system and can produce an early, transient depression in brain activity (*17*). The use of amphetamine as an antifatigue agent in sedentary situations resembling that of the laboratory (for example, sustained motor vehicle operation) can produce a dangerous, transient lethargy, particularly among individuals characterized by CNV's having a slow rise time (type B in Fig. 2). That the paradoxical drowsiness we observed was accompanied by depressed brain activity and subjective reports of a dysphoric mood indicates that principles of psychopharmacology based on amphetamine being solely a centrally acting stimulant drug require review.

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7. All subjects were females between the ages of 18 and 35 (median, 21) and were judged by a psychiatrist to be in good physical and mental health and free of drugs.
8. The time constant for EEG and EOG recordings was 8.2 seconds. High frequency cut-off was 75 hz (50 percent amplitude reduction) with a 12 db per octave roll-off. Trials with eye movements (including eye blinks) and key presses in the S_1–S_2 interval were omitted in off-line averaging. Averaged CNV's were based on 6 to 12 trials per run, the number being constant for a given individual. CNV amplitude was the difference in average voltage between the 512-msec period pre-S_1 and the 256-msec period pre-S_2.
9. In the first hour post-drug, four subjects also verbalized dysphoric mood (for example, "the saddest I ever felt" and "very very blue"). Two individuals displayed tears in their eyes.
10. Ratings were made on a six-point scale for test behavior (5-minute run) and verbalizations made during 5-minute rest intervals: +3, very high ("excited," "euphoric," laughing, and glassy eyes); +2, high ("very alert," "wide awake," and frequent smiling); +1, moderate ("alert" and "awake"); −1, low ("bored" and "tired"); −2, very low ("very tired," head to side, and droopy eyelids); −3, extremely low ("sleepy," "cannot keep eyes open," sleeplike nodding, and eyes closed). The occurrence of more than one indicator of change in alertness resulted in a cumulative rating, for example, a rating of "+5" resulted from the appearance of glassy eyes (+3) *and* the verbalization of feeling "very alert" (+2).
11. Mean ratings on this criterion variable were: −4.85 (range: −1 to −8) for the paradoxical group and +3.29 (range: +1 to +5) for the nonparadoxical group.
12. Means (and standard deviations) of behavioral alertness rating scores in the left half of Fig. 1 for pre-treatment, 1 hour post-treatment, and 2 and 3 hours (combined) post-treatment are as follows: (i) nonparadoxical-drug: −0.29 (0.76), +3.29 (3.45), and +3.79 (2.93); (ii) paradoxical-drug: −0.15 ((0.80), −4.85 (3.31), and +3.19 (2.98); (iii) nonparadoxical-placebo: +0.29 (0.76), −0.43 (0.98), and −1.86 (1.50); (iv) paradoxical-placebo: −0.08 (1.04), −1.08 (0.95), and −1.62 (1.58).
13. All mean differences were evaluated by analysis of variance of simple effects and *t*-tests. Since these two techniques yielded comparable results, the simpler procedure—that of *t*-tests—is presented here. All *P* levels are two-tail values.
14. Means (and standard deviations) of CNV amplitude (μv) for pre-treatment, 1 hour post-treatment, and 2 and 3 hours (combined) post-treatment are as follows: (i) nonparadoxical-drug: 10.84 (2.72), 12.94 (2.56), and 9.90 (3.50); (ii) paradoxical-drug: 13.63 (3.98), 10.87 (4.43), and 13.16 (4.27); (iii) nonparadoxical-placebo: 13.63 (3.27), 12.72 (4.30), and 11.68 (3.71); and (iv) paradoxical-placebo: 13.82 (4.68), 11.73 (3.42), and 11.78 (3.54). The mean pre-drug CNV amplitude was higher for the paradoxical group (13.63 μv) than for the nonparadoxical group (10.84 μv) ($F = 4.49$; d.f. = 1, 18; $P < .05$). Consequently, all raw scores (CNV amplitude in microvolts) were adjusted to remove interindividual variability among subjects in pre-drug and pre-placebo levels [see J. J. Tecce and J. O. Cole, *Psychopharmacologia* **24**, 159 (1972)]. These Adjusted Differences Scores are presented in the right half of Fig. 1 and are the basis of statistical tests. As shown in Fig. 1, a positive value indicates an increase in CNV amplitude after treatment compared to pre-treatment level, whereas a negative value indicates a relative decrease.
15. In the second and third hours post-drug (combined), means of alertness scores were increased ($P < .01$) for both paradoxical and nonparadoxical groups. In the placebo session, both groups showed significant reduction ($P < .05$) in mean behavioral alertness in the second and third hours (combined) post-placebo. No CNV changes were significant in the placebo session. As can be seen in the right side of Fig. 1, the increase in CNV amplitude for the nonparadoxical group in the first hour post-drug disappeared in the second and third hours. During these latter hours, there were reports of cognitive surges ("racing thoughts" and "endless ideas"), which are possible sources of distraction and disruption in CNV development.
16. The classification of each individual's pre-treatment CNV shape as type A or B [J. J. Tecce, *Arch. Gen. Psychiatry* **24**, 1 (1971)] was made by a consensus of two judges who were blind to the experimental conditions.
17. Normal and paradoxical responders do not differ in age, height, weight, use of birth control pills, point in time tested within the menstrual cycle, or time of day amphetamine was ingested (average times for ingestion by nonparadoxical and paradoxical groups were 10:56 and 11:03 a.m., respectively). These groups may differ in rate of drug absorption from the gastrointestinal tract to the circulatory system. The two groups did not differ in amount of sleep reported for the night before testing or in amount of breakfast taken the morning of testing (subjects were asked to keep to their normal sleep hours and breakfasts).
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D(−)-Lactic Acid and D(−)-Lactate Dehydrogenase in Octopus Spermatozoa

Abstract. *The spermatozoa of* Octopus dofleini martini *produce anaerobically* D(−)*-lactic acid and possess a very active* D(−)*-lactate dehydrogenase. In this respect, while resembling certain microorganisms, they differ strikingly from mammalian spermatozoa which produce* L(+)*-lactic acid and contain* L(+)*-lactate dehydrogenase.*

The anaerobic survival and motility of spermatozoa are both strictly dependent on the availability of carbohydrates that can undergo glycolysis. Mammalian spermatozoa depend largely on extracellular carbohydrate, chiefly fructose, provided by the male accessory secretions; the intracellular glycogen content of mammalian spermatozoa is notoriously low and they lack some of the enzymes necessary for glycogenolysis (*1*). On the other hand, in the spermatozoa of certain other animals, particularly in some invertebrates, a different situation is encountered. A notable example is provided by the spermatozoa of the giant octopus of the North Pacific, *Octopus dofleini martini*. In this animal, the spermatozoa are characterized by the presence of a large reserve of intracellular glycogen, and in addition, they possess the enzymes required for glycogenolysis, including phosphorylase and phosphoglucomutase (*2*).

The spermatozoa of *O. dofleini martini* are capable of long survival both in vitro and in vivo. When suspended in seawater and incubated anaerobically at 10°C, that is, at a temperature close to that of the animal's normal habitat in the North Pacific, these spermatozoa retain their motility for several days. In the present study we investigated the metabolism of sperm suspensions incubated anaerobically in vitro, and we have identified lactic acid as a major metabolite, using the following three chemical methods: (i) colorimetric, by means of the hydroxydiphenyl reagent (*3*); (ii) iodometric, by distilling the acetaldehyde formed by oxidation with potassium permanganate in the Lieb-Zacherl apparatus and by determining the acetaldehyde bound to sodium hydrogen sulfite by titration

with iodine (*4*); and (iii) by gas-liquid chromatographic separation of the methyl derivatives of nonvolatile organic acids extracted with ether from the incubation mixtures (*5*). When, however, a further attempt was made to strengthen the chemical evidence for the identity of lactic acid by means of an enzymatic method based on the use of nicotinamide adenine dinucleotide (NAD) and muscle L(+)-lactate dehydrogenase, a negative result was obtained. This alerted us to the possibility that the lactic acid produced by the spermatozoa is not L(+)-lactic acid.

On the assumption that the lactic acid formed by the octopus spermatozoa may be D(−)-lactic acid, we made use of a preparation of D(−)-lactate dehydrogenase from *Lactobacillus leichmannii* and were able to show that, in fact, the lactic acid produced by these spermatozoa was present in the D(−) enantiomorphic form. The rate at which the spermatozoa produced this lactic acid varied, but on the average, at 10°C, about 1 mg of D(−)-lactic acid was produced by 10^9 spermatozoa during 48 hours of anaerobic incubation.

We have good reason to believe that the formation of D(−)-lactic acid also occurs under conditions in vivo. On two occasions, after copulation had been allowed to proceed to completion, we dissected the mated females 24 hours later and recovered from their oviducts the remnants of spermatophores together with a large dilute mass of motile spermatozoa. In this material we found in one instance 5 mg, and in the other 25 mg, of D(−)-lactic acid per 100 ml; L(+)-lactic acid was absent. In this particular type of experiment in vivo, it still remains to be established how much of the D(−)-lactic acid is derived from semen and how much is contributed by the female reproductive tract.

Following the identification of D(−)-lactic acid as a metabolite, we turned our attention to the possibility that the octopus spermatozoa may also contain a D(−)-lactate dehydrogenase. We have, therefore, examined the dehydrogenase activity of aqueous, centrifuged extracts made from homogenized spermatozoa, using an assay system composed of either reduced nicotinamide adenine dinucleotide (NADH) and pyruvic acid, or NAD in combination with either L(+)-, D(−)-, or DL-lactic acid. We were able to demonstrate that the sperm extracts contain a highly active D(−)-lactate dehydrogenase, namely, about 50,000 enzyme units per 10^9 spermatozoa, and that they are capable of both reducing pyruvic acid in the presence of NADH as well as oxidizing D(−)- and DL-lactic acid, but not L(+)-lactic acid, in the presence of NAD. On electrophoretic examination, most of the D(−)-lactate dehydrogenase was found to migrate as a band in a position quite distinct from the multi-isozyme pattern of the L(+) enzyme.

Oxamic acid ($10^{-3}M$), a well-known inhibitor of L(+)-lactate dehydrogenase (*6*), had no effect on the D(−)-lactate dehydrogenase of spermatozoa. The *p*H optimum of the sperm enzyme, examined in a system consisting of D(−)-lactic acid and acetylpyridine-NAD, was above 9, which is nearer to the *p*H optimum of the D(−)-lactate dehydrogenase from *Lactobacillus* (*7*) than to that of the L(+)-lactate dehydrogenase prepared from beef heart or skeletal muscle.

The following conclusions may be drawn from the above observations. The lactic acid produced anaerobically by the spermatozoa of *O. dofleini martini*, is D(−)-lactic acid, as we have been able to prove by using a combination of chemical and enzymatic assay methods for the purpose of identification and determination. We would have missed this interesting fact had we relied solely on the conventional L(+)-lactate dehydrogenase assay method. We have shown, moreover, that the octopus spermatozoa possess a highly active, stereospecific, NAD-dependent D(−)-lactate dehydrogenase, which in some properties resembles the D(−)-lactate dehydrogenase of certain microorganisms, but clearly differs from the L(+)-lactate dehydrogenase commonly encountered in animal tissues and body fluids.

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Probable Fijian Origin of Quartzose Temper Sands in Prehistoric Pottery from Tonga and the Marquesas

Abstract. *Quartzose temper sands included within fired clay bodies of certain prehistoric potsherds from Tonga and the Marquesas have mineralogical compositions wholly different from those of indigenous sands that occur as temper in other potsherds from the same sites but are indistinguishable from sands in potsherds collected from the Rewa Delta of Viti Levu in Fiji.*

Men who travel in boats leave no footprints but may transport with them geologically identifiable artifacts that bear a record of their origins. This fact is significant for reconstructing the migration paths of early islanders across the Pacific. We have traced unusual temper sands in prehistoric potsherds from Tonga in western Polynesia and from the Marquesas in eastern Polynesia to an apparently common source in Fiji (Fig. 1a).

Small islands in the western and southern Pacific are virtual point sources of sand (*1*). On each island, sands available for collection as temper for the manufacture of earthenware by insular potters have restricted mineralogical compositions governed by the limited range of rock types exposed. The limited compositional range prevails across a spectrum of textural types including littoral beach deposits, alluvial and colluvial sands, ash beds, and diverse placers (*2*). The varied tectonic settings of different archipelagoes also allow classification of the potential tempers from various island groups into general categories within which the character of indigenous