ASP-American Geriatrics Society Foundation for Health in Aging Award

AWARD RECIPIENT

Diana R. Kerwin, MD

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PROJECT

"The Association Between Body Mass, Body Fat Distribution, and Vascular Risk Factors on Functional MRI and Cognitive Performance in Postmenopausal Women"

MENTORSHIP TEAM

Edmund H. Duthie, Jr., MD
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Alzheimer's disease (AD) is the most common neurodegenerative disease of aging. Approximately six to eight percent of adults over age 65 years will develop AD, which leads to an irreversible decline in cognition, function, behavior, and, eventually, premature death. Current treatments delay loss of function, but no treatments are available to restore cognitive abilities or halt the progression of neuronal loss. Therapeutic strategies to delay the onset of clinical disease or primary preventive therapies to use in high-risk individuals will significantly benefit the aging population.

Although genetic risk factors may account for 50 percent of the risk for developing late-onset AD, many risk factors are yet to be identified. There is increasing evidence that vascular risk factors and vascular disease influences the risk of developing AD. Several studies have shown an association between AD and vascular disorders such as atherosclerosis, hypertension, coronary heart disease, and diabetes mellitus.

Obesity and overweight increase risk of vascular disorders and may also increase risk of dementia such as AD. A recent case-control study reported that obesity and APOE4 status independently increase risk of AD. Obesity has been suggested as a risk factor for AD in older women and has been associated with poorer cognitive function in men but not in women. In fact, there is some evidence that obesity is protective against cognitive impairment in women possibly related to endogenous estrogens. Body fat mass is a major source of endogenous estrogens in postmenopausal women and higher estradiol levels have been associated with upper body obesity. Estrogen's protective effects on the brain may include promoting cholinergic activity, reducing neuronal loss, reducing cerebral ischemia by improving blood flow and reducing cholesterol levels, and modulating expression of the APOE4 gene.

The proposed study will further elucidate the relationship between obesity as a risk factor for AD in women and the effect of vascular disease, inflammatory markers, hormone levels, and APOE4 status in postmenopausal women. This type of serum and genetic analysis has not been performed and will provide valuable information for aging-related research and further our understanding of AD in women.

I will develop a career in patient-oriented aging research by obtaining advanced training in clinical research design, biostatistics, clinically relevant genetics research, and the genetics of AD. Additionally, I will obtain advanced training in the use of functional magnetic resonance imaging (MRI) in cognitive testing and theory through courses offered in the Medical College of Wisconsin (MCW) Functional Imaging Research Center and the MCW General Clinical Research Center Training Program. I will further develop my career through the mentorship and training obtained through working directly within Dr. Shailendra Patel's genetic laboratory and through continued collaboration with Jane M. Kotchen, MD, and Edmund H. Duthie Jr., MD. I will build upon my previous observational investigations to develop a prospective, clinical investigation of the association and effect of body weight, genetic, inflammatory, and vascular risk factors on cognitive domain function and expanding this to include functional MRI to identify early markers of AD risk.