about a new consent process that was in the planning stages. VET Registry staff worked with human subjects' protection and other oversight committees to create a simpler process than that originally outlined in 2008. Included with this newsletter are the updated consent documents for your continued participation in the Registry.

Please read the documents carefully. They outline important information about what it means to be a member of the Registry. We suggest that you keep the documents in case you have questions or concerns about the Registry in the future. Also included with this newsletter is a frequently asked questions document about what it means to be a Registry member. Of course you may decide not to participate ("opt-out") in the Registry now or at any time in the future. If you opt-out, this means you will not be invited to participate in any studies and we will destroy your contact information. To opt-out, please return the opt-out form included with this newsletter.

If you have questions or comments, please do not hesitate to call us at our toll-free number: 1-866-774-9647. If you leave a message, please speak clearly, leave both your first and last name, and leave a working telephone number so that we can return your call promptly. **Without you the VET Registry would not exist ~ we at the Registry look forward to your continued participation.**

Recently published research papers:

Su, S; Lampert, R; Lee, F; Bremner, D; Snieder, H; Jones, L; Murrah, NV; Goldberg, J; Vaccarino, V. **Common Genes Contribute to Repressive Symptoms and Heart Rate Variability: The Twins Heart Study.** *Twin Research and Human Genetics.* 2010; (13) 1; 1-9

Su, S; Zhao, J; Bremner, D; Miller, A; Tang, W; Bouzyk, M; Snieder, H; Novik, O; Afzal, N; Goldberg, J and Vaccarino, V. **Serotonin Transporter Gene, Depressive Symptoms, and Interleukin-6.** *Circ Cardiovasc Genet.* 2009;2;614-620

Jun Dai, J; Lampert, R; Wilson, PW; Goldberg, J; Ziegler, TR and Vaccarino, V. **Mediterranean Dietary Pattern Is Associated With Improved Cardiac Autonomic Function Among Middle-Aged Men: A Twin Study.** *Circ Cardiovasc Qual Outcomes.* 2010;3: 366-73

(Continued from page 3)

Study Updates

★Family Studies of Health and Behavior

Principal Investigators: Dr. Theodore Jacob, Palo Alto VA, Palo Alto, CA, and Dr. Kathleen Bucholz, Washington University, St. Louis, MO; VETR0105, 1104, 0505

Studies at the VA in Palo Alto, CA focus on the mental and physical health of Veterans and their families with an interest in determining how genes and experiences affect whether people smoke, drink, use drugs, and have depression. In one study, twins are being followed throughout their adult years to determine how their drinking habits change as they age. In another study, the focus is on adult children of twins to determine similarities and differences in health patterns across the generations. It is

hoped these studies will help clinicians design prevention and treatment programs.

At Washington University in St. Louis, MO, the Transition to Adulthood Project (TAP) began collecting data from Registry twin fathers and their families in 2002 and is currently conducting follow-up interviews with the adult children of twins. The TAP team is measuring young adult milestones, like marriage and parenthood, completion of education, occupation and job satisfaction; the team will examine how these milestones relate to health, especially in the areas of mood and the use of alcohol, tobacco and drugs.

★Veteran Health Study

Principal Investigators: Dr. Jack Goldberg, VA Puget Sound, Seattle VA and Dr.

Kathy Magruder, Charleston VA, Charleston, SC; VETR0705-CSP569

The goal of the Veteran Health Study is to better understand the physical and mental health of Veterans as they grow older. Hundreds of twins have already participated in the Veteran Health Study and all twins will be asked to participate. In this study twins complete a pencil and paper questionnaire about their physical health and are interviewed by telephone about their mental health.

The knowledge from this study will help researchers understand how aging affects general health, disability, diabetes, PTSD, depression and other issues. This information will assist the VA in designing programs for prevention and treatment of the health problems of aging Veterans.