A Pilot Study of Some Physiological and Psychological Effects of Caffeine

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Abstract

Eleven volunteers participated in a study to characterize some physiological and psychological effects of caffeine in a double-blind, cross-over study. During one week, the subjects were given a caffeine containing beverage, and during a second week, they were given an identically appearing non-caffeine beverage. Data were accumulated based on urine tests and a medical examination. Diary entries revealed typical effects of caffeine such as increased energy, nervousness and restlessness which were observed after the week of caffeine consumption. A medical examination showed increased adrenal function for those subjects who were non-users or occasional users of caffeine beverages. Habitual users of caffeine beverages showed no obvious adrenal effects. Determination of pH, surface tension and viscosity of urine during the two weeks of the study showed evidence that caffeine is an "anabolic" agent according to a theory suggested by Dr. E. Revici.

Introduction

Caffeine, probably the most widely used drug, is a potent pharmacologic and psychotropic agent (Bolton and Null, 1981 a and b; Goodman and Gilman, 1975). Many studies in both animals and humans have been performed in order to quantify and characterize its physiological and psychological effects.

The research presented in this paper consists of two kinds of observations resulting from consumption of caffeine beverage during a two-week period: (1) effects on adrenal function determined by a medical examination; and (2) physical-chemical measurements of urine, an indication of the anabolic effect of caffeine according to a theory proposed by Dr. E. Revici (1961). In addition, perceived psychological effects of caffeine were studied by means of a questionnaire and daily diary.

Eleven volunteers drank a caffeinated and non-caffeinated beverage during each of two weeks. Subjects were medically examined prior to the study and after each test week. In addition urine samples were tested both prior to the study and after each test week.

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Perceived psychological effects are difficult to quantitate. Goldstein has published several studies in which reactions to caffeinated and decaffeinated coffee were assessed in both caffeine and non-caffeine users using extensive questionnaires (Goldstein et al., 1969). The reactions depended on previous caffeine habituation and use. Heavy users of caffeine had less effects on sleep, and showed less irritability and nervousness as a result of caffeine intake.

Caffeine ingestion stimulates many bodily responses, some of which are opposite in direction (Goodman and Gilman, 1975). For example, after ingesting caffeine, the heart rate is initially decreased, and then increased about an hour after intake. "Caffeine causes increased serum lipids (Bellett et al., 1969) and affects glucose (Darragh et al., 1979) probably through catecholamine mediation."

Subjects who consume high levels of caffeine may, in part, enjoy the effects of the drug which is stimulating their otherwise under-functioning adrenal glands.

Previous experimental work has shown that caffeine increases the output of epinephrine and norepinephrine from the adrenal glands (Goodman and Gilman, 1981). In the present study, this effect of caffeine was measured by physical examination and urine sodium levels in the experimental subjects.

One of the principal objectives of this study was to study the effects of caffeine as an anabolic agent. Dr. E. Revici, after many years of research has proposed that drugs can be categorized by measuring certain physical-chemical properties of urine, as anabolic or catabolic (Revici, 1961).

Methods

Various responses were observed for 11 subjects during a two-week period. Each subject participated in a week of caffeine intake (110 mg daily) from a herbal tea, and a week of consumption of an otherwise identical non-caffeinated tea.

Subjects

The eleven volunteers were healthy persons between the ages of 20 and 35 years. They agreed to drink the test beverages during a two-week period on a double blind basis. Four of the subjects (CE, ZK, AG and AW) were chronic (2 or more years) coffee drinkers (2-6 cups/day). The other subjects either were abstainers or infrequent users of caffeine.

Psychological Effects

In addition to keeping a daily diary, subjects were requested *to* answer a questionnaire prior to, and after each week of the study, as follows:

1. Have you noticed a difference in your energy level?
2. Have you had more or less difficulty falling asleep?
3. Have you had more or less power of concentration and/or attention span?
4. Have you had a decrease or increase in mood, nervousness or depression?
5. Have you noticed any difference in muscular strength, endurance or stamina?

Adrenal Function

In addition to the data supplied by the diary, subjects were given a physical-medical examination to assess adrenal function prior to, and after each week of the study. According to Goodman and Gilman (1975) caffeine stimulates "the release of catecholamines from the adrenal medulla." Caffeine also releases catecholamines due to a central action and by affecting C-AMP.

The tests for adrenal function included the following:

1. Ragland Blood Pressure (Burch and de Pasquale, 1962).
2. Pulse
3. Blood pressure (seated)
4. Pupil size
5. Pupil response to light
6. Sodium content of urine

Ragland Postural Blood Pressure Test; Method and Physiological Basis (Burch and de Pasquale, 1962):

This test is a means of evaluating adrenal activity. It detects diminished adrenal function.

Method: The difference of the systolic blood pressure, measured with the patient in the supine position and in the erect or standing position, is an indication of adrenal function. The patient lies supine for four minutes. The blood pressure is taken in this

position and immediately after the patient stands up.

Upon arising from the supine position and standing erect, the normal subject has a rise or elevation of the systolic blood pressure. The systolic pressure rises approximately 5-10 mm mercury. Since the cardiovascular system must pump blood to the head against the force of gravity, higher blood pressure is required.

When diminished adrenal function is present, the systolic blood pressure taken in the erect or standing position may actually **fall.** The degree of lowering of the erect blood pressure gives some indication of the magnitude of diminished adrenal function.

Adrenal glands have a major role in controlling the tone of the splanchnic veins. These veins do not have valves and are dependent upon nerve function.

Koenigsburg Test for Urinary Sodium-Chloride Excretion (Brooks, 1925):

The adrenal gland produces aldosterone which instructs the kidney to retain sodium. If adrenal gland function is diminished, aldosterone production is decreased and salt is spilled into the urine.

Method: The Koenigsburg Test is a titration procedure. Ten drops of urine are placed in a test tube. One drop of 10 percent potassium chromate solution is added to the urine. 0.74 percent silver nitrate solution is added dropwise until the color of the solution turns brick red. The number of drops required for subjects with normal adrenal function is 17 to 25. Excessive sodium and chloride in the urine will require more silver nitrate regent to turn the solution brick red. The most common reason for spilling sodium into the urine is diminished aldosterone level as a result of diminished adrenal function.

Comparisons of the amount of sodium and chloride in the urine serve as an indirect reflection of aldosterone level and thus, indirectly, adrenal function. In early stages of diminished adrenal function, salt will spill into the urine. However, late in the course of adrenal exhaustion, there is very little salt left in the body and thus there is little salt available to spill.

Description of Pupilary Response to Light

The pupil in the normal subject reacts briskly and remains constricted as long as the light beam is present. If the body is severely sodium depleted, the pupilary constriction does not "hold" and the pupil oscillates. It may even fail to constrict at all. Although salt depletion may occur as a result of many abnormal physiologic processes, the most common is diminished adrenal function and diminished aldosterone and the subsequent chronic loss of sodium and chloride into the urine (Feldman).

Urine Measurements (Revici Anabolic/ Catabolic Index) (Revici, 1961):

Fasting urine was analyzed prior to the study and after each of the two study weeks to determine specific gravity, surface tension (Revici urotensiometer) and pH. These results were combined to form an index to describe the catabolic/anabolic effect of the drug.

According to Dr. E. Revici, the best indication of catabolic/anabolic effect is measured by a composite index of the urine measurements as follows (Revici, personal communication):

Index = I = 2(74 - s.t.) + pH + last two digits of s.g.

Alkaline pH = 5 Neutral pH = 10 Acid pH = 20

For example if s.t. = 70, pH = acid and s.g. = 1.016, the index is 2(74-70) + 20 + 16 = 44.

Values above 40 are considered to be a result of administration of a "catabolic" agent and values below 40 are a result of an "anabolic" agent (See Discussion).

Results

Tables I, II and III present the results of the study. Missing data occurred because the volunteers either did not supply the necessary urine, or diary results, or did not keep medical appointments for examination of adrenal function.

Psychological Effects (Diary and Questionnaire)

Most of the subjects indicated no difference between the two weeks with regard to questions concerning changes in "concentration" and "strength" (questions 3 and 5 in

diary). Differences which were recorded by the subjects are shown in Table I. Three of four subjects indicated more energy during the "caffeine" week. Two subjects reported sleep problems during the second week, both of whom were chronic caffeine users. Five of six subjects reporting an effect were more "nervous" and "irritable" during the caffeine week. This part of the study did not show clear cut effects due to caffeine, because of the small number of subjects and short duration of the study.

Adrenal Function

Table II is a summary of the adrenal function tests performed on ten subjects. The two criteria which were most affected by the ingestion of caffeine were Ragland blood pressure (standing minus supine diastolic blood pressure) and sodium excretion as measured by the "indicating" solution. (See Methods.)

Adrenal function was based on a clinical examination and an overall assessment of the blood pressure and sodium excretion as discussed above. With a couple of exceptions, the pupilary response to light did not show discrimination between the treatment weeks. Although, overall, the two weeks were not differentiated, an obvious pattern emerged. Most of those who were caffeine abstainers (5 of 6) were evaluated as having diminished adrenal function during the week of caffeine ingestion, whereas all of the habitual users of caffeine (4 of 4) showed no difference between the two weeks. Statistical analysis (t test) showed that the difference between the two groups (chronic users and abstainers of caffeine) is statistically significant ($P < 0.05$) for Ragland blood pressure and sodium excretion ($P < 0.05$).

Urine Measurements (Anabolic Effect)

Eight of the eleven subjects had urine measurements taken before the study and after each of the study weeks. The analysis of the urine was performed under blind conditions. (The analyst did not know whose urine sample was being tested nor the beverage being taken.) The results are shown in Table III**.** There is a tendency toward a lower index (see Methods) during the "caffeine" week (Week 2) compared to the "non-caffeine" week. (Interestingly, the pre-study week showed results similar to the "caffeine" week). The ingestion of caffeine results in higher surface tension, more alkaline urine and a lower specific gravity on the average. Six of the eight subjects tested had a lower catabolic/anabolic index during the "caffeine" week compared to the caffeine-free week ($P < 0.10$). This is in conformance with the proposal of Dr. E. Revici (1961): Caffeine is an anabolic agent. Dr. Revici has been engaged in research for more than 50 years, during which he has spent considerable time building up his theory of anabolic/catabolic properties of therapeutic agents. This is the first time such an experiment has been independently carried out by others.

Discussion

The results of this double-blind study indicate that clinical tests show an apparent caffeine effect after one week of use as observed in a relatively small group of subjects.

Psychological Effects Subjects apparently observed some differences in (1) energy (increase with caffeine); (2) sleep patterns (more difficult sleeping with caffeine); and (3) mood (more problems with caffeine). Eight of the eleven subjects observed some difference between the two weeks of caffeine and non-caffeine use. There was no obvious tolerance in the group who were regular caffeine users, although it would be difficult to document such effects in a panel of this small size.

Although there was some suggestion of a caffeine effect in this very small group of subjects, subjective effects of caffeine were not obvious after one week's relatively moderate intake of a caffeine beverage.

Adrenal Function Caffeine has many effects upon body function. One of the major effects is to stimulate the adrenal glands to secrete epinephrine and norephinephrine, resulting in an immediate boost of energy. However, in time, the adrenal glands become exhausted (Feldman).

In our society, the stress of day-to-day living has a tendency to "wear out" our adrenal glands. This diminished activity results in fatigue. In order to revive adrenal function many people ingest moderate to high quantities of caffeine. This is an external stimulant. In time, this stimulation wears out

TABLE I DIARY SUMMARY*

SUBJECT	QUESTION 1 ENERGY	2 SLEEP	3 CONCENTRATION	4 MOOD NERVOUSNESS	5 STRENGTH
SH	More energy 2nd week	------	------	----------	----------
JL	Agitated 2nd week	------	------	----------	----------
CE	-----	------	------	Decreased Nervousness 1st week	----------
AG	-----	-----	------	Calm 1st week	----------
AW	Higher energy 2nd week	Sleep problem 2nd week	Better 2nd week	----------	Less 1st week
JR	More energy 2nd week	------	------	Less irritated 2nd week	----------
AE	-----	Sleep problem 2nd week	Less attention span 2nd week	Jumpy 2nd week	----------
CE	-----	------	------	Less nervousness 1st week	----------

*Only observed differences between WEEK 1 (non-caffeine) and WEEK 2 (caffeine) are reported.

TABLE II - BLOOD PRESSURE AND SODIUM EXCRETION

SUBJECT	MEDICAL EXAMINATION* RAGLAND BP (STANDING SUPINE)				SODIUM EXCRETION**				COMMENTS
	PRE	**WK1**	**WK 2**	**WK 2-1**	**PRE**	**WK l**	**WK 2**	**WK 2-1**	**Adrenal Function**
JC	**0**	**0**	**-10**	**-10**	—	23	65	42	Diminished week 2
SH	**-10**	**-10**	**-10**	**0**	—	55-60	80	25	Diminished week 2
JR	**5**	**5**	**10**	**5**	—	25	23	- 2	B.P., pupil response diminished
AE	**- 5**	**0**	**-18**	**-18**	—	—	—	—	B.P. down second week
JL	**0**	**0**	**- 5**	**- 5**	50	23	23	0	Not much effect
DM	**- 4**	**5**	**- 5**	**-10**	—	45	100	55	Diminished second week
CE* **	**-22**	**10**	**15**	**5**	—	60	40	-20	Not much effect
ZK* **	**- 8**	**-18**	**-10**	**8**	30-35	30	40-45	12.5	Not much effect
AG* **	**0**	**5**	**14**	**9**	—	50-55	40-45	-10	Not much effect
AW* **	**-11**	**0**	**5**	**5**	_ .	50-55	40-45	-10	Not much effect

* Week 2 is the "caffeine" week.
** Koenigsburg Test *** Chronic users of caffeine

the glands. Thus the immediate benefit is at the cost of eventual exhaustion (Feldman).

In day to day clinical practice, many patients come to the doctor's office complaining of fatigue. The severity of this symptom varies from "mild" to "severe". An example of "severe" fatigue is a feeling of being tired and drained of energy even upon awakening from a restful sleep. At the other end of the spectrum, is a diminished ability to work efficiently at the end of the day (Feldman).

Occasionally, the fatigue is a result of anemia, depression, malabsorption, a toxic state or a hypothyroid condition. However, it is our observation that most of the time fatigue is a result of diminished adrenal function or adrenal exhaustion. The level of adrenal function can be ascertained by appropriate physical examination and laboratory testing. As nutritional therapy corrects or improves adrenal gland function the patient's energy improves. If the adrenal gland returns to a normal state of function, the fatigue is minimized or is alleviated (Feldman).

In the active nutritional practice of one of the authors (Dr. Feldman), a recent review of medical records showed that more than 65 percent of new patients complaining of fatigue as a major medical symptom were drinking three or more cups of coffee or tea daily. Many patients reported increased intake of coffee and tea as their day-to-day fatigue became more severe. Upon interview they reported the necessity of coffee, tea, chocolate, or certain soft drink beverages to "boost" their energy. It is very likely that caffeine's ability to stimulate adrenal gland activity accounts for the popularity of caffeine beverages in our society.

In this study, the results of the physical examination and urine sodium excretion evaluation showed that chronic users of caffeine can be differentiated from non-users based on tests which reflected changes in adrenal function during the two test weeks.

Of the six subjects who used little or no caffeine intake prior to the study, four had diminished adrenal function when they were examined prior to the study. Five of this group of six had marked, measurable, diminished adrenal functions after the week of caffeine intake.

Of the four subjects who had a high intake of caffeine prior to the study, all had some degree of diminished adrenal function prior to the study. This diminished adrenal function remained about the same during the week of caffeine ingestion as well as the caffeine-free week.

The diminished adrenal function was mainly characterized by Ragland blood pressure measurements and sodium excretion in the urine.

Anabolic Effect (Revici Index)

A most interesting result was the effect of caffeine intake on certain physical-chemical properties of urine. Dr. E. Revici has developed a theory based on almost 50 years of research that body processes and the effect of drugs on these processes can be categorized as anabolic and catabolic (Dualistic Concept). Agents influencing these metabolic states mostly comprise the usual nutrients. However, drugs and other chemical agents may be categorized as anabolic or catabolic according to which process they stimulate. The result is an excitation of either the catabolic or anabolic effect. Caffeine is considered an anabolic agent because of its ability to donate methyl groups in anabolic processes according to Dr. E. Revici. Dr. Revici has used coffee (with 2 boiled eggs) to help elucidate the nature of symptoms of a disease. If the caffeine and eggs decreased the symptoms, the disease has catabolic character. If it increased the symptoms, the disease is anabolic. Caffeine can then be used to treat anabolic imbalances as a result of the disease.

Urine surface tension, specific gravity and pH are indications of catabolic or anabolic nature of the agent. If surface tension is above 69 dynes/cm, the agent is considered anabolic; alkaline urine is anabolic and a specific gravity below 1.016 is anabolic. The contrary results are catabolic. Each of the individual measures are quite variable, and it would be difficult to accurately categorize an active substance based on a single measure. The best way of analyzing such data is a composite index of all three effects, as recommended by Dr. Revici (1961). (See Methods.)

Conclusions

Caffeine use, at a relatively moderate level (2-3 cups of tea/day), results in distinct

observable effects. In this research we have shown that various physiological and clinical effects can be ascertained after one week of caffeine ingestion compared to a control week.

The moderate intake of caffeine in the subjects not accustomed to caffeine produced marked diminution of adrenal function. In the subjects accustomed to moderate or high caffeine intake, the effects of the moderate caffeine load which we administered were indistinguishable from the baseline prior to the study and the week of no caffeine intake. Apparently, caffeine users become tolerant to these effects of caffeine on the adrenal glands.

Instead of stimulating the glands with caffeine, the adrenals should be supported nutritionally in order to repair them, according to Dr. Feldman. The nutritional program should include:

1. Diminished stressors
2. Learn how to diminish anxiety
3. Pantothenic acid
4. Vitamin C
5. Bovine adrenal gland processed to remove possible toxins and any hormone.

Caffeine ingestion changed the physical/ chemical characteristics of the urine, conforming to Dr. E. Revici's Dualistic Theory. Caffeine appears to be an anabolic agent, stimulating anabolic processes, according to this theory. The results showed a lower index for 6 of 8 subjects during the week of caffeine ingestion compared to the caffeine-free week. (The index also suggested an intake of anabolic substance(s) in the period prior to the study for most of the subjects.) According to Dr. Emanuel Revici, disease may have anabolic or catabolic character. The anabolic nature of caffeine suggests that this drug may be effective in catabolic disease states. However, because of its powerful physiological and psychological effects, the indiscriminate use of caffeine is not warranted. Excessive intake of caffeine is to be discouraged.

TABLE III — RAW DATA - URINE MEASUREMENTS 1

SUBJECT	SURFACE TENSION			PH			S.G*			INDEX		
	PRE	WEEK 1	WEEK 2	PRE	WEEK 1	WEEK 2	PRE	WEEK 1	WEEK 2	PRE	WEEK 1	WEEK 2-1
JC	74	70	66	ALK	ACID	ALK	10	17	29	15	45	50	05
SH	69	66	66	ACID	N	ACID	26	29	29	56	55	65	10
JB	74	71	73	ALK	ACID	ACID	05	12	08	10	38	30	-08
AE	73	63	70	ALK	ACID	ALK	11	33	14	18	75	27	-48
JL	71	72	70	ALK	ACID	N	27	16	08	38	40	26	-14
CE	73	70	72	ALK	ALK	ALK	22	30	23	39	43	32	-11
AG	70	65	72	N	ACID	ACID	23	32	20	41	70	44	-26
AW	72	69	73	ACID	N	ALK	18	25	18	42	40	22	-18
AVERAGE	72	68.25	70.25				17.8	24.3	18.6	32.4	50.8	37.0	-13.8 s=18.1 t=2.15

WEEK 1 is caffeine free and WEEK 2 is with caffeine. Last two digits, e.g., 10=1.010

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