and inshore where large swarms of both species form in the late summer and fall (*16*).

Although the presence of *Epischura* can cause a substantial decrease in the filtering rate of *Diaptomus*, the ultimate effect on the fitness of *Diaptomus* may not be negative. For example, upon sensing the chemical released by *Epischura*, *Diaptomus* may stop feeding and attempt to avoid predation by ceasing to move or by spiraling away (*17*). The reduction in filtering rate could thus be the result of a mechanism for escaping predation that may have evolved because of predation pressure on early instars.

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References and Notes

1. J. L. Li and H. W. Li, *Limnol. Oceanogr.* **24**, 613 (1979); W. C. Kerfoot, *ibid.* **23**, 1089 (1978).
2. A. Sih, *Science* **210**, 1041 (1980).
3. J. J. Gilbert, *ibid.* **181**, 63 (1973).
4. S. A. Poulet and P. Marsot, *ibid.* **200**, 1403 (1978).
5. S. J. Threlkeld, *Limnol. Oceanogr.* **26**, 433 (1981).
6. C. L. Folt, E. Byron, C. Sims, S. Boddy, C. R. Goldman, in preparation.
7. The density of animals in the single-species treatments varied from four to six adults per 125 ml. For the two-species experiments the total density equaled the single-species density, and equal numbers of both species were used. In contact water and dialysis experiments the number of animals was equal to the number in the single-species experiment. There were three to six replicates of each experiment. The densities of animals used in these experiments represent the upper range of in situ densities that we have measured.
8. The animals were heat-killed, rinsed, soaked in a mild phosphate buffer for 2 hours, and solubilized in 0.5-ml Soluene-350 (Packard) for 24 hours at 50°C. Then 10 ml of Dimilume (Packard) was added, and the radioactivity in the animals was counted in a Beckman LS-100 scintillation counter. The food suspension (1 ml) was filtered onto 0.45-μm HA Millipore filters (three replicates). Filters were dissolved in Bray's scintillation fluid and counted. The filtering rates were calculated as milliliters per animal per day = counts per minute in the animal/counts per minute in the food divided by length of feeding period (hours)/24 hours.
9. The data were analyzed two ways with the same statistical result. The difference between filtering rates of animals in all single- versus all two-species experiments was tested by the Mann-Whitney U test ($P < .01$). Filtering rates from experiments at seven different times were pooled for single- and two-species treatments. Analysis of variance resulted in a significant difference between treatments at $P < .005$.
10. The water in the dialysis tubes was stirred several times during the 24-hour incubation period. If the equilibrium was complete for ammonia and other low molecular weight compounds, the result would have been a decrease in concentration to 12.5 percent of the concentration in the contact water. Since the filtering rates were significantly depressed in the presence of dialysis water, we hypothesized that the chemical involved was either equally effective at very low concentrations or was a large molecular weight compound unable to pass through the tubing.
11. As a control for the effect of the manipulation, *Diaptomus* was tested for an effect on itself. The water was prepared in the same way as *Epischura* contact water and dialysis water.
12. Each species was also examined for an effect on the filtering rate that might be due to the physical or chemical presence of the other. The results of the three experiments with *Diaptomus* (alone, in *Diaptomus* contact water, and in *Diaptomus* dialysis water) were pooled and tested for differences from two-species experiments (both species together, *Diaptomus* in *Epischura* contact, and *Diaptomus* in *Epischura* dialysis). The difference was statistically significant ($P < .005$).
13. Although the effect of *Diaptomus* contact water on *Epischura* filtering rates was significant ($P < .05$) with data pooled from experiments on four dates, the effect was not significant for three of four experiments. The overall significance was due to the highly significant depression measured on 14 April 1980.
14. Our data indicate that a depression in *Epischura* filtering rates resulting from exposure to *Diaptomus* occurred only when *Epischura* filtering rates in single-species experiments were above 1 ml per animal per day. On the other dates *Epischura* filtering rates were so low that it may have been impossible to reduce them further without killing the animals. We suggest that *Epischura* may only be affected by *Diaptomus* when its filtering rate is above some threshold value.
15. J. T. Rybock, thesis, University of California, Davis (1979).
16. E. Byron, in preparation.
17. C. L. Folt, personal observation.
18. We thank R. Gersberg, E. Byron, R. Folt, K. Hopper, D. Peart, R. Richards, and an anonymous reviewer for suggestions and assistance and M. Smith for manuscript preparation. Supported by NSF grant DEB79-16221.

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Central Norepinephrine Metabolism During Alcohol Intoxication in Addicts and Healthy Volunteers

Abstract. *The concentrations of the major norepinephrine metabolite, 3-methoxy-4-hydroxyphenylethylene glycol (MOPEG), in lumbar cerebrospinal fluid of alcoholic patients were markedly elevated during intoxication and successively declined during 1 and 3 weeks of abstinence. During intoxication the MOPEG concentration in cerebrospinal fluid showed a statistically significant correlation with the blood alcohol concentration. In healthy volunteers who received 80 grams of ethanol, the MOPEG concentration in cerebrospinal fluid increased significantly. Healthy subjects sampled during intoxication had significantly higher concentrations of MOPEG in the cerebrospinal fluid than did subjects sampled after the end of intoxication. The results indicate that alcohol administration markedly stimulates norepinephrine metabolism in the central nervous system in human subjects, possibly by increasing unit impulse activity of central noradrenergic neurons.*

In spite of extensive research, the mechanisms for the euphoriant effect of alcohol are still unknown. Nor have the psychiatric symptoms dominating the withdrawal reaction in alcohol addicts been definitely correlated to specific alterations of brain biochemistry. In patients with delirium tremens (*1*), elevated concentrations of MOPEG (3-methoxy-4-hydroxyphenylethylene glycol), the major norepinephrine metabolite, have been observed in the cerebrospinal fluid (CSF). This effect has been assumed to reflect an increased release of norepinephrine in the central nervous system in connection with the development of the delirious symptoms. Some animal experiments support this assumption, since a stimulating effect of acute alcohol intake on norepinephrine synthesis and metabolism in the brain has been reported (*2*), but other studies could not verify these results (*3*). The demonstration of a role of the noradrenergic system in the reinforcing effect of ethanol on self-administration of the compound in rats also supports a critical interference of ethanol with noradrenergic mechanisms in the central nervous system (*4*). This view is further supported by the findings that the catecholamine synthesis inhibitor α-methyltyrosine counteracts the stimulating effects of alcohol in rats and healthy volunteers (*5*).

We have reported the presence of elevated concentrations of MOPEG in the CSF of patients during alcohol withdrawal (*6*). This effect was selective, since concentrations of two other major transmitter metabolites, homovanillic acid and 5-hydroxyindoleacetic acid, in the CSF were not elevated or correlated with the MOPEG concentrations (*7*). The stimulation of central norepinephrine metabolism during alcohol withdrawal may be related to direct or indirect effects of alcohol on the noradrenergic system. If the MOPEG elevation in the CSF is related to direct effects of ethanol, it might be correlated with the blood alcohol concentration during intoxication. A MOPEG elevation in the CSF might also be produced during alcohol administration in healthy volunteers.

We analyzed concentrations of MOPEG in the lumbar CSF of alcohol addicts and healthy volunteers and found that in both groups MOPEG concentrations were markedly elevated during intoxication. In the addicts, where very high concentrations of alcohol were found, there was a statistically significant correlation between the alcohol concentration in the blood and the MOPEG concentration in the CSF.

In one group of alcoholic patients ($N = 18$), CSF samples were taken when the patients were intoxicated and immediately after admission to the hospital (day 1). Samples were taken again after

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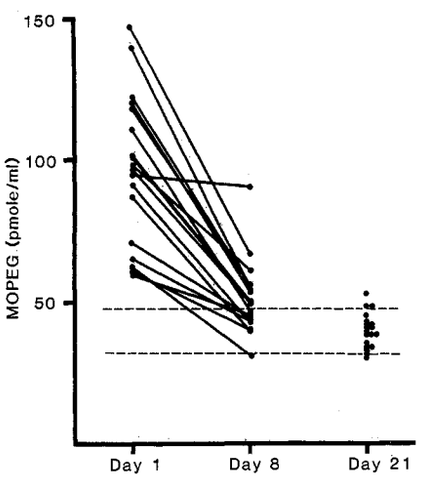
the patients had been in the hospital for 1 week (day 8). In another group of alcoholic patients ($N = 27$), CSF samples were taken after 3 weeks in the hospital (*8*). For reference, data from a group of 27 young, healthy volunteers were used (*9*). The MOPEG concentration was measured by gas chromatography–mass spectrometry and the deuterated compound was used as an internal standard (*10*).

The concentration of MOPEG in lumbar CSF from the intoxicated addicts was markedly elevated above the range in healthy volunteers (Fig. 1). Mean values for controls and patients showed a statistically significant difference on day 1 ($P < .001$). There was a significant decline in the MOPEG concentration between day 1 and day 8 ($P < .001$). The CSF of the second group of alcohol addicts examined 21 days after intoxication showed a distribution of MOPEG concentrations that were largely within the range of the reference values for controls. In the intoxicated alcohol addicts, a statistically significant relation between the blood alcohol concentration and the MOPEG concentration in the CSF was also found ($r = .49$, $P < .05$) (Fig. 2).

In order to examine whether acute alcohol administration also elevates the MOPEG concentration in the CSF of nonaddicted subjects, we studied 13 male volunteers (*8*). Samples of CSF were taken 1 week before and after the oral intake of 80 g of ethanol. The ethanol was diluted in 1 liter of fruit juice and ingested during 2 hours. In one group of these subjects ($N = 6$), CSF was sampled 6 hours after the alcohol intake, when the subjects showed signs of intoxication and alcohol was still present in the blood (Fig. 3). In a second group ($N = 7$), samples were taken 14 hours after the intake, when alcohol was no longer present in the blood. In the first group there was a significant elevation of the MOPEG concentration in comparison with that before alcohol intake ($P < .01$) (Fig. 3). A significant elevation was obtained in the second group as well ($P < .01$). Subjects sampled during intoxication had significantly higher MOPEG concentrations than subjects sampled after intoxication ($P < .05$). In the healthy volunteers the alcohol concentrations were fairly low when CSF was withdrawn. There was no significant relation between the blood ethanol concentration and the MOPEG concentration in the CSF. However, when blood alcohol concentration was plotted as a function of MOPEG concentration in the CSF, the data from the healthy volunteers appeared roughly on the same regression line as that for the intoxicated alcoholic patients (Fig. 2).

Transport of MOPEG from plasma to CSF is markedly restricted by the blood-CSF barrier (*11*). This makes it highly unlikely that the MOPEG elevation in the CSF is secondary to effects of alcohol on the peripheral autonomic nervous system. The MOPEG elevation does not seem to be related to a shift in the central norepinephrine metabolism, since only minor amounts of vanillylmandelic acid have been detected in the CSF during alcohol intoxication (*12*).

The MOPEG concentration in the lumbar CSF is determined by a number of factors, such as (i) transmitter release from central noradrenergic neurons, (ii) the rate of MOPEG formation, (iii) MOPEG transport into and out of the CSF, (iv) CSF hydrodynamics, (v) physical activity, and (vi) drug treatment. Concentrations of 5-hydroxyindoleacetic acid and homovanillic acid were not elevated, and they were not correlated to MOPEG levels (*13*). Therefore the effect of ethanol intoxication seems to be specific for the noradrenergic metabolism. All the healthy volunteers and all the patients sampled on day 1 and day 21 were drug-free. Of the patients sampled on day 8, those who had been receiving amobarbital did not differ in MOPEG concentration from those who had been treated with oxazepam. These results indicate that changes in monoamine oxidase activity, CSF hydrodynamics, metabolite transport, and drug treatment are not causative factors of the MOPEG elevation observed. Specific effects of alcohol on MOPEG transport into or out of the CSF, however, cannot be excluded. The results of previous animal experiments (*2*) suggest that the MOPEG elevation is due to an increased unit activity of central norepinephrine neurons, possibly located in the locus coeruleus. An increase in the functional activity of these neurons, which send axons and terminals down into the spinal cord, has been shown to lead to an increased release of norepinephrine, resulting in



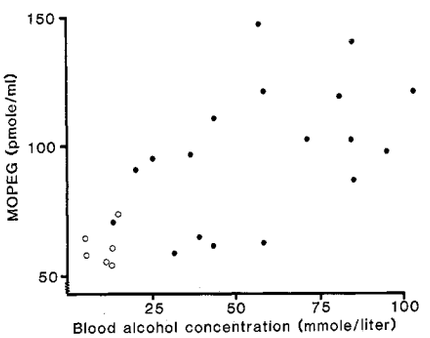


Fig. 1 (left). Concentration of MOPEG in lumbar CSF in alcoholic patients during intoxication (day 1) and after 1 week (day 8) and 3 weeks (day 21) of abstinence. Dotted lines are reference values from healthy adults. Fig. 2 (right). Concentration of MOPEG in lumbar CSF and blood alcohol levels in intoxicated alcoholic patients (●) and healthy controls (○).

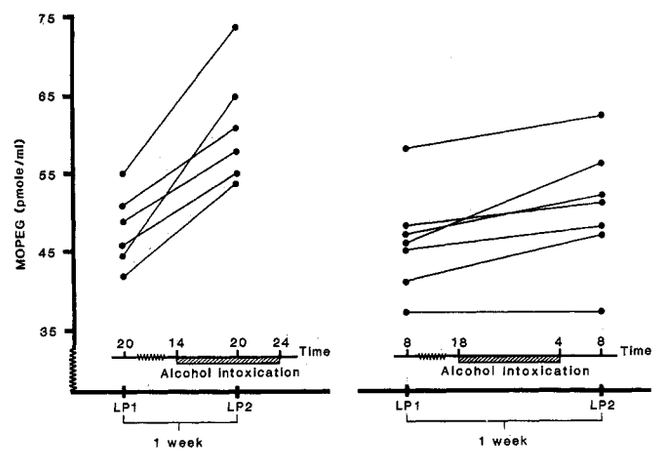


Fig. 3. Concentration of MOPEG in lumbar CSF in healthy male volunteers before (*LP1*) and after (*LP2*) intake of 80 g of ethanol.

elevated MOPEG concentrations in the tissue (*14*).

The quantitative relation found between blood alcohol concentration and the MOPEG level in the CSF of the alcohol addicts further supports the view of a causative effect of alcohol for this biochemical alteration. Whether alcohol has a direct stimulating effect on unit activity of some central noradrenergic neurons or stimulates them by secondary effects on afferent systems to these neurons has not been determined.

Our study supports the idea that ethanol influences brain noradrenergic mechanisms in man. The data also support previous results of animal experiments (*2*). Further studies of the effect of ethanol on central noradrenergic mechanisms may be useful in elucidating mechanisms for psychological changes that occur in connection with alcohol intoxication and withdrawal. A comparison of the time sequences for the euphoriant and anxiety-producing effects of alcohol, the blood alcohol concentrations, and the CSF MOPEG elevation may elucidate the possibly causal relations between these variables.

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References and Notes

1. D. Athen, H. Beckman, M. Ackenheil, M. Markianos, *Arch. Psychiatr. Nervenkr.* **224**, 129 (1977).
2. T. H. Svensson and B. Waldeck, *Psychopharmacologia* **31**, 229 (1973); A. Carlsson and M. Lindquist, *J. Pharm. Pharmacol.* **25**, 437 (1973); G. Bustos and R. H. Roth, *ibid.* **28**, 580 (1976); F. Karoum, R. J. Wyatt, E. Majchrowicz, *Br. J. Pharmacol.* **56**, 403 (1976).
3. K. Gysling, G. Bustos, I. Couche, G. Martinez, *Biochem. Pharmacol.* **25**, 157 (1976); L. H. Pohorecky and B. Newman, *Drug Alcohol Depend.* **2**, 328 (1977).
4. W. M. Davis, S. G. Smith, T. E. Werner, *Pharmacol. Biochem. Behav.* **9**, 369 (1978).
5. A. Carlsson, J. Engel, T. H. Svensson, *Psychopharmacologia* **26**, 307 (1972); S. Ahlenius, A. Carlsson, J. Engel, T. H. Svensson, P. Södersten, *Clin. Pharmacol. Ther.* **14**, 586 (1973).
6. S. Borg, A. Czarnecka, H. Kvande, G. Sedvall, *J. Neural Transm.*, in press.
7. S. Borg, H. Kvande, G. Sedvall, *Prog. Neuropsychopharmacol.*, in press.
8. The age range in the patient groups was 33 to 63 years. All patients were alcohol-dependent according to the criteria of the World Health Organization [*Tech. Rep. Ser. WHO No. 551* (1974)]. None exhibited complicating disorders other than alcoholism. Estimated daily alcohol consumption the week before admission was 250 to 500 g of ethanol. All patients were reported to be drug-free before admittance to the hospital. Toxicological screening of urine showed no signs of drug intake. After the first lumbar puncture (LP) the patients were treated with amobarbital (0.3 to 0.8 g daily) or oxazepam (0.1 to 0.2 g daily) during the first 6 days in the clinic and were then drug-free. The age range of the volunteers was 25 to 60 years. They were all somatically healthy according to physical examination and routine laboratory tests. None had taken drugs 3 weeks prior to the investigation, and all had abstained from alcohol for at least 1 week. Lumbar puncture was performed when subjects were sitting, and 12.5 ml was removed. In the first group of patients samples were taken immediately on admittance and at the same time of the day 1 week later. In the second group and in the group of the 27 healthy volunteers, samples were taken at 8 a.m. after 8 hours of bed rest and fasting. All specimens were immediately frozen and stored at −75°C before the analysis, which was performed within 3 months (*10*). Significant differences were tested by means of *t*-test for correlated or independent samples, or both, and significance of correlation was tested by calculation of the correlation coefficient for ungrouped data [G. A. Ferguson, *Statistical Analysis in Psychology and Education* (McGraw-Hill, New York, 1979), pp. 106 and 164–166].
9. G. Sedvall, B. Fyrö, B. Gullberg, H. Nybäck, F.-A. Wiesel, B. Wode-Helgodt, *Br. J. Psychiatry* **136**, 366 (1980).
10. C.-G. Swahn, B. Sandgärde, F.-A. Wiesel, G. Sedvall, *Psychopharmacologia* **48**, 147 (1976).
11. M. Perlow, M. H. Ebert, E. K. Gordon, M. G. Ziegler, C. R. Lake, T. N. Chase, *Brain Res.* **139**, 101 (1978).
12. B. Sjöquist, S. Borg, H. Kvande, *Substance Alcohol Misuse* **2**, 63 (1981).
13. S. Borg, H. Kvande, G. Sedvall, unpublished data.
14. J. N. Crawley, R. H. Roth, J. W. Maas, *Brain Res.* **166**, 180 (1979).
15. Supported by Swedish Medical Research Council grants B80-25X-05716 and B82-21X-03560.

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Functional Restoration of Vision in the Cat After Long-Term Monocular Deprivation

Abstract. *Recovery of visual acuity was studied in six long-term monocularly deprived cats after removal of the nondeprived eye or reverse lid suture. Although both manipulations improved visual acuity, removal of the nondeprived eye was associated with more rapid recovery and higher final acuity than in reverse suture. These results are in agreement with the known electrophysiological effects of these recovery conditions and are also similar to the effects of reverse occlusion or loss of the nonamblyopic eye in human amblyopes.*

In normal cats, the majority of cells in the striate cortex can be excited by visual stimulation of both eyes (*1*). However, after being reared with monocular deprivation (MD) achieved by lid suture through the first 3 to 4 months of life, only about 5 percent of the cells in the striate cortex respond to visual stimulation of the deprived eye and only a few of these have normal receptive field properties (*2–6*). Correlated with these abnormalities in cortical physiology are the observations that MD cats using the deprived eye are grossly deficient in visually guided behavior, especially in situations requiring form or pattern vision (*7*).

Initial investigations indicated a critical developmental period during which the cells in the striate cortex are sensitive to the effects of MD and that this period ends by 3 to 3.5 months of age (*2*). Most investigations of the ability to reverse the effects of MD outside of this developmental critical period have found little or no effect (*2, 8*). However, Kratz *et al.* (*4*) discovered that removing the nondeprived eye in 4- to 5-month-old MD cats results in an immediate and permanent sixfold increase in the percentage of cells responding to the deprived eye. Recent studies have confirmed this finding in MD cats (*6, 8, 9*) and mice (*10*). The receptive-field properties of these responsive cells are, for the most part, abnormal (*4–6*) and do not improve after visual experience (*6*).

The purpose of this study was to determine whether the increase in the percentage of cells responding to the deprived eye after removal of the nondeprived eye in MD cats was associated with a functional improvement in vision using the deprived eye.

Six kittens from two litters born in the laboratory breeding colony were studied. Lid suture and enucleation procedures have been detailed elsewhere (*4–6*). All kittens had the lids of one eye sutured closed before the time of natural eye opening. The duration of deprivation was 7 months (four cats) or 12 months (two cats) (Table 1).

Training methods have been described elsewhere (*11, 12*). In the jumping stand described by Mitchell *et al.* (*11*), modified to accommodate larger cats, each cat was trained 20 to 30 trials per day, 6 or 7 days a week, first with the nondeprived eye for all discriminations and later with the deprived eye (Fig. 1). Each cat was trained with its nondeprived eye to a criterion of 90 percent correct on a luminance discrimination followed by a striped discrimination, and then visual acuity was assessed (*13*). Approximate threshold acuity was established by a modified staircase procedure (*11, 12, 14*). Final acuity was then determined by giving a minimum of 20 trials at each of three or four spatial frequencies around the approximate threshold randomized in blocks of five trials. Final acuity was defined as the spatial frequency at which

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