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BRIEF COMMUNICATION

A Solid State Device for Measuring Sensitivity to Thermal Pain

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WALKER, J. M. AND W. C. DIXON. *A solid state device for measuring sensitivity to thermal pain.* PHYSIOL BEHAV 30(3) 481–483, 1983.—A simple and inexpensive circuit for use in conducting the tail-flick test is described. The use of digital integrated circuits coupled to a thyristor phase control circuit holds the number of parts needed to minimum. Methods for the use of the device and statistical analysis of the data are also discussed.

Analgesia Tail-flick Pain Opiate

D'AMOUR and Smith [7] introduced a radiant heat method for determining the efficacy of analgesics in small animals. In this test the latency of the animal to withdraw its tail from the heat source is used as an index of pain sensitivity. Various authors have characterized the tail-flick test and compared it to other tests of analgesia [2, 8, 9, 10, 14]. In general higher doses of narcotics are required to produce effects on the tail-flick response than for other measures of pain sensitivity. For example, 6–8 mg/kg of morphine are required to produce significant elevations of tail-flick latency, whereas only 1 mg/kg is required for the phenylquinone writhing test [8]. Thus, a drug or treatment having an effect on this measure is usually considered quite significant. Still, it has been argued that multiple tests of pain sensitivity should be employed before assuming that a particular drug has analgesic properties [12]. The tail-flick test has been used to gauge the potency of a variety of narcotic and non-narcotic agents [9, 13, 15–20]. Hyperalgesia has also been observed [3] as well as analgesic effects from focal electrical brain stimulation [12] and various environmental or physiological [1] manipulations.

Here we describe methods for the design and use of automated tail-flick apparatus suitable for use with rats or mice. The use of current solid state circuitry makes such a device practical and inexpensive.

METHOD

Tail-Flick Apparatus

Figure 1 illustrates the equipment arranged for a typical analgesia test. A simple restraint device is used to position the animal for testing. It should keep the rat in a comfortable position for the experiment while allowing free movement of its tail.

The tail-flick instrument is constructed in two major subassemblies. The smaller unit, the lamp box, interfaces with the animal. The lower portion of this unit is an aluminum box which contains a high wattage quartz projector lamp. The upper surface of the box is covered with felt and has a small (3 mm) hole drilled above the lamp. The combination of aluminum and felt produces a cool non-slip platform for the rat's tail while the small hole provides an abrupt, high temperature source for stimulating the tail. An attached fan runs continuously to prolong the lifetime of the lamp and a small photocell is mounted on an adjustable arm, 13–25 cm above and in line with the source. When the rat's tail is properly positioned on the platform, it occludes the source. When the tail moves, it reveals the source of the photocell providing an indicator of the animals response.

The lamp box is connected by flexible cables to the larger subassembly, the control unit. This unit allows the experimenter to prepare, initiate, and terminate individual trials. It also presents a visual display of the duration of the trials and is capable of being interfaced to a computer for automatic logging of experimental results. Circuitry for the control unit is shown to the right of J1 and J2 in Fig. 2. When the START switch is actuated, flip-flop U2A is preset. Its inverted output causes relay K1 to energize. Depending on the position of the SELECT switch, a predetermined current is delivered via one of the 250K potentiometers to the firing network of thyristor Q1. Firing of the thyristor is phase controlled resulting in the delivery of a full power to the lamp for a preset portion of each power cycle. The voltmeter across the lamp provides a relative measure of the resultant lamp intensity.

At the same time that the lamp circuit is energized, flip-flop U2A also fires one-shot U3. This condition, or an initial application of power to the control unit, causes gates U1B and U1C to reset the timing components, U4, U2B, U5, U6 and U7. U4 is a 10 Hz clock and when the D input of U2B is high, constant duration pulses appear on the CLOCK line to the display.

The display, consisting of U5, U6, and U7, counts in 0.1

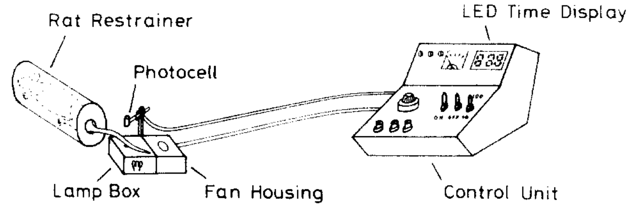

FIG. 1. Arrangement typically used for tail-flick testing of rats. The rat is restrained in an opaque cylinder and is tested using the lamp box which is positioned under the tail. The logic and power control circuits are assembled in the control unit to separate them from the heat generated by the quartz lamp.

second increments until it is halted by one of three mechanisms. Normally the animal's tail will rest on the felt surface of the lamp box and will cover the source hole. When a trial is conducted heat builds up, and the rat will "flick" its tail which uncovers the source. Photocell PC1 then conducts and clears U2A. Alternatively, if the experimenter desires to terminate the trial, he may actuate the STOP switch. If neither of these events occurs, the trial will automatically terminate at either 10 seconds or 100 seconds depending on the position of the TIME switch. Each of these three mechanisms extinguishes the lamp and freezes the elapsed time on the display.

With the unit constructed as shown, relative lamp voltages between 30 and 115 are reliably attainable by adjusting the 250K potentiometers. At around 90 V, most rats will move their tails within four seconds while for analgesic rats the 10 sec limit prevents tissue damage. The wide voltage range and extended time range make testing animals with differing sensitivities feasible.

Some sensitivity to line voltage fluctuation exists in this or any other simple phase control circuit, so periodic note should be made of the relative lamp voltage to insure that the intensity is not varying. Significant line voltage variations can be stabilized by commercially available line voltage regulators. We find that line variations are transferred volt per volt to the output of this device. Such variations thus produce their greatest changes to the unit's output when low voltages are being used. In such a case the use of a lower wattage bulb has been successful here for testing mice. Also, thyristor circuits often produce electromagnetic radiation which can interfere with other sensitive equipment. Line filtering or equipment shielding may be needed if vulnerable equipment is operated nearby. However, in our laboratory we have operated both radios and computers within a few meters of this unit and have experienced no difficulty.

Direct ouput to a computer may be realized by tying the BCD outputs of the TIL 306's to a twelve bit parallel port on the computer. Additionally, a signal can be derived from flip-flop U2A identify data ready.

Testing with mice has been accomplished by replacing the 600 W DVY lamp with a lower wattage unit (300 W) which was fitted to a separate cover for easy changeover. (Both lamps should be available at camera stores). The main benefit of this approach has been to allow for operation at higher voltages where turn-on and line-fluctuations are minimized. Operated in this fashion, bulbs are apt to last for long periods (several years) even when the unit is in daily use.

Tail-Flick Testing

Figure 2 illustrates the arrangement normally used for conducting the tail-flick test. The rat is restrained in plastic

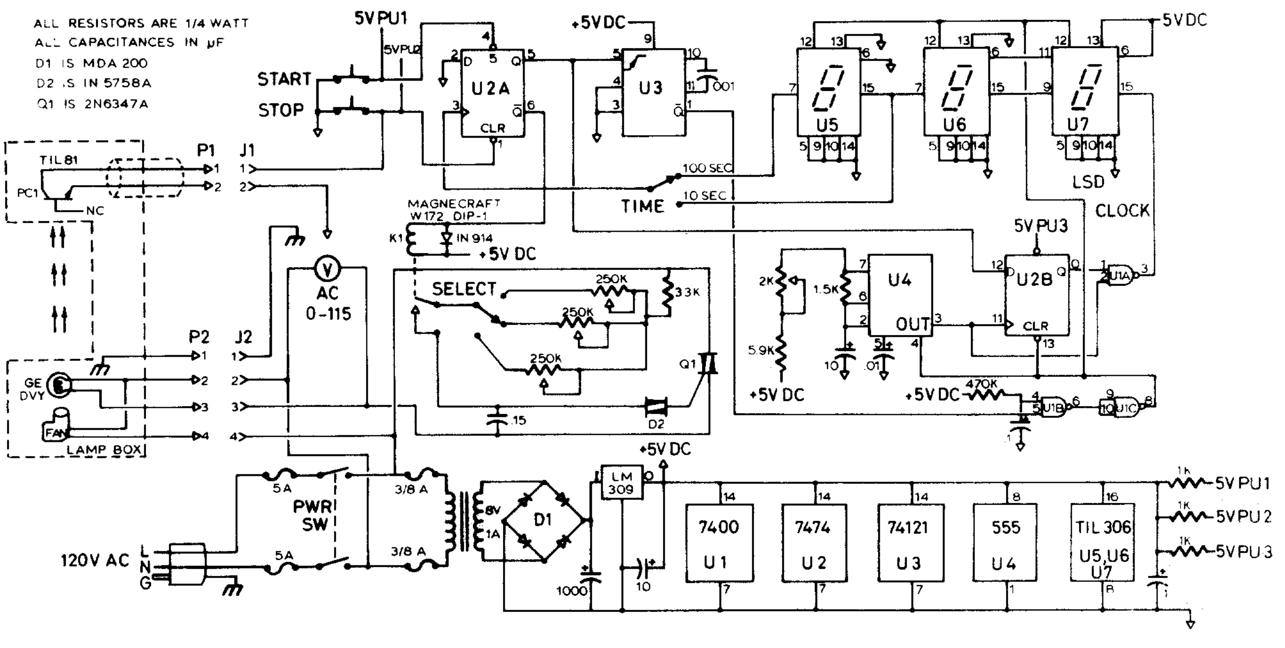

FIG. 2. Schematic diagram for control unit as shown in Fig. 1. The relay isolates power control circuitry from the TTL logic. Layout of the circuit is flexible but should maintain the electrical isolation of these two aspects of the circuit.

tubes approximately 16×6 cm dia. We find that while opaque restrainers reduce behavioral observations, they are far less stressful to the animals than the commonly available clear plexiglass ones. A baseline response rate of 2.5 to 4.5 seconds is achieved by adjusting the lamp intensity and subsequently a number of tail-flick measures are gathered before any treatment is administered. Since the initial design (which has been improved upon several times) many compounds have been tested on a group of functionally identical devices. These include morphine [15], [Met]enkephalin, several enkephalin analogs [6,16], α-, γ-, β-endorphin and substituted analogs [17], dynorphin [18,19], vasopressin and vasopressin analogs [4,5]. ACTH, α-MSH and related substances [15,20], and a variety of cholinergic compounds [13].

The tail-flick measures after the treatment are often adjusted according to the average baseline response. Percent scores have been used [11], although special transformations (arc-sine transform) should be applied to such data because this method puts limits on the natural variation in the data. Others have used mathematical approximations to the integral of the post-treatment time function to obtain an overall measure of the experimental effects which take into account both the duration and the magnitude of the analgesic response [15]. Simpson's approximation of the integral for discrete data has been used in several laboratories [4, 6, 15], and is especially useful for estimating the efficacy of a new agent. This approach does not constrict the variance, but the means and variances are sometimes proportional. This condition can be ameliorated by analysis of the log of the Simpson's integrals. Magnitude and duration of the drug response has also been obtained from tail-flick data [16]. In any case, if the ceiling latency is achieved frequently in an experiment either some attempt should be made to recover homogeneity of variance or non-parametric statistics should be applied.

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