PHYSIOLOGY

Electrophysiological Characteristics of Visual Perception in Volunteers Administered Fluacizine

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Electrophysiological manifestations of disturbed visual perception were studied in 18 healthy volunteers following blockade of M-cholinergic brain structures with the tricyclic antidepressant fluacizine given orally in a single dose of 1 mg/kg. The synchronization of spontaneous electroencephalographic activity observed 2 h after dosing indicated that the cholinergic structures were stably blocked. Evoked potentials were recorded in response to presented images having identical physical parameters but differing in information content (a checkerboard, slanting bands, or circles). When the amplitude-time characteristics of components of visual evoked potentials were analyzed, the brain's electrical response to presented stimuli was found to be altered as compared to the initial (predosing) state: perception of physical parameters of the stimuli was distorted.

Key Words: *visual perception; evoked potentials; fluacizine*

The disturbances of visual perception seen to occur in the context of a central anticholinergic syndrome developing under the action of drugs from the atropine group have been most often associated with hallucinations similar to those typical of delirium [1,2]. However, a psychotic state and extreme disturbances of visual perception develop only in cases of intoxication with very large drug doses. With the techniques available today, in particular those for recording evoked bioelectric activity, it is possible to evaluate alterations in visual perception caused even by minimal doses of psychotropic agents.

The purpose of this study was to determine electrophysiological correlates of visual perception disturbance in healthy human beings exposed to a central cholinolytic.

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MATERIALS AND METHODS

The study was conducted on 18 mentally and physically healthy volunteers aged 26-36 years (body weight 61.2-84.5 kg) with a visual acuity of no less than 0.8. To block the central cholinergic structures, we used the tricyclic antidepressant fluacizine, which is a potent central M-cholinolytic [3]. It was administered once in an oral dose of 1 mg/kg.

The bioelectric activity of the brain was recorded with an electroencephalograph (Nihon Kohden, Japan) in unipolar leads Fz, Cz, O_1, and O_2 using the reference electrode in the form of a combined lead placed upon the earlobes. The filters used had a pass band of 0.5-200 Hz; the time constant was 0.3 sec. Data on bioelectric activity were collected and fed into a Plurimat S computer. The central cholinolytic effect of fluacizine was monitored through evaluation from the spontaneous electroencephalogram (EEG) of its 12 segments

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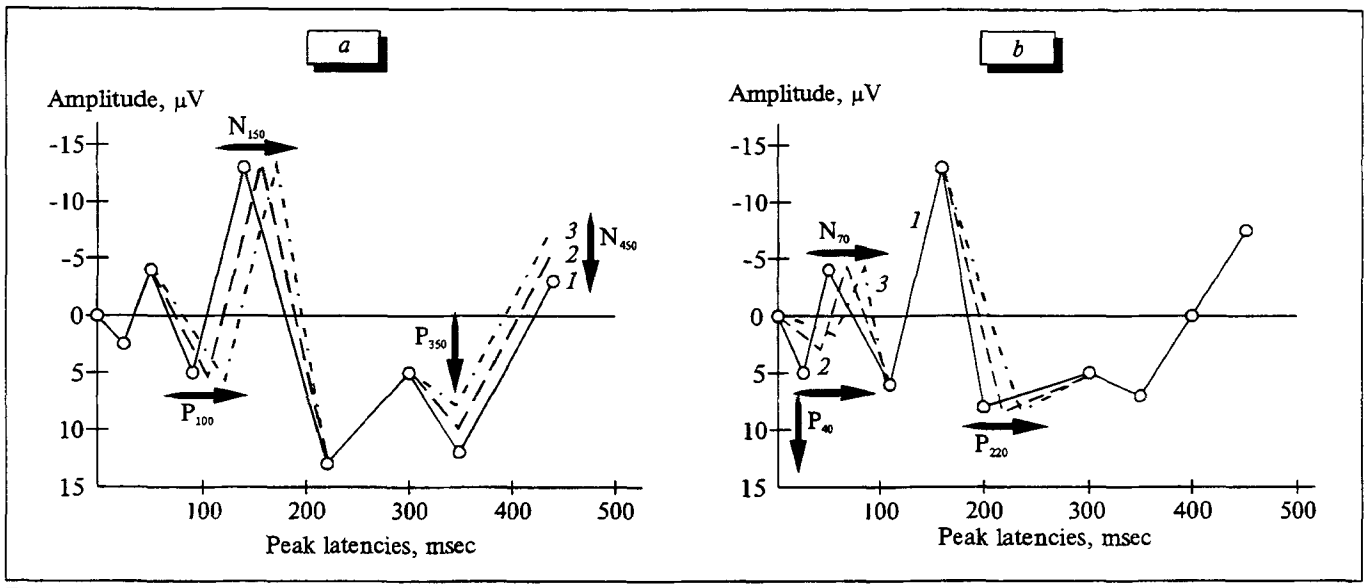

Fig. 1. Schematic representation of the impact of information load during visual stimulation on evoked potential components: *a*) initial state; *b*) state 2 h after fluacizine intake. Significant effects ($F>F_{cr}$) are shown by arrow. *1*, *2*, and *3*: visual evoked potentials upon stimulation with images in the form of a checkboard, slanting bands, and circles, respectively.

of 5 sec by means of fast Fourier transformation; the spectral power and magnitude of the EEG rhythms were expressed in percent [9]. Five frequency ranges - delta, theta, alpha, $beta_1$, and $beta_2$ - were analyzed.

Visual evoked potentials (VEP) were recorded in response to stimulation with black-and-white images of equal brightness (20 cd/m^2) in the form of a checkerboard, slanting bands, or circles presented by a photostimulator (Nihon Kohden); the analysis time was 512 msec and the number of presentations was 20.

With the procedures we used to record and process VEP, the components that are more stable and have higher amplitudes than others include P_{40}, N_{70}, P_{100}, N_{150} P_{220}, P_{300}, P_{350}, and N_{450}. For each of these components the amplitude as deviation of the extremum from the isoline, the peak-to-peak amplitude, and the peak latency were determined from the averaged evoked potential.

The test variables were recorded before fluacizine intake and 2-4 h after it, i.e., during the time when, as indicated by pharmacokinetic data, the activity of fluacizine is at its height [3,7].

In the statistical analysis of the results, Student's *t* test for paired linked samples was used to compare differences from baseline values and Fisher's *F* test for variance analysis to compare differences between parameters of evoked activity.

RESULTS

Two hours after fluacizine intake at 1 mg/kg, the power and magnitude of slow delta and theta waves were considerably increased in all leads, while the alpha waves were decreased in both absolute and relative terms. The most striking changes were registered in the occipital leads, where the contribution of alpha waves had decreased by 20-22% and that of the slow waves had increased by a total of 18-20% ($p<0.05$). These results provide convincing evidence that fluacizine stably blocked cholinergic structures of the brain in the dose used [2,9].

In general, the patterns of change in the VEP parameters in response to the presentation of different structured images were similar, with an increase in the peak latency and a decrease in the amplitude of late components over all brain regions. In order to identify electrophysiologic correlates of visual information processing, we carried out a variance analysis of the amplitude and time characteristics of VEP arising in response to images with differing information loads in the O_1 lead. Image structure was considered to be a factor that varied at three levels and determined the differences between the VEP parameters recorded in the initial state (i.e., before fluacizine intake) and at the height of fluacizine activity.

In the initial state, the information load of the structured images used for visual stimulation (Fig. 1, *a*) had the greatest effect (50% change) on the variance of evoked potential amplitude at 350 msec after stimulus presentation and a smaller effect (25% change) on that at 450 msec. The variance of peak latencies shown by components P_{100} and N_{150} was much less dependent on image structure. The image structure thus determined the signifi-

cance of differences between the initial VEP through differences in the indicated parameters [6].

The analysis of VEP parameters recorded at the height of fluacizine activity (Fig. 1, *b*) showed that the information load of the stimulus no longer determined significant differences between any of the parameters (i.e., the peak latency of P_{100} and N_{150} and the amplitude of P_{350} and N_{450}) as it did in the initial state. Rather, it had the greatest effects on the peak latency variance of P_{40} (33%) and N_{70} (15%), and it also exerted a significant influence ($p<0.05$) on the amplitude of P_{40}. In addition, evoked responses were unequivocally demonstrated for the peak latency of P_{220}.

The method of stimulation with structured images that we chose to use is not a conventional one. In research practice, the dependence of VEP parameters upon the information load factor is usually evaluated using reversed checkerboard patterns [4,8]. The latter technique, however, does not reveal a significant influence of this factor on amplitude/time parameters for exposure to cholinotropic agents given in ethically permissible doses [11]. The use of flashing light, while demonstrating alterations in visual perception [4,10-12], does not permit one to assess how the information flow affects VEP parameters. Stimulation with structured images combines these two conventional methods and thus makes it possible to single out those changes in VEP parameters which are caused solely by the information load [8].

To summarize, fluacizine in a dose of 1 mg/kg distorted the electrical response of the brain to the presentation of images identical in physical parameters but differing in information content.

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