Effect of Mescaline on Nicotinamide Adenine Dinucleotide Synthesis in the Central Nervous System

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Nicotinamide adenine dinucleotide (NAD) synthesis in mouse brain was demonstrated following the intracerebral injection of nicotinamide (500 mg./Kg.). Animals which received mescaline hemisulfate (100 mg./Kg.) 90 min. prior to nicotinamide were found to have higher levels of brain NAD at the 2 and 3 hr. time intervals.

NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD) levels have been increased in various organs of experimental animals by pretreatment with nicotinamide (1–3). Reserpine was found to prolong these levels in rat liver (4), and a similar effect has been demonstrated utilizing mouse brain (5). The participation of NAD in many dehydrogenase systems is well known (5), and alterations in the synthesis or degradation of this coenzyme could conceivably affect metabolic activity in the organism. Since certain psychotherapeutic drugs such as reserpine and chlorpromazine alter NAD metabolism (4), it appeared of interest to examine the effect of a hallucinogenic drug, such as mescaline, on this parameter.

EXPERIMENTAL

Young adult albino mice of both sexes were used as test animals in this study. Two brains were pooled and used for each NAD assay. The preparation of brain extracts was performed according to the method of Ciotti and Kaplan (7). The animals were stunned by a blow to the base of the skull, decapitated, and the whole brains quickly removed, weighed, and transferred to a Ten Broek tissue grinder. Homogenization was then accomplished with 5 vol. of cold 5% trichloroacetic acid. The total homogenate was centrifuged at 2,000 r.p.m. for 5 min., the supernatant liquid shaken with ether, and aliquot portions of the aqueous layer employed in the NAD assays. NAD determinations were made spectrophotometrically at 340 mμ with a Beckman DB spectrophotometer employing an ethanol–alcohol dehydrogenase system (7).

Animals were divided into two groups. Those of the first group received nicotinamide (500 mg./Kg.) intracerebrally in an adaptation of the method of Haley (8). NAD synthesis was demonstrated in the brain tissue by determination of the coenzyme level at various time intervals following the injection of nicotinamide. Animals of the second group received mescaline hemisulfate (100 mg./Kg.) intraperitoneally 90 min. prior to the intracerebral injection of nicotinamide. Determinations of brain NAD content in these animals were conducted at the same time intervals employed in the study of the control group which received only nicotinamide. The values reported represent the mean of at least five NAD determinations. The standard error of the mean was calculated for each set of NAD values and is designated by the vertical line through each point.

In addition, NAD assays were made 30 and 60 min. following the injection of mescaline hemisulfate prior to the intracerebral injection of nicotinamide. NAD measurements were made after intracerebral injections with normal saline in an effort to detect possible nonspecific elevation due to the experimental technique.

RESULTS AND DISCUSSION

Figure 1 illustrates the synthesis of NAD in mouse brain after the administration of nicotinamide. The value at zero time indicates the mean level of NAD before the intracerebral injection of nicotinamide. The brain NAD was not significantly increased until the fourth hour after the nicotinamide reinforcement. The NAD levels remained elevated at the 5 and 6 hr. intervals and then returned to a value comparable to the zero time determination.

Figure 2 shows the brain NAD elevation in experimental animals that received mescaline hemisulfate intraperitoneally 90 min. prior to the intracerebral injection of nicotinamide. These data indicate a greater increase in brain NAD at the 2 and 3 hr. time intervals than was observed in the animals which received only nicotinamide at zero time.

Table I is a summary of the mean values for brain NAD obtained at the various time intervals. Any significant differences in the mean NAD values of the animals receiving only nicotinamide and those which were injected with mescaline before the nicotinamide administration are denoted.

There was no significant change from control values in the brain NAD levels of animals which had received mescaline hemisulfate 30 and 60 min. prior to the determination. The intracerebral adminstration of normal saline did not alter the brain NAD levels.

Bonasera *et al.* (5) have shown that reserpine given

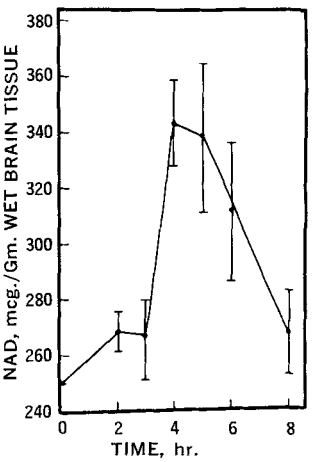

Fig. 1—Synthesis of nicotinamide adenine dinucleotide in mouse brain following intracerebral injection of nicotinamide (500 mg./Kg.) at zero time.

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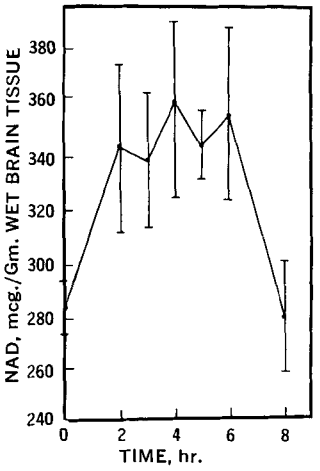

Fig. 2—Synthesis of NAD in mouse brain following intracerebral injection of nicotinamide (500 mg./Kg.) at zero time. Mescaline hemisulfate (100 mg./Kg.) was administered intraperitoneally 90 min. prior to zero time.

enzymatic activities dependent upon its presence. Clark and co-workers have demonstrated that mescaline inhibits the oxidation of pyruvate by brain homogenates; however, no effect was noted on the activity of succinic dehydrogenase (8). Schueler has reported that mescaline does not alter the oxidation of succinate by rat brain minces (9). A considerable amount of evidence indicates that electron transport in the oxidation of pyruvate involves nicotinamide adenine dinucleotide (5). With succinate as a substrate, however, nicotinamide adenine dinucleotide is not required because the electrons enter the transport system at the flavin nucleotide step. It is conceivable that an alteration in NAD metabolism could be a facet in the mechanism whereby mescaline inhibits pyruvate oxidation by brain preparations. This is an important consideration since the major energy source for the brain is glucose. Although the data indicate that mescaline has some effect on NAD synthesis in the central nervous system, it is not possible at this time to correlate any aberration in NAD metabolism with mescaline activity.

TABLE I—NAD LEVELS, mcg./Gm., IN MOUSE BRAIN

Time, hr.	0	2	3	4	5	6	8
Nicotinamide 500 mg./Kg. i.c. at zero time	251 ± 24[a]	269 ± 6	265 ± 13	344 ± 15	338 ± 27	312 ± 24	269 ± 16
Nicotinamide 500 mg./Kg. i.c. at zero time + mescaline hemisulfate 100 mg./Kg. i.p. 90 min. prior to zero time	281 ± 10	342[b] ± 32	336[b] ± 25	358 ± 36	342 ± 12	353 ± 32	278 ± 20

[a] Standard error of the mean. [b] Significantly different from control (nicotinamide 500 mg./Kg. only) $p < 0.05$.

intraperitoneally will delay the peak value of the increase in brain NAD following the administration of nicotinamide intrathecally. In addition, these investigators noted that these values remained elevated for at least 24 hr. after the nicotinamide administration. Earlier, Burton and associates (4) had demonstrated a prolongation of elevated level of liver NAD after nicotinamide administration if animals were pretreated with either chlorpromazine or reserpine.

The NAD values reported in this communication compare favorably with the data available for synthesis of NAD in mouse brain after intrathecal injection of nicotinamide. It is interesting to note that in contrast to the alteration in NAD metabolism effected by reserpine, the apparent changes induced by mescaline indicated an earlier elevation in brain NAD. As in the case of reserpine, the values for the experimental animals receiving mescaline never reached a peak level significantly different from control values of animals receiving only nicotinamide.

Participation of NAD in many dehydrogenase systems is well known and any alteration in the metabolism of this coenzyme could possibly affect

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Keyphrases

Nicotinamide adenine dinucleotide
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Mescaline—nicotinamide adenine dinucleotide synthesis
UV spectrophotometry—analysis