and single doses of hallucinogenic drugs may all be based on neurochemical processes involving dopamine and serotonin.

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13. This pattern of neurochemical changes, 6 hours after the last 15 mg/kg amphetamine injection, is not dependent on the short-term effects of the drug, since essentially the same pattern is seen 24 hours after the last 15 mg/kg injection.
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17. Two facts militate against interpreting these results in terms of a partial anorexia produced by amphetamine. First, the loss of body weight during the experiment was 0.5 kg in the amphetamine-treated group and only slightly less (0.4 kg), in the saline-treated group. Second, the concentrations of L-tryptophan, the dietary precursor of serotonin, were higher in the amphetamine group.
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Auditory Brainstem Frequency Following Responses to Waveform Envelope Periodicity

Abstract. *An auditory frequency following response (FFR) was recorded to four complex stimuli. The FFR corresponded to the waveform envelope periodicity but not to the "missing fundamental" pitch of the stimuli. The FFR may be significant for timbre perception and sound lateralization.*

The importance of periodicity for the pitch perception of complex sounds has long been of interest to auditory investigators. In the 19th century, Seebeck (*1*) showed that the pitch derived from a series of overtones was identical to the pitch of the "missing fundamental." Helmholtz (*2*) later incorporated this finding into his pitch-place theory by supposing that the fundamental was introduced to the ear through distortion. An alternative to the spectrally based theory of Helmholtz was offered when Wundt (*3*) proposed that the cue for pitch was periodicity of nerve impulses that was synchronous with stimulus periodicity. Much later, Schouten (*4*) and Licklider (*5*) disproved the distortion hypothesis of Helmholtz, showing that the fundamental did not have to be present in the ear when its pitch was heard during complex stimulation. This finding generated new interest in periodicity as a pitch cue, and theories of pitch perception that emphasized the periodicity of the waveform envelope (*6*) or the fine structure of the stimulus (*7*) were developed.

Complex waveform periodicity has also been proposed as a cue for the perception of timbre and the lateralization of high-frequency (> 2000 Hz) complex stimuli. In timbre perception, the perceived roughness of a complex sound changes as the prominence of the stimulus envelope is altered (*8*). In sound lateralization, low-frequency sine waves can be lateralized by periodicity cues, but high-frequency sine waves cannot. When the high-frequency signal is complex and has a low-frequency envelope, however, the signal can be lateralized on the basis of its envelope periodicity (*9*). Thus the inherent periodicity of complex stimuli may have significance for the perception of pitch and timbre and for the lateralization of high-frequency sounds.

Recently Smith *et al.* (*10*) recorded a frequency following response (FFR) to the missing fundamental. The FFR is an auditory brainstem response that is generally accepted to be a representation of neural periodicity. The finding of Smith *et al.* is important because it shows that the periodicity of the missing fundamental is available at the brainstem and that it could be used as a temporal cue for

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pitch perception. In their experiment, the missing fundamental of the second, third, fourth, and fifth harmonics of 365 Hz was recorded. The authors inferred that the periodicity of the FFR was directly related to the pitch perception of their subjects. The result is open to an alternative interpretation, however. Since the four harmonics were added in sine phase, the envelope of the waveform had a prominent 365-Hz periodicity. The fact that the FFR corresponded to both the perceived pitch and the waveform envelope leaves open the possibility that the FFR reflected a neural following of the waveform envelope and had no relation to pitch perception.

To test this hypothesis, I conducted an experiment in which the pitch remained constant but the periodicity of the waveform envelope was changed. Three stimuli were generated by amplitude modulating an 800-Hz sine wave at a rate of 200 Hz (Fig. 1A). This amplitude modulation produced complex stimuli composed of the 800-Hz carrier and two sidebands of 600 and 1000 Hz. The amplitude of the carrier was adjusted to alter the periodicity of the waveform envelope. For stimulus 1, the carrier was 6 dB more intense than the sidebands. While this stimulus has no spectral energy at 200 Hz, its envelope has a prominent 200-Hz periodicity, going to zero every 5 msec (arrows, Fig. 1B). For stimulus 2, the carrier and sidebands were of equal intensity, and the 200-Hz periodicity of the envelope was less prominent: where the envelope went to zero in stimulus 1, small peaks now occurred. These small peaks occurred midway between the larger peaks, giving stimulus 2 a component of 400-Hz envelope periodicity. For stimulus 3, the carrier was cancelled, leaving only the sidebands. The 400-Hz envelope periodicity of this stimulus is even more prominent, there being a relatively large peak every 2.5 msec.

Five subjects with normal hearing participated in the experiment. In the first part of the experiment, the subjects matched the pitches derived from each complex stimulus to the pitch of an adjustable sine wave. Subjects switched back and forth between a complex stimulus and the sine wave until a pitch match was made. All subjects matched each complex stimulus five times. All subjects heard the missing fundamental, matching the complex stimuli to within 2 Hz of a 200-Hz sine wave on each match.

In the second part of the experiment, evoked responses were recorded to each of the complex stimuli. Electrodes between vertex and right mastoid were led to an amplifier (Grass 7P54), and responses were sampled (at a rate of ten per millisecond) and averaged by a computer (PDP 11-03). The electroencephalogram was bandpass filtered between 100 and 1200 Hz to restrict recordings to frequencies in the stimulus and stimulus envelope. Each stimulus was presented 2000 times. Stimuli had rise and fall times of 2.5 msec and lasted 30 msec, and each harmonic had a constant starting phase for all 2000 trials. Stimuli were led from an earphone (TDH 49) through 5 feet of plastic tubing (3/8-inch internal diameter) that terminated on a circumaural earmuff. The tubing was used to isolate electrodes from electromagnetic fields of the earphone (*11*). The acoustic delay introduced by the tubing was determined, and a 21-msec recording epoch began as the stimulus reached the ear. High-frequency loss resulting from the tubing (3 dB per octave) was compensated for by frequency equalization. Stimuli were presented monaurally to the right ear at an amplitude of 80 dB (sound pressure level). Before a series of trials began, the amplitude of the stimu-

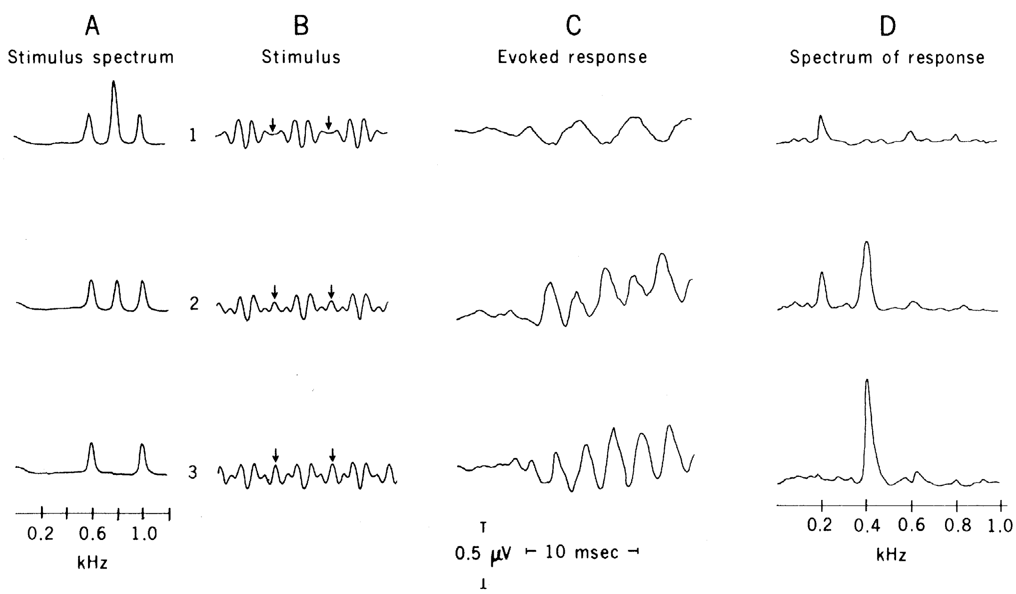

Fig. 1. (A) The spectra of the stimuli. (B) Steady-state portions of the stimuli as recorded by microphone (low-pass noise not present). Arrows point to aspects of envelope periodicity. (C) Composite FFR's for the five subjects (D) The FFR spectra.

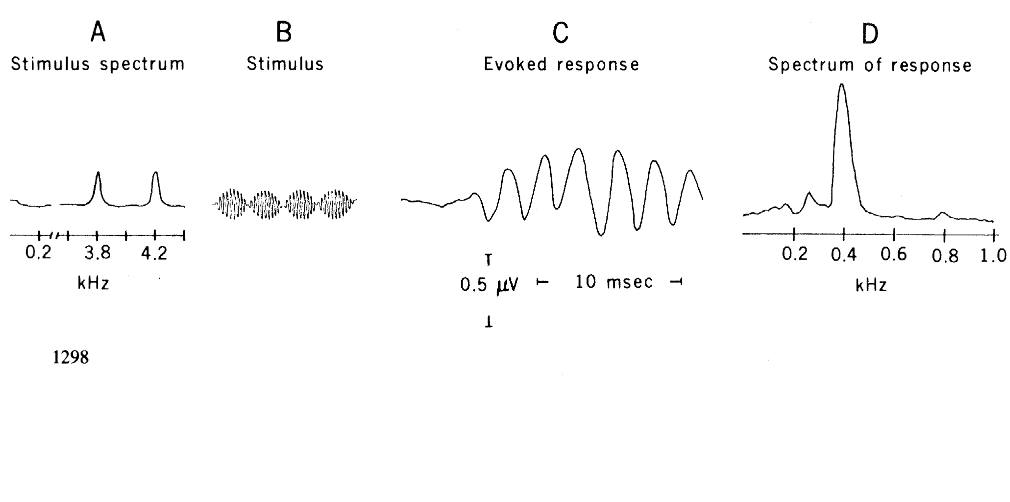

Fig. 2. A complex tone of 3800 and 4200 Hz (A) along with its spectrum (B). (C) The composite FFR to this stimulus, and (D) the spectrum of the FFR.

lus was determined by acoustically coupling the earmuff to a sound level meter (General Radio). The input to the sound level meter was monitored by oscilloscope to ensure proper phase relations. The spectral content of the stimuli was monitored by performing fast Fourier transforms (FFT's) on analog-to-digital representations of the stimuli. A 40-dB low-pass noise with a high cutoff of 450 Hz was present during all stimulation to minimize the possibility of recording a response to low-frequency auditory distortion.

Figure 1C shows the composite FFR's for five subjects to each of the stimuli; and Fig. 1D, the FFT spectrum of the responses. Composite FFR's are shown because the FFR amplitudes and phases were similar across subjects. The FFR correlates well with the periodicity of the waveform envelope: When a 200-Hz envelope periodicity was prominent (stimulus 1), a 200-Hz FFR occurred; when 200- and 400-Hz envelope periodicity was evident (stimulus 2), both 200- and 400-Hz FFR's occurred; when 400-Hz envelope periodicity was prominent (stimulus 3), a 400-Hz FFR occurred.

That the 400-Hz FFR to stimulus 3 did not correspond to the pitch perceived from this stimulus (200 Hz) indicates that the FFR is a reflection of envelope periodicity, but not of the pitch of the missing fundamental.

Although this result does not support temporally based pitch theories, it does indicate that envelope periodicity is an available cue for timbre perception and sound lateralization. Behaviorally, the cue of envelope periodicity is of special significance for the lateralization of high-frequency complex sounds. Therefore, if the FFR is truly a representation of envelope periodicity, it should occur for high-frequency complex stimuli as well as the low-frequency complex stimuli already studied. The stimulus of 3800 and 4200 Hz added in cosine phase provided a high-frequency complex stimulus with a prominent 400-Hz envelope periodicity (Fig. 2, A and B). When this stimulus was presented in the same manner as the previous ones, a clear 400-Hz FFR was recorded (Fig. 2, C and D). This periodicity information could serve as a cue for the lateralization of high-frequency stimuli with low-frequency envelopes.

The results show that the periodicity of the stimulus waveform envelope is represented by the FFR; this indicates that very early in the processing of sensory information, waveform periodicity is reflected. This finding supports the hypothesis that neural timing cues representing envelope periodicity may be used for timbre perception and sound lateralization. The results also show a lack of correspondence between the FFR and the pitch of the missing fundamental.

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Baroreceptor Activation Reduces Reactivity to Noxious Stimulation: Implications for Hypertension

Abstract. *The hypothesis was tested that an acute rise of blood pressure may reduce reactivity to noxious stimuli through a baroreceptor-mediated reduction of cerebral arousal. When blood pressure was raised by an infusion of phenylephrine, rats showed less running to terminate or avoid noxious stimuli than during saline infusions. This effect was not seen in rats with denervated baroreceptors. The results suggest that a rise of blood pressure could have motivational consequences significant for human hypertension.*

Baroreceptor stimulation lowers blood pressure by reflex actions on the heart and blood vessels. In addition, such stimulation has a separate effect: it produces cortical and behavioral inhibition. We have suggested that this less well known effect may reinforce the learning of elevations in blood pressure (*1*). This experiment is an initial step toward exploring that hypothesis.

Weiss and Baker (*2*) investigated a form of fainting which resulted from inadvertent mechanical stimulation of the carotid region and determined that loss of consciousness in carotid syncope could occur without cerebral ischemia or a fall in blood pressure (*3*). Köch (*4*) reported that, in the dog, dilatation of a carotid cul de sac by an implanted balloon would produce prompt and deep sleep (*5*). Bonvallet *et al.* (*6*) reported extensively on the inhibitory electrophysiological sequels of stimulation of the baroreceptor nerves, and they showed these effects to be independent of hypotension. Lacey and co-workers (*7*) suggested that baroreceptor activation could be responsible for changes in response latency observed in vigilance tasks. Ádám and coworkers (*8*) showed that removal of the tonic influence of the carotid sinus by surgical denervation of rats resulted in reduced latency of a learned response and increased inappropriate responding to an unreinforced discriminative stimulus. They also demonstrated that agitated "neurotic" behavior could be more easily stress-induced in denervated rats. Bartorelli *et al.* (*9*) observed that reducing baroreceptor stimulation in decerebrate cats elicits sham rage, whereas increasing such stimulation inhibits it. In preliminary experiments we observed that denervated rats were more sensitive to a variety of noxious stimuli (*10*).

These results suggested a motivational effect of blood pressure that would be of general biological interest and possibly relevance to human hypertension. We designed the present experiment to measure blood pressure–induced changes in the escape-avoidance behavior of rats.

Escape running increases with aversiveness of the motivating stimulation (*11*). We therefore trained rats to escape a periodic aversive stimulus by running on the top of a treadwheel. Then we studied the effect of phenylephrine-induced hypertension on this behavior.

We used 16 male Sprague-Dawley rats (Charles River) weighing 300 to 350 g: ten intact and six with surgically denervated carotid and aortic arch baroreceptors (*12*). Denervation was confirmed by observing heart rate changes in response to an infusion of phenylephrine (*13*). One of the operated rats showed almost normal bradycardia to phenylephrine-in-

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