Egg n-3 Fatty Acid Composition Modulates Biomarkers of Choline Metabolism in Free-Living Lacto-Ovo-Vegetarian Women of Reproductive Age

Allyson A. West, PhD; Yun Shih, MS, RD; Wei Wang, PhD; Keiji Oda, MS; Karen Jaceldo-Siegl, DrPH; Joan Sabaté, MD, DrPH; Ella Haddad, DrPH; Sujatha Rajaram, PhD; Marie A. Caudill, PhD, RD; Bonny Burns-Whitmore, DrPH, RD

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ABSTRACT

The lacto-ovo-vegetarian (LOV) dietary regimen allows eggs, which are a rich source of choline. Consumption of eggs by LOV women may be especially important during pregnancy and lactation when demand for choline is high. The aim of this single blind, randomized, crossover-feeding study was to determine how near-daily egg consumption influenced biomarkers of choline metabolism in healthy LOV women of reproductive age (n=15). Because long-chain n-3 fatty acids could influence choline metabolism, the effect of n-3–enriched vs nonenriched eggs on choline metabolites was also investigated. Three 8-week dietary treatments consisting of six n-3–enriched eggs per week, six nonenriched eggs per week, and an egg-free control phase were separated by 4-week washout periods. Choline metabolites were quantified in fasted plasma collected before and after each treatment and differences in posttreatment choline metabolite concentrations were determined with linear mixed models. The n-3–enriched and nonenriched egg treatments produced different choline metabolite profiles compared with the egg-free control; however, response to the eggs did not differ ($P>0.1$). Consumption of the n-3–enriched egg treatment yielded higher plasma free choline ($P=0.02$) and betaine ($P<0.01$) (vs egg-free control) concentrations, whereas consumption of the nonenriched egg treatment yielded borderline higher ($P=0.06$) plasma phosphatidylcholine (vs egg-free control) levels. Neither egg treatment increased levels of plasma trimethylamine oxide, a gut-flora–dependent oxidative choline metabolite implicated as a possible risk factor for cardiovascular disease. Overall these data suggest that egg fatty-acid composition modulates the metabolic use of choline.
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CHOLINE IS A QUATERNARY AMINE MOLECULE USED to produce the ubiquitous phospholipid phosphatidylcholine (PC) via the cytidine diphosphate (CDP)-choline biosynthetic pathway (Figure). Choline may also be acetylated to form the neurotransmitter acetylcholine or oxidized to the methyl donor betaine. Dimethylglycine is produced when betaine donates a methyl group to methionine (Figure). Sphingomyelin, a choline metabolite, is derived from PC and is a component of lipid membranes and lipoproteins.[1] PC synthesized via the phosphatidylethanolamine *N*-methyltransferase (PEMT) pathway provides a de novo source of choline (see the Figure); however, exogenous dietary choline is required to meet somatic requirements.[2]

The Adequate Intake level for premenopausal women is 425 mg/day,[2] although it is estimated that <10% of American women achieve this recommendation.[3] Women with diets that restrict consumption of choline-rich animal source foods may be particularly vulnerable to choline intakes below current guidelines. The lacto-ovo-vegetarian (LOV) dietary regimen prohibits intake of some choline-rich foods such as red meat and poultry, but allows consumption of eggs, an excellent dietary source of choline.[4] Therefore, eggs may be used to enhance choline intake among LOV women of reproductive age, which is of particular importance during pregnancy and lactation when the demand for choline is high.[5]

The current study is an extension of a feeding study[6] in which the consumption of n-3 fatty-acid–enriched eggs, nonenriched eggs, and walnuts was compared with regard to serum lutein.[6] The aim of this research was to determine the effect of near-daily egg consumption vs egg restriction on circulating choline metabolites in free-living LOV women of reproductive age. The influence of n-3–enriched vs nonenriched eggs on biomarkers of choline metabolism was also investigated secondary to recent reports of a striking relationship between the n-3 fatty acid docosahexaenoic acid (DHA) and PC metabolism.[7,8] Finally, due to associations between trimethylamine oxide (TMAO), a gut-flora–dependent oxidative choline metabolite, and

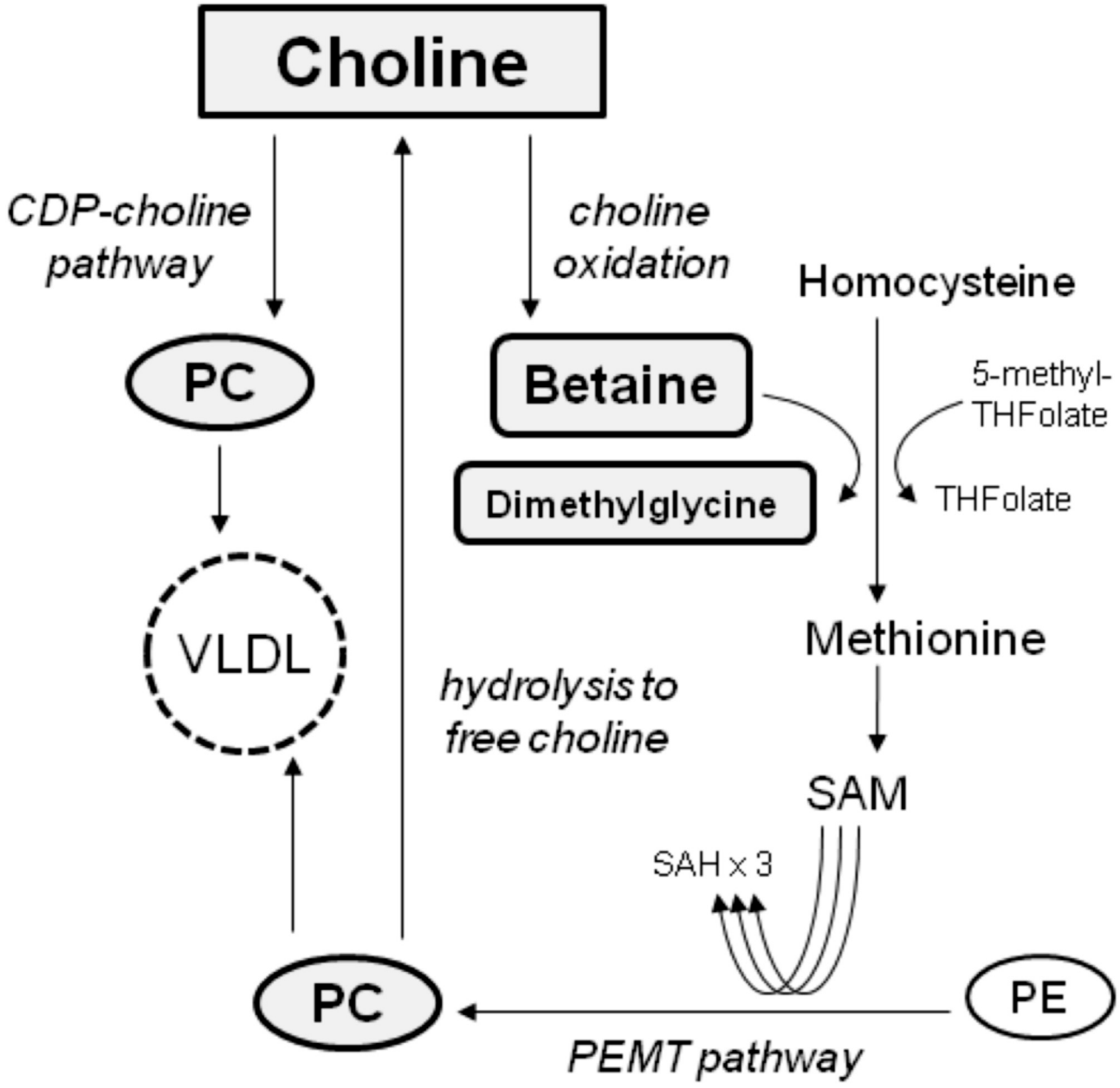

Figure. Diagram illustrating the relationships of choline metabolic products. Choline may be used to synthesize phosphatidylcholine (PC) via the cytidine diphosphate (CDP)-choline pathway or oxidized to betaine. A labile methyl group from betaine may be transferred to homocysteine to form dimethylglycine and methionine, a precursor of the universal methyl donor *S*-adenosylmethionine (SAM). PC can also be synthesized endogenously via the phosphatidylethanolamine *N*-methyltranferase (PEMT) pathway and used to generate free choline. PC molecules produced by the CDP-choline and PEMT pathways are also used for very-low-density lipoprotein (VLDL) synthesis. 5-methyl-THFolate=5-methyltetrahydrofolate. THFolate=tetrahydrofolate. PE=phosphatidylethanolamine; SAH=*S*-adenosylhomocysteine.

cardiovascular disease risk,[9,10] pre- and posttreatment plasma TMAO concentrations were quantified.

STUDY PARTICIPANTS AND METHODS

Study Participants

Healthy LOV adults recruited primarily from the southern California area completed a multistage screening process, as previously described by Burns-Whitmore and colleagues.[6] Participant inclusion criteria of the original study were aged 21 to 90 years, no existing medical condition, no dietary supplement use, nonsmoking, nonalcohol using, LOV for ≥3 months before study enrollment, and willing to follow study protocols.[6] A three-stage screening process that included a self-disclosure on the initial screening questionnaire, a food frequency questionnaire, and an in-person