12 of 17 pairs gave results consistent with the prediction of retaliation following defection (*5*). One pair gave results in contradiction to this prediction, but their response was a brief nonaggressive hover above a model. A sign test showed statistically significant differences in responses before and after replacement of the nestlings (Table 1). Parents that responded to the models after the placement of dead nestlings did not redirect their aggression at their mates or at neighboring breeding pairs. Parents also chased live nonbreeders during the experiment. But, live nonbreeders were ignored if their time of appearance at the nest box precluded the possibility of their committing the defection.

Parent tree swallows displayed the characteristics of the TIT FOR TAT strategy by (i) acting "nice" to the model nonbreeders until after the simulated defection, (ii) being provoked into defecting, and (iii) appearing "forgiving": a significantly larger proportion of encounters (27 of 82) ended in parental chases of nonbreeders before the simulated defection ($z = 2.58$, $P < 0.01$) than did encounters after the simulated defection (18 of 110) at those boxes where parents responded to the models after the simulated defection (*25*). This result indicates a return to normal behavior by the birds in the experiment because parental aggression toward both model and live nonbreeders decreased as the breeding season progressed at boxes outside the experiment (*13*).

These results suggest that the TIT FOR TAT strategy adequately models the restraint shown in the conflict of interest between parent and nonbreeder tree swallows, and that TIT FOR TAT may be fruitfully applied in the analysis of other phenomena in which the genetic relatedness of interactants is inadequate to explain the restraint of conflict demonstrated by the interactants.

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7. An ESS is a strategy such that if all of the members of a population adopt it no mutant strategy can invade (*6*).
8. A. Rapoport and A. M. Chammah, *Prisoner's Dilemma* (Univ. of Michigan Press, Ann Arbor, 1965).
9. A nonzero sum game is one in which the interests of the players are not in direct conflict, making it possible for both players to gain or lose during an interaction. After each interaction, each player receives a payoff that is not only dependent on its own actions but also on those of its competitor. In a biological context, payoffs are in terms of the effects a player's actions have on its fitness [(*5*); S. Riechert and P. Hammerstein, *Annu. Rev. Ecol. Syst.* **14**, 377 (1983)]. Gains or losses are in terms of the payoffs assigned to the outcome of an interaction (*6*). In a symmetrical game the payoffs to each player are equal (*6*). The requirement of symmetrical payoffs can be relaxed as long as the inequalities that define the payoff matrix describing Prisoner's Dilemma are met. Payoffs need only be measured in terms relative to one another [R. Axelrod, *The Evolution of Cooperation* (Basic Books, New York, 1984)].
10. Each player receives a payoff R (reward) for mutual cooperation. But each player is "tempted" to defect because doing so against a cooperative competitor results in the highest payoff T (temptation to defect). In this case, the cooperator receives the lowest payoff S (sucker's payoff). However, if both defect each gets the payoff P (punishment for mutual defection) that is less than R. The payoff matrix is defined by $T>R>P>S$ and $R > (T + S)/2$ (*5, 8*).
11. This is also the solution in biological evolution (*5*). In effect, cooperators quickly go extinct in competition with defectors.
12. A player using TIT FOR TAT is (i) "nice" in that it is never the first to defect, (ii) provocable into a defection by a defection by its competitor, and (iii) "forgiving" in that it only punishes its competitor once for a defection and is willing to play again without an act of restitution (*5*).
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21. On average, fledging = nestling day 20 (*13*).
22. One model was of adult, iridescent blue-green, breeding plumage representing all after-hatching year (AHY) and male nonbreeders and some second year (SY) and all third year (TY) and older female nonbreeders. The second model was of immature, brown plumage meant to represent all AHY and some SY female nonbreeders and all hatching year nonbreeders. Models were presented together so that parental responses were not biased by model-nonbreeder sex, or age, or both. The models were attached to sticks positioned 2 m apart and 1 m from the front of the nest box. Each model was an equal distance from front of the nest box. Each model was an equal distance from the nest box hole. Sticks were 1 m high. Model position, to the right or left of the hole, was determined by a coin flip before each trial.
23. Responses measured were hovers, dives, and contacts (for example, pecks at the model or pulling of feathers from the model).
24. There was no statistically significant change in parental aggression toward live nonbreeders between nestling days 12 and 16 at boxes outside of the experiment (*13*).
25. Difference between proportions test [J. H. Zar, *Biostatistical Analysis* (Prentice-Hall, Englewood Cliffs, N. J., 1974)].
26. I thank H. W. Power, R. Axelrod, W. D. Hamilton, J. D. Ligon, and the reviewers for their criticisms on various versions of the manuscript. The Town of Oyster Bay, N.Y., allowed me to use the J. F. Kennedy Memorial Wildlife Refuge at Tobay Beach as a study site. Supported by the F. M. Chapman Fund of the American Museum of Natural History, Sigma Xi, the Northeastern Bird Banding Association, the Ecology Graduate Program, and a J. Leatham grant from the Zoology Program at Rutgers University.

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Response to Ethanol Reduced by Past Thiamine Deficiency

Abstract. *Ethanol-induced intoxication and hypothermia were studied in rats approximately 7 months after severe thiamine deficiency, when treated rats appeared to have recovered their physical health. Previously induced thiamine deficiency without prior ethanol exposure significantly decreased the area under the curve plotted for the concentration of ethanol in blood and also decreased behavioral impairment and hypothermia due to ethanol exposure. Pathophysiologic changes resulting from thiamine deficiency may contribute to both the pharmacodynamic and pharmacokinetic tolerance to ethanol in chronic alcoholics.*

Alcoholism is characterized by progressive increases in consumption of alcoholic beverages with concomitant alterations in the metabolism of ethanol and its effects on the central nervous system (tolerance) (*1*). Long-term exposure to ethanol can also result in physical dependence (*1*) and chronic pathologic changes in many organ systems (*2*). Alcoholism is frequently associated with thiamine (vitamin B_1) deficiency resulting from inadequate nutritional intake, decreased absorption, or impaired utilization (*3*). The contribution of thiamine deficiency to ethanol toxicity and the resultant dysfunction in organ systems remains controversial (*4*).

Wernicke's encephalopathy is an acute neuropsychiatric syndrome caused by thiamine deficiency most often found in the nutritionally compromised chronic alcoholic (*5*). Treatment with thiamine reverses most of the acute manifestations (*5*), but clinical abnormalities such as memory loss, apathy and social indifference, superficial and labile emotions, and lack of goal-oriented spontaneous activity (Korsakoff's psychosis) may persist together with neurochemical disturbances (*5, 6*). Characteristic neuropathologic findings at autopsy include bilaterally symmetrical periventricular lesions of the brainstem and diencephalon (*5, 6*).

Discrete regions of the rat brain show alterations in glucose uptake (as measured by the ^{14}C-labeled deoxyglucose technique) during thiamine deficiency. These metabolic changes parallel behavioral and histologic abnormalities that resemble clinical-anatomic findings in patients with Wernicke's encephalopathy (*7*). Serotonergic and cholinergic neurotransmission are reported to be specifically affected by acute thiamine deficiency (*8*). Furthermore, thiamine deprivation has been shown to increase voluntary ethanol consumption in the rat (*9*). Many of these abnormalities are reversed quickly after administration of thiamine (*10*), but the extent of residual dysfunction of the central nervous system has not been elucidated. We postulated that changes in response to ethanol may persist long after recovery from severe thiamine deficiency and tested this hypothesis by studying ethanol-induced intoxication and hypothermia in rats approximately 7 months after their recovery from thiamine deficiency. We now report that severe, previously induced thiamine deficiency without prior exposure to ethanol significantly decreased intoxication and hypothermia caused by ethanol.

Sprague-Dawley rats (Taconic Farms) weighing 200 to 250 g each were fed on freely available thiamine-deficient or control diets (BioServ). Thiamine-deficient rats were injected intraperitoneally with 50 mg of thiamine hydrochloride (25 mg per milliliter of saline) per kilogram per day for 3 days; control rats received 0.9 percent saline (2.0 ml/kg) when rats in the other group exhibited severe symptoms of thiamine deficiency (*7, 8, 10*). Thiamine-deficient rats weighed significantly less than controls at the time of their first injection (males, 170 ± 4 g compared to 447 ± 11 g; females, 200 ± 6 g compared to 261 ± 5 g; $P < 0.001$ for both genders); after this injection both groups were given a standard diet (Ralston Purina).

After a recovery period of 7 to 8 months, the mean weights (± standard error of the mean) of previously thiamine-deficient rats [males (n = 12), 491 ± 16 g; females (n = 10), 294 ± 6 g] and control rats [males (n = 10), 531 ± 17 g; females (n = 5), 292 ± 10 g] were not significantly different ($P > 0.2$). All female rats were in estrus as determined by vaginal smears at the time of ethanol administration. The male and female groups were studied by the same protocol but on different days. All animals were given ethanol (4 g per kilogram, 20 percent weight by volume) by gavage at 0800 hours after a 12-hour fast. The severity of intoxication was rated blindly every 90 minutes thereafter by means of a validated observational scale of neuro-

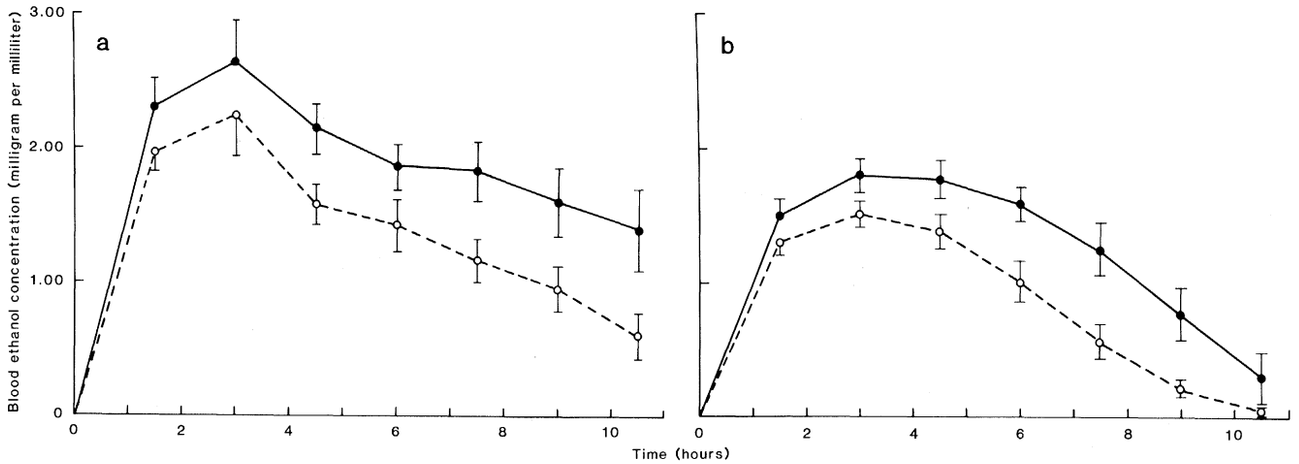

Fig. 1. Blood ethanol concentration (mean ± standard error of the mean) in rats recovered from thiamine deficiency (○) and in control rats (●) after administration of ethanol (4 g/kg) in (a) males (n = 12 treated rats and 9 control rats) and (b) females (n = 10 treated rats and 5 control rats).

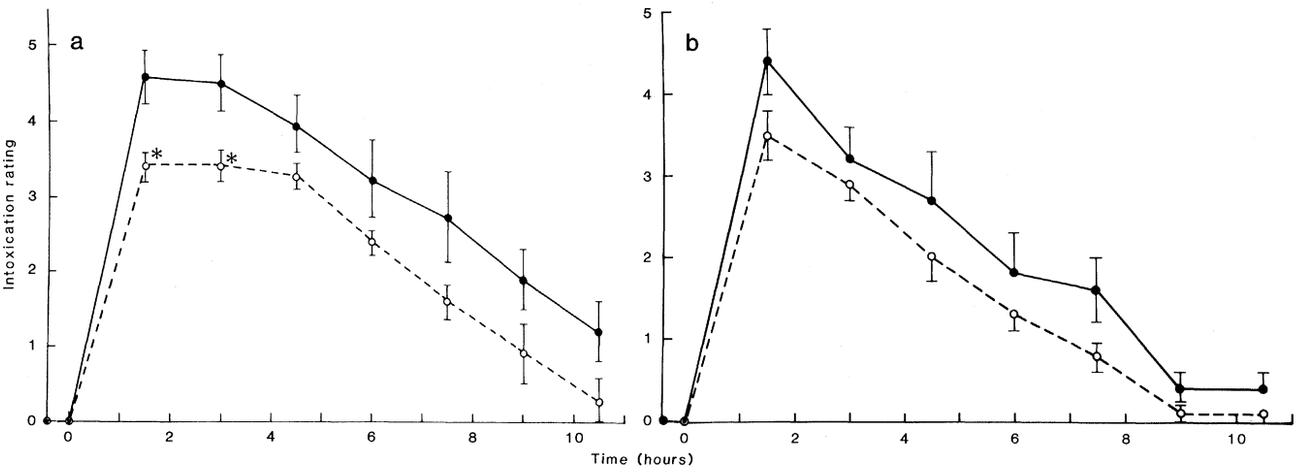

Fig. 2. Behavioral rating of intoxication (mean ± standard error of the mean) (*11*) for rats recovered from thiamine deficiency (○) and for control rats (●). (a) Males (n = 12 treated rats and 10 control rats). (b) Females (n = 10 treated rats and 5 control rats). (*) $P < 0.02$ (Bonferroni inequalities).

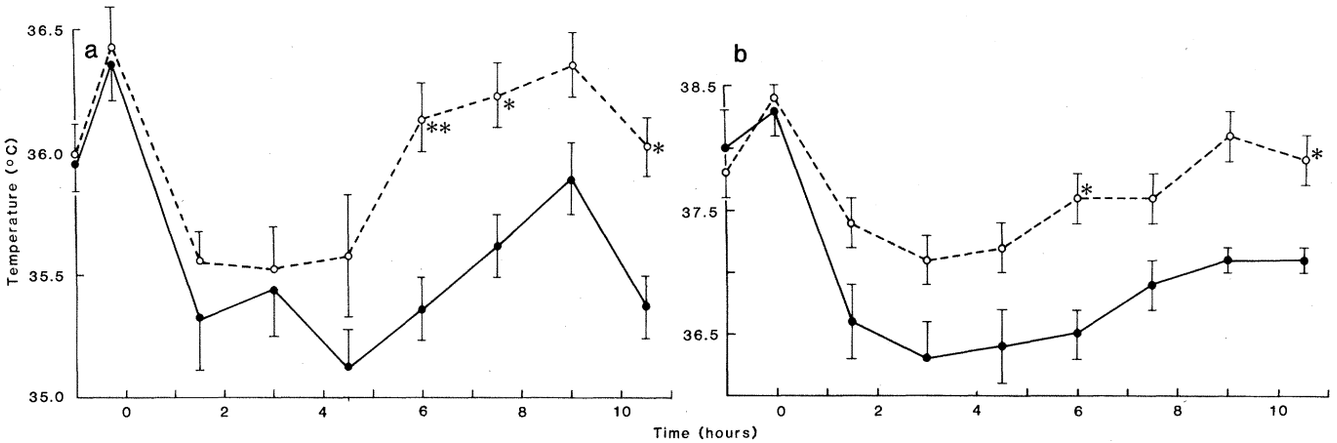

Fig. 3. Ethanol-induced hypothermia in rats recovered from thiamine deficiency (○) and in control rats (●). (a) Males (n = 12 treated rats and 10 control rats). (b) Females (n = 10 treated rats and 5 control rats). (*) $P < 0.05$; (**) $P < 0.02$ (Bonferroni inequalities).

behavioral impairment (*11*). Rectal temperatures were obtained twice before administration of ethanol and every 90 minutes thereafter (YSI Telethermometer, Yellow Springs Instruments). Blood samples were taken from the tail veins to 10.5 hours after administration of ethanol; blood ethanol concentrations (BEC's) in these samples were determined by means of a gas chromatographic method (*12*).

Ascending BEC's (90 and 180 minutes after ethanol administration) were not significantly different in rats recovered from thiamine deficiency and control rats ($P > 0.05$, unpaired t-tests), but both treated and control males (Fig. 1a) had higher BEC's than the respective female groups (Fig. 1b) ($P < 0.025$, unpaired t-tests). The area under the BEC curve (milligrams per milliliter per hour) from 0 to 10.5 hours was reduced by approximately 30 percent in the treated groups (males, 1451 ± 131; females, 907 ± 92) compared to the control groups (males, 1976 ± 221; females, 1326 ± 128; $P < 0.05$, unpaired t-tests) (Fig. 1).

Baseline behavioral ratings (*11*) and rectal temperatures were essentially identical in rats recovered from thiamine deficiency and control rats (both males and females) (Figs. 2 and 3). However, the treated groups appeared to be significantly less intoxicated than controls [$F(1, 33) = 6.68$; $P < 0.02$], and male rats (Fig. 2a) appeared to be more impaired overall than the females (Fig. 2b) [$F(1, 33) = 8.87$; $P < 0.01$]. Four of ten control male rats, but none of those recovered from thiamine deficiency, lost their righting reflexes ($\chi^2 = 5.87$, $P < 0.02$); three of five control females and one of ten treated females lost their righting reflexes ($\chi^2 = 4.26$, $P < 0.05$). Male rats recovered from thiamine deficiency were significantly less behaviorally impaired than controls at 1.5 and 3 hours after administration of ethanol ($P < 0.02$, unpaired t-tests). An analysis of covariance with BEC as a covariant showed that male rats recovered from thiamine deficiency were significantly less impaired at the time of peak effect (1.5 hours) than controls (adjusted group means, 3.5 ± 0.2 versus 4.2 ± 0.2; $P < 0.02$). The behavioral impairment of treated females was not significantly different from that of controls at either 1.5 or 3 hours. Although rates of recovery were similar for treated and control groups, female rats recovered earlier, a finding consistent with the reduced area under the BEC curve.

Ethanol-induced hypothermia was significantly less severe [$F(1, 33) = 11.1$, $P < 0.005$] in both male and female rats recovered from thiamine deficiency, with a significantly greater effect in females [$F(1, 33) = 6.12$, $P < 0.02$] (Fig. 3). The mean maximum decrease in body temperature in treated rats (males, 1.1° ± 0.17°C; females, 1.1° ± 0.21°C) and control rats (males, 1.3° ± 0.20°C; females, 2.0° ± 0.46°C) was not significantly different. Rectal temperatures were higher in the females overall [$F(1, 33) = 111$, $P < 0.0001$]. In males, body temperature was significantly higher ($P < 0.02$) in rats recovered from thiamine deficiency (36.1° ± 0.1°C) than in control rats (35.4° ± 0.1°C) by 6 hours after administration of ethanol; this was because the temperatures of more of the treated rats (9 of 12 compared to 1 of 10 controls) had returned to baseline by this time ($\chi^2 = 9.29$, $P < 0.01$) (Fig. 3a). In females, body temperature was significantly higher ($P < 0.05$) in those recovered from thiamine deficiency (37.6° ± 0.2°C) than in controls (36.5° ± 0.2°C) by 6 hours after administration of ethanol (Fig. 3b).

Our findings show that the pharmacologic response to ethanol as measured by a behavioral intoxication scale (*11*) and hypothermia was significantly diminished in rats approximately 7 months after severe thiamine deficiency, a time at which they appeared to have recovered their physical health. Consistent with earlier reports (*13*), we found that ethanol was more rapidly metabolized in female rats. Previously induced thiamine deficiency reduced the area under the BEC curves after administration of ethanol by approximately 30 percent for both male and female rats. The similar shapes of the BEC curves for treated and control rats suggest that there are no major differences in absorption and that the major changes from past thiamine deficiency are due to increased volume of distribution or metabolism (or both) of ethanol. Rats recovered from thiamine deficiency and control rats were indistinguishable in terms of overall appearance and body weight at the time of ethanol administration, suggesting that increased metabolism is more likely to be the case. There is evidence that acute thiamine deficiency stimulates microsomal drug metabolism by the liver (*14*). Increased microsomal enzyme activity has been shown to augment ethanol metabolism (*1, 15*). Our results demonstrate a prolonged alteration in ethanol disposition after thiamine deficiency in the rat.

There also appear to be important behavioral changes in response to ethanol during the ascending BEC curve that are not explicable by differences in BEC between the groups recovered from thiamine deficiency and the control groups. Significantly fewer recovered animals of both sexes lost their righting reflexes

after administration of ethanol compared to controls. These observations suggest alterations in sensitivity of the central nervous system to ethanol, perhaps as a result of residual brain dysfunction from past thiamine deficiency.

Characteristic neuropathological findings of Wernicke-Korsakoff syndrome were found in 1 to 2 percent of all human brain specimens at autopsy in recent general hospital surveys; most cases occurred in alcoholics, only a small proportion of whom had been diagnosed during life (*5, 16*). Randomly selected alcoholics showed microscopic and biochemical evidence of demyelinization in the mammillary bodies, a brain region known to be damaged in Wernicke-Korsakoff syndrome (*17*). Certain memory abnormalities and other neuropsychologic deficits of chronic alcoholics are qualitatively similar to those of Korsakoff patients (*6, 18*). Behavioral manifestations and brain neuropathologic changes similar to those in Wernicke-Korsakoff syndrome have been reported in normally nourished rats exposed to ethanol over long periods as well as in thiamine-deficient animals not exposed to ethanol (*4*). Therefore, in the animal model, long-term consumption of ethanol, even with an adequate diet, may result in functional thiamine deficiency sufficient to cause damage to the central nervous system. These findings should only be extrapolated to humans with caution. However, it is possible that reported abnormalities in neurotransmitter function of the central nervous system in alcoholism and related psychopathological syndromes (*19*) as well as protracted withdrawal signs in abstinent alcoholics (*20*) may be related to enduring brain dysfunction sustained during cumulative subclinical episodes of thiamine deficiency throughout a course of extended alcohol abuse (*16*).

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Suppression of Gamma Interferon Production by Inactivated Feline Leukemia Virus

Abstract. *Supernatants from cultures of normal feline lymphocytes stimulated with* Staphylococcus *enterotoxin A showed antiviral activity, characterized as a gamma-like interferon. With the addition of inactivated feline leukemia virus, markedly less interferon was produced. The reduction in interferon production was not attributable to lowered lymphocyte viability or reduced mitogenic properties of* Staphylococcus *enterotoxin A and appears to be a direct retroviral effect. This finding may reflect clinically relevant events that may contribute to the development of the feline or human states of acquired immunodeficiency.*

Feline leukemia virus (FeLV), a contagious retrovirus transmitted primarily through salivary secretions, causes neoplastic or nonneoplastic diseases in the infected cat, including a state of immunodeficiency characterized by diminution of cellular and humoral immunity. Retrovirus-induced immunosuppression, the most frequent sequela of persistent FeLV viremia, predisposes the animal to secondary illness of infectious or autoimmune origin and accounts for most FeLV-related deaths (*1*). Viremic cats have suppressed blastogenic responses to T-cell mitogens, reduced mobility of lymphocyte membrane concanavalin A (Con A) receptors, suppressed antibody responses to synthetic polypeptides, prolonged allograft rejection times, and various degrees of hypocomplementemia, thymic atrophy, and depletion of the paracortical zones of lymph nodes (*2*). In addition, peripheral blood and splenic lymphocytes from FeLV-infected cats, when stimulated with T-cell mitogens, cannot be induced to produce interferon, or when induced produce only low titers thereof (*3*). Although little