DO LOW FOLATE AND HYPERHOMOCYSTEINEMIA CONTRIBUTE INDEPENDENTLY TO VASCULAR DYSFUNCTION?

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Hyperhomocysteinemia (HHcy) is a risk factor for arterial disease. Previously we observed that HHcy evoked by folate depletion caused vascular dysfunction in rats. However, evidence exists that low folate (LF) concentrations alone, also contribute risk toward cardiovascular disease. Therefore, it is not clear whether the dysfunction we observed earlier was due to HHcy, LF concentrations, and/or their combination. In this study we tested the independent contributions from HHcy and LF, as well as their combination (HHcy+LF), to vascular dysfunction of rat mesenteric resistance arteries (~ 180 μm, internal diameter). Rats consumed standard chow (10 mg folate/kg chow) and water that was not (Con) or was (HHcy) supplemented with 1% methionine. Additional animals consumed LF chow (0.4 mg folate/kg feed) and water that was not (LF) or was (HHcy+LF) supplemented with 1% methionine. After ~12 weeks, plasma homocysteine (Hcy; μM) and liver folate [μg folate/g liver] were assessed to confirm the efficacy of our dietary manipulations.

Our data indicate that relative to Con animals: 1) HHcy rats had elevated Hcy but normal folate; 2) LF animals had normal Hcy but low folate; and 3) HHcy+LF animals had elevated Hcy + low folate concentrations. Therefore, we were able to test our hypotheses that: 1) HHcy and LF evoke arterial dysfunction independently and that 2) arterial dysfunction is exacerbated in the presence of HHcy + LF. Endothelium-dependent (Ach) and endothelium-independent (SNP) vasorelaxation were assessed by performing dose response curves, using wire-type myographs. Our results indicate that while Ach-evoked vasorelaxation (left side figure) was blunted (p<0.05) in all groups relative to Con animals, SNP-evoked vascular function (right side figure) was similar among groups. These data suggest that dysfunction was successfully produced by the LF as well as the HHcy animals. The significance of our findings is that we were able to observe the greatest amount of dysfunction in the HHcy + LF animals.

![Graphs showing vasorelaxation data](image-url)