DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

We propose to determine if long-term exposure to solvents is associated with adverse central nervous system (CNS) outcomes, specifically cognitive function (CF) and metrics from structural magnetic resonance imaging (MRI) of the brain. No prior studies of the CNS effects of neurotoxicants has evaluated a large number of older adults without current exposure, with quantitative assessment of long-term exposures, combining neurobehavioral assessment, neuroimaging, and assessment of vascular health and genetic polymorphisms known to influence CNS health or chemical kinetics or toxicity. Moreover, no prior studies have evaluated diffusion tensor imaging, an MR technique that allows for better white matter measurements. We propose a study of 1,080 former workers at Los Alamos National Laboratory in New Mexico, between the ages of 50 and 70 years, with a broad range of exposure to chlorinated, aromatic, and other solvents. All subjects will complete neurobehavioral testing, and a random sample (N = 300) will also complete structural MRI with diffusion tensor imaging. Several measures of vascular health and genotypes of five polymorphic genes (ApoE, ACE, GSTM1, GSTT1, NAT2) will be assessed. The population is stable, has a wide range of educational levels and solvent exposures, we have been working with them for six years, and extensive industrial hygiene sampling data are available. Detailed exposure assessment will be completed in year 1, before subject recruitment. In order to ensure a sufficient sample size, we propose a cross-sectional study and will enroll subjects over 27 months, rather than enroll a smaller number and do repeat testing. The relations among cognitive functions, solvent exposure, aging, vascular health, genetic polymorphisms, and neuroimaging measures are of great interest for the former solvent workers under study and to public health concerns regarding the role of neurotoxicants and the aging brain.

PERFORMANCE SITE(S) *(organization, city, state)*

Johns Hopkins University, Bloomberg School of Public Health (BSPH), Baltimore, MD
Johns Hopkins University, School of Medicine (SOM), Baltimore, MD
University of Pennsylvania School of Medicine, Philadelphia, PA

KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below. Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

| Name | Organization | Role on Project |
|---|---|---|
| Schwartz, Brian S., MD, MS | Johns Hopkins BSPH | Principal investigator |
| Bolla, Karen I., PhD | Johns Hopkins SOM | Co-investigator |
| Breysse, Patrick, PhD | Johns Hopkins BSPH | Co-investigator |
| Davatzikos, Christos, PhD | University of Pennsylvania | Co-investigator |
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***Disclosure Permission Statement.*** Applicable to SBIR/STTR Only. See instructions. ☐ Yes ☐ No