A NEW HALLUCINOGEN: 3,4,5-TRIMETHOXYPHENYL-β-AMINOPROPANE

WITH NOTES ON THE STROBOSCOPIC PHENOMENON*

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3,4,5-Trimethoxyphenyl-β-aminopropane (TMA) is structurally related to both amphetamine and mescaline, as is shown in Figure 1.

Because of this structural relationship of TMA and amphetamine, methedrine, and mescaline, one could anticipate a clinical response to the compound which would represent certain phenomena characteristic of each of these drugs. This presented an intriguing problem as to whether or not, in actuality, this would be the case.

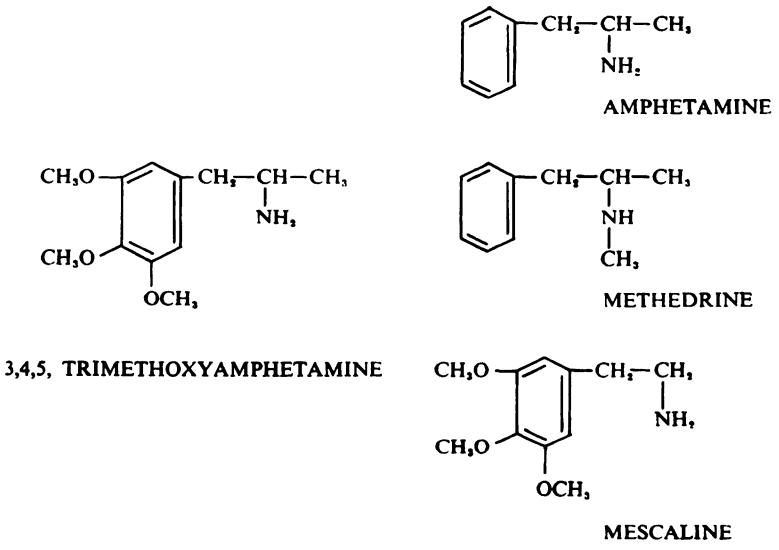

FIG. 1.—Structural similarities of TMA, amphetamine, methedrine and mescaline.

Amphetamine is a central nervous system stimulant which raises the blood pressure, causes sleeplessness, and is said to place the majority of subjects in a more communicative frame of mind (Grahn, 1950). It is not reputed to produce

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a "model psychosis" in a single dose. Methedrine has been reported to produce hallucinations in a single dose of 100 milligrams (Fischer, 1954) and in a single dose of 60 milligrams in schizophrenic subjects (Liddell and Weil-Malherbe, 1953). It also increases the ease by which a person can communicate his emotional problems. It has been used as an adjunct to psychotherapy, but it has the disadvantage that it produces tachycardia and hypertension. Methedrine is contraindicated in hypertension, heart disease, and thyrotoxicosis.

Mescaline is a central nervous system depressant, and causes visual hallucinations when administered in adequate doses. The hallucinations represent, to some extent, a bringing to the foreground of past experiences which had highly impressed the person (Stockings, 1940). The question is now brought to mind: Would a structure which combined all the structural aspects of amphetamine and mescaline manifest itself clinically by increasing the ease of communication of emotional problems, while at the same time producing hallucinations similar to those produced by mescaline? It is true that mescaline does in some cases increase communication, but this effect is not constant. Furthermore mescaline has been known for over fifty years and has not been used as an adjunct to psychotherapy to any extent. Possibly the reason for this has been that investigators seem always to have used large doses (200–400 mgm.). The effects of smaller doses of mescaline are not fully known.

There are so few hallucinogens known that we must study intensively the types of subgroups and molecules which cause hallucinations if we are to come to any understanding of the phenomenon itself.

3,4,5-Trimethoxyphenyl-β-aminopropane (Trimethoxyamphetamine, TMA) was first synthesized by Hey in 1947 (Hey, 1947) who was impressed with its euphoric properties (private communication). The Imperial Chemical (Pharmaceuticals) Limited, of Manchester, very kindly prepared a supply of this compound for us.

We tested the toxicity of TMA by administering it intraperitoneally on mice. Our doses ascended from 5–80 mgm./kgm. body weight in geometric progression. Five mice were studied at each dosage level. There were no deaths within 48 hours in any group. The only signs of toxicity were tremors over the body, and an intermittent scratching of the ears with the hind paws, at a very rapid rate, starting with the 20 mgm./kgm. group. Both these signs were maintained for seven hours, after which time they passed off with no apparent ill effect. These mild toxic signs started with a proportionate dose 15 times that needed to produce hallucinations in humans.

After the toxicity had been established in mice a series of experiments was run on dogs. These were planned to show effects on blood pressure, pulse rate, respiration, and the response to various anticipated antidotes. In four Nembutal-anaesthetized dogs, which had a manometer cannulated into the carotid artery for blood pressure readings, we found that so long as the TMA was administered intravenously at a rate less than 6 mgm./minute there was no change in blood pressure or respiration, even after 420 milligrams had been administered (equivalent to 36 mgm./kgm. body weight in one dog). If the drug was given intravenously at a rate in excess of 10 mgm./minute there was a sudden drop in blood pressure of approximately 40 mm. Hg (Fig. 2). If the drip was continued this drop in blood pressure was found to be self-limiting, starting to rise again, but at a very slow rate. If the intravenous drip was stopped, as indicated in Figure 2, there was a rapid rise in blood pressure to its normal base line. It was found, as would be expected, that with this drop in blood pressure there was a corresponding increase in heart rate. If the drip was not stopped after the fall

in pressure the administration of adrenaline, amphetamine, or neosynephrine would instantly raise the blood pressure above its normal base line (Fig. 3).

In most of these dogs there was no mydriasis noted but this could be explained on the basis of the Nembutal used.

Amphetamine in doses smaller than the dose of TMA used caused a rapid

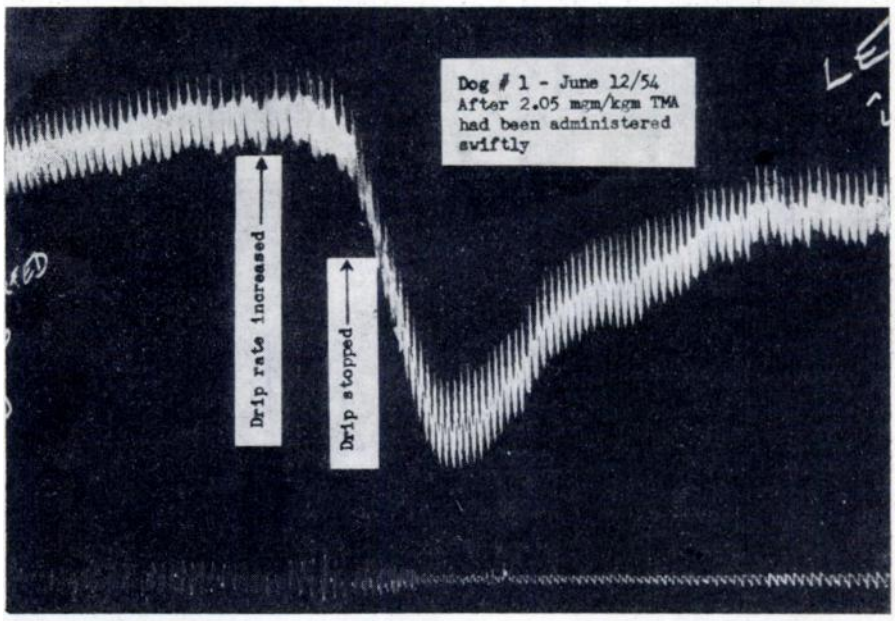

FIG. 2.—The effects on blood pressure and respiration in a dog after administration of TMA at a rate in excess of 10 mgm./minute intravenously.

rise in blood pressure when given intravenously (Fig. 3). This is interesting since it would be either one or more of the three methoxy groups which is responsible for this reverse action from amphetamine. The effects of mescaline on blood pressure are not well known. However Stockings (1940) reports a slight rise in blood pressure with large doses of mescaline by mouth. Chaumerliac and Roche (1949) report a marked vasodilatation of the cutaneous and retinal vessels with unspecified amounts of mescaline given to prisoners at Dachau in 1944.

We then administered TMA intravenously to unanaesthetized dogs. If the drug is administered in a fairly concentrated solution (20 mgm./ml.) we found that after 1·2 ml. had been given (24 mgm.) the dog would react with a non-productive heaving of the abdomen for a few moments and then present an acute "catatonic" reaction which lasted for the next 2 or 3 hours. During this phase the animals had all four limbs on the ground, their heads cocked at a slight angle, and a marked droop to the head. Their tails were kept between their legs. Within a few minutes of the onset of the "catatonic" phase the animal would start to sway from side to side but never falling. The dog would not respond to calling. On pulling on the dog's leash the animal would walk a few steps and then stop, assuming the same position described above. As the dogs walked they showed an ataxia but seldom fell, recovering rapidly when they did. A mydriasis was noted in each case. After 35 or 40 minutes the animal would lie

down, after which it could only be encouraged to stand up with a great deal of prompting. We found that although the animals appeared to be aware of their surroundings they did not respond to painful stimuli. Respirations were normal and regular.

Amphetamine had no effect on this "catatonia", but Nembutal (5 mgm./kgm. body weight) appeared to relieve the reaction in about 20 minutes if given intravenously. When the animals were examined 24 hours later no signs of deviation from the normal could be found. During the period of recovery the animals were ataxic.

If the intravenous dose was given slowly in dilute solution no "catatonia" developed even after large cumulative doses had been given. There was, however,

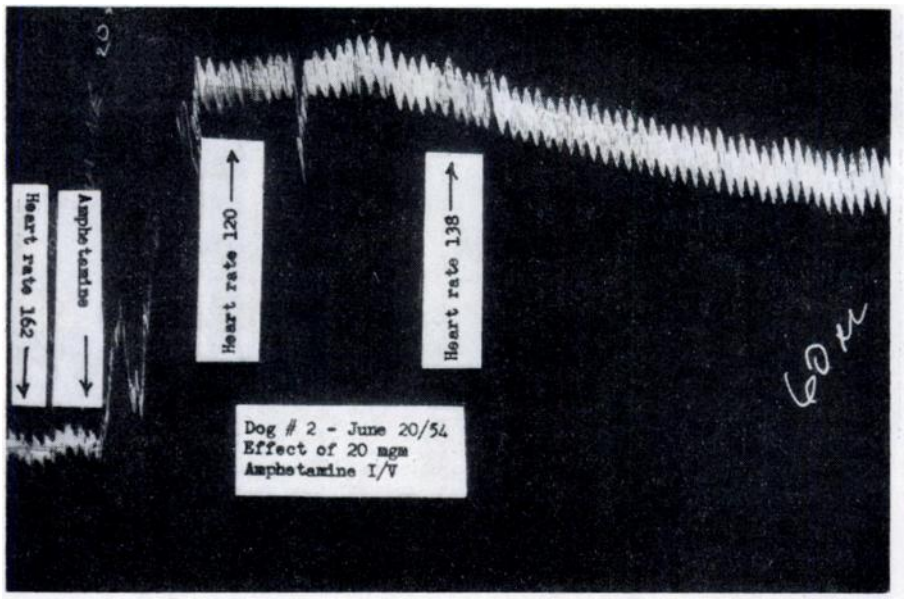

FIG. 3.—The effects on blood pressure of intravenous administration of 20 mgm. of Amphetamine Sulphate.

a marked ataxia. The animals recovered from this inco-ordination within 3 hours. There were no deaths, every animal appearing completely normal when examined 24 hours after administration of the TMA. Three dogs were used.

It was now felt that we had established enough information about trimethoxyamphetamine to be justified in administering it to human volunteers. We started with doses of 0·8–1·2 mgm./kgm. body weight (this was equivalent to a total dosage of 50–100 mgm. in the nine subjects used) by mouth and we found that in this range the following general syndrome was experienced:

About one hour after administration by mouth a slight transient headache was noticed. This passed rapidly, to be followed, in most cases, by a slight nausea which remained for 15 minutes to one hour. Occasionally this nausea was severe enough to discourage eating but in no case did a subject vomit. We found later that if 50 milligrams of beta dimethylaminoethyl benzohydryl ether 8-chlorotheophyllinate (Gravol, Dramamine), an anti-nauseant, were given 30 minutes before administration of the TMA, no nausea was experienced. One to two hours after administration by mouth of the TMA there was a sudden onset

of giddiness and the subjects would remark something like "I feel drunk or lightheaded". This was soon followed by an increase in movements, a rather marked increase in communicativeness, and a decrease in inhibitions. This phase remained for the ensuing 3 or 4 hours and then fell off rather rapidly so that 6–7 hours after the TMA had been administered there were no signs of abnormality. During this excitement phase the subject was slightly incoordinated, to the extent that he had to concentrate on what he was doing with greater intensity than normally and therefore he found that it was so much trouble to perform any muscular movements that he preferred to remain at rest in whatever position he found himself. After two hours the average subject presented a bilateral hyperreflexia in deep tendons and a rise in pulse rate by about 10 per minute, but no change in blood pressure. There was no significant change in blood pressure throughout the 24 hours succeeding the administration of the drug by mouth in any subject.

After administration of TMA at doses of 1·0–1·2 mgm./kgm. body weight, electroencephalographic recordings were made which showed very little change from the controls. The subjects on the above dose said that the experience was pleasing. None of them complained of any anxiety or discomfort aside from the slight initial nausea (which in subsequent subjects was combated with Gravol).

It was now decided to try to elicit hallucinations in subjects by use of a stroboscope stimulator. We administered a dose equivalent to 1·6 mgm./kgm. to a 22 year old white male. This subject was given an EEG before and after administration of the drug. During the control run the record showed a good regulation of the spontaneous tracings. The alpha rhythm was prominent and of good voltage, appearing symmetrical in both parieto-occipital regions with a frequency of 10 cycles per second. Recordings were carried out with the stroboscopic stimulator (eyes closed) at frequencies ranging from 4–20 c.p.s. There was a following of the alpha rhythm up to 12 c.p.s. The best response, with harmonics at 12, 18, and 24 c.p.s., was elicited with a frequency stimulation rate of 6 cycles per second. The second EEG was carried out 2 hours after oral administration of the TMA. On this record the spontaneous tracings were of much lower voltage and were not as well regulated. The alpha rhythm showed a tendency towards a faster rate, and frequencies of 11–12 c.p.s. appeared. The response to photic stimulation was more marked than previously. A response was noted up to 20 c.p.s. in short intermittent trains. Again the best response, with harmonics of 12, 18, and 24 c.p.s., was elicited in the 6 c.p.s. band.

Before administration of the TMA the subject saw small fine patterns of squares with fine lines, with the stroboscope set at an intensity 4 and frequencies varying from 4–20 cycles per second. The colours were predominantly white with some red and blue. The stroboscope was shut off, the TMA administered by mouth, and the subject allowed to relax for the ensuing two hours.

One hour after administration he felt "drunk" but claimed not to have the numbing effect around his mouth that he does with alcoholic intoxication. This subject had not been given Dramamine, therefore he experienced nausea and did not want to eat. He was shivering very slightly and said that he felt dizzy. He said that he did not want to stand up, but could easily sleep. The nausea subsided within one hour of its onset. He said that he felt "rubbery" in his legs and was "trembling slightly all over as if anticipating some daring feat".

Upon applying the stroboscope two hours after administration of the TMA, the subject, with his eyes closed, saw mosaics (which he described as being similar to those seen in the "movie version of Turkish Temples"), the letters of the alphabet, neon signs which raced up and down his field of vision as

on the marque of theatres, green snow falling, gold and silver rain falling, and firework displays. All these were seen in various pastel colours. The subject denied any excessively bright colours. He said that he had never before seen some of the colours. He was intensely fascinated and said that the experience was most pleasing. He was talking rapidly, and in a loud voice described all these things without interjection by the examiner. The subject also saw several large catlike animals with "great fangs" which were green in colour. He claimed that these animals were not molesting him, but were simply in his field of vision. The subject described himself as being "in the middle of what I see". The scenes were in three dimensions which the subject said were so exaggerated as to be almost unreal.

The examiner wished to test the response of the hallucinations to suggestions given to the subject. He asked the subject if he had ever seen Shakespeare's *Hamlet*. Immediately the bright pastel colours of the subject's hallucinations were replaced by dark purples and blacks. He saw the figure of Hamlet standing upon a turret which was obviously made of wood (as on the stage). In the next instant he was asked if he could see natives in the South Sea Islands. Immediately the subject reported various bright colours: yellow, green, red and blue, and he visualized, in a most spectacular three dimensional view, the islands in the distance with United States Navy ships floating about the ocean. The correlation of this with the Broadway play *South Pacific* is clear. The subject was disturbed by the fact that there were bridges connecting the ships with the islands and that automobiles were riding over the bridges.

After all these phenomena were experienced we tried to elicit hallucinations without the aid of the stroboscope. We were successful to the extent that the subject saw various patterns and designs with his eyes closed. The subject remained euphoric and very communicative for the next two hours. He complained of weakness in his legs, especially around the thighs. As the euphoria wore off he complained of sleepiness. He was taken home by automobile and at this time showed signs of a paranoid reaction: He said that the driver was driving far too fast, although in reality the speed was 25 m.p.h., and that the driver was trying to alarm him by driving at this "excessive speed". He felt that people were looking at him and he even entertained the idea that possibly the examiners had arranged for these people to stare at him. This, however, lasted but a short while. All this while he had insight and when his intelligence was appealed to he responded well.

On trying to sleep, in the afternoon, five hours after administration of the TMA, he woke up at intervals because of nightmares that he was having while asleep. By 8 hours after taking the drug all its effects had worn off. The subject slept well that night, having no unusual dreams.

The next day the subject related to one of us that at one time during the previous day's experiment he had imagined that he was either dead or dying, but that suddenly the Queen Mother appeared in Royal Purple and at this he said to himself that he could not possibly be dead if the Queen Mother were alive. The experience made the subject anxious for a few moments.

Our next subject was a 22 year old white, rather extroverted, female. Before giving the TMA to this subject she was given 50 mgm. Dramamine. Fifteen minutes later we administered 100 mgm. of TMA by mouth. This was equivalent to 1·6 mgm./kgm. body weight.

Before administering the TMA we did a control run with the stroboscope set in the range 4–20 c.p.s. The subject saw a red dot in the centre of the field for the first few seconds. This was followed by predominantly white and black circles

or hexagons. The fields were always symmetrical. There was no suggestibility on the part of the subject. She stated that she usually dreamt in colour. The stroboscope was used in one minute bursts at fifteen minute intervals following administration of the TMA with the following results: After 15 minutes the stroboscopic stimulations elicited flashes and spots of red, blue, mauve, and black. The subject was not suggestible and showed no evidence of increased communicativeness. After 30 minutes there were no changes of note to report. The colours were as in the previous stimulation in this subject except that there was much more blue (cyanopsy) in the fields and a pattern of "plus signs" appeared. The field was entirely symmetrical. It is of interest to note the increased blue colouration or cyanopsy. Chaumerliac and Roche (1949) observed the same phenomenon in persons given large doses of mescaline. One hour after administration the subject saw more blues and the other colours were more prominent. The subject said that there was less symmetry in the patterns which she now saw. She was becoming suggestible, and said "If you were a modern artist you could have a wild time painting the things that I am seeing". One hour and 15 minutes after administration she said that she felt as if she had been to a cocktail party—by this she meant that she was light-headed. She experienced no nausea.

One hour and a half after administration of the TMA we elicited the first structured hallucination. The subject, with her eyes closed, was watching the stroboscope and she described the following scene: "A woman is walking down Fifth Avenue (or is it Park Avenue?), she has a dog with her." The examiner asked what kind of a dog and she answered, "It's a poodle. It's walking in front of her and she is walking away from me." The examiner questioned again, asking if the scene was in three dimensions. She answered, "Yes, in fact it's in six dimensions." When asked to explain this she did so by saying that there were objects which she could not describe which were spinning in various parts of her visual field with their axes of rotation through various planes. She then saw bridges "like the Golden Gate with sailing boats sailing in the blue water". The sea seemed to be prominent in all her hallucinations. She described the scenes as being sketched in fine penned India Ink which had been coloured in later.

The stroboscope was then shut off. The subject said that her muscles felt lax. She was talking excessively and laughed at trivial incidents. The subject did not hallucinate without the stroboscope. She presented a mydriasis but did not complain of poor vision.

Two hours after administration of the compound, the stimulator was again turned on and the scenes became more and more like strange patterns of brocade and prints on materials. She was extremely enthusiastic and said that it would be ideal for an artist or designer to have these kind of visions. The scenes were described as being in the form of a pie cut in six pieces, each piece contained a different scene and, at will (or from suggestion of the examiner after she had described the scenes to him), she could "go into one of these scenes and become part of it so that you are sitting in the middle of what is going on". She did this several times for us, describing flowers, print designs, wallpaper pattern designs, and many whirling patterns which were going in every conceivable direction.

Two hours and fifteen minutes after the TMA had been given the subject saw, with photic stimulation, an oriental bridge across a stream in an oriental garden. This impressed her greatly and she said that she could still see the scene, but that it was changing, even though the stroboscope had been shut off immediately after this scene had been elicited. The colours were beige, maroon and green. The whole was in an exaggerated three dimensional form. Then (with the stroboscope turned off) she saw cities which were large and displayed in front of

her eyes as if she were flying over them in an aeroplane. At this time the subject switched to designs seen on materials, which she kept describing in superlative terms. She kept remarking that "this is what poets and artists and designers must take to get their inspirations". She was talking excessively and continuously. On suggestion she saw among other things, jet aircraft flying over a city, fields of flowers, and many pattern designs.

About this time a Paisley design appeared in the foreground. We found that if the stroboscope were started while an hallucination was fixed and "steady" it would "break up" the vision and produce a Paisley design. All her visions were in three dimensions. She then presented hallucinations of being in various countries of the world, describing story book scenes from each country. Seven hours after the administration of the TMA the subject had returned completely to normal.

Our last subject, a 23 year old medical student, was thought to be particularly suitable for several reasons. He was an accomplished artist and could therefore paint his impressions of the hallucinations. He had also had the drug previously in a dose of 0·8 mgm./kgm., and had at that time become quite nauseated, so that this was a means of testing the effects of Dramamine as an anti-nauseant.

This subject was given 50 mgm. Dramamine, by mouth, half an hour before administration of 125 mgm. of TMA—equivalent to 2·0 mgm./kgm. for his body weight. His control stroboscope impressions, with his eyes closed and situated 2 feet from the lamp, had been black and red in colour and consisted of a perfectly symmetrical field which was perforated. Above 12 c.p.s. the field became more blue and the whole perforated field spun counterclockwise. Fifteen minutes after administration of the TMA there was no change in the response to the stroboscope. At 25 minutes the subject felt slightly lightheaded. There was no nausea.

Thirty-five minutes after administration, the stroboscope elicited black chevrons moving in from the four corners to the middle of the field (Fig. 4). The basic field was white. The rotation was said to appear more like a real wheel now, with spokes. There were both clockwise and counterclockwise rotations at

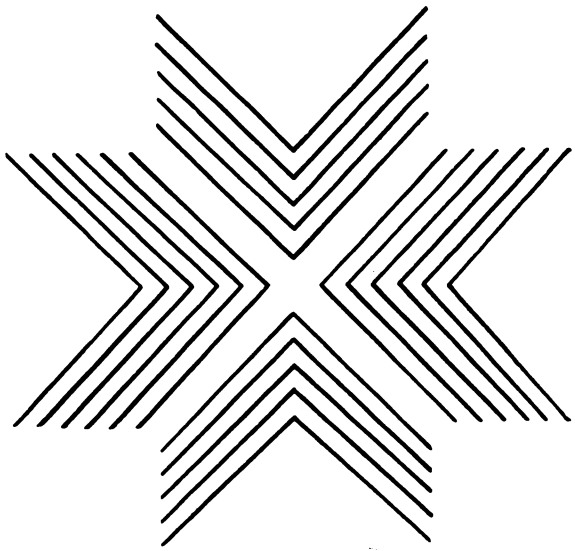

FIG 4.

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different times. These seem to be correlated with the frequency of the photic stimulator.

In forty-five minutes the patient said he was "giddy" but showed no signs or symptoms of nausea. The stroboscope impressions at 50 minutes had not changed from what they were at 35 minutes. At 60 minutes the subject saw "wall-paper designs" and "bright blue whirls with showers of brilliant blue stars in the whirl". As the frequency of the stroboscope was increased to 8 c.p.s. the whole field started rotating. The colours were all in pastels with the exception of the brilliant blue mentioned above.

At 1 hour and 20 minutes the subject felt pleasantly excited and wished to laugh at insignificant things. At this time we gave 30-second bursts with the stroboscope (intensity 4 at 10 c.p.s.). With the first burst the subject saw snow flakes with red middle and black periphery. These snow flakes were falling all around him. There were tiny brilliant blue dots interspersed (Figs. 5 and 6).

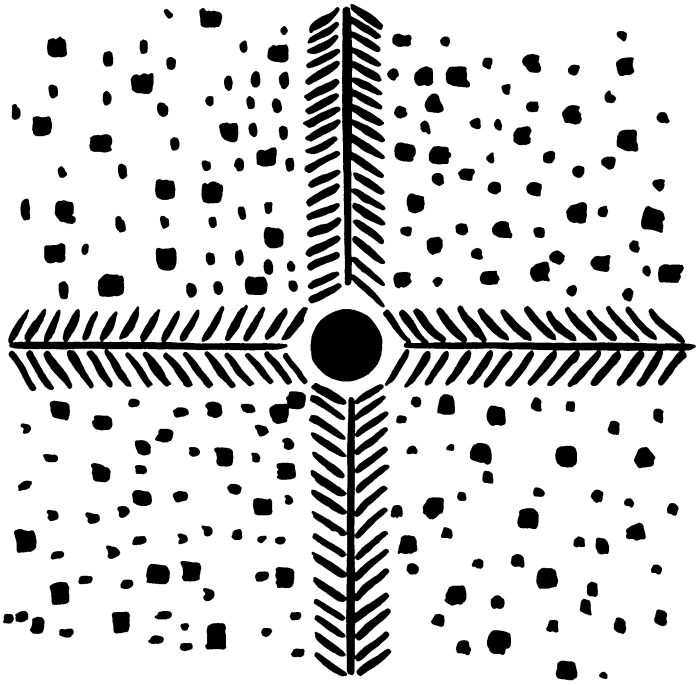

FIG. 5

The whole field was rotating. Then some yellow colours appeared for the first time in this subject.

After 1½ hours he said, "I feel silly as hell but don't really care." The subject normally does not use profanity of this sort and cares very much if he is silly or not. The subject at this time stated that he felt that his temperature perception and taste were more acute than normal.

There was no effect noted on ordinary vision. His mydriasis responded to accommodation. The subject's pulse, in one and a half hours, had risen from 72 to 84. It did not rise above this latter figure at any time recorded, his blood pressure did not rise throughout the experiment.

At 1 hour and 35 minutes the subject reported snow flakes, similar to those

already seen, at photic rates up to 16 c.p.s. Above this figure the pattern remained, but the colours became brighter.

At 1 hour and 45 minutes the subject reported very slight visual distortion. This lasted only a few minutes. He showed a marked increase in his speed of talking. He reported that he felt euphoric and he certainly gave this impression to observers.

At 1 hour and 55 minutes he reported some "shadowy patterns" without the stroboscope "but the colours were much brighter with the stroboscope".

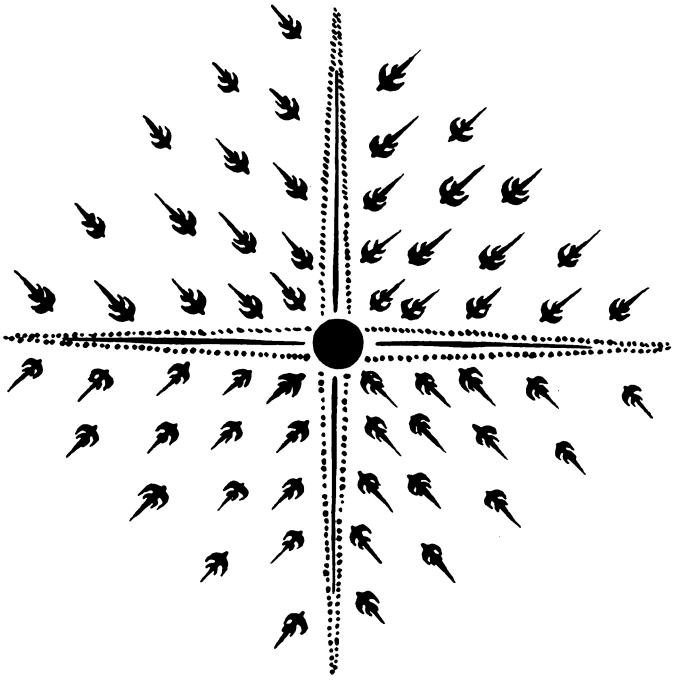

FIG. 6

Two hours after administration of the TMA the subject reported that he was very happy, felt slight tremors all over his body, and was not tired. So far the subject had seen no "real-life" scenes. They had all been patterns of a geometric nature. He had reported some hallucinations of "flashes of brilliant blue—like a welding arc".

At 2 hours and 40 minutes he saw a tunnel moving at a great rate and a great distance. He felt he was looking down this tunnel and this gave the effect of greatly exaggerated perspective. He kept talking about this "beautiful three dimensional effect". In this same hallucination he saw, for the first time, men standing on a spiral staircase. He thought that they might be "midshipmen preparing for their graduation at Annapolis (the United States Naval Academy), or a choir of men". The colours were rich reds and golds, with white and blue. He thought he was there while this was taking place—"it wasn't a picture". He felt that in the last few minutes the response to photic stimulation had changed: the scenes were from real life and were not symmetrical designs any longer.

We found that at this time he could hallucinate without the aid of photic stimulation. He saw façades of buildings in spectacular three dimensions,

Venetian architecture, a pool with explosions of brilliant amethyst and sapphire colours, peacocks' tails in iridescent colours, small streamlined fish, a chain of "plus signs" and red dots winding in and out of each other: a large number of black mice ran by at intervals. These and many similar scenes were experienced. Everything in the scenes was moving to and fro or across the field. The subject offered the information that he "got a modern interpretation of everything". By this he meant that many things were presented not as they really appeared in life but as a modern artist might present them. The subject is, as stated above, an amateur artist.

It is of interest to note that if the stroboscope was flashed in single flashes after an image had been formed without the stroboscope the general response would be that the initial complex image would be replaced by a more primitive one such as hexagonal designs or bright beads. This was not always the case. Exceptions were, for instance, that a flash brought the initial picture into sharp relief as though illuminated by a lightning flash, or a flash might initiate a series of red "plus signs" on a previous image of a blue tablecloth.

The subject stated that he felt very lax throughout the experience. He felt very pleasant, having not a care. Nothing could distress him. About 5 hours after administration he would see in his hallucinations anything that was in the conversation at the moment. He could do this with his eyes open or closed although he felt he saw more with his eyes closed. From the 4th to the 6th hour everything he looked at appeared to have a serpentine movement in it.*

At 5 hours he did not want to take the Nembutal offered to him when he was told that this would stop his hallucinations. However he was persuaded to take the capsule ($\frac{3}{4}$ gr.) of Nembutal. In half an hour he said he thought that the objects in the room weren't moving as much as before. One hour later he was almost normal except that when he closed his eyes he could have hallucinations. After the 8th hour he presented no abnormal signs or symptoms. That night he slept well with no unusual dreams. There was nothing unusual noted by the subject on arising next morning. All the subjects slept well after the experiment and did not have nightmares nor later recurrences of hallucinations.

We were interested in studying the excretion of TMA, by a modification of the spectrophotometric method of Woods *et al.* (1951). This is based upon the formation of a coloured compound when bromocresol purple is mixed with certain organic amines. This gives a yellow colour, the optical density of which, at 410 μ, is proportional to the concentration of the amine (in this case TMA). By this method we found that:

1. During the first 2 hours after administration of TMA by mouth there was a minimal excretion (Fig. 7). This rapidly increased during the latter half of the first two hour period to maintain a fairly steady plateau during the next three hours. This plateau was formed earlier as the actual dose taken by mouth increased.
2. The proportion of TMA recovered from the urine during half hourly samples for 22 hours was between 20 and 35 per cent.
3. The drug was not detectable in the urine after 22 hours.
4. In all cases the drug was detectable in the sample of urine which was taken half an hour after administration of the TMA.
5. There was a correlation between the subjective feeling of "drunkenness" on the part of the subjects and the start of the rapid climb up to the plateau in the urinary excretion.

* This was the only change noticed by our subjects in their perception of the external world.

We wished to determine if the amine excreted was identical with that ingested. We did this by two methods: the urine of the subjects was extracted with chloroform and the picrate of the amine was produced. The melting point of this amine picrate was then determined and compared with the melting point of 3,4,5-trimethoxyphenyl-β-amino propane picrate. Both these compounds were found to fall in the range 188–190° C. A mixed melting point determination was then done and no depression of the melting point was found. We next calculated the theoretical amount of the compound which would be necessary

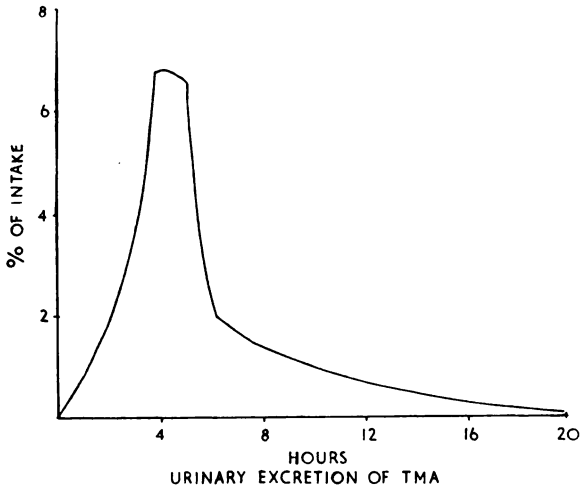

FIG. 7

to produce a certain quantity of nitrogen by the Kjeldahl method. When this quantity was weighed out and the Kjeldahl determination done we found a 4 per cent. relative error in the amount of nitrogen produced. This was well within the mechanical error of weighing. Both the above tests are not absolutely conclusive evidence, the amines having rather wide melting point ranges. The analytical procedures used showed that 65–80 per cent. of the ingested amine was not excreted as the original product. The other possible routes of excretion would be in the bile and perspiration. It is possible that this remaining 65–80 per cent. is metabolized in the liver and excreted as a breakdown product.

DISCUSSION

From the description given it will be noticed that TMA, as might be expected from its formula, produces symptoms similar to those produced by mescaline and amphetamine. The fact that it does not produce any hypertension and only a slight increase in heart rate, and that it does not interfere with sleep, may prove it to be superior to amphetamine and methedrine as adjuncts to psychotherapy. Caution however should be observed in its use, as with all such drugs, and a subject having taken it should be under constant supervision for 24 hours. He should not be allowed to drive an automobile for 12 hours following administration.

Blaschko (1940) has shown that amines with the group on the penultimate carbon of the side chain are inhibitors of amine oxidase. This enzyme is involved with metabolism in the higher brain and it is possible that the phenomenon of hallucinogenesis is involved with the inhibition of amine oxidase.

Summary

1. The structural formula of TMA (trimethoxyamphetamine) lies between those of mescaline and amphetamine. It is nontoxic to humans in doses up to 2·0 mgm./kgm. of body weight. In mice it produced no fatalities in doses up to 80 mgm./kgm. of body weight. In lower doses (0·8–1·2 mgm./kgm.) in man it produced euphoria and a loosening of emotional restraint. In higher doses (1·6–2·0 mgm./kgm.) it caused visual hallucinations in addition.

2. In humans hallucinogenic doses produced no significant effect on the blood pressure or respirations, and only a mild increase in heart rate.

3. Very high doses (above 20 mgm./kgm.) in mice produced a tremor and a scratching of the ear with the hind feet. In anaesthetized dogs a large dose, given in excess of 10 mgm. per minute intravenously, caused a self limiting fall in blood pressure of about 40 mm. Hg. In unanaesthetized dogs it produced a catatonia-like condition when given by rapid intravenous injection.

4. The drug was not detectable in the urine 22 hours after administration by mouth. In humans the peak urinary excretion was between the second and fifth hours after administration by mouth. This peak fell off sharply after the fifth hour. Twenty to 35 per cent. of the ingested drug was recovered unchanged in the urine.

5. A single flash of light from a stroboscope will cause a change in the type of hallucination present at the instant of the flash:

(i) The hallucination may change to a more primitive, less organized type.

(ii) The previous scene may remain but with a difference in the lighting effect so that the patterns stand out in relief. Some details may be added to the pattern.

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