(disappearance quantum yield of 0.04). DDE was not detected as an irradiation product of DDT in hexane, possibly because it reacts as rapidly as it is formed (disappearance quantum yield of 0.26).

These initial products, DDD and DDE, absorb ultraviolet light and react to form a number of secondary products which were identified only by retention times on the gas-liquid chromatograph (Table 1). To determine the photolytic products resulting from DDE and DDD, each compound was irradiated separately in *n*-hexane solution and the reaction mixture was analyzed by gas-liquid chromatography. Irradiation of DDD produced only one major peak at R_F of 2.76 minutes. Products from DDE irradiations had R_F values of 2.29, 2.60, and 3.30 minutes. Irradiation of DDT yielded a mixture with the major products having R_F values of 1.49, 2.29, 2.60, 2.76, and 4.40 minutes (DDD). It is possible, therefore, that the DDT products with R_F values of 2.29 and 2.60 resulted from initial DDE formation, and the product with R_F value of 2.76 originated from DDD photolysis.

To determine the effect of HCl on the reaction process, sufficient *n*-butylamine was added to the DDT solution to neutralize the HCl produced. In the presence of *n*-butylamine, no change in the rate of either DDT disappearance or DDD formation was observed. These observations indicated that the progress of the reaction was not dependent upon HCl production.

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1. Abbreviations are: DDT, 1,1,1-trichloro-2, 2-bis (*p*-chlorophenyl) ethane; DDE, 1,1-dichloro-2, 2-bis (*p*-chlorophenyl) ethylene; DDD, 1,1-dichloro-2, 2-bis (*p*-chlorophenyl) ethane; DDC=O, 4,4′-dichlorobenzophenone; BA, *p*-chlorobenzoic acid; DDA, bis (*p*-chlorophenyl) ethanoic acid; tetrakis, 2,3-dichloro-1,1,4,4-tetrakis (*p*-chlorophenyl) butene.
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Relation of Pharmacological and Behavioral Effects of a Hallucinogenic Amphetamine to Distribution in Cat Brain

Abstract. *The hallucinogen 2,5-dimethoxy-4-methylamphetamine, also known as STP, accumulates in specific areas of cat brains. The unchanged compound was detected in the brain for at least 6 hours, whereas its behavioral effects lasted for about 4 hours. The coincidental pharmacological and behavioral effects of the compound apparently indicate a relation between the anatomical distribution and action.*

The hallucinogenic agent 2,5-dimethoxy-4-methylamphetamine, also called either DOM or STP, has, in humans, psychedelic effects which are about 60 to 100 times more potent than those of mescaline, but it is 30 to 50 times less active than lysergic acid diethylamide (LSD) (*1*). In rabbits this drug provokes an abnormal electroencephalogram by a mechanism different from that provoked by *d*-amphetamine (*2*).

We have studied the tissue distribution and elimination of STP-H^3 in mice, rats, rabbits, and cats (*3*) and have synthesized the analogs of STP to test the chemical structure on animal behavior (*3*). We also report on the correlation of the behavioral and pharmacological effects of STP to its sites of accumulation in the cat brain.

By a trituim-hydrogen exchange reaction (*4*), STP was synthesized and labeled with tritium in positions 3 and 6. Labile tritium atoms were removed until a constant specific activity of 360 μc/mg was achieved. The chemical and radiochemical purity of the compound was ascertained by thin-layer chromatography (silica gel G) and by its infrared spectrum. The chromatograms were developed in chloroform and methanol (1 : 1); butanol, acetic acid, and water (4 : 1 : 1); and isopropanol, butanol, acetic acid, and water (10 : 1 : 1 : 1). Autoradiograms and ultraviolet fluorescence were used to detect STP-H^3 on the plates.

Six cats (one female) (1.8 to 3.0 kg) were anesthetized with ether, and STP-H^3 (10 mg/kg; 3.6 mc/kg) was

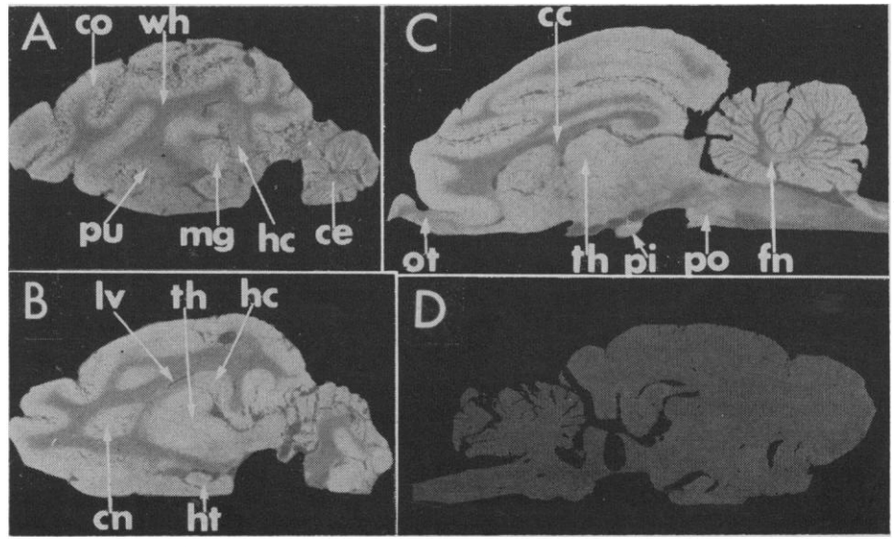

Fig. 1. Distribution of the radioactivity (light areas) in cat brains 15 minutes (A–C) and 6 hours (D) after injection of STP-H^3 intravenously. Abbrevations: *cc*, corpus callosum; *ce*, cerebellum; *cn*, caudate nucleus; *co*, cortex; *fn*, fastigial nucleus; *hc*, hippocampus; *ht*, hypothalamus; *lv*, lateral ventricle; *mg*, medial geniculate nucleus; *ot*, olfactory tract; *pi*, pituitary; *po*, pons; *th*, thalamus; and *wh*, white matter.

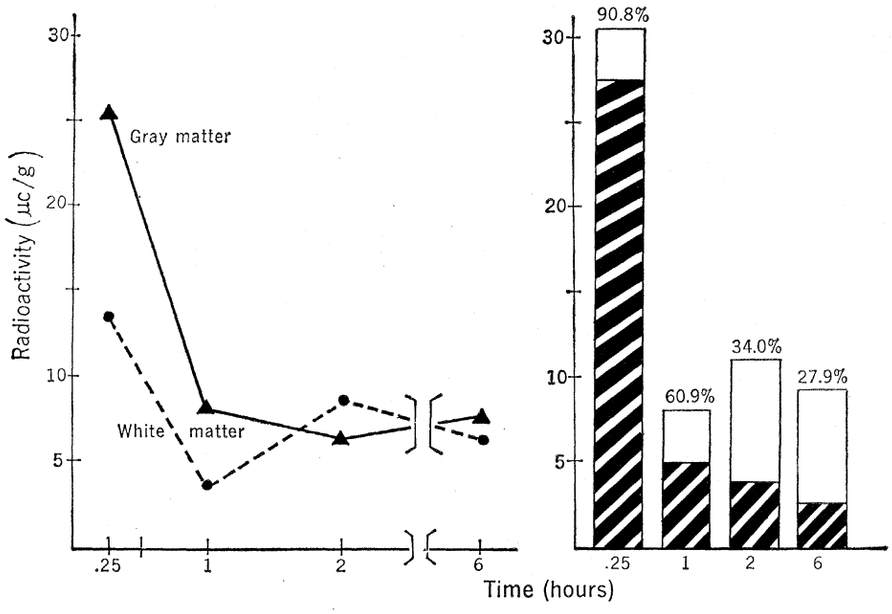

Fig. 2. (Left) Accumulation of radioactivity in gray and white matter. (Right) Amount of unchanged STP-H^3 in the cat brain; (hatched areas) STP-H^3; (plain areas) metabolites.

infused into the femoral vein as the cats were beginning to awaken so that anesthesia would not mask behavioral effects. The animals were killed by bleeding, either 15 minutes or 1, 2, or 6 hours after administration of the drug. The brains were dissected and frozen immediately in hexane cooled to about -70°C with solid carbon dioxide. Sagittal sections of whole brain (30 to 60 μ) were cut at -10°C with a Jung model "K" microtome. The autoradiography of the brain sections and the evaluation of the results were performed as described (*5*). Samples of the brain were homogenized with methanol (200 mg of tissue per milliliter of homogenate), and unchanged STP-H^3 was identified by thin-layer chromatography with the above solvents. The radioactivity was assayed by liquid scintillation. The amount of labile tritium in tissue homogenates was 0.3 to 0.5 percent. The identity of the isolated compound with authenic STP was ascertained by the isotope dilution method and by the mixed melting point test.

During the injection of the drug there was an immediate recovery from the remaining light anesthesia, but a catatonic-like state was produced when more compound was introduced. The pupil constriction was at maximum, and transient difficulties in respiration occurred in some animals. During the catatonic stage, the legs were held tightly against the body and the eyes were open. Tremor was noted and the animals were unable to walk. Approximately 10 minutes after injection, the cats began to attempt movements about the cage. Intermittently, they had a fixed stare not directed to particular objects, and they continually made pawing motions in the direction of their stare. Animals did not respond to visual stimulation, but became very angry and aggressive if touched or subjected to a loud noise. They growled, hissed, and threw themselves against the cage, biting and clawing. These behavioral effects were evident for 4 hours after injection.

To correlate the onset of effects with the distribution of STP-H^3, two cats were killed at 15 minutes. In the most lateral sagittal sections through the brain (Fig. 1A), there were accumulations of STP-H^3 in the hippocampus and the amygdaloid nucleus. Also, the medial and lateral geniculate bodies and the putamen showed high radioactivity. In the sections closer to the midline (Fig. 1, B and C) accumulations in the thalamic nuclei, caudate nucleus, and hypothalamus were detected. The drug appeared to be concentrated in the cerebellum, fastigial nucleus, and in the olfactory nuclear area in the frontal region of the brain. The cortex showed higher radioactivity than the white matter, but there were so specific accumulation sites in the cortex.

Some of these STP-accumulation areas in the brain are interesting in relation to their function in brain physiology and behavior. The hypothalamus and amygdala influence emotional behavior (*6*). Stimulation or destruction of certain areas of the hypothalamus can produce violent rage with growling and hissing in cats (*7*). The hypothalamus also functions in sleep and waking. The hippocampus supposedly modifies the information from the eye, ear, and skin and is regarded as an association area in the brain (*6*). Further, the neural pathways controlling muscle tone pass through the nucleus fastigi.

The permeability of the blood brain barrier, the blood flow, and the vascularity affect the accumulation of drugs in brain (*8, 9*). Furthermore, the site of accumulation of a drug does not necessarily correspond to its site of action. However, we found high concentration of STP in these areas which could account for the emotional behavioral disturbances; there was also accumulation in visual pathways which could be related to the production of hallucinations which have been reported to occur in man.

Instead of dilatation of the pupils, maximum constriction was noted. When STP was applied locally in the rabbit eye, pupil constriction and relaxation of the nictitating membrane was observed (*3*). It seems possible, therefore, that STP has an adrenergic beta-receptor antagonizing effect. Consequently, the remaining parasympathetic effect on the pupil causes constriction.

The white matter had lower concentrations of STP than the gray matter up to 2 hours after administration (Fig. 2, left). The delay in establishment of an equilibrium concentration could be caused by necessity for penetration of multiple membranes of the laminated myelin sheath (*9*). From our studies, the unchanged STP-H^3 in the brain was 91 percent at 15 minutes and 61 percent at 1 hour (Fig. 2, right). The difference in the amount of STP between 2 and 6 hours is small. The equilibrium in the concentration of STP in gray and white matter was achieved at the time when the behavioral and pharmacological effects of this compound had subsided at about 4 hours. Thus, a change in the distribution of STP in the brain (Fig. 1, A–D) rather than the decrease in total brain concentration of STP due to the conversion into its metabolites (Fig. 2, right), may have caused the disappearance of its effects.

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Objective Measure of the Dynamics of a Visual Movement Illusion

Abstract. *Apparent movement in peripheral vision can be induced by sequential flashing of two dots that are spatially unresolved. Subjects used this illusion to make forced-choice estimates of the directional sequence of the two dots. Performance at this task defines spatiotemporal conditions that induce the illusion without reliance upon subjective distinctions of "movement" from "successivity" and "simultaneity." The dynamics of the illusion, defined in this way, are measured and compared with those for after-flash inhibition and the perception of real movement.*

Two small brief sequential flashes of light in the human peripheral field of vision, separated spatially by a fraction of a degree and temporally by about 50 msec, induce a strong illusion of movement of a "single dot," in the direction of the sequence (*1*). We find that the illusion remains strong, and is still a reliable index of sequential order, even though the dots are so closely spaced (for example, 6 minutes of arc, if presented 22° peripheral to the fovea) that they appear as one dot when flashed simultaneously. This situation, illustrated in the inset of Fig. 1, permits an objective study of the spatiotemporal conditions that induce the illusion; subjects used the direction of the movement illusion to estimate (forced choice) the sequential order of the two unresolved dots. At sufficiently short intervals, subjects reported a single flash with no clear directional properties. At sufficiently long intervals, the illusion also fails and two flashes, spatially superposed, are reported. In both extremes, performance in estimating sequential order falls to chance levels. At intermediate intervals one obtains "band-pass" performance curves, which may define characteristic dynamics of the mechanism underlying the illusion. In contrast with this experiment the usual methods (*2*) of investigating conditions adequate for apparent movement rely upon subjective reports of "simultaneity," "good movement," and "successivity" by highly trained subjects viewing sequential flashes of two spatially distinct lights.

As illustrated in Fig. 1, a digital computer (Digital Equipment Corp. PDP-8) randomized (*3*) a list of 24 different two-flash stimuli with respect to right-left order and time interval between flashes. In response to the subject's pushing a button signifying "ready," the computer counted out a 1-second wait, rang its typewriter bell (ready-fixate signal), and after another 1-second wait presented the appropriate pair of flashes 22° peripheral to the fixation point. Subjects, viewing the stimulus monocularly and with heads in a chin rest, responded by pushing one of two buttons signifying "toward the right" or "toward the left." After presenting all 24 trials of one subset, the computer rerandomized the list and awaited the next "ready" command. After a suitable number of trials, the computer printed a summary of performance versus time interval. Data from several such experiments are shown in Fig. 2. Naive subjects produced similar curves, after a few minutes of practice with "easy" (50-msec) time intervals, in sessions of about 240 responses to the computer. Inclusion of "blank" (nearly simultaneous) presentations yielded no significant directional bias at the dot luminances used in the experiment of Fig. 2. Performance as in Fig. 2 is relatively insensitive to luminance level of the dots and the surround, and to the position or orienta-

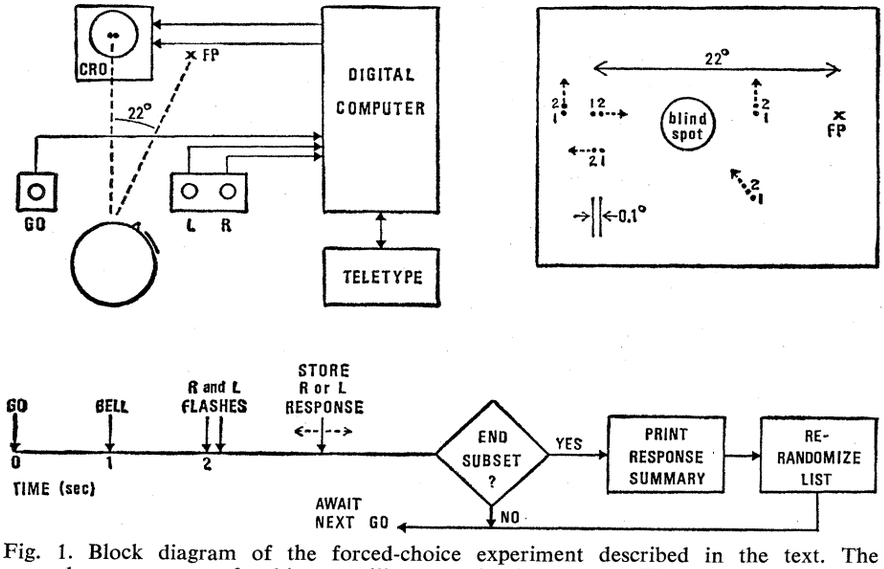

Fig. 1. Block diagram of the forced-choice experiment described in the text. The general arrangement of subject, oscilloscope, fixation point (*FP*), and computer are shown at the upper left. At the bottom of the figure, the sequence of events associated with one stimulus presentation is summarized. Inset: the visual field of the left eye, schematizing the subjective "fine-grain" movement illusions generated by the flashing of two dots separated by 0.1° in various retinal positions, spatial orientations, and sequential orders (first dot labeled "1"; second dot labeled "2," flashed 50 msec later). The dashed arrows suggest the illusory movement as described by most observers.