roditic *Corbicula* attains sexual maturity when it reaches 7 to 10 mm in length (*3*). Histological sections of clams in this study also revealed mature ova in clams as small as 6 mm. That the clams may reach sexual maturity at this size range, in conjunction with their ability to disperse by flotation, indicates that rapid population blooms could occur in areas previously devoid of *Corbicula*. Also, because they reach maturity in 4 to 6 months (*1*) and because of their brooding capabilities, gravid or potentially brooding adults can quickly populate a new area rather than there being a delay in population growth resulting from larval settlement.

There have been sporadic reports of juvenile *Corbicula* composing important parts of the drift fauna of various streams. Numerous small *Corbicula* (3 percent of the total drift fauna) were recovered during a study of the lower Mississippi River (*15*). These clams were recovered in particularly high concentrations in June and August, times that may reflect reproductive peaks for this clam. Small adult or juvenile clams may settle out from a flotation mode in a relatively (or at least temporarily) static area, where they would fall out of the drift. Thus rapidly growing juveniles and mature but small adults could populate a relatively calm area. With the high degree of fluctuation seen in southern North American streams, the clams may be carried downstream from this static area in spurts and bounds.

Reports of population dynamics from a single area must be regarded with care, since the populations reported may not represent a single grouping but may instead be the result of multipopulation invasions over relatively short periods of time. This type of transport may be reflected in the variety of size classes seen in a given lotic population. In some Mississippi streams, *Corbicula* populations usually break down into three discernible size classes. Typically, however, there are anomalous intermediate sizes, which have frequently been allocated to individual growth variations. We cannot any longer assume that these intermediates are part of a single population. Instead, they may reflect a growth stage from a different upstream population that recently drifted in. Also, small adults may drift together and settle in an already populated environment, adding a secondary and artificial growth stage for that given locality.

Britton and Morton (*3*) maintain that "the genus *Corbicula* contains species primarily adapted to flowing water environments . . . periodically subjected to seasonal flooding." Flooding may allow floating clams to transfer stream systems. In view of this potential mode of transport, we must add active dispersal behaviors to the morphological and physiological invasive advantages that this "weed" species has evolved.

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Event-Related Brain Potentials in Boys at Risk for Alcoholism

Abstract. *Recent neurophysiological findings have demonstrated that abstinent chronic alcoholics manifest deficits in event-related brain potentials. To explore possible biological antecedents of alcoholism the present study examined boys at high risk for alcoholism. Event-related brain potentials were recorded from biological sons of alcoholic fathers and matched control boys. Differences in the P3 component of the potentials were obtained between the high-risk and control subjects.*

Brain dysfunction or brain damage has been observed with the use of neuropsychological and neuroradiological techniques in chronic alcoholics (*1*). Studies of evoked brain potentials (EP's) have demonstrated a number of functional aberrations in chronic alcoholics (*2*). Several investigators have studied auditory brain stem potentials in chronic alcoholics and have reported electrophysiological evidence of increased neural transmission time (*3*). Moreover, event-related potential (ERP) studies in chronic alcoholics have demonstrated deficits in the P3 component with the use of information processing paradigms (*4*). The presence of these deficits in the central nervous system has been presumed to reflect the consequence of chronic alcohol abuse (toxic effects of alcohol on the brain, nutritional deficits, or an interaction of alcohol and nutrition-related factors). Although the neurophysiological deficits observed in chronic alcoholics are presumed to be alcohol-related effects, it is possible that some of these deficits may be present in subjects at high risk for alcoholism and therefore antecede the onset of alcohol abuse.

Genetic factors may be involved in the development of alcoholism. Sons of alcoholic fathers represent a special group at high risk for developing alcoholism (*5*) even when they are separated from their biological parents soon after birth. Studies of male adoptees indicate that the biological rather than the adoptive parent is predictive of later drinking problems (*6*). Further evidence for a genetic predisposition comes from twin studies indicating that the concordance rate for alcohol abuse among identical twins is almost double the rate for fraternal twins (*7*); patterns of alcohol consumption are also highly concordant among identical twins (*8*). This evidence suggests that a genetic factor may be involved in the presence of neural pathophysiology associated with alcohol abuse.

The identification of a suitable biological marker that is genetically transmitted is important in identifying individuals before the onset of the disease. Moreover, biological markers can provide fundamental data on the etiology of alcoholism. The search for such a marker must focus on a biological variable known to be genetically determined and prevalent in abstinent chronic alcoholics. There is good evidence to indicate that EP waveforms are genetically determined. Monozygotic twins manifest EP waveforms that are as concordant with each other as those obtained from the same individual tested twice (*9*).

We now report the presence of P3

deficits in the ERP's obtained from subjects at high risk for alcoholism compared with those of control subjects. Twenty-five sons of alcoholic fathers between the ages of 7 and 13 with a mean age of 11.9 (standard deviation, 2.1) were tested. In each case, the father had received the exclusive diagnosis of alcoholism (DSM III) and had at one time or another been in treatment for alcoholism. We excluded boys whose mothers were alcoholics or who had ingested alcohol during pregnancy or drank excessively after giving birth. Only boys without medical problems and without exposure to alcohol or other substances of abuse were included in this study.

The 25 normal control (NC) subjects were boys who were matched for socioeconomic status and age to the high-risk (HR) subjects. The NC group had a mean age of 12.5 years (standard deviation, 2.4) and did not differ significantly in age from the HR group. They were included only if they had no exposure to alcohol or other substances of abuse, and had no history of alcoholism, or other psychiatric disorder in first- or second-degree relatives. Except for alcohol history, the same exclusion criteria were used as for the HR group. All subjects were paid volunteers.

Subjects were seated in a sound-attenuating chamber facing a computer-controlled display (cathode-ray tube). They were told to look at a fixation point displayed in the center of the screen. The experiment consisted of a visual head-orientation task. The nontarget stimulus was a frequently occurring plain oval presented in the center of the cathode-ray tube to which the subject did not respond (n = 160). The target stimulus was an aerial view of the head with the nose and only one ear drawn in, rotated in four different positions: nose up and right ear (n = 20), nose up and left ear (n = 20), nose down and right ear (n = 20), nose down and left ear (n = 20). Subjects pressed one of two microswitches as quickly as possible (reaction time) with either the right or left index finger to indicate whether the right or left ear, respectively, was present in the display.

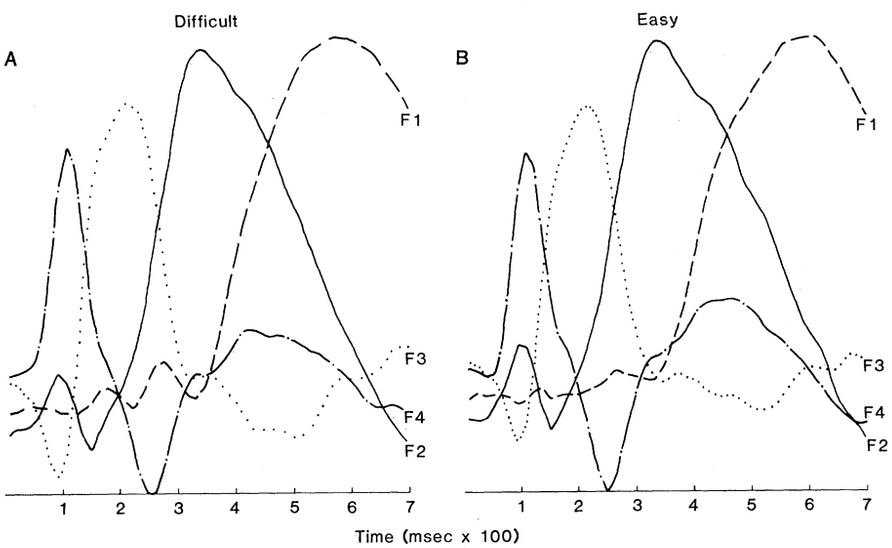

Fig. 1. Factor loadings of the first four factors obtained after principal component analysis with varimax rotation (PCAV) for the difficult (A) and easy (B) target and nontarget stimuli for both groups of subjects (normal control and high risk) at all four electrodes.

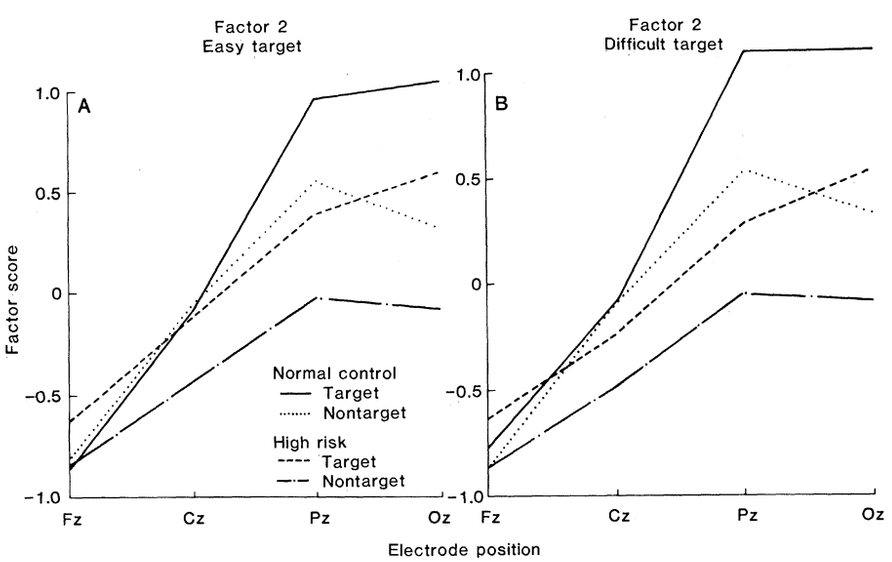

Fig. 2. Factor scores of factor 2 (P3) plotted according to electrode for the easy (A) and difficult (B) target and nontarget PCAV.

In the "easy" condition, the head was facing forward (nose up on screen), and the left or right ear appeared directly on the side corresponding to the appropriate button. In the "difficult" condition, the head was facing back (nose down on screen), and either the left or right ear appeared on the side of the screen opposite the corresponding button. A total of 240 stimuli were randomly presented—160 nontargets and 80 targets (20 per target condition). The stimuli were 25 msec in duration and subtended 2.9° of arc; interstimulus intervals varied randomly between 2 and 4 seconds. The ERP's and behavioral data were under computer control (*10*).

Reaction times for easy stimuli were significantly shorter than for difficult stimuli [$F(1, 48) = 110.64$, $P < 0.0001$]. There were no significant reaction time differences between groups. The number of correct behavioral responses was significantly less for the HR group for easy [$t(48) = 2.76$, $P < 0.01$] and difficult stimuli [$t(48) = 3.65$, $P < 0.001$].

All ERP data were subjected to an eye-movement correction procedure (*11*). ERP's to all stimuli regardless of side of appearance, were combined for easy and difficult targets. Furthermore, ERP's obtained in trials with correct behavioral responses were subjected to a latency corrected average procedure (*12*) to reduce possible latency jitter. The P3 baseline-to-peak voltage and latency measurements obtained from these latency corrected average data were then analyzed across groups, conditions, and electrodes with a repeated measures analysis of variance (*13*). No differences in the latency of P3 were obtained between groups. In addition to the baseline-to-peak voltage measurements, the entire raw data set was subjected to a principal component analysis with varimax rotation, through the use of the covariance matrix (PCAV) (*13*). As the results of our statistical analyses were

identical with both procedures, only the results of the PCAV procedure will be presented here.

Separate PCAV's were performed on the easy target and nontarget ERP's, and the difficult target and nontarget ERP's for the HR and NC groups separately. As the factor structures of the two groups were the same (*14*), the data from the two groups were combined to perform two separate PCAV's for the easy and difficult conditions. Figure 1 indicates the component loadings of the first four factors obtained for the easy and difficult conditions. The first four factors account for 96.1 percent of the variance for the easy condition and 96.4 percent for the difficult condition. Factor 1 is a rather broad component that peaks at 598.5 msec for the easy and at 570.5 msec for the difficult conditions (slow wave). Factor 2 is maximum at Pz and peaks at 332.5 msec for both the easy and the difficult conditions (P3). The factor scores for each of the four factors were subjected to a repeated measures analysis of variance (*13*). Factor 1 (slow wave) was significantly different for electrodes [easy: $F(3, 144) = 18.06$, $P < 0.0001$; difficult: $F(3, 144) = 19.74$, $P < 0.0001$] and stimuli (target, nontarget) [easy: $F(1, 48) = 43.36$, $P < 0.0001$; difficult: $F(1, 48) = 53.29$, $P < 0.0001$], but not for groups. Factor 3 was significantly different for electrodes [easy: $F(3, 144) = 46.95$, $P < 0.0001$; difficult: $F(3, 144) = 56.67$, $P < 0.0001$] and stimuli [easy: $F(1, 48) = 21.72$, $P < 0.0001$; difficult: $F(1, 48) = 19.44$, $P < 0.0001$], but not for groups. Factor 4 was significantly different only for electrodes [easy: $F(3, 144) = 38.9$, $P < 0.0001$; difficult: $F(3, 144) = 28.70$, $P < 0.0001$]. Factor 2 (P3) was also significantly different for electrodes [easy: $F(3, 144) = 57.50$, $P < 0.0001$; difficult: $F(3, 144) = 64.54$, $P < 0.0001$] and stimuli [easy: $F(1, 48) = 16.16$, $P < 0.0002$; difficult: $F(1, 48) = 22.15$, $P < 0.0001$]. In addition, factor 2 was significantly different between high- and low-risk groups for the difficult condition [$F(1, 48) = 5.22$, $P < 0.02$].

The component scores for each of the four factors were then subjected to a repeated measures analysis of variance for each electrode separately. Again these results indicated that only factor 2 (P3) differed significantly between groups. This group difference was significant at the parietal lead (where P3 is maximum) for both easy [$F(1, 48) = 6.49$, $P < 0.01$] and difficult [$F(1, 48) = 9.92$, $P < 0.002$] conditions, as well as at the occipital lead for the difficult condition [$F(1, 48) = 4.21$, $P < 0.04$] (Fig. 2).

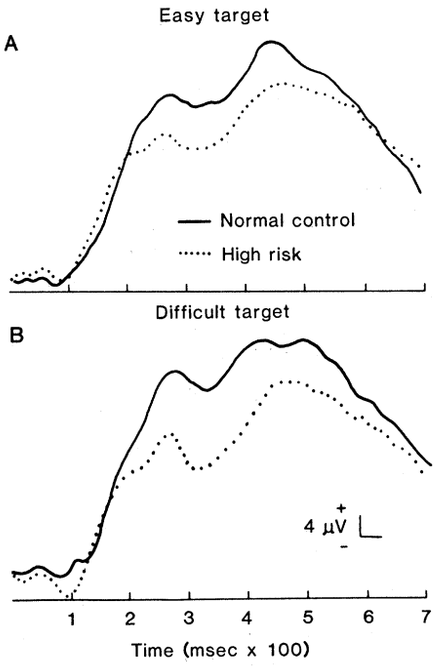

Fig. 3. Grand mean ERP waveforms for the easy (A) and difficult (B) targets at the parietal electrode (Pz).

Figure 3 illustrates the differences between the ERP's obtained from both groups for the easy and difficult targets at the parietal lead, where these differences were greatest.

These findings indicate a significant difference in P3 voltage between boys at high risk for alcoholism and normal control boys, without exposure to alcohol. As reaction times did not differ between groups, it is unlikely that these differences are due to attention deficits. We have obtained similar results in alcoholic patients. Perhaps the differences are due to differences in speed versus accuracy strategies. Although possible, it is unlikely that differences in P3 voltage between these two groups are due to differences in maturational level. Differences in evoked potentials and electroencephalograms have recently been reported between males with some family history of alcoholism and control subjects in response to a challenge dose of alcohol (*15*). Our findings are particularly striking in that they were obtained without the administration of alcohol.

We have reported similar P3 voltage decrements in abstinent chronic alcoholics with many P3 procedures (*2*). Recently, we have investigated the reversibility of electrophysiological deficits observed in alcoholics with prolonged abstinence from alcohol. Although we have found improvement in brain stem potential delays, we have not observed any change in P3 voltages (*16*). These results suggest that rather than being the consequence of years of heavy drinking, the P3 voltage decrements observed in chronic alcoholics antedate alcohol abuse.

The significance of a reduced P3 component in high-risk boys may be interpreted at two different levels. At the neuroanatomical level, recent intracranial recordings in humans (*17*) have indicated that the hippocampus and amygdala may make substantial contributions to the P3 potentials recorded from the scalp. In addition, a study using the magnetoencephalographic technique has also suggested the hippocampus as a possible neural generator of this late positive ERP component (*18*).

At the functional level it is by now well established that the amplitude of P3 indexes stimulus significance (*19*) and plays a role in memory (*20*). Thus the significantly reduced P3 amplitude in high-risk boys suggests a reduced capacity to assess significance or allocate the necessary neural resources for encoding a specific event. To the extent that P3 reflects processes involved in revising current representations in working memory, this specific neurophysiological deficit in HR subjects suggests that sons of alcoholics may manifest deficits in memory. This has recently been observed in adolescent sons of alcoholics who performed significantly more poorly than control subjects on memory tasks (*21*).

The present neurophysiological observations in boys at high risk for alcoholism are striking in that they were obtained without the use of alcohol in sons of alcoholics not previously exposed to alcohol or other drugs of abuse. Our data do not allow us to infer whether the observed P3 deficit in high-risk male children represents a predisposing factor for subsequent alcohol abuse. Longitudinal studies to examine the relationship between the present neurophysiological findings in male children and future patterns of alcohol intake are necessary.

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Neuroendocrine Response to Estrogen and Sexual Orientation

Abstract. *A neuroendocrine component, the positive estrogen feedback effect, thought to be related to sexual orientation and, indirectly, to sexual differentiation, was evaluated in healthy, noninstitutionalized research volunteers. Men and women with a lifelong heterosexual orientation and men with a lifelong homosexual orientation were administered an estrogen preparation known to enhance the concentration of luteinizing hormone in women but not in men. The secretory pattern of luteinizing hormone in the homosexuals in response to estrogen was intermediate between that of the heterosexual men and that of the women. Furthermore, testosterone was depressed for a significantly longer period in the homosexual men than in the heterosexual men. These findings suggest that biological markers for sexual orientation may exist.*

A fundamental question of human psychosexuality is whether there are biological influences on sexual behavior and sexual orientation. Of particular interest is whether hormonal correlates exist for the development and expression of patterns of sexual behavior. The results of previous efforts to relate the plasma concentration of androgen (primarily testosterone) or estrogen (chiefly estradiol) to homosexual or heterosexual orientation were not convincing (*1*). Currently, a biological explanation of homosexuality is being pursued most vigorously in the hypothalamic-pituitary-gonadal axis, a neuroendocrine system. Presumably the endocrine responsiveness of this system is sexually dimorphic, perhaps reflecting organizing influences of hormones during critical periods of sexual differentiation (*2*). It has been suggested that such differences in neuroendocrine responsiveness are linked to sexual orientation (*3, 4*). Because of the importance of these controversial findings, we measured the neuroendocrine response to estrogen administration in men and women who differ in their sexual orientation. We found that men declaring a lifelong homosexual orientation had patterns of luteinizing hormone (LH) and testosterone secretion in response to estrogen that were intermediate between those of men and women declaring lifelong heterosexual orientation.

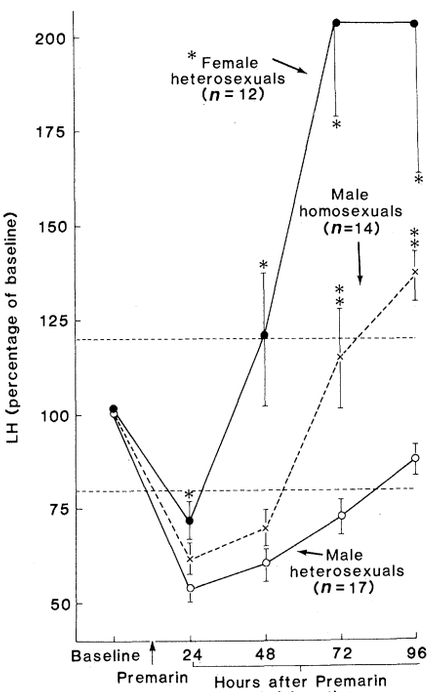

Fig. 1. Changes in LH in response to a single injection of Premarin. Values are means ± standard errors (vertical bars). Dashed lines indicate the 95 percent confidence interval for baseline values for all groups. Group comparisons: (*) female heterosexuals significantly different from male heterosexuals and homosexuals at all times ($P < 0.05$, Newman-Keuls multiple comparison test) and (**) male homosexuals significantly different from male heterosexuals at 72 and 96 hours ($P < 0.05$, SNK). All groups show a decrease from baseline at 24 hours.

During the follicular phase of the menstrual cycle, increasing concentrations of estrogen initiate a transient decrease in LH (negative feedback) that is soon followed by a sharp increase in LH (*5, 6*). The ability of increased estrogen to enhance the release of LH (positive feedback) is thought to reflect the adult consequences of hormone-mediated sexual differentiation. Such an LH response pattern, typically seen in females, presumably reflects the "female" differentiation of the brain; the typical absence of this response in males presumably reflects "male" brain differentiation (*7*). Exposure to high concentrations of androgen during a critical period of development in males results in a relatively steady LH secretion pattern. Females, not ordinarily exposed to such levels of androgen during this period, secrete LH in the cyclical pattern related to the ovulatory cycle. A brief negative feedback response of LH to estrogen followed by a late rebounding of LH above pretreatment levels (positive feedback) was recently used to explore, indirectly, human sexual differentiation and interrelationships of brain function, hormone responsiveness, and sexual orientation (*3, 4*).