# Social and Environmental Influences on Blood Serotonin Concentrations in Monkeys

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• **Dominant male adult vervet monkeys have whole-blood serotonin concentrations approximately twice those of subordinate adult males. We examined the effects of spontaneous and induced changes in social status, temporary isolation from the social group, and membership in single male groups on whole-blood serotonin concentrations. We found that in male vervet monkeys, elevated blood serotonin concentration is a state-dependent consequence of active occupation of the dominant male social position, and we believe that a reinterpretation of the significance of hyperserotonemia in humans may be warranted.**

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Biologic studies in psychiatry are often restricted to the examination of peripheral tissues. Consequently, whether and how abnormalities in these tissues reflect CNS function are of considerable importance. A peripheral measure of interest to psychiatric researchers is blood serotonin because alterations in its concentration have been reported in a variety of disease states. Hyperserotonemia has been observed in a substantial subset of autistic children,[1,2] mentally retarded persons without aminoacidemias,[3] and chronic schizophrenics in whom the elevation can be associated with enlarged ventricles.[4] Because blood serotonin concentration is dependent on peripheral tryptophan metabolism and platelet physiology, its elevation in different clinical populations may result from diverse mechanisms. As with any clinical variable, studying the mechanisms underlying hyperserotonemia in different disease states may be more revealing than the observation of its association with a variety of diseases.

The relationship between blood and brain serotonin levels has yet to be fully specified. Under some conditions, changes in blood serotonin levels parallel changes in brain serotonin levels. For example, both are similarly affected by pharmacologic interventions that augment precursor availability (eg, tryptophan loading[5,6]), that inhibit biosynthetic enzymes (eg, *p*-chlorophenylalanine treatment[7]), that disrupt serotonin storage (eg, fenfluramine hydrochloride administration[8-10]), or that alter enzymes catalyzing serotonin degradation (eg, treatment with the monoamine oxidase inhibitor clorgyline[11]). However, in other conditions such as carcinoid syndrome, blood and brain serotonin levels do not appear to be associated.[3] Furthermore, because blood serotonin is stored exclusively in platelets, an association between blood and brain serotonin levels would not necessarily be expected in diseases of platelet physiology.[12,13]

An important issue in assessing the significance of hyperserotonemia is whether its incidence is trait or state dependent. In normal men, blood serotonin concentrations are remarkably stable over long periods of time (up to ten years[13]). This observation suggests that blood serotonin concentrations are trait dependent. Among autistic children, blood serotonin levels exhibit somewhat more intraindividual variability, although this variation may be largely due to maturational changes.[2] In partial contrast, there are reports that in Huntington's chorea[14] and motor neuron disease,[15] blood serotonin levels are state dependent and in motor neuron disease, correlate with the severity of the clinical condition. Alterations in blood serotonin concentrations also appear to be associated with the onset of migraine attacks.[16] Interpretation of these studies is complicated in part because they are largely cross sectional across populations rather than longitudinal within subjects. Nevertheless, they are compatible with the view that blood serotonin concentrations can be state as well as trait dependent.

While investigating the contributions of serotonergic mechanisms to the mediation of overt social behavior in captive groups of adult vervet monkeys (*Cercopithecus aethiops sabaeus*), we examined the behavioral effects of tryptophan, 5-hydroxytryptophan, *p*-chlorophenylalanine, and the monoamine oxidase inhibitor clorgyline, alone and in combination.[17] To verify the effectiveness of these pharmacologic interventions, we measured blood serotonin levels before, during, and after drug treatment. We noted

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Table 1.—Group Types and Housing Conditions

| Study | Housing | No. of Groups | Adult Males/Group | Comments |
|---|---|---|---|---|
| 1 | Stable multimale | 10 | ≥3 | . . . |
| 2 | Spontaneous dominance changes | 4 | 3 | Previously used in study 1 |
| 2 | Behaviorally manipulated multimale | 9 | 3 | One group excluded from analysis |
| 3 | Multimale, dominant and subordinate isolated | 7 | 3 | Subjects isolated without visual contact with group members |
| 3 | Multimale, dominant and subordinate isolated | 3 | 2 | Subjects isolated with visual contact with group members possible |
| 4 | Single male | 4 | 1 | . . . |

that prior to drug treatment, in each of six groups, one male had blood serotonin levels about twice those of the other males. In each group this male was identifiable behaviorally as the dominant male. Subsequently this association between dominant male social status and high blood serotonin concentration was confirmed in 11 additional stable multimale groups.[18] In groups of captive vervet monkeys, male social status may be manipulated behaviorally. Removal of the original dominant male leads to the emergence of another behaviorally defined dominant male.[19] Return of the original dominant male within ten weeks of his removal results in the interim dominant male resuming his original subordinate position. Thus, the trait or state dependency of the association between dominant male social status and an elevated blood serotonin level in vervet monkeys may be determined experimentally. In this article, we report on the intraindividual stability of blood serotonin concentrations among adult male vervet monkeys in multimale social groups under conditions of stable status relationships, and on the effects of a variety of socioenvironmental influences on blood serotonin concentration. Our investigations on the mechanisms underlying the elevated blood serotonin levels in dominant vervet monkeys will be reported elsewhere.

## SUBJECTS AND METHODS

### Subjects

The subjects were adult male vervet monkeys. All were ferally reared, had fully erupted canines, were free of diarrhea and other diseases, weighed between 5.4 and 8.5 kg, and had been in captivity for at least five months prior to the onset of the present studies. They were maintained on isoniazid-free commercial monkey chow supplemented once or twice weekly with fresh fruit. Chow and water were available ad libitum.

As shown in Table 1, four studies were conducted using subjects housed in the following six conditions: stable multimale groups (study 1); multimale groups in which spontaneous shifts in dominance occurred (study 2); behaviorally manipulated multimale groups (study 2); multimale groups from which the dominant and a subordinate male were temporarily isolated (study 3); multimale groups from which the dominant male was temporarily isolated (study 3); and stable single-male groups (study 4). Ten stable multimale groups were used in study 1. They lived in indoor-outdoor enclosures ranging in size from $4 \times 3 \times 2$ m to $30 \times 24 \times 3$ m. Each of these groups contained three or more adult males, three or more adult females, and their immature offspring. Four of these groups subsequently had spontaneous shifts in dominance relationships and were used in study 2. This study also used nine behaviorally manipulated groups, each of which originally contained three adult males and three adult females. These groups were housed in $4 \times 3 \times 2$-m enclosures. One part of study 3 used seven multimale groups from which the dominant and one subordinate male were simultaneously isolated. When isolated, these 14 animals were housed individually in $3 \times 2 \times 1$-m cages and were unable to see or be seen by members of their original groups. All of these seven groups contained three or more adult males, two or more adult females, and their offspring. One of these groups was originally used as one of the ten stable multimale groups. Study 3 also used three other multimale groups from which the dominant male was temporarily isolated in an individual cage containing a one-way mirror that enabled him to see but not be seen by members of his group. These three groups originally contained at least two males, two females, and their offspring. In study 4, four single-male groups each containing three or more adult females were used. After the male was added to these groups, no changes in group composition occurred.

Table 2.—Behavioral Repertoire

| Behavior | Reliability | Description |
|---|---|---|
| Threaten | 0.89 | Jerking head, opening mouth, staring, retracting ears, lunging toward |
| Contact aggress | 0.93 | Slapping, pushing, pulling fur, biting |
| Display | 0.86 | Exaggerated bouncing, circling movement with tail over back; jerking penis in sagittal plane |
| Avoid | 0.94 | Retreating from threat, turning or moving away |
| Submit | 0.86 | Squealing, screaming, hopping backward, pawing ground |
| Be vigilant | 0.94 | Scanning environment outside enclosure, shaking fence with rigid tense posture, threatening neighboring groups |

### Methods

**Social Status.**—In the stable and behaviorally manipulated multimale groups, the behaviors described in Table 2 were recorded. Social status was assessed by noting the subject's success in dyadic intermale aggression. Subject A was regarded as successful in a dyadic agonistic encounter with subject B if B submitted to or avoided A when A threatened B, displayed to B, or engaged in contact aggression with B. In each group the male with the highest percentage of success in intermale dyadic encounters was regarded as the dominant male. All remaining adult males were regarded as nondominant or subordinate. In these studies, the only behavioral distinction made was between the dominant male and the subordinate males. No attempt was made to rank order the subordinate males. Every dominant male won at least 91% of his dyadic intermale agonistic encounters with outcomes, and no subordinate male won more than 48% of his dyadic agonistic encounters. For all groups, intergroup vigilant behavior was scored.

**Interrater Reliability.**—Interrater reliability was measured before and during the present studies, as described in detail elsewhere.[20] Briefly, for the six behaviors (threatening, displaying, engaging in contact aggression, submitting, avoiding, and being vigilant) recorded in these studies, interrater reliability between

observer A and observer B was assessed by dividing the number of times a behavior was scored by both observers by the number of times it was scored by either one or both. As indicated in Table 2, for all behaviors, interrater reliability was at least 86%.

**Blood Collection Procedures.**—Subjects were deprived of fruit for at least 48 hours and fasted overnight prior to blood collection. Subjects were rendered tractable with an intramuscular 7- to 12-mg/kg dose of ketamine hydrochloride (a procedure that does not affect blood serotonin concentration), and blood samples were obtained by femoral venipuncture within 15 minutes of ketamine administration.[21] Two to four milliliters of blood was collected into a sterile plastic syringe, immediately transferred to a tube containing edetic acid, inverted, and stored on ice. Within 90 minutes of collection, blood samples were transferred from the edetic acid tubes to polypropylene tubes and frozen either at −70 °C or in liquid nitrogen until assayed one to four months later. Neither circadian nor seasonal rhythms in whole-blood serotonin concentration have been observed in vervet monkeys,[21] and in our study all blood samples were obtained between 6:30 and 8:00 AM.

Blood serotonin concentration was determined by the fluorimetric method of Yuwiler et al.[22] All samples were run in duplicate on 0.7 to 0.9 mL of whole blood. An intra-assay coefficient of variation was ascertained on five occasions. Each intra-assay coefficient of variation was based on six determinations of a pool (mean, 780 ng/mL), and the mean intra-assay coefficient of variation was 1.7% (range, 1.4% to 2.3%). An interassay coefficient of variation was determined by measuring the same pool on six different assay runs. The interassay coefficient of variation was 1.8%. Recoveries were determined by adding known amounts of serotonin creatinine sulfate to blood samples at the time of collection. The mean recovery rate for ten such additions was 99% (range, 95% to 102%). Because of the high recovery rate, the reported blood serotonin concentrations are uncorrected values.

**Experimental Design and Data Analysis.**—Four studies were completed. Study 1 assessed the intraindividual stability of blood serotonin concentrations in behaviorally stable multimale groups. Blood serotonin concentration was measured in 33 males living in ten groups. For each subject, blood serotonin concentrations were determined on at least five occasions. For every animal, consecutive samples were obtained at least 11 days apart, and samples were obtained over a minimum of 90 days (mean, 128 days). The intraindividual stability was determined by obtaining intraindividual Pearson product-moment correlations between the separate sample points (eg, first-second, first-third, second-third) and by calculating intraindividual coefficients of variation across the five sample points.

Study 2 assessed the effects of spontaneous and induced changes in social status on blood serotonin concentrations. In one part of these studies, four previously stable multimale groups (of study 1) underwent a spontaneous alteration in social status. A formerly dominant male became subordinate and a formerly subordinate male became dominant. Blood serotonin concentrations were measured at least four times before and three times after these status changes. The effects of these status changes on blood serotonin level were assessed by a two-group (formerly dominant and formerly subordinate) by two-condition (before and after status change) analysis of variance (ANOVA) with repeated measures.

In the other part of study 2, changes in social status were experimentally elicited in the nine groups by the removal and return of the original dominant male. These groups were observed for a 70-day baseline period, a 60- to 70-day period after removal of the original dominant male from the group, and a 50- to 65-day reunion period after the original dominant male had been returned. During the removal period, in each group, one of the two formerly subordinate males became dominant. In eight of nine groups, this interim dominant male resumed his subordinate position in the reunion period. In the ninth group this initially subordinate male remained dominant in the reunion period. Data from this ninth group were excluded from analysis. The other nine originally subordinate males remained subordinate in all periods. For each animal, blood serotonin concentration was measured at least five times in each period. The effects of this gain (from subordinate to dominant) and loss (from interim dominant to subordinate) of status on blood serotonin concentration were assessed by a two-group (always subordinate and interim dominant) by three-condition (baseline, removal, and reunion) ANOVA with repeated measures.

During the removal period of study 2, the nine originally dominant males were divided into three groups of three males each, and each group was combined with a previously formed group of three females. Six of the nine originally dominant males (two from each group) became subordinate. On return to their original groups, eight of these nine animals regained their dominant status. Only data from these eight groups are reported. The effects of this loss of and subsequent gain in status on blood serotonin concentration were assessed by a two-group (always dominant and interim subordinate) by three-condition (baseline, removal, and reunion) ANOVA with repeated measures.

Study 3 examined the effects of temporary isolation on blood serotonin levels. In one part of this study, the dominant and a subordinate male from seven groups were isolated without visual access to their groups for 21 to 28 days. These animals were subsequently returned to their groups. Blood serotonin concentration was measured at least twice before isolation, three times during isolation, and twice after return to their groups. The effects of this temporary isolation were assessed in a two-group (dominant and subordinate) by three-condition (before, during, and after isolation) ANOVA with repeated measures. In the other part of this study, three dominant males were isolated from their groups for 16 days. When isolated, the animals had visual access to their groups through a one-way mirror and were able to initiate displays and threats to other group members. Blood serotonin was measured before, six times during, and after isolation. The effects of this isolation treatment on blood serotonin concentration were assessed by comparing these animals with three dominant males who remained in their groups. Data were analyzed by a two-group (temporarily isolated and remaining in group) by three-condition (before, during, and after isolation) ANOVA with repeated measures.

Study 4 examined the effects of membership in a one-male group on blood serotonin concentrations. Each of four males who had been dominant in multimale groups was placed in a previously formed group of three adult females. Subjects were the only adult male in these groups for at least 60 days, and for each subject blood serotonin concentration was measured at least three times before the subject became a member of a one-male group and five times when it was a member of the one-male group. The effects of being in a one-male group were assessed by a paired $t$ test.

## RESULTS

### Study 1

Whole-blood serotonin concentrations in subjects living in stable multimale groups exhibited little intraindividual variation. For no subject did whole-blood serotonin concentration vary more than 19% between any two sample points, and for each of the 33 subjects, all sample values were within 12% of the mean. This intraindividual stability was reflected in the low intraindividual coefficient of variation across the five sample points (mean, 6.1%; range, 2.2% to 9.6%) and, as shown in Table 3, by the high intrasubject Pearson product-moment correlation across all pairs of sample points ($r \geq .91$ for all pairs of sample points).

### Study 2

In four groups used in study 1, a spontaneous change in dominance relationships occurred. Prior to this change the initially dominant males won about 95% of their dyadic intermale aggressive encounters (range, 92% to 100%). After this change, the new dominant males won a similar percentage of such encounters (range, 91% to 98%). As shown in Table 4, the transition from subordinate to dominant position was accompanied by a rise in whole-blood serotonin concentration, while concentrations in the four initially dominant males that became subordinate declined. There was a significant interaction between status (initially dominant or initially subordinate) and time (before or after dominance shifts) ($F[1,6] = 85.37$, $P < .001$). During the periods of social stability both before and after the dominance shifts occurred, blood serotonin concentrations showed marked intraindividual stability (intrasubject Pearson product-moment correlations both before and after dominance changes in these eight animals were $r \geq .95$, $n = 8$, $P < .05$).

Table 3.—Intra-animal Stability of Whole-Blood Serotonin Concentration*

| | Sample Time | | | |
|---|---|---|---|---|
| | 1st | 2nd | 3rd | 4th |
| 2nd | 0.96 | . . . | . . . | . . . |
| 3rd | 0.92 | 0.97 | . . . | . . . |
| 4th | 0.93 | 0.91 | 0.95 | . . . |
| 5th | 0.91 | 0.92 | 0.93 | 0.95 |

*Intra-animal Pearson product-moment correlations across the five sample times (n = 33, $P<.001$ for all pairwise comparisons).

Table 4.—Spontaneous Dominance Changes and Whole-Blood Serotonin Concentrations*

| | Serotonin Concentration, ng/mL | |
|---|---|---|
| Initial Role | Before | After |
| Dominant | 950 ± 20 | 506 ± 64 |
| Subordinate | 674 ± 54 | 933 ± 57 |

*Serotonin concentrations were determined before and after spontaneous shifts in dominance in four initially dominant and four initially subordinate males. Data are expressed as mean ± SEM.

Table 5.—Effects of Induced Changes in Social Status on Whole-Blood Serotonin Concentration of Initially Subordinate Males*

| | Serotonin Concentration, ng/mL | | |
|---|---|---|---|
| Group | Baseline | Removal | Reunion |
| Always subordinate | 608 ± 81 | 593 ± 71 | 588 ± 69 |
| Interim dominant | 654 ± 40 | 1,059 ± 68† | 617 ± 39 |

*Serotonin concentrations were based on the mean of each animal for each period. Each cell represents the mean concentration (± SE) for the eight animals in each group.
†$P<.01$ compared with other cells by Scheffe's test.

Table 6.—Changes in Social Status and Whole-Blood Serotonin Concentration in Initially Dominant Males*

| | Serotonin Concentration, ng/mL | | |
|---|---|---|---|
| Group | Baseline | Separation | Reunion |
| Always dominant | 980 ± 63 | 999 ± 71 | 956 ± 37 |
| Interim subordinate | 1,019 ± 48 | 598 ± 43† | 1,010 ± 46 |

*Serotonin values are based on the mean of each animal's values for each period. Each cell represents the interanimal mean concentration (± SE) for each period for the three always-dominant or the five interim-subordinate subjects.
†$P<.01$ compared with other cells by Scheffe's test.

As shown in Table 5, similar changes in whole-blood serotonin concentration occurred in the eight groups in which dominance relationships were experimentally altered. Concentrations in each of the three periods (baseline, removal, and reunion) exhibited little intraindividual variation (intraindividual $r \geq .92$, n = 16, $P<.01$ for each period). Accordingly, the effects of the induced status change on serotonin concentration were assessed by using each subject's mean concentration for each period. After removal of the initially dominant male, one of the two initially subordinate males became dominant. When dominant, these males were behaviorally indistinguishable from the initially dominant males. They won about 94% of their intermale aggressive encounters and were vigilant at the same rate as the initially dominant males. In the reunion period these animals resumed their subordinate positions after reintroduction of the initially dominant male. The other eight initially subordinate subjects (one per group) remained subordinate throughout all three periods. As Table 5 shows, blood serotonin concentrations in the eight subjects who became dominant in the removal period increased about 60%. In contrast, blood serotonin concentrations were unchanged in those animals that had remained subordinate. The interaction between status (always subordinate or initially dominant) and period (baseline, removal, reunion) was significant ($F[2,28] = 31.82$, $P<.001$).

Comparable alterations in blood serotonin concentration were shown by the initially dominant subjects in these eight groups. As Table 6 shows, three of these subjects were dominant in all periods and they had unchangingly high concentrations of blood serotonin. The five males that became subordinate during the removal period manifested a parallel 40% decline in blood serotonin concentration. The interaction between status (always dominant and interim subordinate) and period (baseline, removal, and reunion) was significant ($F[2,12] = 23.47$, $P<.001$).

### Study 3

Figure 1 shows the effects of temporarily isolating seven dominant and seven subordinate males from their social groups for 30 days. When the animals were caged individually without visual or tactile contact with members of their groups, the whole-blood serotonin concentrations of the dominant males declined to about 53% of their preisolation levels. On return to their social groups, the temporarily isolated dominant males regained their dominant position and their mean blood serotonin concentration (± SEM) rose from 545 ± 56 ng/mL to 1,036 ± 69 ng/mL. In contrast, the whole-blood serotonin concentrations of the subordinate males were unaltered by temporary isolation ($F[6,72] = 36.58$, $P<.001$ for the interaction between dominant or subordinant states and sample time).

The effects of temporary isolation were examined in three other dominant males. These animals could see, but could not be seen by, their group members. During their 16-day isolation these subjects threatened and displayed to, but received no responses from, their group members. As shown in Fig 2, these isolated males exhibited about a 40% decline in blood serotonin concentration. After returning to their groups, these animals regained their dominant positions, and their blood serotonin levels returned to preisolation levels. Blood serotonin concentrations in three dominant males that remained in their groups were unaltered. The interaction between housing (isolated or not isolated from group) and sample time was significant ($F[7,28] = 12.63$, $P<.001$).

### Study 4

The effects of living in a one-male group on the whole-blood serotonin concentration were assessed in four subjects that previously had been dominant in multimale groups. As shown in Table 7, in the single-male groups these subjects continued to engage in intergroup vigilant behavior at the same rate as when they were in multimale groups but obviously were not submitted to or avoided by other male group members. These subjects showed little intraindividual variability in blood serotonin concentration either when in their multimale groups (average intra-animal coefficient of variation, 3.5%; range, 2.2% to 5.1%) or when in the single-male groups (mean coefficient of variation, 3.8%; range, 2.5% to 6.0%). Consequently, the effects of living in a one-male group were assessed by using each subject's mean blood serotonin concentration for each living condition. Living in a one-male group resulted in a significant decline in mean blood serotonin concentration (± SEM) from 998 ± 41 ng/mL to 606 ± 51 ng/mL ($t = 14.9$, $df = 3$, $P<.001$ for correlated samples).

### COMMENT

These results indicate that, in adult male vervet monkeys, whole-blood serotonin concentrations can be influenced by social and environmental factors. In both single-male or multimale groups, whole-blood serotonin

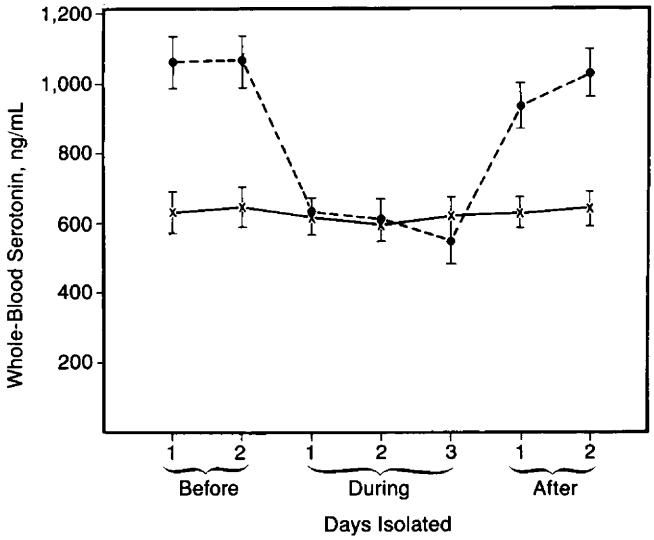


Fig 1.—Effect of temporary isolation without visual access to subject's social group on whole-blood serotonin concentrations. Dots indicate seven dominant males, and x, seven subordinate males. Data are expressed as mean ± SEM.

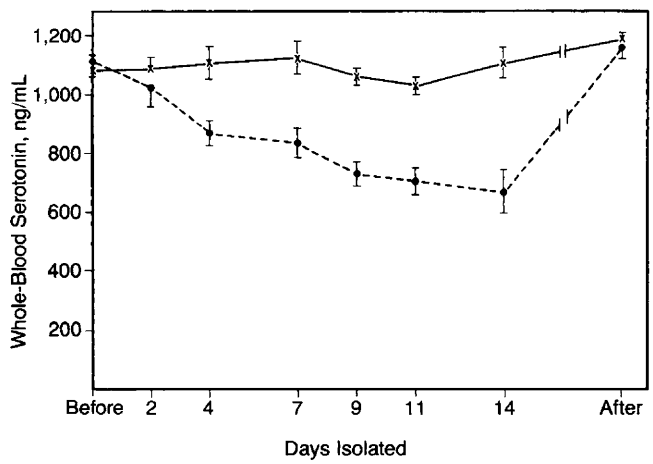


Fig 2.—Effect of temporary isolation with visual access to subject's social group on whole-blood serotonin concentrations. Dots indicate three isolated dominant males, and x, three dominant males remaining in groups. Data are expressed as mean ± SEM.

concentrations show little intraindividual variation as long as dominance relationships are stable. Dominant males have substantially higher whole-blood serotonin concentrations than do subordinate males or males living in single-male groups. Spontaneous and induced gains or losses in social status are accompanied by corresponding increases or decreases in whole-blood serotonin concentrations. Temporary isolation, with or without visual access to group members, reduces whole-blood serotonin concentrations in dominant males to levels exhibited by subordinate males. Males in single-male groups continue to engage in intertroop vigilant behavior, and temporarily isolated males continue to threaten and display to their group members. The elevated blood serotonin concentrations exhibited by dominant males therefore are probably contingent on both initiating aggressive and receiving submissive behavior from other adult male group members. In any case, among

Table 7.—One-Male Groups and Whole-Blood Serotonin Concentrations*

| | Group | |
|---|---|---|
| | Multimale | Single-Male |
| Status | Dominant | . . . |
| Vigilance, events/hr | 5.5 ± 0.8 | 6.1 ± 0.9 |
| Serotonin concentration, ng/mL | 998 ± 41 | 606 ± 51 |

*Four males that were dominant in multimale groups were transferred to groups containing three females. Vigilance behavior was unchanged but serotonin concentrations declined significantly ($P<.001$ for correlated $t$ test). Data are expressed as mean ± SE.

male vervet monkeys, elevated blood serotonin concentration is, at least in part, a state-dependent consequence of active occupation of the dominant male social position.

The biologic mechanisms underlying the linkage between blood serotonin concentration and social status are currently unknown. Whole-blood serotonin is largely derived from intestinal tryptophan metabolism and is contained in platelets that vary in size, number, serotonin uptake, and serotonin storage capacities.[12,23,24] The differences in blood serotonin concentration between dominant and subordinate males might thus be due to alterations in tryptophan metabolism or platelet physiology. The extent to which any of these factors is susceptible to the hormonal and physiologic concomitants of dominant social status is unknown. Preliminary data indicate that the status-related differences in blood serotonin concentration observed in these studies are not due to differences in serum or plasma tryptophan concentration, platelet number, platelet size, or platelet monoamine or plasma amine oxidase activities. However, relative to subordinate males, dominant males appear to exhibit a much greater relative and absolute rise in whole-blood serotonin concentrations following an acute (20 mg/kg) tryptophan load. This observation suggests that there may be a status-related difference in tryptophan hydroxylase activity. An increased peripheral uptake and conversion of tryptophan in the hyperserotonemia of autism and schizophrenia was suggested by Freedman et al.[24]

Previous investigations of the impact of social status on peripheral physiologic variables in nonhuman primates have focused on cortisol and testosterone concentrations. However, the relationship between these measures and male social status is controversial. For example, basal cortisol concentrations have been observed to be both positively and negatively correlated with male dominance.[25-28] These apparent inconsistencies may result, in part, from methodologic differences in determining social status or from differences in housing conditions.[29] Nevertheless, the lack of a convincing relationship between these variables and dominance may also be due to the extreme intraindividual variability in these measures. Cortisol and testosterone are released in a pulsate fashion and exhibit circadian and circumannual rhythms.[30-34] In Old World monkeys, twofold to fourfold intra-animal variation in concentration in samples collected within 24 hours is common. This intra-animal variation in cortisol and testosterone levels contrasts with both the intraindividual stability of the whole-blood serotonin concentration and the persistent and consistent nature of dominance relationships in captive vervet monkeys. Among captive vervet monkeys, although the rate of intermale agonistic encounters may vary daily, the pattern of outcome is strikingly stable over long periods of time. Whether the association between whole-blood

serotonin concentrations and male dominance generalizes to free-ranging vervets, to other species where dominance relationships shift more frequently, or to species with clear linear dominance hierarchies has yet to be determined. Nevertheless, recording the specific biologic and behavioral processes that account for the elevated blood serotonin concentrations exhibited by captive dominant male vervet monkeys is of interest in providing a model for investigating the mechanisms underlying hyperserotonemia. In addition, to the extent that blood and brain serotonin are related, vervet monkeys may be useful in defining the impact of social status on central serotonergic function. This potential relationship is being explored by measuring CSF 5-hydroxyindoleacetic acid (5-HIAA) level in basal conditions and following administration of probenecid with and without tryptophan loading.

The influence of social status and other socioenvironmental factors on blood serotonin concentration in humans has not been studied but may have clinical relevance. Our findings that blood serotonin concentration is correlated with a behavioral state suggest that the association between shifts in blood serotonin concentrations and clinical conditions in diseases such as Huntington's chorea, motor neuron disease, and bipolar depression needs to be investigated. However, conducting such studies in humans requires a more detailed characterization of human social status than is usually available. One of the characteristics of human societies is that each person is entwined in many social groups and many simultaneously occupy several dominant and subordinant status positions. Indeed, social influences on blood serotonin concentrations may be detectable only following major changes in life situations such as retirement, job demotion, extended personal crisis, or the assumpton of leadership in a small, relatively closed group. We are currently studying some of these situations.

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