（人間環境医工学専攻生体環境学コース）　　（別記様式第８号）
（課程・論文博士共通）

論　文　内　容　要　旨

※ 整理番号		（ふりがな） 氏名（自署）	こが　　のりえ 印
論文題目	Altered polyunsaturated fatty acid levels in relation to proinflammatory cytokines, fatty acid desaturase genotype, and diet in bipolar disorder （双極性障害における多価不飽和脂肪酸濃度と炎症性サイトカイン・脂肪酸デサチュラーゼ遺伝子型および食生活との関連）		

論文内容要旨

Objectives
Inflammation and altered polyunsaturated fatty acid (PUFA) levels have been implicated in bipolar disorder (BD). A recent genome wide association study identified a locus in the fatty acid desaturase (*FADS*) gene cluster conferring susceptibility to BD. In this study, we examined PUFA levels in patients with BD in relation to proinflammatory cytokines, *FADS* genotype, and dietary habits.

Methods
We enrolled 83 patients with BD and 217 healthy controls who underwent plasma PUFA measurement. A subsample of 65 patients and 90 controls underwent plasma interleukin (IL)-6 and tumor necrosis factor alpha (TNFα) measurement, and three *FADS* single nucleotide polymorphisms (SNPs) were genotyped. Information on fish consumption was obtained by a self-reported diet history questionnaire.

Results
In comparing PUFA levels between patients and controls, significant differences were found for all 7 PUFAs tested. Specifically, n-3 eicosapentaenoic acid (EPA) level was decreased, and n-6 arachidonic acid level was increased in the patients ($p<0.0001$ for both). Plasma IL-6 and TNFα levels were both significantly increased in the patients. Plasma EPA level was negatively correlated with IL-6 and TNFα levels. The *FADS* genotype, which was associated with increased n-6 PUFA levels, was also associated with marked elevation in TNFα levels. Less frequent fish intake was associated with low EPA and high IL-6 level.

Conclusions
Taken together, our results provide strong evidence for altered plasma PUFA and proinflammatory cytokine levels in patients with BD. Furthermore, *FADS* genotype and fish consumption may contribute not only to altered PUFA levels but also to inflammation in BD.

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