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A Nonferrous Instrumental Joystick Device for Recording Behavioral Responses During Magnetic Resonance Imaging and Spectroscopy

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LUKAS, S. E., M. DOBROSIELSKI, T.-M. CHIU, B. T. WOODS, S. K. TEOH AND J. H. MENDELSON. *A nonferrous instrumental joystick device for recording behavioral responses during magnetic resonance imaging and spectroscopy.* PHARMACOL BIOCHEM BEHAV **46**(4) 781–785, 1993.—A nonferrous joystick device was developed to permit subjects to continuously report ethanol-induced alterations in subjective mood states while undergoing a magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) procedure. The device utilizes air pressure (supplied by a small compressor) that is directed to a series of tubes that terminate in a hand-held unit. The hand-held unit easily fits inside the magnet and resembles a standard computer game joystick except that the ends of the air hoses replace the buttons. The control unit contains three pressure transducers, which are triggered when the tubes are occluded by the subject, activating different pens on an event marker located 6 m from the whole body imager. The unit is safe to use inside a 1.5-Tesla magnetic field and does not disrupt the MRI and MRS recording procedures. Subjective reports of ethanol-induced euphoria and intoxication paralleled the MRS detection of ethanol in the brain. This device could prove to be useful in numerous behavioral studies involving whole-body MRI and MRS.

Behavioral responses Magnetic resonance imaging (MRI) Magnetic resonance spectroscopy (MRS) Ethanol Human subjects

MAGNETIC resonance imaging (MRI) and spectroscopy (MRS) are relatively recent techniques that have expanded our understanding of both the anatomical and biochemical aspects of living tissue. Both techniques operate on the concept of inducing fluxes in protons with a large magnetic field. The resultant spatial resolution of MRI has surpassed that of all other imaging techniques. The potential use of MRS in diagnostic medicine and neuroimaging research is rapidly growing.

One area of research that requires further development is the behavioral correlates of changes in brain chemistry. Although there have been a number of studies measuring the behavioral effects of psychoactive drugs and glucose utilization using Positron Emission Tomography or PET (1–4,9, 10,17–19), similar studies using MR technology have not been conducted. The PET studies were conducted using behavioral rating scales such as the Addiction Research Center Inventory, and since the time domain for acquisition of the signal is long, such procedures are acceptable. Equivalent MRI and MRS studies are more difficult to conduct because the instrumental device must be made of nonferrous material. In addition, with the development of echo-planar MRI, the time domain is markedly shorter, requiring a more rapid assessment of changes in subjective mood states. These restrictions led us to develop a nonferrous instrumental joystick device that could be used by subjects to communicate their levels of ethanol intoxication as the MRS detection of ethanol in their brains was monitored. The results of the MRS studies have been previously reported (15); the details of the development of the joystick device is the focus of the present paper.

METHOD

Subjects

Seven, healthy, adult male volunteers (ages 23–26) provided informed consent to participate in this study. All subjects were normal weight (77.5 ± 3.7 kg), with normal height/weight ratios, and reported consuming alcoholic beverages on an occasional basis (two to six drinks per week). No subject had either a direct or a family history of alcohol or drug abuse and dependence. All subjects had normal physical and psychiatric examinations. Blood hemogram, blood chemistry studies, and urine drug screens were negative at initial evalua-

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tion. Following an overnight fast, subjects reported to the McLean Hospital Brain Imaging Center. On arrival, subjects provided a urine specimen for drug screening and all were negative. A Kowarski-Cormed butterfly catheter was inserted into an antecubital vein for blood sampling and plasma ethanol levels were determined. Plasma concentrations of ethanol were measured in duplicate using a sensitive and well-validated gas chromatographic method described by Gentry et al. (8), who modified a procedure described earlier by Freund (7).

Joystick Device

The entire system consists of five components: a hand-held joystick device, a pressure transducer interface box, an air pressure pump, a control unit, and an event marker. The hand-held unit was modified from a commercially available computer joystick by removing the buttons and replacing them with small-bore Tygon tubing (see Fig. 1). The interface box contains three pressure transducers that are sensitive to small changes in air pressure. The compressor was used to maintain a steady pressure of 9.5 mmHg, which increased when the end of the tubing (in the hand-held unit) was occluded by the subject. The control unit (mounted under the event marker) contains pen solenoid drivers, power supplies, and activity indicator light-emitting diodes. The increased pressure produced by closing the end of the tube activates the transducer's contacts, completing the circuit to a pen on an event marker located 6 m from the whole-body imager.

Subjective Mood State Reports

Subjects held the device in their right hand and were asked to cover one or more of the three pressure switches or transducers when they experienced the following: initial detection of an ethanol-induced change in feeling state; very good feelings or euphoria; very bad feelings or dysphoria. Subjects were told to cover the tubing hole for as long as they experienced the particular change in mood state. Responses from all three switches were registered on the cumulative recorder, which was run at a speed of 1 cm/min.

Ethanol Solution

Beverage grade ethyl alcohol (vodka) was mixed with orange juice and placed in a modified thermos bottle (16). Subjects consumed the 0.7-g/kg dose (350 ml total volume) through a special straw over a 15-min interval. The straw had a 10-ml reservoir in which a 70% vodka/orange juice solution was added to both active and placebo drinks to provide a strong initial taste in an attempt to mask the identity of the drink.

^1H Spectroscopy Procedure

Magnetic resonance imaging (MRI) and spectroscopy (MRS) procedures were carried out with a G. E. Signa 1.5-Tesla (General Electric, Milwaukee, WI) whole-body imager. Subjects were laid supine on the MRI table and a reference position (the intersection of the axial and sagittal light beams) was located at the glabella. The chosen voxel of interest (VOI) was localized based on a series of T1 weighted (TE = 30 ms, TR = 600 ms) coronal and sagittal images. VOI utilized in all studies included the medial frontal and cingulate gyri, the ventricles, the medial portion of the basal ganglia, the centrum semiovale at the level of the anterior commissure, and the splenium of the corpus callosum. Voxel localization was achieved with the STEAM pulse sequence (5,6), and the magnetic field homogeneity was optimized by shimming on the water signal. Using this sequence, a water line width of 4–8 Hz was achieved over a voxel size of 4 × 4 × 4 cm in less

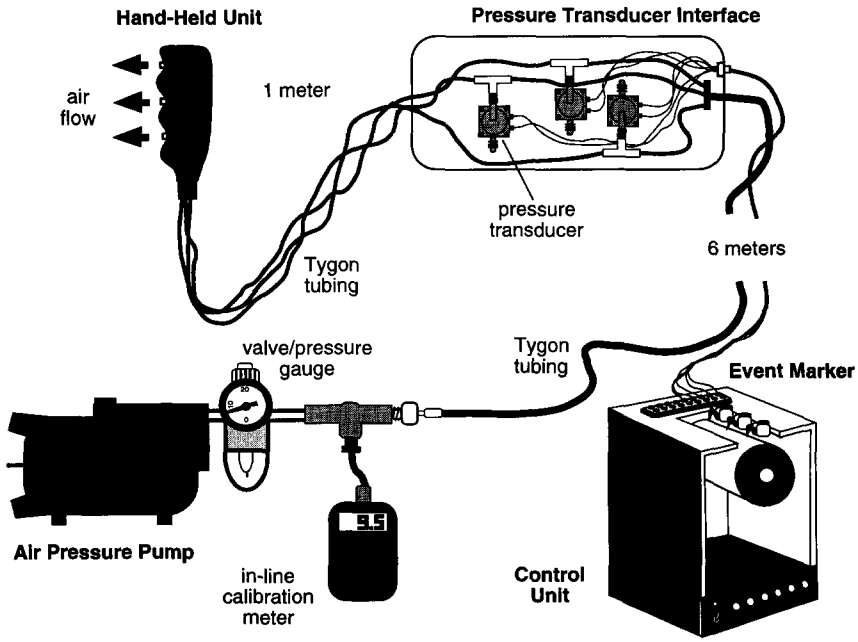

FIG. 1. Details of the instrumental joystick device. The hand-held unit is kept at the subject's side while the transducer interface is anchored to the table. The air compressor and event recorder are located 6 m from the whole-body imager.

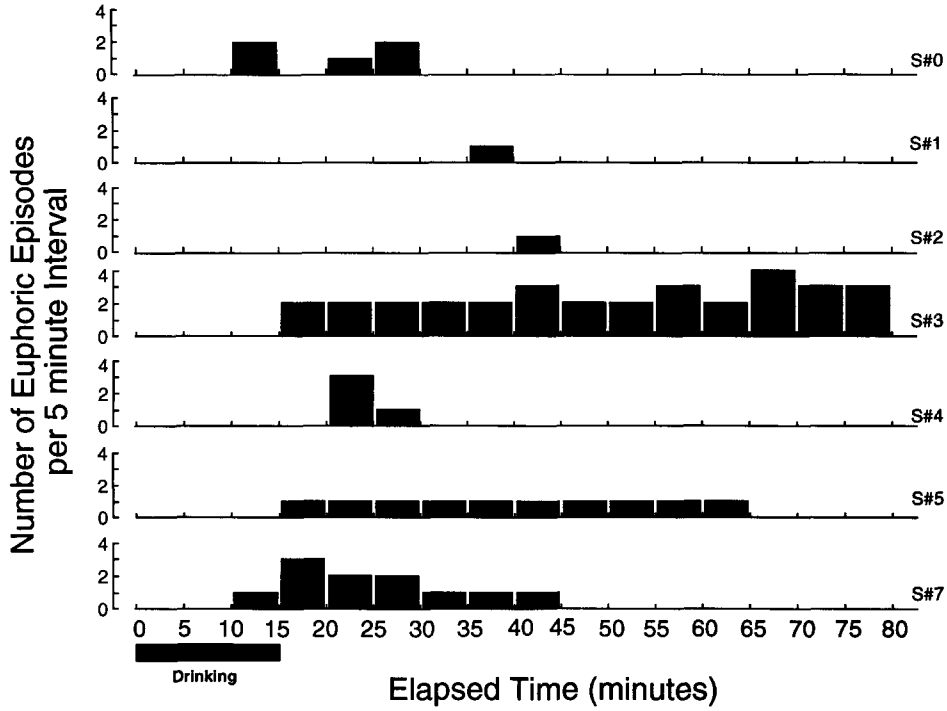

FIG. 2. Individual profiles of joystick responding after 0.7 g/kg ethanol in all seven subjects while they laid in the whole-body imager.

than 10 min. Water suppression was achieved with a presat pulse and an additional sat pulse between the second and third slice selective RF pulses of the STEAM sequence.

After a control spectrum was obtained for the chosen VOI, the subject sat up and drank the ethanol solution. After completing the drink, the subject was repositioned inside the imager, using the reference markings at the glabella, and the VOI was reshimmed. A total of 128 scans were collected at an echo time (TE) of 270 ms, mixing time (TM) of 90 ms, and a repetition time (TR) of 1500 ms. The free induction decays (FID) were initially processed on the 1280 spectroscopy data station (General Electric) with exponential line broadening (1 Hz), zero-filled to 2 K points and Fourier transformed. Subsequently, analyses were conducted on a SUN Sparc-2 workstation with the GE SA/GE Spectroscopy software package. Brain ethanol concentration (mM) was determined by measur-

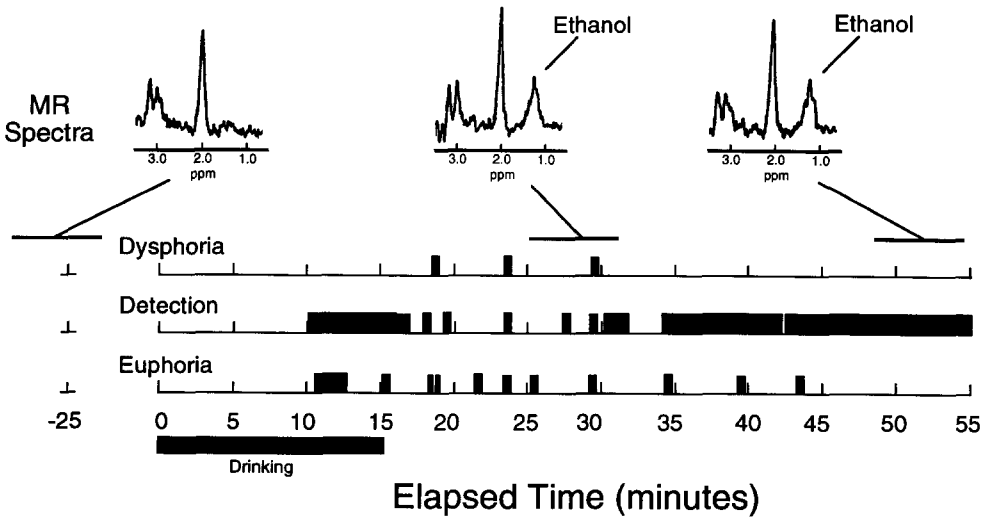

FIG. 3. Microanalysis of joystick responding (dysphoria, euphoria, and detection) by one subject (#7) and corresponding MR spectra at various times before and after 0.7 g/kg ethanol administration.

ing the areas under the *N*-acetyl aspartate (N-AA) and ethanol peaks, and then multiplying the ratio ethanol area/N-AA area by 7 (the reported brain N-AA concentration in mM).

RESULTS

The behavioral profile of joystick responding for each subject after ethanol is shown in Fig. 2. Although there is variability in the number and duration of ethanol-induced euphoric episodes, all subjects reported ethanol effects within 5 to 10 min after drinking ceased. The highest density of euphoric events occurred in the 15- to 30-min period after drinking. Figure 3 shows the actual spectra obtained in one subject during joystick responding over the 80-min experiment. The appearance of the ethanol peak at about 1.2 ppm is clearly evident at the 15-min time point when the subject had clearly detected ethanol effects and was reporting episodes of euphoria. Brain ethanol levels began to decline toward the end of the study. This subject also reported a number of brief dysphoric events during the ascending portion of the brain ethanol curve. Plasma ethanol levels paralleled the detection of ethanol in the brain; details of these findings have been previously reported (15).

DISCUSSION

These data demonstrate that continuous measures of changes in behavioral mood states can be obtained from subjects while they are in a magnetic resonance whole-body imager using a nonferrous instrumental joystick device. The device was easy to use and did not interfere with any other aspect of the study. The instructional set of only three options (detection, euphoria or good feelings, and dysphoria or bad feelings) was purposely kept simple to ensure that reliable data would be obtained from the subjects while they were inside the imager. Furthermore, the simplicity of the instructions was necessary because subjects were required to respond continuously before, during, and after consuming ethyl alcohol. Since subjects frequently became intoxicated, it is essential that they have a minimum of responses from which to choose, especially since they did not receive any prompts to respond.

The paroxysmal nature of euphoric events after ethanol has been noted previously using a different style joystick device (12,13). Further, the simultaneous appearance of both euphoria and dysphoria reports during the ascending phase of the brain and blood ethanol curve illustrates the often contradictory and complex subjective effects of ethanol intoxication (14). Rapid and transient changes in mood states occur during the ascending phase of the brain ethanol curve and suggests that the present device may be useful in correlating such measures with ethanol-induced changes in other neurophysiologic and neuroendocrine measures (11). The simultaneous measurement of behavioral, neurophysiologic, and neuroendocrine function should permit a more precise understanding of how ethanol affects brain function and behavior. This multidisciplinary approach may not only provide new insights into mechanisms underlying ethanol-induced tolerance and dependence, but could be adapted to study behavior/brain chemistry relationships in a number of other disciplines as well.

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