A PILOT INVESTIGATION OF THE EFFECT OF TRYPTOPHAN MANIPULATION ON THE AFFECTIVE STATE OF MALE CHRONIC ALCOHOLICS

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(Received 12 January 1999; in revised form 18 March 1999; accepted 25 April 1999)

Abstract — A pilot study was conducted to investigate the hypothesis that dietary tryptophan manipulation would influence self-report affective status in alcoholic males. No significant effect of dietary manipulation was observed on the tryptophan/large neutral amino acids ratio or psychological indices of affect. The notion that dietary manipulation may be utilized in improving mood state in alcoholic males was not supported.

INTRODUCTION

Serotonin (5-hydroxytryptamine, 5-HT) is a major neurotransmitter implicated in both mood control (Lucca et al., 1992) and alcoholism (Otter and Martin, 1996; Badawy et al., 1998). Tryptophan is the natural amino acid precursor in 5-HT biosynthesis. Availability for production of 5-HT in the brain is largely dependent on the transport of tryptophan across the blood–brain barrier (BBB) (Struder et al., 1997). Competition for BBB transport proteins occurs between tryptophan and the other large neutral amino acids (LNAA) tyrosine, valine, isoleucine, leucine, phenylalanine, and lysine. The ratio of tryptophan to the sum of these LNAA provides an index of the potential for 5-HT production in the brain. The clinical usefulness of tryptophan supplementation, particularly its adjunctive use with antidepressants in the treatment of psychiatric disorders, has received recent attention (Eriksson and Walinder, 1998).

Although brain metabolism can be altered by amino acid supplementation, these changes may also be achieved by dietary manipulation (Young, 1991). This approach can be explored by modulating the proportions of carbohydrates and proteins in the diet (Wurtman and Wurtman, 1995). The rationale for this is that a high carbohydrate meal will induce an insulin surge by modulating the proportions of carbohydrates and proteins in the diet (Wurtman and Wurtman, 1995). Therefore, the consequence of tryptophan manipulation increasing 5-HT and reducing anxiety and depression may be of potential therapeutic efficacy in appropriately motivated individuals (Møller, 1992) and therefore appropriately motivated patients with alcohol dependence. The aim of the present pilot study was to determine whether manipulation of tryptophan by diet alone significantly influences self-report affective status of alcohol-dependent subjects.

SUBJECTS AND METHODS

Subjects

Subjects were 18 alcohol-dependent males (mean age ± SD 47.1 ± 9.5 years) who were currently on a rehabilitation programme following in-patient detoxification. All subjects satisfied the DSM-IV criteria for alcohol dependency of the American Psychiatric Association (1994) and were alcohol- and drug-free for at least 2 weeks following detoxification. All subjects volunteered to participate and signed an informed consent form.

Experimental design and statistics

The study used a counterbalanced, repeated measures design in which high carbohydrate (CAR), high protein (PRO) and nutritionally balanced (NUT) breakfasts were supplied to subjects on three separate days. Blood samples were collected (at 08:30) before breakfast, which was taken at 09:00, and 2.5 h after each breakfast (i.e. at 11:30). Self-report measures of affective state were then administered to the subjects. The independent variable was diet type (CAR/PRO/NUT). The psychological dependent variables were sum scores on a battery of self-report affective state measures. The biochemical component, the nutritionally balanced breakfast, consisted of: cereal with almonds/milk or a glass (200 ml) of semi-skimmed milk, fish (haddock), poached or boiled egg, non-fat cheese/soya food, and one piece of toast. The high carbohydrate meal consisted of cereal with almonds/milk or a glass (200 ml) of semi-skimmed milk, and two slices of bread. The high protein meal consisted of haddock/poached or boiled egg/non-fat cheese/soya food, and one piece of toast. Coffee/tea was taken in all cases as normal. Statistical analysis was performed using one-way analysis of variance (ANOVA).

Biochemical analysis

The blood samples were collected via 9-ml Vacutainers (Becton Dickinson) and serum was separated by centrifugation at 3000 rpm for 10 min and the supernatant separated into Eppendorf tubes as follows: 200 μl of serum plus 200 μl of 5% (w/v) sulpho-salicylic acid, for amino acid analysis; 200 μl of serum and other aliquots set up for analysis of tryptophan metabolites and liver function tests. The samples were stored at –80°C until analysis. Amino acids were measured by the method of Teerlink et al. (1994).

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**Psychological measures**

The psychological test battery comprised self-report measures that have been widely clinically evaluated and have established psychometric properties (Martin and Thompson, 2000). The following instruments were used: (1) Hospital Anxiety and Depression (HAD) scale (Zigmond and Snaith, 1983); (2) Beck Depression Inventory (BDI; Beck et al., 1961); (3) Spielberger State–Trait Anxiety Inventory (STAI; Spielberger et al., 1983); (4) Locus of Control of Behaviour (LCB) scale (Craig et al., 1984).

After giving the blood sample at 11:30, subjects were asked to complete the self-report questionnaires at 11:35. This procedure was repeated on days 2 and 3 when the subjects were assigned (crossed over) to the alternative meals (CAR/PRO/NUT).

**RESULTS**

**Biochemical analysis**

The mean level of each individual post-breakfast amino acid and associated $F$ and $P$ values are shown in Table 1. Dietary manipulation was observed to have a statistically significant effect on all the amino acids measured except tryptophan. No significant effects of dietary manipulation were observed on the post-breakfast tryptophan/LNAA ratio, $F(2, 34) = 0.15, P = \text{n.s.}$

**Self-report affective measures**

The mean score and standard deviation of each self-report affective measure as a function of dietary condition is shown in Table 2 with calculated $F$ and $P$ values. No statistically significant effects of dietary manipulation were observed on any of the self-report affective state measures.

**Sample size estimation**

Replication sample size estimations were conducted on the self-report affective measures and calculated on the basis of power set at 0.8 and $\alpha = 0.05$ with a calculated pooled variance term using the method specified by Cohen (1988). A replication sample size of $n = 318$ was calculated in order to find a significant effect of dietary manipulation on all the self-report affective measures.

**DISCUSSION**

The biochemical observations will be discussed prior to an examination of the psychological material. No significant effect of dietary manipulation was observed on the post-breakfast tryptophan/LNAA ratio. It could be concluded that dietary manipulation of carbohydrate does not affect tryptophan availability in humans unless a highly restrictive and abnormal diet is pursued. However, the observation of a post-breakfast significant effect of dietary manipulation on all the amino acids measured with the exception of tryptophan suggests that the dietary manipulation was indeed affecting amino acid uptake via the anabolic process. This finding is consistent with the view of Young et al. (1988) that the mechanism of tryptophan metabolism within the mammalian brain is a complex, multi-factorial one and is at present poorly understood. Additionally, no significant dietary effect on affective state was observed on any of the psychological measures, therefore the use of this approach as a potential clinical intervention to improve mood in alcoholic males cannot be currently endorsed or recommended.

These results are therefore disappointing, since they suggest that a biological basis for improving mood via conscientious dietary choice, and without the use of prescribed...
pharmacotherapy, is unsupported. Alternatively, the relatively small sample size in this pilot study may be a fundamental limitation in terms of the lack of dietary effects observed on either the biological or psychological measures used. Power estimations revealed that, in a larger subject population of marginally more than 300 subjects, a significant effect of dietary manipulation is likely to be observed on all the self-report affective measures.

However, relating any observed dietary effect on mood status to biological substrates in a larger replication study would be problematic in view of the incomplete state of knowledge regarding tryptophan metabolism, and there would be little clinical significance of a result that required such a large sample to demonstrate.

Acknowledgements — We are grateful to Dr A. A.-B. Badawy for advice on dietary factors and to Professor D. R. Thompson and Professor C. C. H. Cook for comments on an earlier version of this manuscript.

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