trous females and placed on the lip of ovariectomized females treated with AMN. The males spent significantly more time contacting the facial regions of target females carrying the saliva from estrous females and, as expected, exhibited no difference in their contact times with ventral gland or anogenital regions (Fig. 1C). The results suggest that salivary stimuli may act as reproductive chemosignals, perhaps in parallel with ventral gland cues.

In developing gerbils, mouthing interchanges emerge relatively early in life and became most salient during weaning; they persist in a similar, species-typical form throughout the juvenile and adult phases of life. Our results suggest that all of these interchanges use a common source of chemical signals, arising from saliva of social partners. The type of information and functional role of the signal may vary with the age, sex, or experience (*10*). Further tests are needed to directly examine whether the saliva preferences reflect actual social partner preferences in normal interchanges.

Other investigators have established that saliva plays a role in the suckling behavior of neonatal rats and the aggressive behavior of adult mice (*11*). Our data extend these findings and provide evidence that saliva-related cues may act as chemosignals in all aspects of rodent social development. Using a common chemosignal source for various social interactions during development would provide a mechanism that not only maintains the structure of social investigations (naso-oral or oro-oral contacts), but also modifies or transforms the outcomes of social interchanges when the signal is altered by age and environment. Saliva-related stimuli may also contribute to the establishment of filial or juvenile interchanges and relationships that could have enduring effects on those adult social interactions that are also dependent on saliva cues. Although our study was not specifically designed to test these hypotheses, the data we have presented do provide an empirical base for more direct investigations of these questions (*12*).

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3. The amount of time the pups in this experiment spent contacting their fathers was not significantly greater than the time pups in the previous experiment spent with fathers paired with untreated mothers ($P > .05$).
4. The effectiveness of a saliva sample as an attractive stimulus appears to depend on the contextual features of the substrate on which it is deposited; when the saliva is applied to substrates which differ from the normal morphological context (for example, the mouth), the behavioral responses are significantly diminished (*2*).
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Auditory Brainstem Potentials in Chronic Alcoholics

Abstract. *Auditory brainstem potentials were recorded from abstinent chronic alcoholics and control subjects. The latencies of peaks II, III, IV, and V were significantly delayed in the alcoholic patients compared to control subjects. Brainstem transmission time was longer in alcoholics than in controls. This study provides systematic evidence that chronic alcohol abuse results in brainstem deficits suggesting possible demyelination of auditory tracts.*

Chronic alcoholism is known to result in aberrations of the central nervous system. At the structural level, these deficits have been studied with the use of neuropathological methods (*1*), pneumoencephalography (*2*), and computerized tomography (*3*). At the functional level, these changes have been examined with neuropsychological tests (*4*), electroencephalography (*5*), and cerebral blood flow studies (*6*). More recently, event-related potentials (*7*) have been used to assess the functional integrity of the brains of alcoholic patients. These electrophysiological studies have demonstrated functional deficits reflected in specific components of the event-related potential (ERP). The N1-P2 component of the ERP has been found to be depressed in chronic alcoholics, regardless of whether the response is to a relevant or irrelevant stimulus modality (*8*). Furthermore, abnormal P300 components have been reported in abstinent chronic alcoholics (*9*). Investigations of the structural (*1-3*) and functional (*4-9*) brain aberrations in alcoholics have produced consistent findings indicating that chronic alcohol abuse affects primarily the cerebral cortex and leaves relatively intact the primary sensory pathways.

Potentials generated in the auditory nerve and brainstem auditory pathway consist of seven positive waves occurring at specific latencies (*10*). Each peak is presumed to reflect the activity of different neural sites, with the first wave generated in the auditory nerve, the second in the cochlear nucleus, and the third in the region of the superior olivary complex. The fourth wave is postulated to emanate from the lateral lemniscus and the fifth peak from the inferior colliculus (*11, 12*). The neural sites responsible for the activity of the last two peaks are at present unknown. Investigators have reported that the time interval between peak I of the compound auditory nerve response and peak V of the inferior colliculus in the midbrain may prove valuable as a measure of brainstem transmission time (BTT) (*13*).

Several studies have demonstrated that a single dose of alcohol causes significant increases in the auditory BTT in rats (*14, 15*), cats (*15*), and man (*16*). However, functional brainstem deficits have not been reported in alcoholic patients practicing abstinence. We now report that transmission time in the auditory brainstem pathways of alcoholic patients is significantly slower than that in control subjects.

Seventeen hospitalized male alcoholic patients with a mean age of 38 ± 2.1 years (± standard deviation) were tested in this study. All patients met the Research Diagnostic Criteria (*17*) for alcoholism. Alcoholic patients with a history of hepatic encephalopathy, a history of

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Table 1. Mean latencies (± standard deviation) of auditory brainstem potentials of peaks I through V and the latency of each peak with respect to peak I for the alcoholic and control groups. The level of statistical significance (P) between the alcoholic and control groups is indicated for each measure (N.S., not significant).

Subjects	Mean latencies for peaks					Interpeak latencies			
	I	II	III	IV	V	I and II	I and III	I and IV	I and V
Controls	1.84 ± 0.22	2.73 ± 0.29	3.57 ± 0.23	4.95 ± 0.34	5.88 ± 0.39	0.88 ± 0.22	1.72 ± 0.24	3.11 ± 0.40	4.04 ± 0.43
Alcoholics	1.82 ± 0.22	3.04 ± 0.39	4.15 ± 0.51	5.77 ± 0.51	6.81 ± 0.58	1.22 ± 0.45	2.33 ± 0.62	3.95 ± 0.56	4.99 ± 0.59
P	N.S.	.02	.001	.001	.001	.01	.005	.001	.001

head injury, seizures not related to alcohol withdrawal, or abuse of other psychoactive drugs were not included in the study. The patients had been drinking heavily for an average of 16 years and a minimum of 6 years. All patients were totally abstinent for a minimum of 3 weeks and medication-free for a minimum of 2 weeks.

Seventeen age-matched and education-matched males were used as control subjects. They were recruited from among hospital employees and paid for their participation. All control subjects were prescreened for drinking and medical histories and were medically examined prior to the experiments; only subjects who were occasional "social drinkers" and were free of medical problems and medication were accepted for the study. Auditory brainstem potentials were evoked monaurally with the use of 2000 stimuli consisting of 0.5-msec clicks presented through earphones (TDH 39) at a rate of ten stimuli per second. Each ear was tested randomly across all subjects. Stimulus intensity was 70 dB above threshold. Monopolar recordings were taken between a vertex electrode and the ipsilateral earlobe, with an electrode on the forehead serving as the ground. The potentials were amplified 100,000 times and were subjected to a digital filter with a bandpass of 100 Hz to 2000 kHz (*18*). Brain electrical activity was sampled at a rate of 40 kHz (one point every 25 μsec) for 10 msec following the onset of the click. We measured the latency of the first five peaks including the interpeak latencies (BTT) between peak I and each successive peak. The interpeak latency between peaks I and V is inversely related to the conduction velocity in the ascending pontine segment of the auditory pathway.

Since there was no significant difference between ears for either group of subjects the data for both ears were pooled. The differences in mean latencies for the five peaks and four interpeak latencies between the two groups of subjects were assessed initially with the use of a two-way analysis of variance with repeated measures, and an appropriate correction being applied to the degrees of freedom (*19*). The individual group means were further assessed with the use of individual t-tests.

The brainstem potentials for one control subject and one alcoholic subject are shown in Fig. 1. The statistical analysis yielded significant differences between groups [$F(1, 32) = 30.51$, $P < .01$] and between trial factors [$F(1, 32) = 111.08$, $P < .001$]. The interaction between groups and trial factors was also significant [$F(1, 32) = 10.15$, $P < .01$]. Peak I did not differ significantly between patients and controls. Peak II differed between groups ($P < .02$) as did peaks III, IV, and V ($P < .001$). Interpeak latencies were all significantly different as follows: between I and II ($P < .01$), I and III ($P < .005$), I and IV ($P < .001$), and I and V ($P < .001$).

These findings provide systematic electrophysiological evidence of increased neural transmission time in the brainstem of alcoholic patients who show no clinical signs of corticobulbar or corticospinal tract deficits. Our data indicate that while the most peripheral part of the auditory pathway is not affected (peak I), there is a significant increase in latency of each succeeding peak. This significant slowing in neural transmission time reflects a decrease in conduction velocity not elicited by deficits at the peripheral organ, but suggesting pathological changes in the medulla and the pontine formation.

Various morphological abnormalities of the auditory brainstem potential have been described in patients with neurological disorders, and electrophysiological deficits have been found to be related to specific neuroanatomical lesions (*12*). Interpeak latencies of the auditory brainstem potential are stable and not influenced by factors such as attention or motivation (*20*). A significant slowing in conduction velocity of the auditory brainstem potential was reported in two patients with quadriparesis and multiple cranial nerve deficits. These patients had a long history of alcohol abuse and were suspected of central pontine myelinolysis (*21*). The pathological changes usually involve the central part of the base of the mid- to upper pons and are characterized histologically by loss of myelin sheaths and oligodendroglia whereas nerve cells, axis cylinders, and blood vessels remain relatively intact. Demyelination of the auditory tracts and nuclei at the level of the caudal and mid-pons adjacent to the basis pontis has been shown to result in a significant increase in BTT (*22*). This demyelination cannot readily be identified by clinical diagnosis, and in most cases its presence is only detectable during postmortem examinations of the brain.

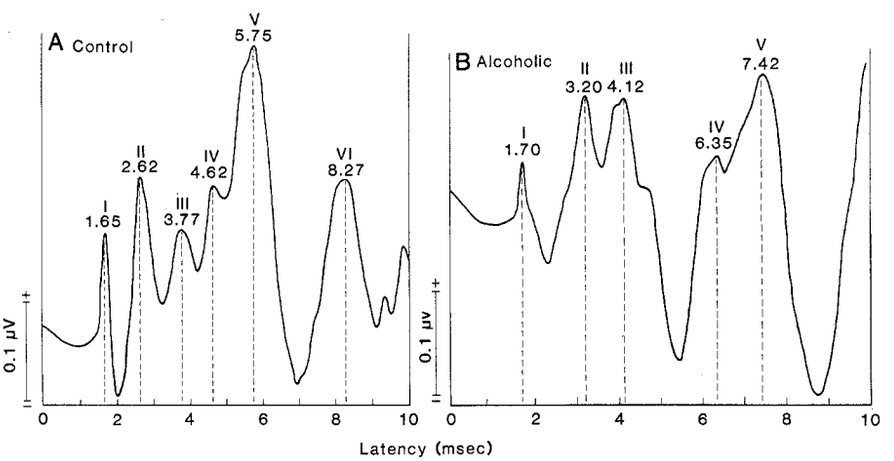

Fig. 1. (A) Auditory brainstem potential for one control subject indicating the latencies of peaks I to VI. (B) Auditory brainstem potential for one alcoholic subject, with the latencies of peaks I to V indicated. Wave VI is delayed beyond 10 msec and therefore is not shown.

Our data provide evidence for the involvement of brain areas other than neocortex in chronic alcoholism. The increase in neural transmission time within the auditory brainstem may reflect a direct pathological process of demyelination; this effect has been suspected in alcoholic patients (*23*) and observed in rats fed on alcohol for long periods (*24*). These results could also be caused indirectly by the aberrant fluidizing effects of chronic alcohol intake on cell membranes (*25*), which may result in edema. The use of auditory brainstem potentials may provide critical prognostic information about the progress of brainstem deficits in chronic alcoholics and their potential recovery with prolonged abstinence.

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Dialysis in Schizophrenia: A Double-Blind Evaluation

Abstract. *Eight chronic schizophrenia patients completed a research program consisting of ten weekly sessions of active hemodialysis and ten weekly sessions of sham dialysis in a double-blind design. Previous reports of therapeutic efficacy were not substantiated. None of the patients improved during active dialysis; four patients worsened.*

Feer *et al.* (*1*) reported in 1960 that three out of five schizophrenic patients improved after only one or two hemodialyses. No further attempts were made known until 1977, when Wagemaker and Cade (*2*) reported dramatic improvement in five physically healthy schizophrenic patients treated with weekly dialyses for up to 16 weeks. Since that report there has been intense interest in this area of clinical investigation as evidenced by reports of both positive (*3*) and negative (*4, 5*) clinical psychiatric findings, technical reports about dialysis (*6*), and biochemical papers exploring possible mechanisms of action of dialysis in relation to endorphins (*5, 7*). In a recent literature review (*8*) it was noted that of 92 physically healthy schizophrenics who had been dialyzed 42 showed marked or some improvement. However, these reports do not all include information about the diagnostic criteria of schizophrenia employed, duration of illness, method of behavioral evaluation, and type and quality of improvement, or precise description of dialysis equipment. Our double-blind study of weekly hemodialysis of schizophrenic patients was undertaken to investigate the therapeutic claims made for this procedure. Since we finished our study two other double-blind studies have been published to date (*9*): Linkowski *et al.* observed improvement in six of seven patients on real dialysis and in three of five on sham dialysis, and Diaz-Buxo *et al.* observed no effect in four patients.

The patients in our study were five women and three men admitted to the Clinical Center at the National Institutes of Health and diagnosed schizophrenic

Table 1. Means and standard errors of psychiatrists' ratings of their patients' symptoms during the 2 weeks prior to the dialysis sessions, the last 2 weeks of sham dialysis sessions, the last 2 weeks of active dialysis sessions, and the 2 weeks immediately following the last dialysis session. Ranges for the ratings were: global psychosis and depression, 1 to 15; total Brief Psychiatric Rating Scale, 24 to 168; thought disorder cluster, 3 to 21; individual items, 1 to 7. N.S., not significant.

Symptom	Period				*F*	*P*
	Before dialysis	Sham dialysis	Active dialysis	After dialysis		
Global psychosis	8.0 ± .6	9.1 ± .8	8.9 ± .5	9.1 ± 1.0	1.2	N.S.
Global depression	5.2 ± .9	5.5 ± 1.2	5.3 ± 1.0	5.1 ± .8	.08	N.S.
Total BPRS	63.2 ± 4.3	67.7 ± 5.1	65.4 ± 4.2	66.9 ± 5.2	.6	N.S.
Thought disorder cluster	11.4 ± 1.4	11.8 ± 1.5	11.6 ± 1.3	11.4 ± 1.5	.1	N.S.
Hallucinatory behavior	3.4 ± .7	3.4 ± .8	3.3 ± .7	3.3 ± .7	.3	N.S.
Unusual thought content	4.4 ± .6	4.4 ± .5	4.3 ± .5	4.2 ± .6	.1	N.S.
Conceptual disorganization	3.7 ± .6	4.1 ± .6	4.0 ± .5	3.9 ± .6	.6	N.S.
Suspiciousness	4.4 ± .7	4.5 ± .7	4.4 ± .8	3.9 ± .8	1.4	N.S.

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