

Vascular Disease Risk Factors (VDRF) in MS is Associated with Brain ATP Abnormalities: Dysmetabolism May Drive MS Disease Progression.

Vijayshree Yadav^{1,2}, Allison Fryman², Michael Lane^{1,2}, Frank Bittner^{1,2}, Manoj Sammi¹, William Rooney¹
¹Oregon Health & Science University, ²Portland Veteran's Affairs Medical Center

Objective: To determine if VDRF accelerate disease progression by decreasing cerebral blood flow and brain metabolism in people with MS.

Background: VDRF, such as hyperlipidemia, hypertension, obesity, diabetes, and heart disease, appear to significantly increase the risk of disability progression in MS, however the underlying mechanisms are not well understood.

Design/Methods: This is a 3-year prospective, observational, single-site, study with two arms (MS subjects with and without VDRF). 7T MRI brain data collected at baseline, 12, 24 and 36 months. Outcome measures include changes in: 1) high energy phosphate metabolites in cerebral gray matter assessed by ³¹P 7T MR imaging (MRSI) and cerebral blood flow and blood volume detected by dynamic contrast-enhanced 7T MRI, 2) brain parenchymal volume assessed using SIENAX, 3) clinical impairment, disability, and quality of life.

Results: We performed cross-sectional analyses of the baseline MRI data was available for 50 subjects. Mean age/gender was 54.5 years with 72% female) (+VDRF, N=28, mean age 56.4 years, 82% female) and -VDRF, N=22, mean age 52.2 years; 59% female). We analyzed a volume of interest in the occipital region for changes in phosphate metabolites using 7T MRSI. Adenosine triphosphate (ATP) to total phosphate signal ratio was decreased in +VDRF subjects by 4.5% (P<0.05) compared with -VDRF subjects. +VDRF female subjects had a 3.9% decrease in normalized brain tissue volume (P=0.02) compared to -VDRF. Cerebral blood flow data and clinical correlates will be presented.

Conclusions: This is the first study to assess brain metabolism and cerebral blood flow in MS patients with and without VDRF. We demonstrate here that MS subjects with VDRF have significantly reduced brain ATP compared with MS subjects without VDRF. ATP depletion may reflect mitochondrial dysfunction resulting from cerebral blood flow abnormalities and contribute to MS disease progression as suggested by the increased brain atrophy in those with VDRF.