BIO-PSYCHOLOGICAL INFLUENCES OF AIR IONS IN MEN:

EFFECTS ON 5-HYDROXYTRYPTAMINE (5HT) AND MOOD

by

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ABSTRACT

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Air ions are naturally occurring meteorological phenomena which can be recreated in the laboratory. They have effects at levels of biological system organization from the cell membrane to the community member. Diverse mechanisms have been postulated to account for the biological activity of air ions: one of these, the serotonin (5HT) hypothesis, is of especial importance. It is stated as follows: positive air ions release 5HT from tissue stores and negative air ions accelerate its oxidation.

Serotonin is a neurotransmitter that has been implicated in changes in affective state. The specific aims of this study were to examine some of the biochemical and psychological effects of air ions in men and to consider the mechanism(s) by which they exert their influence. The main issues were to:

1) examine the effects of positive and negative air ions on mood

(assessed by the Profile of Mood States [POMS] adjective check list).

2) examine the effects of positive and negative air ions on 5HT as indicated by urinary 5HIAA, a major product of 5HT catabolism, and on urine volume.

Sub-issues explored were:

1) charge specificity of ion effects.

2) the time-course of ion-related events.

3) subject selection.

Thirty-three volunteer men, who were selected for self-reported mood lability, "weather-sensitivity" and/or minor health problems were exposed to air ions under the following conditions: thirty minutes of ambient ions (ca 2-300 ions/cc); two hours of positive (or negative) air ions (ca 100,000 ions/cc); two hours of negative (or positive air ions; then 30 minutes of ambient ions. Control subjects were exposed to ambient air ions for five hours (positive/negative [N = 13]; negative/positive [N = 13]; ambient control [N = 7]). Subjects were randomly assigned to treatment or control groups. Mood and urine measures were obtained at 15 minute intervals throughout the five hour session.

Statistical analyses were performed on each of 10 mood and urinary dependent variables. Comparisons across experimental groups were performed separately for the AM and PM data. There were planned contrasts for treatment vs control and positive vs negative comparisons.

The results of the main issues were:

1) Analyses of covariance (ANCOVA) comparing groups means revealed

differences between the treatment groups and the control groups for the POMS mood indicators Vigor and Friendliness in the AM (P = 0.037; P = 0.046). Repeated measure analyses of variance (ANOVA) for Group x Time interactions revealed a difference in slope between the treatment vs control groups for POMS Vigor and Friendliness in the AM (P = 0.002; P = 0.014). Repeated measure ANOVAs by group showed that the difference in slope was due to a significant negative trend for the control group and no linear trend for the treatment groups (Vigor, P = 0.033; Friendliness, P = 0.043). The treatment vs control differences in group means observed for Vigor and Friendliness in the AM were enhanced in the PM: the treatment subjects reported higher mean levels of Vigor and Friendliness while the control subjects' reports remained low. The effects on slope for Vigor and Friendliness were not observed in the PM as the control group which showed a negative linear trend in the AM remained down in the PM.

2) The results of the ANCOVAs comparing group means revealed that for AM periods the amount of urinary 5HIAA was higher in the control subjects' urine than in the treatment groups' (P = 0.021). The treatment vs control group mean differences were not found in the PM urines. However, a significant PM difference between treatment vs control groups means was shown for the volume of urine (higher in the control subjects (P = 0.026). The results of the repeated measure ANOVAs for Group x Time interactions revealed a difference in slope between the treatment vs control groups for 5HIAA concentration and amount of 5HIAA in the PM

(P = 0.032; P = 0.016). Repeated measure ANOVAs by group for concentration showed positive linear time trends for the treatment groups and no linear trend for the control group (positive ions, P = 0.013; negative ions, P = 0.066). All groups showed an increase in the amount of 5HIAA: the treatment vs control group contrast for slopes was, however, significant (P = 0.021).

Significant differences between treatment and control groups were found for the mood indicators Vigor and Friendliness: the control groups reported significantly less Vigor and Friendliness over time. Urinalyses showed significantly higher amounts of 5HIAA in the AM and urine volume in the PM, for control vs treatment subjects. These data demonstrate a bio-psychological influence of air ions in human subjects. The results of this study are significant for a given dose and population. Different and/or charge related effects may be evident at dose levels approaching the environmental norm.

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†Santek, Inc., Hollywood, Florida (formerly Klykon); manufacturers of ion generating and measurement equipment

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I. OVERVIEW: EXAMPLES OF ION EFFECTS AND MECHANISMS OF ACTION

Air ions are part of the atmospheric envelope surrounding the earth. They have effects at levels of biological system organization from the cell membrane to the community member. The accelerated plant growth induced by ions of either charge is an example of air ion effects at the cellular level. The growth is explained as the result of an ion-induced increase in cytochrome C (cytochrome C is an important compound for cellular respiration). An example of air ion effects at the tissue level involves the trachea. In living and in vitro preparations, positive air ions decreased the efficiency of tracheal clearing mechanisms used to clean debris from inspired air: cilia beats and mucosal flow were slowed; blood vessels in the tissue were easily ruptured. The latter effect could cause tissue damage during coughing to clear clogged air passages. Negative air ions reversed the effects of positive ions on the clearing mechanisms and have been used therapeutically to ameliorate respiratory distress in asthmatic people. Air ion therapies have also been used to treat other disorders such as migraine headaches, anxiety neuroses and gastritis.

Diverse mechanisms of action have been proposed to account for the varied influences of air ions. Generally a single mechanism is proposed for a given level of system organization. Thus, the increase in cytochrome C is said to account for accelerated plant growth. The relatively

simple explanation is sufficient to account for the effect: the explanation has intralevel consistency. Where cells are organized into tissue, such as in the trachea, serotonergic mechanisms are implicated. Serotonin (5HT) transmits information among some cells organized into tissue. It is also a vasoconstrictor. It is the latter action of 5HT that is invoked to account for tissue vulnerability to mild mechanical trauma such as a cough. Serotonin is present at the level of system organization studied, tissue, and the proposed mechanism of action is consistent with some of its known effects.

However, when air ion studies are conducted at higher* levels of system organization, single mechanisms may or may not suffice to account for their influence. Since higher levels incorporate membrane, cell, tissue, organ, etc. components, the possible hierarchical ordering of the different mechanisms of air ion action must be considered. For instance, it is not known whether the mechanism(s) underlying the 5HT effect in tissue is cytochrome dependent. Cytochromes are present in some tissues where 5HT is found and the oxidation of 5HT is cytochrome linked. Does one effect "cause" the other; or do they operate with relative independence?

A few researchers have studied the effects of air ions on two or more response indicators at the same time. Olivereau (1971a) studied the effects of air ions on brain tissue, adrenal weights and electrolyte

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*The terms higher and complex or more complex are used to denote systems which incorporate smaller unit components of other systems. For a good discussion of levels of system organization see Wimsatt, 1976.

(NaCl and KCl) consumption in hundreds of rats. He found air ions affected each level of system organization (tissue, organ, behavior). The mechanism(s) of action hypothesized involved the antidiuretic hormone (ADH). ADH is part of a complex homeostatic process for balancing water and mineral metabolism. If an animal is in a water-deprived state, the need for fluids is signalled at some level or levels that will induce behaviors sufficient to satisfy the need. Olivereau also reported effects of air ions on 5HT in the blood and brains of these same or similarly treated rats.

Did the 5HT effects "cause" the ADH effects, or vice versa? were they independently influencing the same operant behaviors? in combination, etc.? Any hypothesis that implied linear signal systems from the cellular to behavioral levels of response is probably too simplistic. Though the order of events has not been specified, it is known that water and mineral metabolism is kept in balance by several feedback loops and there is evidence that both 5HT and ADH are involved.

Gilbert's (1971) work is another example of research carried out to study the effects of air ions on more than one response indicator at the same time. In his investigation, emotionality and 5HT content in rat brains were examined. Gilbert found that exposure to negative air ions reduced the rats' levels of emotionality as well as the content of 5HT in the brain. Whether the ion effect on brain 5HT had anything to do with ion effects at other levels of system organization where 5HT is localized is not known. Though studies such as this are complex, they

are of particular interest to some scientists because they test hypotheses that cross disciplinary lines. That is, air ions may influence one or more pools of 5HT (a biochemical effect), they may influence emotionality (a psychological effect), they may influence 5HT and emotionality in combination or independently (a bio-psychological effect). The complexity of interpretation of Olivereau's and Gilbert's work demonstrates that: 1) at complex levels of system organization, more than one mechanism of air ion action may be operating; and 2) the sequence of causality among the mechanisms hypothesized cannot be implicitly assumed.

One mechanism that accounts for much of the data in the field of air ion research involves 5HT. It is invoked as the mechanism underlying effects at several levels of system organization. Some effects of air ions on 5HT are described by the serotonin hypothesis: positive air ions release 5HT from tissues and negative air ions speed up its oxidation. Serotonin appears to have an important role in mental processes, although the details are not yet understood. For instance, chlorpromazine, the first major antipsychotic agent introduced in the United States, was believed to work on the basis of its pharmacological antagonism of 5HT. The accumulated findings of psychiatric pharmacology and air ion studies justify a prediction about the interactions among air ions, 5HT and mood: positive air ions will release 5HT and induce some form of dysphoria and negative air ions will decrease circulating 5HT and lead to euphoria (or a related state). This dissertation research tested the above predictions.

FOLK HISTORY

The observation that certain winds occasion disorder and sickness dates back to 400 BC and Hippocrates' Greece. Stories of the "witches winds" and their ill effects are common in the popular literature and even find their way into medical journals, but even these are generally anecdotal. In the United States and elsewhere, air ion technology has been applied in educational and commercial settings. Stories abound. In schools where ionizing units were installed, a reduction in student absenteeism was reported. In a Swiss bank, when employees were exposed to negatively ionized air a marked decrease in the incidence of respiratory illness was reported. Working time lost, as compared to a control group, was reported to be less by a factor of 16. Hansell (1960), somewhat playfully, speculated that, "The bush that burned with fire, but was not consumed," was the product of a naturally produced corona (creating ions) and that Moses was sensitive to its effects. Whether or not divine inspiration has a greater frequency of occurrence atop mountains, where ions are more plentiful, has not been systematically studied. However, the ability of air ions to influence other psychological states, such as mood, has been documented.

For years, natural philosophers and observers of behavior have noted many animals' ability to "predict the weather." Hansell (1960) recounts the following anecdote:

> "The loose sandy soil of Long Island seems to provide a favorable environment for ants, and they frequently were a nuisance. These ants lived in burrows underground where

> water due to rain storms must have presented them with a major survival problem. They seemed to be able to anticipate rain and to prepare for it, so that they reappeared again in good shape as dry weather returned. On the other hand, if they were subjected unexpectedly to water from a hose and sprinkler, on a fine day when no rain was approaching, they apparently were surprised and unprepared so that they suffered disaster. Thus nature seems to have provided the ants with a weather predicting ability. The mechanism may very well be positive air ionization, accompanying falling barometric pressure. Ants, like people and animals, must be made nervous, apprehensive and pessimistic by positive air ionization accompanying falling barometric pressure..."

Most recently, air ions have been linked to animal behavior and the prediction of earthquakes. This is a difficult phenomenon on which to get an adequate sample, but personal accounts of bizarre behavior changes wrought by pre-earthquake stimuli have apparently been ardent enough to interest researchers at Stanford University. In their primate laboratories, animal behaviors and geological indicators are being monitored to see if changes in the two systems are correlated. Mechanisms by which the earth's deformation generates pockets of high air ion densities have been postulated (Lipinski, 1977). But the validity of these hypotheses awaits confirmation.

OCCURRENCE IN NATURE

The word "ion" was coined by Michael Faraday, who wished to stress its ability to migrate, as did the ancient Greek Ionians (Sulman, 1976). Ionization of the air is the result of collisions among particles. The charged air molecules formed, air ions, are the products of energy transfer. In nature, the sources of energy necessary for this process are varied. For instance, cosmic rays can induce ion formation. Cosmic

ray particles arriving from outer space have velocities far greater than the velocities of molecules influenced by temperatures alone (Hansell, 1961). When these high energy units combine with other energetic radiations and impact with a molecule of one of the common atmospheric gases, an air ion is formed. First, the outermost electron of the gaseous molecule becomes agitated and accelerated. If enough energy is transferred to an electron, it is torn out of its molecular orbit and a positively charged molecule is left behind.

Once an electron separates from its nuclear core, it may recombine with another positive ion to form a neutral molecule. The opposite charges attract one another, but as an electron is pulled toward a positive ion, it rapidly accelerates. It tends to arrive at the ion with such great velocity that it flies right on past its target. Only when some third particle gets in the way of the electron is it slowed enough to permit recombination with the attracting positive ion, forming an electrically neutral molecule (Hansell, 1961).

Radioactive substances produced in the soil are also responsible for the formation of air ions. For instance, radon and thoron are released and carried into the atmosphere by diffusion. The high energy emissions from the radioactive source displace an electron from a gaseous molecule. The remaining nucleus takes on a positive charge while the liberated electron is easily captured by an adjacent molecule which becomes negatively charged. Ions collide with neutral molecules in air at a rate of about 10^9 impacts/sec/cc. Energy transfer occurs so that

positive charges eventually reside on molecules with the lowest ionization potential. Electrons are captured by species with high electron affinities and greatest stabilities. The formation of oxonium, hydronium, oxygen and hydroxyl ions is predicted by this theory.

Waterfalls and the pounding of the surf are other natural sources of air ion production. The shearing action of the water droplets (The Lenard effect [Lenard, 1892]) causes them to break up into smaller electrically charged components. The heavier, positively charged ions tend to fall with cascading water. The lighter, negative ions are carried into the atmosphere by the fine spray (Sulman, 1976). Measurements of ion densities at health spas and water resorts confirm their presence in concentrations as high as 37,000 ions/cc (Davis, 1963). In general, however, areas remote from polluting foci will contain an average of 2,500 ions/cc in the atmosphere.

Weather variables such as temperature, relative humidity and barometric pressure as well as rain and other forms of precipitation influence ion densities. Solar flares and other meteorological influences on the earth's electric field have also long been known to influence ion densities. Small air ions have been reported to peak in spring and fall and are at their minimum in winter and summer (Vasiliev, 1951; 1966). The daily course of light ions has a maximum in the late night through early morning hours. It is lowest around midday. The maximum and minimum can range from no measureable ion level to the 37,000 ions/cc reported at Bad-Gastein in Europe (Davis, 1963).

Other natural electric field phenomena also are known to influence ion production. For instance, particles blowing along surfaces can create electric fields when dissimilar materials separate after having exchanged charges during contact. The hot, dry winds (i.e. the Sharav) blowing in from certain desert regions are examples of this type of ion-formation. Sand particles, swept across the land by large air masses help form fields characterized by a high positive to negative ion ratio (Robinson and Dirnfield, 1961). Bodies of aircraft, automobiles and trucks can build up high potentials in the same way. Vehicles transporting flammable materials are often required to drag a grounding chain along the highway to discharge this energy build up.

Clouds can also produce electric fields large and intense enough to cause the formation of ions. The electrostatic phenomenon called lightning is an example of this. When clouds form, charges are built up due to the friction between the air and the water droplets forming the clouds. The clouds will take on a positive or negative charge depending on which type of charge predominates in the water droplets. When the dielectric strength of the air is exceeded, charge is transferred to other clouds or to the earth, often in the form of lightning. Lightning rods, like the drag chains mentioned above, can direct this energy to safe grounding sources.

Lightning rods directly neutralize clouds too. Due to induction, electrons are pulled to the point of a lightning rod by the electrostatic forces of a positively charged cloud. The accumulated electrons

pass off to the cloud and its positive charge is neutralized. This process reduces the threat of lightning. When the clouds' positive charge cannot be balanced by the electrons available on the rod, electrons will be drawn up from the earth. Thus, lightning rods can be electron ejectors.

According to Hansell (1961), a phenomenon which is more common than lightning, but less frequently observed, is the electrical discharge which can take place from points of vegetation and other objects. These electron ejector points work on the same principles of induction as the lightning rod. That is, atmospheric conditions can cause electrons to be drawn up from the ground and discharged near the earth's surface. This temporarily reverses the earth's normal positive charge to negative.

PHYSICAL PROPERTIES

> For original sources the reader is referred to the following material: Beckett and Krueger, 1960; Chalmers, 1967; Joint Committee on Atmospheric Electricity, 1967; Loeb, 1947; Mohenen, 1970; Siegel and Fiet, 1976.

The following is a summary of some basic physical properties of air ions: Small or or light air ions travel comparatively rapidly in an electric field. The unit used to describe the size of air ions is based on their mobility; the number of centimeters the ion moves per second in a field of one volt per centimeter (cm/sec/V/cm). The mobility of small air ions is on the order of one to two cm/sec/V/cm. Over dry land and

in each cubic centimeter (cc) of air, about 10 ion pairs are formed per second. They have a life span of seconds to minutes, and are continuously associating and dissociating from other molecules. These particles readily give up their charge to surrounding objects, such as building surfaces, or combine with dust, smoke particles or water vapor. These reactions deplete the atmosphere of small air ions and induce the formation of intermediate and/or large air ions.

Intermediate ions are defined as those moving at rates of 0.01 to 1.0 cm/sec/V/cm. It has been suggested that this group is rarely encountered in nature and is considered primarily an intermediate step in the process of forming large ions. Sulman (1976) however, suggests that these aggregates do not settle and therefore contribute to the ambient air ion pool.

Large air ions, or Langevin, named after their discoverer, move slower than 0.01 cm/sec/V/cm. These are frequently referred to as condensation nuclei, meaning they have the ability to condense water vapor into water drops (see Table 1). These ions tend to settle out of the atmosphere and are therefore effective as deionizing agents. As their density increases, the density of small air ions decreases. The single greatest ion depleting source outdoors is the internal combustion engine (Hansell, 1961). Indoors, this distinction goes to cigarettes (Hansell, 1961), though the high temperatures generated by striking a match can momentarily double the total ion count in a small room (Chiles et al., 1960).

TABLE 1: Comparison of Ions with Other Particles in the Air (size in cm)

Molecules	10^{-8}
Light or small air ions	10^{-7}
Average or intermediate air ions	10^{-6}
Heavy or large air ions	10^{-5}
Fog Particles	10^{-4} to 10^{-3}
Raindrops	10^{-2} to 10^{-1}
Limit of visibility to the eye	5.0×10^{-3}
Limit of visibility in microscope	2.0×10^{-5}

(from Vasiliev, 1951, p. 7)

ISSUES AND OBJECTIVES

Methodological Issues

There are four main methodological issues in air ion research: 1) ion generation; 2) ion quantification; 3) subject dose; and 4) subject response. Some of these topics have been reviewed elsewhere and appear here in summary form (Frey, 1965; Gualtierotti et al., 1968; Kornblueh, 1962; Krueger, 1969; Krueger and Sigel, in press; Vasiliev, 1951).

1) Ion Generation. There are two main sources of ion generation in the laboratory: radiation from isotopes such as ^{3}H or ^{210}Po, and corona discharge. Radioactive generators do not maintain high concentrations of ions in large, enclosed spaces and are generally not useful for human experimentation. Corona discharge generators, in the past,

produced unacceptable amounts of ozone (0.050 ppm) along with oxides of nitrogen and other large charged molecules such as magnesium oxide. These molecular species are not considered to have the biological activity of small air ions, so some of the results of the studies carried out through the 1930's must be viewed with circumspection (Dessauer, 1931; Kimura et al., 1939; Tchijevsky, 1933; Yaglou et al., 1933).

The charge and size of air ions formed by any generating source is contingent upon physical events in the ambient atmosphere: amount of polluting materials, geographic location, season, temperature, barometric pressure and relative humidity. When the relative humidity in an experimental chamber exceeds ca 80%, the formation of electroaerosols is likely. Electroaerosols are essentially charged water droplets. They are related to air ions, but are technically not ionic-phenomena. The biological effects of electroaerosols have been extensively reviewed by Wehner (1962; 1969).

2) Ion Quantification. Methods for quantifying ion densities in the past 20 years have been improved over the earlier measurement systems. Nonetheless, atmospheric vicissitudes are always changing the state of air ionization. Since the atmosphere cannot be absolutely controlled in most experimental situations, air ion densities cannot be specified with precision greater than ca ± 30% for any given moment. However, the average concentration of ions/cc of air over a period of several hours may vary less than 15%.

3) Subject Dose. The issue of subject dosage of air ions is of the same type encountered in studies with other gaseous material. For

instance, how much marijuana is inhaled in a given inspiration? Different people have varying lung capacities and methods of smoke inhalation (oral and/or nasal). Therefore dose absorbed cannot be precisely specified. In addition, the distribtion of THC (the active ingredient in marijuana) may not be homogenous in the marijuana cigarette. Both problems are analogous to events in air ion studies.

The inspiration of air ions will vary as a function of tidal lung volume, frequency of respiration and method of breathing. The effects of air ions may even vary depending on differences between nasal and oral breathing (Knoll et al., 1961). The processes of diffusion tend to distribute air ions homogenously in space. However, air ions are attracted to particular surfaces and repelled by others so that the local densities of air ions will vary markedly in a room with a bed, a rug, a person and various wall coverings (Bach, 1967). Frey (1965) has described the distribution of ion clouds on the basis of physical elements in the room.

Precise dosage cannot be determined, but an investigator can insure that some air ions reach their target by electrically grounding the subject. Earlier air ion studies were frequently marred by their failure to ground or report grounding of the subjects. If subjects are not grounded, their bodies tend to build up an electrostatic surface charge that repels the ions they are supposed to be inhaling. This technical difficulty can be easily overcome by supplying the subject with clothing made from cotton and by attaching a lead from some part of the body to a grounded source (Frey and Granda, 1962; Frey, 1965).

Research in air ions will benefit from technological advances in other disciplines. For instance, apparatus designed to deliver a precise amount of anesthesia to a patient by way of a facial mask fitted with a pre-set valve may be adapted for the administration of air ion bursts. Some devices in electroaerosol and inhalation therapy approximate the mask arrangement suggested.

4) Subject Response. The issue of subject response is related to subject dose. Dose-response relationships have generally received cursory attention in air ion research, especially at more complex levels of system organization, i.e. behavior or psychological state. One reason for the neglect is the absence of an indicator of ion effects, such as a performance or mood measure, that is both reliable and sensitive. More often than not, ion doses are selected on the basis of generator capacity; the idea being that a strong stimulus will maximize the probability of subject response. The assumption that "more (ions) is better" may be fallacious. Several reports in Chapter III indicate that subjects do respond to high (50,000 ions/cc) concentrations of positive and negative air ions. However, sometimes positive and negative ions have the same, rather than opposite effects. Some possible explanations of such paradoxical effects will be discussed in Chapter VII.

General Issues

Some important general issues in air ion research are: 1) the non-specificity of the serotonin hypothesis; 2) the lack of models for conceptualizing interactions among electrical, chemical and psychological factors; 3) the influence of air ions on health; and 4) the role of

air ions in the environment.

1) Serotonin Hypothesis. The serotonin hypothesis is stated as follows: Positive air ions release 5HT from tissue stores and negative air ions speed up its oxidative deamination. This hypothesis was developed from observations on tracheal tissue by A.P. Krueger in the early 1960's.

When extirpated tracheal tissue is exposed to air ions, the site of air ion action is directly observable and the source of 5HT is reasonably obvious. Serotonin is stored in tracheal tissue and new amounts of 5HT cannot be contributed from other tissue or blood sources in the isolated preparation. However, when the intact organism is exposed to air ions, identifying the site and source of air ion effects is a different matter because: 1) there may be more than one site of action; skin, trachea, alveoli, other?; 2) there may be more than one source of 5HT (or other chemical mediator); platelets, peripheral nervous system tissue (trachea), central nervous system tissue (brain), etc.; and 3) there may be more than one mechanism by which mediators are affected: release, oxidation, charge carrying properties of blood, end-product inhibition, and so on. Any or all of these influences can contribute to the 5HT pools and make the hypothesis in its present form relatively non-specific.

Another problem of non-specificity by the serotonin hypothesis is related to the one above, and is also the result of extending the original hypothesis beyond the level of system organization from which its

principles were derived. It involves the measurement of 5HIAA, a metabolic breakdown product of 5HT.

It is not always feasible to obtain a tissue or blood sample to measure 5HT when working with humans or other intact organisms. Urine samples provide a non-invasive means for biochemical analyses. Serotonin is absent in urine or present only in very small amounts, but its breakdown product can be measured to make inferences about 5HT's metabolism. However, when 5HIAA is measured to index air ion effects, the amount of 5HT converted to 5HIAA cannot be predicted. Both mechanisms of the serotonin hypothesis, release and oxidation, should result in a net increase of 5HIAA. Thus, the non-specificity of the serotonin hypothesis refers to: difficulties in identifying the source of 5HT for studies at more complex levels of system organization; and its inability to predict amount of 5HIAA relative to the mechanisms hypothesized. Nonetheless, statements that air ions influence serotonergic systems can be made.

It must be remembered that the original tissue preparations from which the hypothesis was derived allowed for fairly direct examinations of 5HT. It is actually the extensions of the serotonin hypothesis that lack specificity.

2) Lack of Models. The serotonin hypothesis is an issue of general interest because it describes an interaction between two stimuli with very different physical properties, ions and 5HT. Serotonin has also been correlated with changes in psychological state. A response to

the question "How do air ions induce chemical changes that influence affective states?" requires insights from the disciplines of physics, chemistry and psychology. Gaseous molecules, of which air ions are a subset, are studied by the physicist. Organic chemicals, of which 5HT is an example, are studied by the biochemist. The mental realm is studied by the psychologist. The absence of a model for conceptualizing the relationships among electro-psycho-chemical events limits testing hypotheses of the phenomena, especially at more complex levels of system organization.

3) Health. The effects of air ions on specific health problems, respiratory distress, wound healing and migraine headaches, will be discussed later. The influence of air ions on health is not known. The lack of information has to do with stymied research efforts because: 1) it was argued, inappropriately, that air ions are present in too dilute a concentration to be biological agents; 2) irregular research funding interrupted studies which had already begun; and 3) the study of subtle, as opposed to clearly pathogenic, vectors is not an area of general support. The topics of air ion concentrations and research trends have been reviewed elsewhere (Andersen, 1972; Gualtierotti et al., 1968; Krueger, 1969; 1972; Krueger et al., 1966a; Krueger and Sigel, in press).

The broader health issue, that of subtle or long-term ion influences, raised here is primarily theoretical because of the lack of evidence. Longitudinal or epidemiological studies have not been carried

out (see Vasiliev, 1951). Nonetheless, it is known that air ions are natural components of the air and because their charge and size make them attracted to smoke and dust, they form condensation nuclei and settle out of the atmosphere. About 2,500 air ions/cc exist in unpolluted air. Industrialized cities contain as few as 80 ions/cc of air (Beckett, 1959; Kornblueh et al., 1973; Maczynski et al., 1971). Crowded offices may have no measurable ion levels. Occupational safety legislation may some day regulate air ion standards. In the interim, it may be prudent to consider if there is a detriment to human health when ions are continually depleted from the air. Tchijevsky (1933) indicated that animals reared in ion-depleted environments became sick and died.

4) Environment. The environmental issue concerns air ions and their role in meteorological phenomena. All weather is related to the electrical properties of the air. Wind, lightning, rain and other forms of precipitation are the result of electrostatic events, mediated in part by air ions. Depletion of ions from the air may actually affect local atmospheric conditions. These in turn can affect plant and animal life, and an entire ecosystem can be disrupted as a result of an imbalance in the electrical properties of the air.

Molecules essential to life evolved in ionized air. The presence of the first living forms altered the original chemical and electrostatic milieu, but the changes were not lethal. Advances in technology have caused the magnitude of organic changes to be expanded to the point where life is endangered. Technology is a potentially lethal develop-

ment and particular advances must be considered in the general context of health and survival.

Objectives

The issues in air ion research described above span interests across different levels of system organization. This dissertation research was carried out at the level of the intact human organism.

The specific aims of the present study were to examine some of the biochemical and psychological effects of air ions in men and to consider the mechanism(s) by which they exert their influence. Since progress in air ion research requires indicators for each level of organization, the development or identification of reliable and sensitive indices such as mood and 5HT was primary. For these purposes it was necessary to:

1) examine the effects of positive and negative air ions on mood;

2) examine the effects of positive and negative air ions on 5HT as indicated by urinary 5HIAA, a major product of 5HT catabolism, and on urine volume.

The sub-issues explored were:

1) whether positive and negative air ions have different effects;

2) the time course of ion-related events;

3) subject selection.

Volunteer men who were selected for self-reported mood lability, "weather-sensitivity" and/or minor health problems were exposed to air ions (ca 100,000 ions/cc) under the following conditions: thirty minutes of ambient ions; two hours of positive (or negative) air ions; two

hours of negative (or positive) air ions; then 30 minutes of ambient ions. Mood and urine measures were obtained at 15 minute intervals. The rationale for the specific details of the protocol will be discussed in Chapter III.

II. BIOLOGICAL EFFECTS

SUMMARY: NON-MAMMALIAN

Extensive research on the influence of air ions in microorganisms, plants and insects has been carried out. Comprehensive reviews of these studies have been published elsewhere (Gualtierotti et al., 1968; Krueger, 1969; Krueger and Reed, 1976; Krueger and Sigel, in press). Illustrative excerpts of studies from these reports follow.

In 1933 Tchijevsky and his associates conducted a long series of experiments with agar plate cultures of Staphylococcus aureus, Vibrio chlorerae and Salmonella typhi. In all instances, small air ions (charge not specified) inhibited colony formation. They also observed that small air ions reduced the viable cell count of the normal microflora of air in enclosed spaces. A similar effect was achieved when the air was enriched with artificially generated bacterial aerosols. Lethal effects of air ions were reported for the mold Neurospora crassa (Fuerst, 1955), Penicillium notatum (Pratt and Barnard, 1960), Escherichia coli (Kingdon, 1960), Staphylococcus aureaus (Biró et al., 1969; Krueger et al., 1957) and on four bacteriophages of the T group (Biró and Sváb, 1970).

Since the 1960's Krueger's laboratory has been reporting increases in the growth of seedlings exposed to air ions. Ions of either charge produced significant acceleration of growth as measured by stem length, integral elongation, fresh weight and dry weight (Krueger et al., 1962a).

Ionized atmospheres increased the biosynthesis of cytochrome C, a compound associated with cellular respiration (Krueger et al., 1963a; 1963b). Stimulation of the synthesis of cytrochrome C was associated with enhanced plant activity.

The evidence for this mechanism of ion action in plants led Krueger and his associates to study the silkworm (Bombyx mori) whose development is also linked to the action of cytochrome C. Exposure to air ions was found to increase the rate of larval growth, cause spinning to start earlier and to increase the weights of cocoon and silk layers. Edwards (1960) observed a marked increase in the flight activity of blowflies exposed to positive ions. Helson and Penham (1970) found that a shift in air ion concentrations triggered the mass flight of Wiseana ssp.

A review of studies with mammals is particularly relevent in this dissertation. Work carried out at increasingly complex levels of system organization for the past 20 years has confirmed an effect of air ions on living matter. Much of this work supports the hypothesis that air ion effects are mediated by or correlated with changes in 5HT.

MAMMALIAN TISSUE

The early studies of air ion effects on tracheal tissue were incisive (Krueger, 1962a; 1962b; Krueger & Smith, 1957; 1958a; 1958b; 1959; 1960a; 1960b; 1962). The selection of in vitro and in situ preparations for the study of air ion effects was well conceived: 1) tracheal tissue receives air ions deposited during normal respiration.

Therefore the site and possibly mechanism(s) of air ion action could be studied directly; 2) tracheal tissue has cilia-lined mucosa that is representative of the coverings of the major distribution channels of the respiratory tree. Findings at this level of system organization could be generalized to most air breathing organisms; and 3) tracheal tissue is accessible to study.

In extirpated tracheal strips, positive air ions were noted to contract the wall of the trachea, eliminating the peristaltic action normally associated with the clearing mechanism; dry the mucosal surface; and render the cilia vulnerable to mild mechanical trauma, abolishing their activity in exposed areas. These effects were reversed by negative ion treatment. The restoration of moisture to the dried mucosal surface was an occasional exception. It has been suggested that the high water vapor saturation required to keep the tissue viable may have, at times, yielded the production of electroaerosols (Andersen, 1972).

Each of the above tissue effects was replicated by in vivo studies on rabbits, mice, rats, guinea pigs and monkeys. In these experiments animals were anesthetized and air ions were administered directly to the mucosa through a surgical opening in the trachea. In addition to the effects found in vitro, positive ions increased animal respiration and vasoconstriction in the tracheal wall. All of the effects were reversed by negative air ions.

The ability of negative air ions to reverse signs of distress (vasoconstriction, decreased cilia-beats and mucosal flow) in tracheal tissue

suggested they might be useful in the treatment of asthma. Clinical studies of air ion effects tend to be methodologically flawed or weak, but these studies are the ones that attract general attention and interest.

Boulatov (1968) reported the complete remission of dyspnoeic attacks (for over six months) in 55% of the 830 patients receiving air ion therapy. The severity and frequency of attacks was reduced in an additional 35% of the cases and no improvement was noted in 10% of the patients. Negative air ions were considered to "improve general health and act as a normalizing agent on a number of physiological parameters including the central nervous system" (in Gualtierotti et al., 1968). In view of the favorable results obtained on a large group of patients, the "popularization of aeroion-therapy is highly recommended."

Palti et al. (1966), reported similar successes in the management of asthma with 19 infants aged two to 12 months. After establishing measurement categories for spasticity and respiratory rates, it was determined that "negative ions, without any other supportive treatment (including antibiotics) terminate the spastic attack after a much shorter period than that required by the conventional mode of treatment." The absence of side effects with negative ion treatments, as opposed to frequent reactions to traditional drug regimens, was of particular benefit for the young patients. Statistical analyses were not reported. Jones et al. (1976) found negative ion treatments were not efficacious in the routine management of seven cases of asthma. The significance of these negative results is difficult to ascertain for only seven cases.

After Krueger demonstrated that air ions had biological effects, he sought to elucidate their mechanism(s) of action. Empirical observations suggested to him a 5HT link because: 1) 5HT was localized in tracheal tissue; 2) 5HT was a known smooth muscle constrictor; and 3) intact animals exposed to positive air ions had diarrhea, a sign associated with the hyperproduction of 5HT in patients ill with carcinoid syndrome. The following laboratory studies supported the 5HT link suggested by Krueger's empirical observations.

Excised tracheal tissue from rabbits was divided into three sections. The anterior and posterior sections were not exposed to air ions and served as controls. The mid section was exposed to negative air ions. Small but reproducible decreases in tissue 5HT were found for five of the six animals tested. Two additional control animals showed no differences in 5HT content for the three tracheal sections. The largest decrease observed from control values (ca 35%) was recorded after 30 minutes of exposure.

Continued experimentation demonstrated that all of the tissue effects attributed thus far to positive air ions (contraction of the tracheal wall, decreased cilia beats and mucosal flow) could be duplicated by the intravenous injection of 5HT to a living tracheotomized animal (Krueger and Smith, 1960a). These findings provided direct support for the involvement of 5HT in the mediation of air ion effects.

Indirect confirmation of the serotonin hypothesis was provided by tissue studies using reserpine and iproniazid. Reserpine is a compound

long used as an antihypertensive and in the treatment of depressions. It has a bimodal action. First, reserpine releases tissue stores of 5HT. The 5HT is catabolized. Following its destruction by monoamine oxidase (MAO), the system is in an overall 5HT depleted state. The latter is the dominant and longer lasting reserpine effect. If Krueger's assertion is correct, and negative air ions induce a functional depletion of 5HT, then one would expect reserpine to mimic negative ion effects in the mammalian trachea. Such was found to be true.

Negative air ions and reserpine both increased ciliary rates (Krueger and Smith, 1960). An added prediction in the absence of 5HT would be a scarcity of "typical" effects of positive ions. For instance, if 5HT normally mediates the contraction of the tracheal wall, and there is none present due to prior reserpine treatment, then the contraction phenomenon should not be displayed in the presence of the positive air ions. Krueger has tested this prediction and results were in the expected direction (Krueger and Smith, 1960a). In contrast, drugs that accumulate 5HT should reproduce positive ion effects. Iproniazid is such a drug. It works by blocking the MAO normally engaged in the destruction of 5HT after it is released. In cases where animals were treated with iproniazid, positive ion effects have been reinstated. Iproniazid-induced effects are reversed by negative ion treatments.

Krueger's tracheal tissue studies provided extensive documentation of the effects of air ions on tissue and suggested possible mechanisms of air ion action. Many observations were considered to support the

serotonin hypothesis; however, other observations had no obvious connection with it. Tissue studies at the level of the intact organism (burn patients) provide examples of several mechanisms for the mediation of air ion effects which can function at the same time and may or may not involve 5HT.

For ten years, more than 200 patients with various kinds and degrees of burns were treated with negative air ions by Kornblueh, the pioneer of clinical studies in the United States. Though statistical procedures were not carried out, in the medical opinion of Kornblueh and other consulting physicians, ion therapies were efficacious in the treatment of burned patients.

At the skin surface, negative air ions seemed to reduce infection, diminish exudation from wounds and promote the early formation of eschars (Kornblueh, 1967). The bacteriocidal effect of air ions is implicated by these findings, which were complemented by Worden's (1961) study. In a group of 24 animals tested (Golden hamsters), healing of surgical incisions and regeneration of severed femoral nerves were enhanced by positive and negative ion treatments. Though the action of 5HT was not ruled out in the healing studies, the bacteria killing properties of air ions might be sufficient effector mechanisms.

Intravenous injections of 5HT produce pain. However, pain is a complex phenomenon, involving sensory (or peripheral) and perceptive (or central) elements which cannot always be distinguished. Nonetheless, Kornblueh (1967) reported that in a majority of burned patients, cessation

of local pain was achieved after 10 to 15 minutes of negative ion exposure. The reduction of pain, in theory, can be linked to the decrease of circulating 5HT induced by negative ions and can therefore be considered indirect support of the serotonin hypothesis.

Animal studies support the above finding of an analgesic effect of negative air ions. Olivereau (1971a) found that when mice were placed on a hot plate following 25 minutes of negative air ion exposure, the appearance of signs of pain, i.e. paw licking, were significantly delayed compared to controls ($P < 0.02$). Positive air ions significantly decreased the latency of pain responses ($P < 0.005$). While these data support the implication of 5HT in the production of pain, it must be remembered that the contributing influences of central and peripheral 5HT have not been specified (Olivereau, 1971a).

At the cognitive level, a study on post-operative pain in burn patients showed that negative air ions had a significant sedating or calming effect for patients matched for type of surgery, age and sex ($P < 0.02$) (David et al., 1962). The above studies confirm the effects of air ions demonstrated on tracheal tissue and extend them to other levels of system organization. The effects of air ions at the psychological level will be discussed more fully later.

Blood

It is difficult to localize the source of air ion effects in living organisms because of the close association of blood and tissue in vivo. However, in vitro blood analyses, like the in vitro tissue studies, can

provide direct tests of the serotonin hypothesis. The study below supports observations that air ions affect 5HT in blood (Tal et al., 1976).

Human blood was drawn from the cubital vein and transferred to test tubes containing 1/10 volume of a mixture of 15% K_3EDTA and 0.02% potassium sorbate to prevent clotting. The pH of the treated blood was 7.6 to 7.8. A five ml sample was spread on a glass Petri dish and exposed to ions of either charge (ca 36,000 ions/cc). After 10 minutes of exposure, positive ions were noted to increase 5HT in: 1) total blood (+40%); 2) plasma (+90%); 3) erythrocytes (+40%); and 4) thrombocytes (+240%). These effects were significant in all instances at $P = 0.05$ or less. Negative ions reversed each of these conditions at the same levels of significance. Changes in blood pH were not reported. These are enormous effects. If they can be replicated, they may reveal some of the ways in which air ions act once they interface with blood and tissue.

Krueger's efforts to elucidate the mechanism(s) of air ion action continued with a series of in vivo blood studies in mice (Krueger et al., 1963). The experimental question he asked was: will positively ionized air produce a rise in the blood level of 5HT?

Controlled conditions for temperature and relative humidity and the absence of atmospheric pollutants were maintained throughout. By the seventh day of a 17 day treatment regimen, the control and experimental groups differed significantly ($P < 0.05$). The positive ion-treated

animals showed an increase (ca 25%) in the level of blood serotonin. Both groups had demonstrated moderate (ca 10%) increases in blood 5HT by the third day of confinement, but this was attributed to the stress of an unnatural environment. The assumption proved warranted as the control groups resumed baseline status by the seventh day. The treated groups continued to show elevated blood 5HT levels (ca 15% above day three). There was no significant change in either group during the subsequent 10 days of the experiment.

These results were confirmed in a second and third experimental series. Over the course of six years' investigations the results were extended to include negative ion treatments. These treatments produced the predicted decrement in blood 5HT (Krueger et al., 1968). The in vitro work cited previously supports the interpretation that at least some of the in vivo effects reported by Krueger were the result of the influence of air ions on blood.

Brain

Based on earlier studies in tracheal tissue and blood, Krueger hypothesized that positive air ions would increase the presence of 5HT in brain samples and that negative air ions would deplete 5HT. These predictions were partially confirmed in mice continuously exposed to ions of either polarity for up to 72 hours.

Analyses of brain samples carried out after 12 hours of exposure showed that low doses (2,000 to 4,000/cc) as well as high doses (350,000 to 500,000/cc) of ions of either polarity induced a significant decrease

in brain 5HT ($P < 0.05$). At 24 hours only the mid dose (30,000 to 40,000/cc) positive ion group exhibited a significant reduction in 5HT ($P < 0.05$). By 48 hours none of the ion-treated groups varied appreciably from the untreated animals. But at 72 hours significant reductions in brain 5HT were found among all the ion-treated animals with the exception of those in the mid dose positive ion group ($P < 0.05$). These results do not show the charge related differences expected for animals in paired time and dosage groups. When positive and negative air ions acted at all, they both tended to decrease brain 5HT.

Studying the influence of air ions in brain tissue is a difficult task since the effects are presumably not direct. Turnover studies could clarify patterns of 5HT and other biogenic amine metabolism by focusing on local rather than whole brain changes. They could also circumvent the problem of trying to identify the separate sources of 5HT in the brain tissue homogenate because when the sample is pulverized, all of the 5HT in the tissue is pooled, and differences between free (circulating) and bound (stored in tissue) 5HT are not distinguishable.

The original serotonin hypothesis was derived from observations in tracheal tissue exposed directly to air ions. Since the brain is presumably sealed off from the direct impact of air ions, it is not surprising that the 5HT hypotheses were only partially confirmed. Nonetheless, an effect of air ions on brain 5HT was demonstrated. Just how this happened is not known. The effect on 5HT could be the indirect result of behavioral changes induced by air ions, such as increases in

locomotion, or the influence of an ion-induced psychological state on a biochemical substrate.

Regardless of their putative mechanism(s) or action, the effects of air ions have been demonstrated at progressively higher levels of system organization. Gilbert's (1973) work was cited earlier as an example of research carried out on response indicators at two levels of system organization and is reviewed below.

Gilbert studied the relationships among air ions, 5HT and emotionality. The purpose of his study was to determine the effects of both continual and intermittent negative ion inhalation on the emotional level and content of brain serotonin of rats experiencing prolonged isolation. He predicted that rats raised in isolation and treated with negative ions will have lower levels of serotonin and will develop less emotional behaviors than rats subjected to isolation only. These predictions were based on earlier observations that negative air ions cause a depletion of brain 5HT and that 5HT was widely recognized as a biochemical correlate of some psychological states. Emotionality was defined operationally by handling reactions: startle response, vocalization and resistance to being picked up.

At 170 days of age rats were randomly assigned to one of four housing conditions: Group Housed (GH), Individually Housed (IH), Continuously Ionized-Individually Housed (CI-IH), and Intermittently Ionized-Individually Housed (II-IH). Six animals were assigned to each group. Negative ion densities were about 3,000 ions/cc for CI-IH and II-IH units and about 500 ions/cc for IH and GH groups. Positive ion

densities were on the order of 800 ions/cc for all four groups. After 100 days, each animal was tested for emotional behavior (Korn and Moyer, 1968). Immediately following the testing paradigm each animal was sacrificed by decapitation. Brain tissue was analyzed for 5HT content.

Composite behavioral ratings for emotionality indicate that IH animals were significantly more reactive than either the GH animals ($P < 0.005$) or the CI-IH animals ($P < 0.025$). The II-IH animals were more reactive than the GH animals ($P < 0.05$). Serotonin levels of the IH group were significantly higher than those of the CI-IH group ($P < 0.05$). The II-IH group had higher 5HT levels than the CI-IH group ($P < 0.06$). These results were in accordance with the hypothesis that negative air ions induce a reduction in the emotional behavior of rats. The concurrent prediction that negative ions reduce brain 5HT was also supported.

This study suggests the involvement of 5HT in the mediation of air ion effects at the behavior and psychological levels of system organization, and is especially significant because it was carried out under what appear to be well controlled conditions by modern standards. Other brain or behavior studies which do not attempt to test hypotheses about 5HT or the underlying mechanism(s) of air ion action will be reviewd later.

Olivereau (1971a) undertook an extensive series of studies of air ion effects in animals and discovered mechanisms involving 5HT, monoamine oxidase (MAO) and antidiuretic hormone (ADH). In one study, cells

along the hypothalamic-hypophyseal axis were examined for histological changes.

Thirty rats were subjected to daily negative ion treatments over a period of 23 to 37 days. Densities were on the order of 200,000 ions/cc. Exposure lasted 15 to 30 minutes per day. Analyses of cell size were made. By comparison with controls the volume of the nuclei increased 20% ($P < 0.01$). The volume of the nucleoli increased 60% ($P < 0.001$). In addition, more neurosecretory materials were observed in migration along the axons. These modifications reflected the classic histophysiological picture of intensified neurosecretory activity, according to Olivereau.

Identical results were obtained after continuous exposure to negative ions in lower (20,000/cc) concentrations. Ten rats underwent treatment for 20 days. As in the earlier work, hypertrophy of the nuclei and nucleoli was noted. Modifications of neurosecretory granules were observed in both studies. There appeared to be an increase in the discharge of ADH which Olivereau linked to the increased volume of the organelles. A subsequent study of the posterior lobe of the hypophysis confirmed suggestions of the increased liberation of ADH. Olivereau showed the hypersecretion of ADH was related by a complex series of events involving homeostatic and accessory systems' management of "hydromineral" metabolism.

Several dozens of other experiments by Olivereau demonstrated air ion effects at all levels of system organization measured, from the cellular to gross motor behaviors. Some of these implicated 5HT (spon-

taneous activity, sexual behavior, sensitivity to heat); others did not (adrenal weights, ingestion of food, thirst).

Urine

Excess materials from the brain find their way to the urine along with by-products from the rest of the body. The waste contributions to the urine from varied sources were noted to make biochemical assessments difficult to interpret because the source of a given product cannot be identified, nor can the mechanism by which it was liberated. It was noted above that the mechanisms of the serotonin hypothesis, release and oxidation, both suggest an increase in urinary 5HIAA. Preliminary findings by Krueger and Smith (1960b) indicated that when three guinea pigs were exposed to negative air ions for 24 hours, the level of 5HIAA in urine rose in all three cases. No report on the effects of positive air ions was made.

Sulman et al. (1970) extended Krueger's findings to include urinalyses in over 200 patients suffering from Sharav weather conditions. The Sharav is the name given to the hot, dry desert winds that sweep across parts of Israel and are said to account for a diversity of clinical complaints. It is generally characterized by a rapid decrease in relative humidity to values 25 to 30% below normal, an increase in temperature five to 10° C above the seasonal average and an elevated positive ion density which precedes the winds by 10 to 12 hours (Robinson and Dirnfield, 1963; Sulman et al., 1970). The 5HT and 5HIAA data were reported as follows:

Parameter studied	Units/24 hr.	Normal days	Sharav or weather front days
5HT	µg	1-50	50-500
5HIAA	mg	1-9	5-25

At first it appeared that the predicted decrease of 5HIAA by positive air ions was not confirmed. However, this may be accounted for as follows. Serotonin increased 10 to 50 fold in urine. This outcome is predicted as a result of the positive air ions' release of 5HT. The increase in the presence of 5HIAA in urine is less than three to five times that of normal value. It is possible that the elevated levels of 5HIAA are a reflection of the extraordinary increase in the amounts of 5HT present in the urine and not an indication of accelerated metabolism per se. This interpretation bears a striking resemblance to the one proffered by Krueger to account for the single deviant finding in his earlier tracheal studies for 5HT (Krueger and Smith, 1960b).

The studies reviewed so far have demonstrated air ion effects in tissue, blood, brain and urine. Serotonin was frequently identified as both the mechanism and indicator for air ion effects. In this sense, 5HT is considered a primary indicator. How and when 5HT is engaged by air ions must be worked out. There are numerous sites of 5HT release and metabolism in the intact organisms, and it is possible that only some of these are affected by air ions under varying conditions of time and dose. Serotonin may be only one of several primary biochemical indicators.

MAMMALIAN BEHAVIOR

Air ion effects have been sought at levels of system organization more complex than tissue, such as behavior. A primary indicator at this level has not been identified. What would a primary indicator at the behavior level look like? An answer involves determining whether biochemical agents are causal for higher level effects or vice versa. The lack of models for conceptualizing inter-level interactions makes it difficult to know if the issue of causality (as raised here) is even relevant (Knapp, 1976).

Although these theoretical questions are important, they cannot be answered here, so in the following review section mostly intra-level questions will be considered. For instance: are there effects of air ions on behavior variables? what is the direction of the air ion effect, improvement? normalization? how do air ions interact with other subject variables, such as age, gender, level of activation or stress? can any mechanisms be postulated?

Behavior is a term that can be applied to describe responses to stimuli at just about any level of system organization. To the microbiologist the cell "behaves" in a particular fashion when exposed to various stimuli. In the context of air ion studies, behavior generally refers to neuromuscular and skeletal responses of the intact organism. Responses such as reaction time are classified as elemental or simple behaviors. Responses such as maze running are examples of gross or complex motor activity. Maze running has both learning and performance aspects to it.

The differences between elemental and gross behaviors are not important for demonstrating the effects of air ions: they can be shown for either type of response. However, the distinction between the two is necessary when the outcomes of one behavior are used to predict the other. The strategy of working with the relatively simple to understand the relatively complex is certainly reasonable, but methods of generalization must be carefully applied. The assumption that understanding the elemental performance variables will shed light on how air ions influence more complex activity such as work capacity or efficiency is unwarranted in the absence of data. There are likely to be significant emergent and confounding events to consider before data obtained in one response system can be utilized to predict another, more complex. Examples from the in vitro and in vivo 5HT studies demonstrate possible discontinuities between simple and more complex events such as identifying the source of 5HT in blood for in vivo, as opposed to in vitro studies. This caveat has eluded consideration by some unwitting or unscrupulous entrepreneurs, whose health claims for air ionizers far exceed their data base.

Elemental or Simple Behaviors

In the early 1960's several researchers undertook to demonstrate the effects of air ions on simple performance measures in human, i.e. reaction time, finger tapping and vigilance tasks. Slote (1961) studied the influence of positive and negative air ions on 16 men for three performance variables: Flicker-Fusion Frequency (FFF), Simple Visual

Reaction Time (SVRT) and Finger Tapping (FT). The dependent measures chosen were thought to represent a sensory response, a sensorimotor response and a motor response, respectively. The more impulses processed or the more responses emitted per time unit, the better the functional state was reasoned to be. According to this speed of processing criterion, negative air ions (ca 20,000/cc) improved performance across all test conditions. FFF and FT values increased and response time (RT) decreased. Positive air ions (ca 20,000/cc) had the opposite effect. All results were statistically significant except for the positive ion decrease on FT ($P < 0.05$).

The major objective of Slote's study was to determine whether positive and/or negative air ions "affect human performance." The FFF, SVRT and FT indices demonstrated an effect of air ions on relatively simple performance variables: they do not necessarily indicate that air ions influence other performance measures. However, Slote has identified three sensitive indicators of air ion effects which are considered to indirectly reflect the functional state of the organism. The indicators are generally suited to evaluate how an agent can interact with other variables likely to affect overall performance, such as age or level of motivation or noise because they have short latencies (15 to 20 minutes) and are easy to measure. By varying the conditions under which FFF, SVRT and FT were studied, to round out response contingencies, extrapolations to other aspects of human performance such as work efficiency could be more substantive, as the generalizations were derived from data obtained under simulated work conditions.

Knoll et al. (1961) confirmed that air ions can influence SVRT, but whether reaction times increased or decreased could not be predicted. Several hundred subjects were investigated on over 12,000 tests. Exposure time was 30 minutes or less and ion doses varied from 1,000 to 1,000,000 ions/cc. The effects of systematically varying time and dose were not studied, though "there was nearly always an effect on reaction time." It was reported that:

1) as ion concentrations decreased from about 1,000,000 ions/cc to 2,000, the reaction time was faster in an increasing percentage of the experiments;

2) the effect of both positive and negative ions was small, though statistically significant; variations in no case were greater than 10% from the mean.

3) either positive or negative ions decreased some subjects' reaction time and increased others';

4) ions of the same polarity had opposite effects on the same subjects for some repeated trials. Reaction times were decreased by ion exposure and then increased a few hours later. Whether reaction times were increased by ion exposure and then decreased was not mentioned.

Knoll et al. were unable to account for the variability of outcomes. They suggested that the action which air ions produced depended on the "homeostatic mechanism of the body." This position, if specified in detail, is amenable to experimental investigation. For instance, does "stress," as a homeostatic disruptor, enhance the probability of an

ion-improved performance? So far, only a few researchers have taken up the question. In their investigations "stress," interacting with other subject variables, has tended to confound interpretations of ion effects. These studies will be discussed in more detail later.

For the moment it is sufficient to note that reaction time might be an indicator of air ion effects, and this is important for the advance of air ion research. Studies on reaction time are also important because its measurement may provide insight into a little studied mechanism of air ion action: effects on muscle chronaxy. Chronaxy is the minimum time that a current of twice the threshold strength must flow in order to excite a tissue or muscle. It is a concept infrequently encountered by English speaking physiologists today, but still used by some noted Russian investigators (Skorobogatova, 1962; Vasiliev, 1951). They are primarily responsible for the research on air ion effects and muscle chronaxy.

How air ions effect changes in chronaxy is not known. Guillerm et al. (1967) suggested that negative air ions increased oxygen utilization and thereby reduced chronaxy. Minkh (1963) said that negative air ions enhanced the metabolism of water-soluble vitamins. Minkh's subjects did show an improvement in work capacity that was correlated with the vitamin/ion effect. It is the supposed improvement on speed and endurance performance measures that presumably motivates the use of air ion treatments in some athletic regimens. There is limited work to affirm or negate the efficacy of this type of program (Deleanu and Mozes-Lorinez, 1975; Derevenco et al., 1977; Hamburger, 1962).

Appropriate generalizations from the relatively simple to the more complex require information from many intermediate steps. The jump from shortened muscle chronaxy to improved athletic endeavor is not well supported, as intervening data have not been obtained. However, it is true that an individual in ill-health has decreased functional capacities that increases in reaction time and muscle chronaxy could index. Therefore studies on air ions, reaction time and chronaxy may provide an important transitional step. The suggestion has merit, as a site, a mechanism and indicator of air ion effects can be examined in a single system at the behavioral level of organization. This was the power of the early 5HT tissue studies carried out by Krueger.

As an indicator of ion effects, the reliability of reaction time is suspect. Like FFF, reaction time is susceptible to changes induced by extraneous stimuli such as temperature, noise or time of day. The fluctuations in elemental performance variables are likely to make the influence of air ions on more complex activities even more difficult to predict.

McDonald et al. (1967) did not find effects of air ions on reaction time, but they did find that positive air ions (ca 1,000,000 ions/cc) improved performance on a fast presentation vigilance task ($P < 0.05$). Barron and Dreher (1964) studied the influence of air ions on four sensorimotor measures, including reaction time, but found no statistically signficant effects. The authors noted that the subjects in this experiment were test pilots who were in excellent health and conditioned to perform efficiently even under duress. The subjects' peak physical

conditions suggested a "ceiling effect" was achieved: pilot performances already approached upper limits of efficiency and therefore reduced the likelihood of significant improvment (by ion treatment). Similarly, their specialized training in emergency procedures reduced the probability of performance deterioration in response to stressful stimuli, e.g. temperature extremes or fatigue. Biochemical indicators of stress such as blood glucose, urinary catecholamines, 17-ketosteroids, etc. were assayed and reported only as "not significant." The authors concluded that the performance and biochemical measures must be considered as inconclusive, especially due to the sample size (10) and superior constitution of the pilots. These negative data are suggestive: air ions do interact with other subject variables such as age, level of activation or stress; but the inference ought to be considered in its weakest form.

Wofford (1966) summarized the results of many studies in this field by saying, "...ionization has a significant behavioral effect on relatively simple tasks, but does not significantly influence more complex forms of behavior." He may be correct, or it may be that appropriate strategies have not been developed yet for generalizing from simple performance variables to more complex activity. Little work on this issue has appeared since 1966.

Gross or Complex Behaviors

Neither elemental nor gross motor performance indicators can be used to directly test hypotheses about mechanisms of air ion action at

the biochemical level. However, correlations among variables may be found so that mechanisms can be inferred.

In 1961, Frey proposed a "rational framework for interpreting the behavioral effects of atmospheric ions." He intended his paper to stimulate physiological, as opposed to cellular, research. In it he suggested that "negative ions stimulate the secretion of the glucocorticoids, and positive ions either stimulate the secretion of the mineralo-corticoids or inhibit the glucocorticoid secretion." The hypothesis was derived from a study of selected findings relating air ion effects to: histological changes in the adrenal cortex, stress and pituitary ACTH stimulation of corticoids, and corticoid effects in numerous physiological processes (allergy, blood pressure, cardiac condition, pain, shock, etc.). Frey concluded that, in general, negative ions normalize subjects under some stress and positive ions have debilitating effects.

Duffee and Koontz (1965) considered Frey's hypothesis concerning the effects of air ions on behavior one of the few amenable to experimental investigation. The purpose of their study was to determine whether stress was a necessary precondition for ions to affect behavior. As a corollary to Frey's hypothesis they suggested that, "the normal balance of adrenal corticoids cannot be influenced by air ions unless the balance has already been disturbed in some way." Their statement operationally defined stress as an adreno-chemical imbalance. The definition is not in keeping with Selye's concept of stress, charac-

terized by the General Adaptation Syndrome (GAS), whereby a clearly delineated pattern of changes in various organs is described. A second objective of the research was to investigate the relationships between ion polarity and age on learning and performance in rats.

Stress was induced by the administration of an electrical shock. Two age groups, three and 14 months of age, were tested. Average concentrations of positive ions were 290,000 ions/cc. Negative ions were on the order of 140,000 ions/cc. The duration of ion exposure preceeding testing is not explicitly stated, but appeared to be 33 days of continuous exposure. Criteria for learning and performance were the number of errors and time in a water maze. The shock was administered to half of the experimental animals prior to maze trials. The remaining, non-stressed animals were controls.

The effects of three independent variables, ion-polarity, stress and age, on learning and performance were examined using an analysis of variance technique. Results indicated that older rats learned more slowly in general, and suggested that ions of either polarity, especially negative ions, enhanced learning of the maze (not statistically significant). For performance trials, both polarity and the interaction effects of polarity and age were significant ($P < 0.05$). Performance of the older animals living in a negatively ionized atmosphere was especially improved. Stress was not observed to be a necessary precondition for ions to affect behavior.

In this study, age and stress were treated as independent variables. However, they may not be unrelated. Aging processes may disrupt

the normal balance of adrenal corticoids and, in this way be considered a stressor in the classical histological sense of Selye (1936; 1946). If age were a stressor, then the Duffee and Koontz study supports findings that stress may be a necessary precondition for ionized air to affect behavior. Behavior effects have been reported in organisms that do not appear to be stressed, and these will be reviewed. However, a weak form of Frey's hypothesis may serve heuristically: vulnerability to stress enhances or maximizes the ion effect.

An incidental, but powerful effect reported by Duffee and Koontz supports the idea that age, whether considered a stressor or not, increases susceptibility to ion effects. When young and old animals which spent 18 days in the positive ions were transferred to an atmosphere with negative ions, the water maze performance of the total group improved by 350%. This was a result of the improved performance of the older animals. This "contrast" phenomenon has not been well studied and Duffee and Koontz raised the question of whether the improved performance was attributable to polarity or the sudden change in polarity. They did not interpret this finding as indirect support for the hypothesis that age is a significant variable for demonstrating ion effects.

Jordon and Sokoloff (1959) studied the effect of air ions, age and maze learning in rats and concluded that the benefit derived from exposure to air ions was at least in part a function of age. A multiple-T-pattern maze with escape-from-water motive was used to assess age differences for ion effects. Trials to criterion for three and 22 month

old rats were compared. Each group consisted of 150 animals. Animals were exposed to negative ion densities on the order of 8,000 to 9,000 ions/cc for three hours prior to the water-maze trial.

The results were as follows: Under ambient atmospheric conditions, the young rats showed a much higher learning ability than the old rats as measured by number of errors and average total time. When both old and young rats were subjected to negative air ions, the older rats reduced the average number of errors from 79 (in normal atmosphere) to 39, roughly a 50% improvement. Their average time scores approximated those of the young rats. For young rats, neither the number of errors nor the time scores was altered significantly. The effects of positive air ions were not studied.

What is it about older animals that seems to enhance their susceptibility to ion effects? This question has not been systematically treated. Duffee and Koontz (1965) suggested that some performance improvements may be a function of increased respiratory capacity. They noted that older rats are prone to murine virus pnemonia and tend to suffer latent lung consolidation when placed under minimal stress. Perhaps the older rats' impaired function of lung tissue was ameliorated by negative ion exposures (even as short as three hours [Jordon and Sokoloff, 1959]) and their renewed capacity positively influenced performance. Perhaps the negative ions reduced stress responding so the respiratory dysfunction was not activated. There are any number of possible explanations. For the moment it must suffice to point out that: 1) age and stress may not be independent factors; and 2) some

tests, such as the water-maze, may place older animals at a particular performance disadvantage whereas they may perform at least as well as younger animals under conditions such as those requiring the acquisition and performance of passive avoidance skills.

The preceeding studies show that some subject variables such as physical condition, age or stress level can provide information about some of the more arcane mechanisms of air ion action. Air ion dose is another factor that generally receives only secondary consideration, yet it too may provide valuable insights about how air ions effect certain changes. For instance, ion concentrations of a given intensity may engage one set of effectors; ions at another dose may recruit, at least in part, an independent set of responses. No comprehensive and systematic studies of dose specific, ion-dependent phenomena have been found.

Technical difficulties have been cited for the general failure to carry out dose-response determinations, i.e. the lack of a reliable and sensitive indicator of ion effects, especially at the behavior level of system organization, or the disparity in quantification between the numbers of ions generated in a given experimental situation and the actual amounts ingested by the subject via nasal/oral inhalation and/or extra-nasal reception. These methodological issues are infrequently resolved (see Vasiliev for opposite view). Given these limitations, a few experimenters have attempted the generation of empirical dose-response curves.

Bachman et al. (1966) were specifically interested in determining whether reports by other researchers tended to contradict one another because the effects observed were, unbeknown to the authors, dose-specific. To test their hypothesis, they randomly assigned 99 male rats to one of nine groups, 11 rats per group. Three groups were subjected to positively ionized air, three negatively ionized air, and three "electrically neutral" air. The treatment conditions were divided into high, medium and low ion exposures. Dosages were reported as 4,900,000, 188,000 and 61,000 ions/cc respectively. Animals were placed individually in an activity chamber. Activity was recorded continuously for 45 minutes. Fecal pellets and the presence of urine were recorded.

Analyses of variance indicated a significant interaction between polarity and ion concentration. The effect of a particular ion polarity on activity was dose-dependent. For example, with the low dose, gross motor activity was lower with both positive or negative ions than with "no ions." Activity increased with increasing positive ion concentrations. At the highest positive ion dose, activity equalled control values. Low negative ion concentrations decreased activity levels below control values, medium negative ion concentrations increased activity above control levels, and high negative ion concentrations decreased activity to levels attained for low concentrations. The effects of ion concentrations on activity were significant for both negative and positive ions ($P < 0.01$; $P < 0.05$). Observations on "attacks on foil," urination and number of fecal boli were characterized by functions with

discontinuous slopes. The greatest changes in behavior (ca 50%) were shown for ion concentrations below 200,000 ions/cc.

The authors concluded that small changes in ion concentration and polarity produce profoundly different effects. If one assumes that other variables, both biological and psychomotor, are similarly sensitive to these ion parameters, then it is easy to see how the inconsistencies of the literature have arisen. Bachman et al. stated that the task remained of determining to what extent results with rats are applicable to humans.

The conditioned emotional response (CER) is a performance variable used to index fear in rats. The technique requires pairing a response, usually a bar press, with an unconditioned stimulus, e.g. a tone, and an unavoidable painful stimulus such as electric shock. After paired presentations, the tone, in the absence of any shock, elicits a "freezing" response which effectively inhibits bar pressing rates.

Frey (1967) used the CER technique to study the effects of negative air ions and reserpine drug treatments on 18 male rats. The levels of ions reaching the subjects, defined by the current flow to ground, was 5 $\pm$ (3×10^{-10}) amp. These data were not transformed into the customary numbers of ions/cc. It was hypothesized from previous studies that negative air ions and reserpine would reduce the inhibition of lever pressing.

Conditioned emotional responding was established by the conventional means outlined. Experimental trials began following stable (70%)

inhibition of lever pressing. Rats were divided into reserpine-treated (R), small negative ion (N), and no-treatment (C) groups. Data analyses allowed for the known inhibitory effects of reserpine on motor output. The bar-press differences between Group C and Groups N and R were significant ($P < 0.05$). The reserpine and negative ion treated groups showed a disinhibition of the CER. The differences in bar-pressing between the treatment groups N and R were not significant. A second experiment replicated these findings. Differences between negative air ion and control groups were significant at the $P < 0.005$ level. Frey concluded that small negative ions had a significant effect upon rats in this situation: negative ions reduced the inhibition of their lever pressing.

Frey's findings are also notable because they demonstrated an effect of air ions that proved to be reproducible in a highly controlled experimental situation. Elaborate procedures were undertaken to insure the reception of the air ions by the rats and to minimize the effects of confounding subject variables and extraneous stimuli. The success of the replication study argued well for the attention to detail and underscored the care necessary to demonstrate some air ion effects.

Olivereau's (1973) study complemented the CER findings that negative air ions can reduce fear or anxiety-induced performance deficit in animals.

> "Adaptation to a stressed situation was daily studied (24 rats for seven to nine weeks) with a new psychophysiological behavior test. Rats hanging on a ring over a cold water bath had to learn to dive to shorten this period

> of stress. After a short negative air ion treatment (20 minutes, 150,000 ions/cc) the hanging time significantly decreases, but this only in the most fearful rats by plunging earlier. This anxiolytic effect is in agreement with the hypothesis that brain serotonin is involved in the effect of air ions. A few paradoxical results show that treatment with negative air ions may also increase muscular endurance" (Eng abstract).

The studies on elemental and gross behavior variables demonstrate air ion effects at the behavior level of system organization. It has been shown that the influence of air ions is not easily predicted. Some of the ambiguity in estimating effects is a function of: 1) interactions of air ions with subject variables such as age, level of activation or stress; 2) inappropriate extrapolations from the simple to the more complex behaviors; 3) dose-specific indicators; or 4) weak experimental design.

The mechanisms of air ion action postulated to operate at the behavior level, muscle chronaxy, adrenal hormones and 5HT, have received little extended study. The rules for defining primary indicators have not been clearly specified. Nonetheless, air ions can influence behavior variables, and some of these, such as indices of emotional experiences, can guide future research at higher levels of system organization.

PSYCHOLOGICAL BEHAVIOR

It is difficult to make a smooth transition from elemental or gross behaviors to the psychological state of system organization. More than any other hierarchy nexus, the intersection between the behavior

and psychological levels highlights the lack of conceptual models for dealing with inter-level interactions. Some scientists contend that psychological state should be construed as mental behavior and can be studied as an experimental psychologist would study any overt behavior such as reaction time or gross motor activity. However, the assumptions about the nature of mental events, implicit in the behavioristic paradigm, are likely to obscure what may be fundamental differences between mental and behavioral phenomena. The dilemma is considerably more than a philosophical issue: it is rooted in most scientific and other human endeavors (see Knapp, 1976). Nonetheless, behavioral protocols can be advanced that elucidate principles of psychological functioning but circumvent some basic issues. The conditioned emotional response (CER) is an example of such a protocol. Psychophysiological studies are another.

The electroencephalogram (EEG) is an indicator that has demonstrated sensitivity to air ion effects (Assael et al., 1974; Silverman and Kornblueh, 1957). When 10 subjects were exposed to 35,000 ions/cc for 45 minutes, the frequency of alpha waves was reduced from 10 or 11 to 9 or 7 Hz and the amplitude increased by up to 20%. An advance of the alpha rhythm from occipital to frontal areas, with a general synchronization of both hemispheres was found. Control and experimental periods were interchanged at random. No statistical tests were reported (Assael et al., 1974).

Slowed alpha rhythm may be non-specific and can appear under a variety of circumstances, but interhemispheric synchronization is gener-

ally considered a sign of quiescense or relaxation. The authors considered the observed decrease in alpha frequency as a sign of relaxation. The interpretation is consistent with their subjective data which included reports of increased relaxation and these confirm earlier reports that humans are capable of telling when they are in an ionized atmosphere (McGurk, 1959; Winsor and Beckett, 1958).

The psychophysiological effects of ionized air on psychiatric patients were examined by Monaco and Acker (1963). The study was proposed as an exploratory investigation of the effects of positive and negative air ions on the subjective feeling state and physiological reactions of psychiatric patients. It was deduced from previous studies that relative to the effects of positive or no-ion conditions, negative air ions would reduce autonomic arousal and improve "feeling tone."

Forty-eight psychiatric patients of various diagnoses were subjects along with 24 non-patient men and women. The physiological measures; heart rate, respiration and skin temperature, were monitored continuously or at three minute intervals. A paired-comparison adjective list was administered at the end of each session as a psychological measure. Each subject received three ion conditions, positive, negative or ambient for 20 minutes each, with order of exposure counterbalanced among six order groups.

Analyses of variance for the adjective list revealed no significant main effects. For the physiological variables in the patient group, negative ions decreased systolic blood pressure and increased skin

resistance and pulse finger volume. The results were significant in the predicted direction, though slight in terms of amplitude (P not given). A signifcant effect for pulse finger volume, in the unpredicted direction, was found in the non-patient group.

The authors concluded that the "psychophysiological effect of ionized air represents a worthwhile area for future research." It is perhaps unfortunate that they did not apply their own recommendation for the control of "pre-stimulus levels of activation" in the statistical treatment of the data. The oversight may have obscured some otherwise clear-cut ion effects in this well designed study.

In a widely cited study, it was reported that ca 80% of the people in an anxiety syndrome clinic benefitted from treatment with negative air ions (Ucha Udabe et al., 1968). The criteria for "improvement" were not specified, but synopses of the 35 clients' clinical symptoms were published along with the report. According to these, psychoneuroses, apprehension and fear responses remitted or diminished considerably in the manifested syndrome. Most conspicuous was the absence of somatic complaints. Attempts to replicate these findings have not been found. Indirect support of the observation that air ions can benefit patients with illnesses considered to have psychosomatic components is provided by the pain and asthma studies reviewed earlier.

Charry (1976) undertook a study that utilized a psychophysiological model from neurology and psychiatry. Eighty-six subjects were exposed to both positively ionized and ambient air ion level environments. Two

experimental sessions were run in counterbalanced, within-subjects repeated measures design. The positively ionized atmosphere ranged from 20,000 to 30,000 ions/cc. Ambient ion levels averaged from 0 to 300 bipolar ions/cc. Measures of performance (complex and simple reaction time tasks), mood (affective states as assessed by the Adjective Check List and Sulman's Questionnaire) and "physiological activation" (skin conductance) were taken for both days.

The results were analyzed on the basis of two different measures of ion-sensitivity: Lacey's autonomic lability score (ALS) and Sulman's physical sensitivity to serotonin irritation (PS) measure. Statistical analyses demonstrated significant negative affect for all subjects on an adjective check list under positively ionized as compared to ambient conditions ($P = 0.05$ or less). No significant differences between ionized and ambient conditions for either reaction time or skin conductance were found. However, when the data were analyzed on the basis of high or low physical sensitivity (ALS and PS) significant effects of positive air ions were observed: low ALS/PS subjects showed increased reaction times, whereas high ALS/PS subjects showed no changes; low ALS/PS subjects showed depressed skin conductance, whereas high ALS/PS subjects showed opposite responses, and low ALS/PS subjects reported decreased elation and increased fatigue, whereas high ALS subjects appeared unaffected.

When age, sensitivity and ion condition (positive or ambient) were considered simultaneously, two significant three-way interactions emerged.

For simple reaction time, younger subjects with high sensitivity had the slowest reaction time in the ionized condition, and older subjects with both high and low sensitivity to ionized air did not show significant changes in their reaction times ($P < 0.03$). For the measure of tension, older sensitive subjects showed higher levels in the ionized atmosphere compared to ambient conditions ($P < 0.03$).

The relationships between "level of activation" and the effects of air ions on performance were discussed in some detail. "Low ALS is equivalent to a less efficient balancing of, or recovery from, the effects of environmental stimuli, so that shifts in activation would be likely to be associated with performance deficit, which is the case with these subjects."

Charry demonstrated that it is important to consider the pre-stimulus state of an organism before the effects of a (ion) stimulus are interpreted. He went on to suggest that certain physiological measures indicate that some individuals are more sensitive to the influence of air ions than others, and their behavior as social community members could be linked to changes in the electrostatic environment. He concluded that "...These findings support the need to examine more closely the underlying mechanisms which produce these changes as it would appear that significant changes in any one or a combination of affective, cognitive, or behavior states could produce serious performance deficit leading to deterioration in mental health, and aggravation of existing social problems, especially in urban areas where positive air ions are likely to exist in high concentrations."

Sulman's (1970; 1971) studies on naturally occurring ion-phenomena complement Charry's laboratory findings. They also support Charry's observation that the contributions of the environment to the social milieu are important factors to consider in describing social processes. Sulman and his colleagues analyzed biochemical and clinical outcomes of the Sharav effect. The main biochemical results were reported earlier. The clinical results are based on data compiled for over 500 weather-sensitive subjects (Sulman, 1971; Sulman et al., 1970; 1974; 1975).

Clinical complaints during Sharav conditions range in variety and severity from sleeplessness and irritability, to vomiting and diarrhea, respiratory distress and abdominal pain. Sulman has grouped frequently occurring complaints into three major categories. Each category is described by its biochemical and symptom profile. They are:

1) The Serotonin Hyperproduction:Irritation Syndrome, reported to occur in 43% of the people studied. Complaints in this category include: sleeplessness and migraine to vasomotor rhinitis and polyuria;

2) The Adrenal Deficiency:Exhaustion Syndrome. This accounts for 44% of the complaints which include hypotension, fatigue, depression and hypoglycemic spells;

3) The Hyperthyroidism:"Forme Fruste" group covers the remaining 13% of the population sampled.* Many symptoms in this category overlap those in the Serotonin Hyperproduction:Irritation Syndrome. In this

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*In a later paper (1974) hyperthyroid patients were reported to be diagnosed using a thyroxine urine assay developed by Sulman and Tal (1972).

group, allergic reactions, acne and assorted contradictory conditions (increased appetite-weight loss; overactivity-fatigue) are encountered (see Table 2 for biochemical profiles for each syndrome [Sulman et al., 1970]).

TABLE 2: Results of urinalysis in 200 persons suffering from Sharav in relation to their clinical complaints on Sharav days, compared with normal days. The quantitative definition of the changes found by urinalysis is compiled in Table 1, every patient serving as his own control*)

Group No.	Syndrome	Serotonin 5-HIAA	Sodium potassium	17-KS 17-OH	Adrenaline, Noradrenaline	Histamine, creatinine	Percentage of cases
1 86 patients	Serotonin Hyperproduction: Irritation Syndrome	+	0	0	0	0	43
2 88 patients	Adrenal Deficiency: Exhaustion Syndrome	0	0	-	-	0	44
3 26 patients	Hyperthyroidism Forme Fruste	+	+	+	+	+	13

*) Increase +. Decrease -. No change 0.

(from Sulman et al., 1970, p. 49)

Based on the clinical descriptors, Sulman has deduced that the "Sharav effect" resembles Selye's General Adaptation Syndrome (GAS). In this characterization, Stage I is an alarm reaction, Stage II is resistance, and Stage III is exhaustion. From this pattern of responding, Sulman predicted that tourists and new immigrants would not suffer from the Sharav and that long time residents would. His rationale was as

follows: First, the hot, dry weather brings about "passive dilation of the peripheral blood vessels and augments perspiration." Newcomers respond to the change with the alarm reaction (Stage I), a hypersecretion of catecholamines. The alarm response reduces the immediate discomfort of heat stress, but secondary effects, consequent of catecholamine excess, may be experienced. However, with continued exposure to local climatic conditions, resistance (Stage II) is developed and the individual achieves an optimal balance of vessel dilation and perspiration. Long term exposure, Sulman says, erodes the body's capacity to maintain a homeostatic balance for catecholamine secretion because the dilation of the peripheral blood vessels can no longer be compensated. This represents the time when long-term "weather-sensitives" gradually enter the exhaustion phase (Stage III) and are medically at risk. Urinalyses bear out these predictions: new immigrants hypersecrete and veterans hyposecrete catecholamines (Sulman et al., 1970; 1975).

According to Sulman, 5HT hyperproduction is provoked by a steep increase in the positive ionization of the air during the Sharav. Positive air ions are associated with many distress responses supposed to be mediated by 5HT. If drugs are administered which reduce the availability of 5HT, then the aversive effects of positive air ions should be eliminated. Sulman tested this hypothesis. Eighty subjects were treated with antiserotonin drugs in counterbalanced fashion. Subjective assessments were made on pre- and post-treatment conditions for 10 clinical complaints. A "good" reaction to the drugs was reported

in approximately 90% of the cases for all 10 symptoms. Positive placebo responses were reported no more than 10% of the time. No statistical evaluations were carried out (Sulman, 1971). In a later series, Sulman et al. (1974) reported that 75% of 129 subjects suffering from 5HT ailments benefitted from treatment with negative air ions (35,000 ions/cc). Detailed experimental and statistical protocols were omitted. Sulman concludes that, "Our blood serotonin assays (1975), and therapeutic results, with either 5HT antagonists or negative air ionization...confirm the hypothesis of Krueger": positive air ions release 5HT and negative air ions accelerate its oxidation.

SUMMARY

In the early 1960's Krueger and his colleagues investigated the effects of air ions on tracheal tissue. The selection of tracheal tissue preparations was well conceived because:

1) air ions are deposited on tracheal tissue during normal respiration. Therefore the site and possibly mechanism(s) of air ion action could be studied directly;

2) tracheal tissue has cilia-lined mucosa that is representative of the covering of the major distribution channels of the respiratory tree;

3) tracheal tissue is accessible to study. For in vitro and in vivo preparations positive air ions were noted to contract the wall of the trachea, dry the mucosal surface and render the cilia vulnerable to mild mechanical trauma.

After Krueger demonstrated that air ions had biological effects, he sought to elucidate their mechanism(s) of action. Preliminary observations suggested to him a 5HT link because:

1) serotonin was localized in tracheal tissue;

2) serotonin was a known smooth muscle constrictor;

3) intact animals exposed to positive air ions had diarrhea, a sign associated with the hyperproduction of 5HT in patients ill with carcinoid syndrome.

Numerous animal studies were undertaken: negative air ions were shown to decrease tissue 5HT; intravenous injections of 5HT were shown to duplicate all of the tissue effects attributed to positive air ions; and reserpine (a 5HT depletor) mimicked negative ion effects while iproniazid (a 5HT "accumulator") reinstated positive ion effects. From these findings the serotonin hypothesis of air action was evinced: positive air ions release 5HT from tissue stores and negative air ions accelerate its oxidation.

The serotonin hypothesis has been extended to make predictions about the effects of air ions on blood, brain and urine studies. The hypothesis is non-specific for such applications because:

1) there are several pools of central and peripheral nervous system 5HT likely to be affected by air ions;

2) release and oxidation of 5HT both result in a net increase in 5HIAA.

However, the hypothesis can be used to predict that air ions will influence serotonergic systems.

While Krueger and his colleagues studied the effects and mechanisms of air ions at tissue levels of system organization, another group of scientists investigated ion effects on behaviors of the intact organism. Once again early results seemed reasonably straightforward: negative air ions improved the performance of elemental tasks such as reaction time and positive air ions had the opposite effect. However, before long it was noted that though air ions "nearly always had an effect," whether performance would improve or decline could not be predicted. As work progressed it soon became evident that subject variables, such as age and gender, as well as individual differences such as level of stress or motivation, moderated numerous of the ion effects. It also became evident that ion dose was an important experimental variable, but since it was hard to identify a reliable indicator of ion effects, systematic dose-response determinations were not widely undertaken.

Interest in 5HT as a moderator of ion effects was renewed when researchers examined more complex forms of behavior such as emotion or pain. The research tended to split along disciplinary lines: either non-human animals and biochemical events assumed to underly experiences with "inferred emotional content" (anxiety) were studied, or humans and emotional experiences with inferred biochemical content (5HT) were. Both groups were finding correlational data to support the statement that air ions influenced 5HT and emotion and that negative air ions were especially stress-relieving. However, the consensus, soon to be reached by responsible parties, triggered a premature celebration by certain

commercial parties. By the latter part of the 1960's, scandal and federal intervention extinguished most air ion research in the United States.

The accumulated evidence provides links, but does not explain the arcane relationships among electrostatic, biochemical and psychological events. The body of data reviewed does indicate that biological organisms, under certain testing conditions, are capable of detecting and responding to the presence of ionized stimuli. A renewed interest in air ions, a knowledge of the past trials and errors and an awareness of the need for interdisciplinary models to conceptualize their influence and guide research should advance progress in this field.

III. RATIONALE

Air ions influence the behavioral and psychological levels of system organization (see previous review). Studies referring specific ion effects to dose, duration of exposure, route and other conditions of administration are, however, lacking. One reason for the paucity of parametric studies is that a reliable and sensitive indicator of air ion effects on behavior has not been clearly identified. What is required is a human bio-assay like those developed in pharmacology for measuring drug effects, such as the guinea pig ileum for 5HT contraction of smooth muscle, or the "wet dog shake" for narcotic analgesia. The mood tests and urine measures applied in this study were tested as indices of air ion effects in humans.

The effects of air ions on psychological and on biochemical indicators were examined independently. The dependent measures used were: scores on a seven category adjective check list and urine volume and 5HIAA content.

INDICATORS

Mood Measures

The Profile of Mood States (POMS) test was administered to assess the effects of air ions on mood (McNair et al., 1971). The POMS inventory is a 65-item adjective check list compiled to index seven independent mood states (McNair et al., 1971): Tension-Anxiety (T),

Depression-Dejection (D), Anger-Hostility (A), Vigor (V), Fatigue-Inertia (F), Confusion-Bewilderment (C) and Friendliness (Fr) scales. The five point rating scale for each adjective ranged from "not at all," scored as 0, to "extremely," scored as 4 points (see Appendix A).

The POMS test is used in assessing "transient, fluctuating, affective states" (McNair et al., 1971). It was used in this study for the following reasons:

1) The test is self-administered and takes only three to five minutes to complete. Subjects filled out the tests without disrupting the experimental protocol which required isolation from the experimenter in an air ion chamber for five hours.

2) The test is simple to understand: the authors state that no more than a seventh grade education is required to respond to the items (McNair et al., 1971).

3) Learning effects did not confound the test, as is frequently the case for performance variables.

4) An adjective check list similar to the POMS was previously used to demonstrate air ion effects on mood (Charry, 1976). The POMS test was especially chosen because it could be administered at 15 minute intervals to measure mood change (McNair, 1976). It was not known whether the other check list could be applied at repeated intervals.

Biochemical Measures: Urine

Volume of urine. This variable was included because air ions have been reported to effect changes in diuresis (Tromp, 1963; Olivereau,

1971a; 1971b); and urine volumes are easily determined. Tromp (1963) reported "that the amount of urine excreted is very closely related to the environmental conditions; in fact, it is probably one of the most sensitive of biometeorological thermometers" (p. 330).

5-hydroxyindoleacetic acid (5HIAA). 5HIAA, a metabolite of 5HT, was thought to reflect one of the basic mechanisms of air ion action and might be correlated with changes in mood. The benefits of using the urine indicators developed were as follows:

1) 5-hydroxyindoleacetic acid (5HIAA) is the oxidation product of 5HT and is therefore used to estimate its elimination rate. It is 100 times more concentrated in urine than 5HT. Urinary 5HIAA was measured as an indirect test of the serotonin hypothesis.

2) Voluntary urine elimination is a safe and non-invasive method of sample collection. Although blood studies examine a more proximate site of air ion action than urine, the collection procedure is traumatic. The probable biochemical changes induced by the stress of venipuncture procedures could interact with air ion effects in human studies.

3) Sulman used 24 hour urine samples which were assayed for 5HIAA by MacFarlane's method (1956). In the present study, a modification of a more modern protocol was used (Korf and Valkenburgh-Sikkema, 1969). Urine samples were analyzed on the same day they were collected and the assay was simple enough to allow for the convenient measure of 20 samples in a single run.

In criticizing urine studies on transmitter substances, it is frequently remarked that, "the brain is a long way from the bladder."

This comment reflects the many drawbacks to using urine analyses to monitor CNS effects. Some of the analytical problems have been reduced in magnitude as follows:

1) In urine, other waste products may mimic the substance being assayed. Extraction and purification procedures which primarily isolated 5HIAA were used (see Methods), thereby reducing the non-specific reactions of the assay.

2) There are substances present in urine which interfere with the transmission of light and therefore inhibit the fluorescence readings. These were corrected for in two ways. First, a small urine sample was used. This reduced the amount of the interfering substances relative to the 5HIAA extracted. Second, an internal standard, to which a known amount of 5HIAA was added, was used for computing the 5HIAA content per sample. The internal standard served as a correcting factor. These procedures reduced the contribution of extraneous factors to the urine assay.

3) No literature references on the biological variability of the content of 5HIAA for short sampling times (less than 24 hours) were found. The expected range of 5HIAA concentration was estimated from Sulman's 24 hour collections of urine (1970).

Two theoretical issues have not been resolved. First, the assay procedures cannot deal effectively with problems concerning the origins of 5HIAA. Serotonin is present in other sources in the body besides the CNS: platelets, mast cells and enterochromaffin cells of the intestinal

mucosa. All of these contribute to the 5HIAA pool in the final analyses of human urine samples. These non-CNS contributions make urine a "noisy" system in which to identify biogenic amines related to specific central neuronal events. Second, according to the serotonin hypothesis, discussed in the Issues section, positive air ions release 5HT, and negative air ions speed up its catabolism. Both mechanisms should result in a net increase in urinary 5HIAA. Urine studies would not distinguish between mechanisms of action leading to enhanced 5HIAA content, or differentiate between positive and negative ion effects expected by the serotonin hypothesis.

Sub-issues

Time-course. Information is needed on the time-course of ion-related events. Latencies reported for air ion effects range from two minutes for the remediation of hay fever symptoms (Winsor and Beckett, 1958) to years for inducing some aspects of the Adrenal Deficiency Syndrome (Sulman et al., 1970).

Mood and urine measures were particularly suitable for assessing short-term response latencies. Mood, by definition, refers to transient, fluctuating affective states. While the biochemical measures no doubt have longer term components (diurnal, seasonal, yearly), they may reflect changes in the immediate environment as well. Fifteen minute analyses were chosen as the shortest interval for which urine and mood assessment samples could be obtained.

The distinction between primary and secondary ion effects is not often explicitly considered. In this study, information on 5HT and mood

response times was sought to provide insight into the phenomenon. For instance, if biochemical changes were highly correlated with mood changes, one could infer a relationship between the two. If the biochemical changes consistently lagged behind the mood changes or vice versa, an inference about primary and secondary effects could be made. However, the inference might be inaccurate. For while the two response indicators may demonstrate different lag times, it is possible that the events they were chosen to index do not. Thus, the assignment of primary and secondary status must be conferred with circumspection.

Ion-sensitivity. It was evident from the literature reviewed that air ions exert a stronger influence on some subjects than on others (Duffee and Koontz, 1965; Frey, 1961; Gilbert, 1973; Jordon and Sokoloff, 1959; Olivereau, 1971a; 1971b; Sulman et al., 1970). In this study it was reasoned that if subjects could be selected for sensitivity, ion effects would be more pronounced.

Three screening questions were formulated to serve as selection criteria. They were:

1) Do you have or have you ever had any: allergies, bronchial irritation, migraine headaches, stomach illness, any health history or chronic illnesses?

2) Do you consider yourself a weather-sensitive person?

3) Do you consider yourself a person whose moods change pretty easily throughout the day? Do you consider yourself particularly sensitive to your immediate surroundings?

The first question was included on the basis of the literature reviewed that suggested that stressed individuals are more responsive to ionized atmospheres. The effects of air ions on "stress" has not been well tested, particularly in humans. The exploratory nature of this investigation did not justify exposing the old or infirm to any medical risk. Therefore young males with some mild history of illness were chosen. In this study stress was not deliberately induced, but it is possible that psychophysiological procedures to detect stress labile responders would have aided the selection procedures. Charry (1976) used such measures to identify ion-sensitive subjects.

The second question was included as a result of Sulman's finding that ca 25% of the Israeli population is identified as "weather-sensitive." It is these people with whom Sulman frequently works. The inclusion of this selection variable reproduced one aspect of his sample.

The third question was included to:

1) Help identify subjects who were accustomed to noticing their responses to changes in the environment;

2) Help select individuals capable of using the POMS test to report mood change;

3) Select men with enough response variability to register affective change. Subjects with stable POMS would not be expected to indicate ion-related effects.

It was considered that use of these selection criteria might reduce between-subject variability. Age restrictions were imposed to reduce

some of the likely variability due to differences in physiological function such as liver or kidneys. The range chosen, ages 18 to 29 years, was somewhat arbitrary, but considered the relative availability of younger men as experimental volunteers. Men who chose not to be tobacco-deprived for the five hour experimental session were also excluded from this study.

The California Psychological Inventory (CPI) was administered as a measure of whether or not the individuals selected for the study had similar or related personality characteristics (Gough, 1975). The CPI is a 480-item true/false personality inventory. It included 18 standard scales grouped into four categories (see Appendix B). The test is self-administered and takes 45 to 60 minutes to complete. The inventory has been used for testing in non-psychiatric populations aged 12 to 70 years in the assessment of "characteristics of personality [as opposed to mood] which have a wide and pervasive application to human behavior..." (brackets mine) (Gough, 1975). The Eysenck-Maudsley Personality Inventory (EPI) was considered for use because it contained a somatization scale (neuroticism) which was analogous to one of the questionnaires used by Sulman to assess ion-sensitivity, and was used in another air ion study (Rim, 1977). The CPI was chosen, however, because it included a measure for somatization (well-being) along with other scales. The CPI also has a broader popularity among United States researchers and clinicians and more normative data to support its application to theory (Cline, 1972).

IV. METHODS

SUBJECTS

Advertisements (see Appendix C) for participation in an air ionization study were placed in publications with a circulation throughout the San Francisco Bay Area (The Bay Guardian, The Chronicle, The Foghorn at the University of San Francisco and the Phoenix at San Francisco State University). Over 200 responses were received. Thirty-three males between the ages of 18 and 29 were eventually selected for inclusion in this study. Subjects were randomly assigned to treatment or control groups.

Screening procedures were carried out in two stages. The first was a telephone interview. The subject was asked the following questions:

1) How old are you?

2) If you smoke cigarettes can you go without one for five hours?

3) Do you consider yourself a weather-sensitive person?

4) Do you have or have you ever had any: allergies, bronchial irritation, migraine headaches, stomach illness (Crohn's disease, ulcer, spastic colon), any health history or chronic illnesses?

5) Do you consider yourself a person whose moods change pretty easily throughout the day? Do you consider yourself particularly sensitive to your immediate surroundings?

Subjects who gave negative responses to questions 3, 4 and 5 or who expressed a lack of interest, were not processed further. If the sub-

ject answered "yes" to questions 3, 4 or 5 the processing continued. If the interviewee requested clarification of the term weather-sensitive, the following statement was read: "Do you find the weather pretty significant in determining how you feel physically and/or mentally? Do changes in the weather affect your mood or cause any bodily changes of which you are aware?" In response to inquiries on the nature of the experiment, the following explanation was read:

> In this study we're looking at some of the biochemical and psychological effects of certain types of air, ionized air. To help us do this, you'd be asked to fill out a mood questionnaire and provide a urine sample every 15 minutes. The whole experiment would take about 5½ hours and you'd be paid $2.50/hour. The procedures are entirely safe and simple.

Supplementary information was given on a few occasions when requested.

Those who responded affirmatively to one or more of the "sensitivity" questions (numbers 3, 4 or 5) were told that a packet of forms would be sent to them. The contents were then explained by the interviewer. The subjects were requested to complete all items and return the information by mail. The processing of these returned data comprised the second stage of the screening procedure.

The following forms were contained in the packet:

1) A 135-item health questionnaire (see Appendix D);

2) A human subjects consent form. This explained the experiment in more detail and outlined potential risks, hazards, and benefits (see Appendix E);

3) A University of California addressed return mail envelope;

4) A breakfast menu. Subjects were requested to restrict foods that would interfere with the biochemical analyses (see Appendix F);

5) Three POMS lists, marked "MORNING," "NOON" and "EVENING." Instructions on the adjective check list were modified to read:

> Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE space under the answer to the right which best describes HOW YOU ARE FEELING RIGHT NOW (see Appendix G).

Subjects were instructed to fill out the forms at the designated times on the same day. All subjects were told that they would receive payment of $2.00 for the return of the completed materials. Eighty-five percent were returned.

Subjects who had said "yes" to the "health sensitivity" question during the telephone interview had these responses cross-checked with the health inventory. It was planned that if a medical risk were disclosed, a consulting physician would determine the feasibility of a subject's inclusion in the study. No medical risks were evident from the health inventories returned so consultation was not required.

The POMS tests were scored. Average Range and Total Mood Disturbance (TMD, POMS manual) were used as response lability indicators for the seven mood categories. Range and TMD were calculated as follows:

> Range: The difference between the highest and lowest scores for a given mood variable on a given day. For instance, if the Tension-Anxiety scores for MORNING, NOON and EVENING were 2, 12 and 20, respectively, the range on the T scale would be calculated as 18. Summing all categories and dividing the number of categories gave the average range score for that subject.

TMD: Sum of scores for POMS categories: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia and Confusion-Bewilderment less those for Vigor and Friendliness for the three samples.
TMD = (T + D + A + F + C) - (V + Fr)

Responders with a TMD totalling less than 185 and/or an average range of less than 5.0 were excluded from the study at this time. Values of this magnitude were considered low: these subjects frequently filled in numbers in the "not at all" or "a little" range of the POMS scales. Such response tendencies reduced the likelihood of demonstrating some ion effects because:

1) A low level of pre-stimulus responding precluded registering "less affect"--a basement effect; and

2) If subjects did not show affective change in any given, normal varied day, they were considered unlikely to show affective change induced by air ions.

"Non-responders" were sent a check for $2.00 and thanked for their cooperation. No experimental day was scheduled.

ION-TREATMENT ROOM

The ion-treatment room measured 3 x 4 x 3m. A three meter plywood partition divided the room in half lengthwise. Its surface was covered with aluminum foil to which a grounding wire was attached. A poster of a forest scene covered the center of the plywood partition. Eight ion "discharge heads" (Klykon Remote Discharge Head, Model 1501) in a 2 x 4 matrix faced the poster (see Appendix H for schematic). A battery operated telephone intercom (Archer Z-Station Transistor Intercom,

Catalogue No. 43-211, Radio Shack, Division of Tandy Corp., Fort Worth, TX) was used for subject-experimenter communications. Light was screened out by covering the window. Overhead fluorescent fixtures provided illumination. The room was sound-attenuated with acoustic tile. A synthetic fiber carpet covered the floor. Subjects rested on a lounge covered with a cotton bedspread. Two small tables held plastic containers for urine samples, liquids for ad lib consumption (de-ionized water, preservative-free apple and grape juice) and assorted children's games and puzzles. Temperature was maintained at 25° C ± 1.5°. A small electric fan created a masking white noise and circulated air from an outside ventilator duct through the room throughout the course of the experiment. The laboratory site was within one mile of the ocean and was considered to be relatively free of particulate matter (Krueger, 1976). One subject was tested per day.

WEATHER MEASURES

Barometric pressure, relative humidity and general weather conditions were recorded for each session along with ambient ion levels (Airguide Compensated Barometer, Airguide Instrument Company, Chicago; Abbeon Certified Hygrometer and Temperature Indicator, Model HTAB 169 B, Abbeon, California, Inc., Santa Barbara, CA). Barometric pressure averaged 29.84 inches ± 0.18 S.D. Relative humidity was generally stable at 52% ± 4% S.D. Ambient levels of positive ions were on the order of 200 to 300 ions/cc. The presence of small negative ions was not detected. Data were collected from March, 1977 to March, 1978.

GENERATION AND QUANTIFICATION

Ions were generated by the corona discharge method (Klykon Laboratory Generator, Model 140, Klykon, Inc., Miami, FL). These generators are said to produce almost no ozone (< 0.002 ppm, Klykon manual).

Ion counters extract ions from an air stream passing across a set of charged metal plates. Ions are attracted to the plates depending upon the strength and polarity of the electric field of the plates and the size and charge of the ions. Ions give up their charge to the grounded plates. Because the charge on an air ion has electrical polarity, it is possible to collect specific ions by applying an appropriate d-c potential to the polarizing plates. Ions of a given polarity and size can be deflected into contact with collector plates where their charge is neutralized. An electric current is generated by the ions deposited and is measured by a micromicroammeter.

The unit used in these experiments could be adjusted to selectively measure ions having a specified mobility range (Klykon Volumetric Ion Counter, Model 1901, Klykon, Inc., Miami, FL). The 66 v polarizing voltage was chosen, as this collects only ions with mobilities greater than or equal to 66 v/cm/cm/sec. These include ions of the 22 v mobility and greater. Measurements recorded on 10 separate occasions, under varying atmospheric conditions, showed no differences between the 22 v and 66 v settings. Because the readings are cumulative, this indicated that small air ions were being generated rather than those of the intermediate (less mobile) type.

Before the subject arrived, the ion collector was placed on the lounge with the sampling port situated to approximate the subject's head position while supine. An electrometer was connected to the ion collector (Micromicroammeter, Model 240, E-H Research Laboratories, Inc., Oakland, CA). The instruments were turned on and allowed to reach stable operating temperatures (15 minutes). Leakage currents to the electrometer were recorded for "blower off" and "blower on" positions and intake port sealed conditions. These readings were subtracted from all readings to zero the equipment.

After ambient ion levels were recorded, the ion generator was operated at maximum output. Positive and negative ion concentrations (ca 100,000 ions/cc) were determined by the same procedures outlined above. In pilot studies, measurements were recorded at the end of each experiment. Variation in ion densities before and after was less than ± 15% of the mean value. Subsequently, post-session measurements were discontinued.

The difficulties of precise measurement of air ion concentrations with subjects in the room have been addressed elsewhere (Frey and Granada, 1962; Frey, 1965). They are principally: subject movement; type of clothing; absorption of ions on surfaces and ion-cloud distortion. These factors make the statement of ion concentration with a precision of more than ± 15% difficult.

EXPERIMENTAL PROTOCOL

The subject was exposed to ambient ions for the first 30 minutes; two hours of positive (or negative) ions; two hours of negative (or positive) ions; then 30 minutes of ambient ions. A tone on the intercom signalled the end of each 15 minute segment. At the signal, the subject filled out the numbered POMS test corresponding to that time period and then provided a urine sample. Thus there were twenty 15 minute segments: 20 data points for mood and urine (see Figure 1).

Figure 1:

PRE	AM (Positive or Negative)	PM (Negative or Positive)	POST
	* * *	† * *	
1 2	3 4 5 6 7 8 9 10	11 12 13 14 15 16 17 18	19 20

*Entry of experimenter for equipment change or counterfeit noise.
†Lunch.

All subjects were requested to report at 9:00 AM on the assigned day. They had been advised to wear a cotton shirt and pants (cotton is less likely to build up an electrostatic charge). A cotton lab coat was provided if necessary. Subjects were escorted to the experimental room.

Instructions to subjects:

1) If you would like to use the men's room before the experiment begins it is just down the hall to your right.

2) Please write what you ate for breakfast on the back of test #1.

3) While taking the mood tests, try to be as sensitive as you can be to the full range of choices and record even slight changes.

4) Feel free to make any observations or comments on the back of the mood tests about what you are experiencing. Sometimes the mood tests do not list a particular feeling and your notations may be helpful to us.

5) You will periodically be hearing noises. They are not necessarily correlated to any changes in the air environment. Some of them are included to keep you from trying to guess what changes are taking place.

6) A light lunch will be served after test #12. The experiment will continue. There will be no break. If the intercom sounds while you are still eating, please complete the required tasks and then resume eating. (Lunch consisted of: a small lettuce, apple and raisin salad with French dressing; salted pretzel sticks; and a vanilla-flavored sponge cake with cream filling [Hostess Twinkie]. These foods were used in accordance with recommendations for diets which do not interfere with the biochemical analyses performed [UCSF Dieticians' Manual]).

Urine: Each sample you provide will be used. For analysis we only need a very small sample. However, make sure you empty your bladder completely each time. That way each 15 minute segment will start with freshly formed urine. Because we need such a small sample you DO NOT have to drink a great deal; just enough water for urine formation is necessary. When samples are too dilute (light colored) they are a little harder to work with, so try to balance your liquid intake between being able to provide steady samples and still retaining a strong yellow color. A glass of liquid every sixth time should be a good start. That would be after test numbers 1, 6, 12 and 18. Try to use this pattern, but if it is not working, you may alter it to suit yourself.

PLEASE ASK ANY QUESTIONS YOU MAY HAVE ABOUT THIS.

These instructions were given verbally and in written form. The subject was requested to attach the grounding lead to his ankle (the electrodes were two silver dimes, glued to a velcro band. No electrode paste was used). When the experimenter was clear that there were no questions, she left the room.

During the course of the experiment, the room was entered several times. Some of these were equipment switching times and some were counterfeit entrances. All such entries were carried out at the same

times during subject runs. The experimenter was completely hidden from subject view on all entrance times. When the tests for the 20th time interval were completed the experimenter was signalled by the subject on the intercom. The subject was instructed to detach the ground wire from his ankle and to meet in an interviewing room at the opposite end of the hall. In the closing interview the following questions were asked:

1) Did you notice any changes? When?

2) Were they good or bad?

3) If you were to break the time into halves, could you call one half better than the other?

Responses were recorded. The experimenter asked if there were any other comments or questions. At the end of the interview, the subject was supplied a California Psychological Inventory (CPI) and requested to mail back the completed form. This completed the experimental trial. Payment was contingent upon the return of the CPI.

BIOCHEMICAL ANALYSIS

Collection of Urine

Urine samples were collected at 15 minute intervals. Each sample was contained in a plastic beaker with seal. The urine samples remained at room temperature until they were analyzed later in the day; preliminary studies indicated that 5HIAA concentrations were unchanged over a five to seven hour period.

Volume

Total volume of each sample was recorded. An aliquot was removed for 5HIAA analysis.

5-Hydroxyindoleacetic Acid (5HIAA) Assay

Principle. The 5HIAA was extracted first into ether from an acid urine and then from the ether into a buffer, pH 7. The solution was treated by the o-pthalicdicarboxyaldehyde (OPT) method for fluorophore formation (Korf and Valkenburgh-Sikkema, 1969). Calculations for the estimation of 5HIAA were based on the use of an internal standard.

Reagents, Solutions and Equipment.

1) Water: De-ionized water was used throughout;

2) Phosphate buffer (0.5 M PO_4, pH 7). This solution was made weekly;

3) Cysteine (L-cysteine hydrochloride hydrate). Calbiochem. A 1.0% solution in water and a 0.4% solution (Reagent B) in the phosphate buffer were made daily;

4) Ether ($[C_2H_5]_2O$). Mallinckrodt;

5) Hydrochloric acid (HCl). Mallinckrodt. Concentrated HCl and 6N HCl were used;

6) 5-Hydroxyindoleacetic acid (5HIAA). Sigma. 1.0 mg/ml of 5HIAA in water; can be used for a week if kept refrigerated. A 1:100 dilution in the phosphate buffer was used in the preparation of the standards made daily;

7) o-pthalicdicarboxyaldehyde (OPT). Aldrich. 0.1% OPT in 95% ethanol. This solution was stable for about a week if kept refrigerated;

8) Quinidine sulfate. 0.03 µg/ml;

9) Sodium chloride (solid) (NaCl). Mallinckrodt;

10) Sodium metaperiodate ($NaIO_4$). G. Frederick Smith. 0.1% in water. This solution was made weekly;

11) Test tubes. Screw cap (teflon-lined);

12) Spectrophotofluorimeter. Aminco-Keirs, American Instrument Co., Silver Springs, MD;

13) Readout: A Data Precision Corp. Model 3500 Digital Volt-Ohmmeter was connected to the recorder output of the Aminco microphotometer. Three condensers, totalling 20,000 µF were connected across the output of the volt-ohmmeter to smooth voltage fluctuations. Readings on the 10 scale were 4.6 times those of the transmission scale.

Procedure. Urine sample size for use in the ether extraction procedure was determined on the basis of total urine sample volumes:

Urine (ml)	Sample (ml)
0-20	0.1
21-50	0.2
50-100	0.5
> 100	1.0

Reagent B was used to equalize sample sizes to 1.5 ml for use in the ether extraction step.

Extraction. In a test tube were combined: the urine sample; the appropriate amount of Reagent B; 6N HCl; NaCl; and ether. All tubes were capped, checked for leaks by olfactory testing, and placed on a

rotator. The ether was transferred to a test tube and the phosphate buffer was added. Test tubes were capped and placed on a rotator. The upper ether layer was removed and discarded. The remaining aqueous layer was retained for use in the fluorescence assay.

	Standard (ml)	Sample (ml)
Reagent B	1.5	1.4
Urine	-	0.1
6N HCl	0.3	0.3
NaCl (1g)	+	+
Ether	10	10
	Cap and place on rotator at medium speed 10 min. Transfer 8.5 ml of ether to a test tube	
Phosphate Buffer	4.0	4.0
	Cap and place on rotator at medium speed 10 min. Remove and discard upper ether layer	

Fluorescence Assay. Three tubes were used for each urine sample. Tubes "A", "B" and "C" contained the extract. Tube "B" was used as a blank by periodate oxidation destruction of the 5HIAA. Tube "C" was an internal standard to correct for recovery. The aqueous extract was added to each tube. Quantitative variability was shown to be less than 8% with duplicate samples.

	Tube A	Tube B	Tube C
Aqueous extract	1.0	1.0	1.0
Phosphate buffer	0.1	0.1	-
5HIAA (1 μg/ml)	-	-	0.1
1.0% cysteine	0.1	-	0.1
0.1% $NaIO_4$	-	0.1	-
	Mix tubes in rack by manually shaking two min.		
Concentrated HCl	2.0	2.0	2.0
	Mix solutions in tubes on vortex mixer 10 sec.		
0.1% $NaIO_4$	0.1	-	0.1
0.1% OPT	0.1	-	0.1
	Cap all tubes "A" and "C." Wait 30 min.		
1.0% cysteine	-	0.1	-
0.1% OPT	-	0.1	-
	Cap remaining tubes "B." Boil all tubes 10 min. Cool in water five min.		

Fluorescent Readings. The excitation/emission wavelengths used were 365/475. The quinidine solution was used to standardize the daily readings by adjusting the digital volt-ohmmeter to read 270. The adjustment was accomplished by manipulating the sensitivity dial on the spectrofluorimeter when the slit width and meter multiplier were set at 1.0 and 0.1 respectively.

Calculations. The concentration of 5HIAA in urine was determined by the following equation:

$$C_o = (0.4706/V_u) \times (\Delta A/[\Delta C - \Delta A])$$

where:

C_o = the concentration of 5HIAA in the original urine sample;

V_u = the volume of urine used;

ΔA = the fluorescence readout of tube "A" minus the fluorescence readout of tube "B";

ΔC = the fluorescence readout of tube "C" minus the fluorescence readout of tube "B"

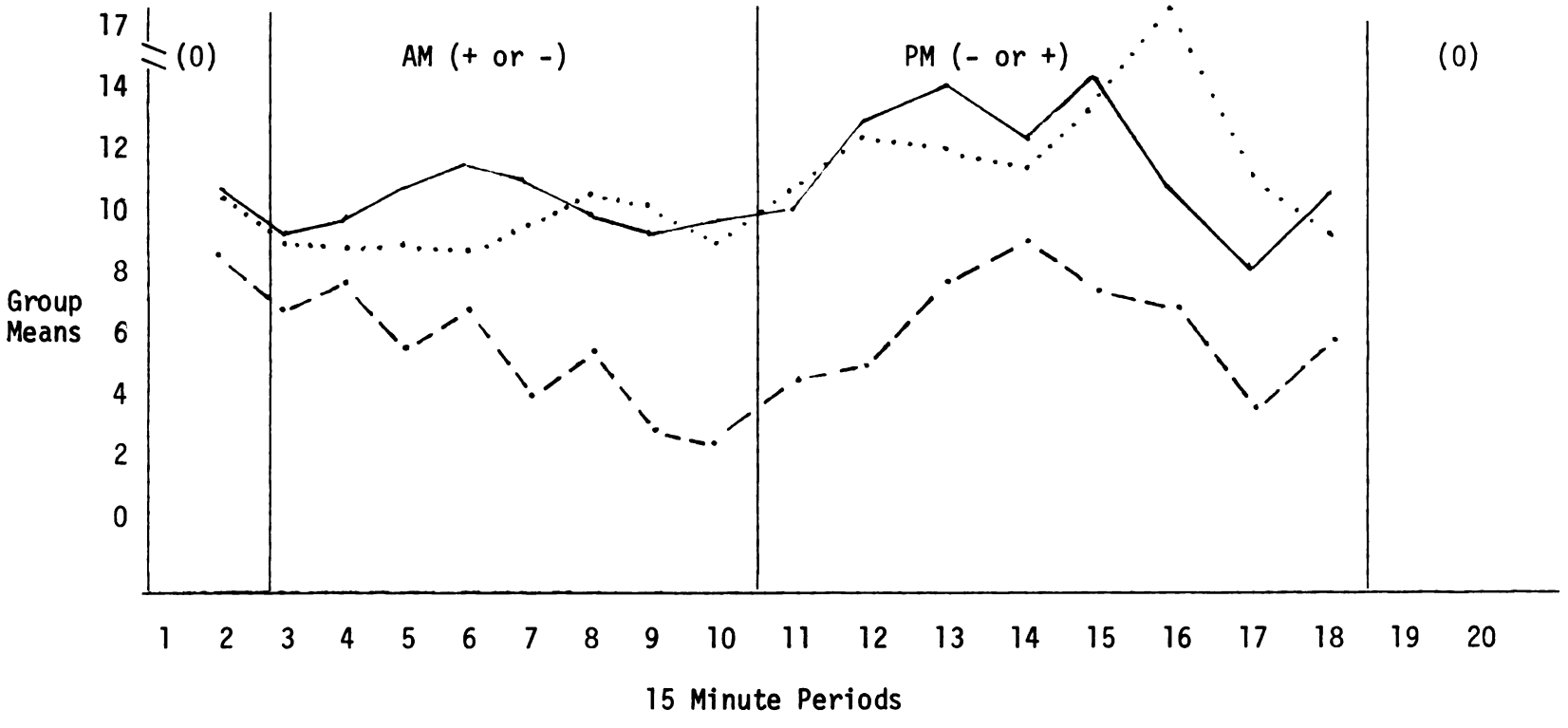
The derivation of this formula is shown in Appendix I.

DATA ANALYSIS

After all subjects were tested, visual inspection of the data showed a marked deviation from overall response level at or near period 12. The variation was observed for most of the dependent variables and was independent of ion-treatment order (see Figures 2, 3 and 4). It was noted that lunch was served during this interval and it appears that the anticipation and/or metabolism of the food influenced the PM dependent measures so that within-subject analyses of AM vs PM periods (positive vs negative) were inappropriate. Across subject analyses were therefore performed, in which the AM treatment periods (3 to 10) and PM treatment periods (11 to 18) were considered as separate and complete experiments, as each contained data from positive (N = 13), negative (N = 13) and control (N = 7) groups. Therefore, for a given dependent variable, the effects of air ion treatment were sought by comparing the differences in

FIGURE 2 (Graph of Table 10): Means for POMS variable Vigor for each 15 minute period in the AM and PM

Note deviations from overall response level at or near period 12 (lunch).



Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

——— = positive AM/negative PM ion treatment (N=13)
..... = negative AM/positive PM ion treatment (N=13)
.— — = ambient ion treatment in AM and PM (N=7)

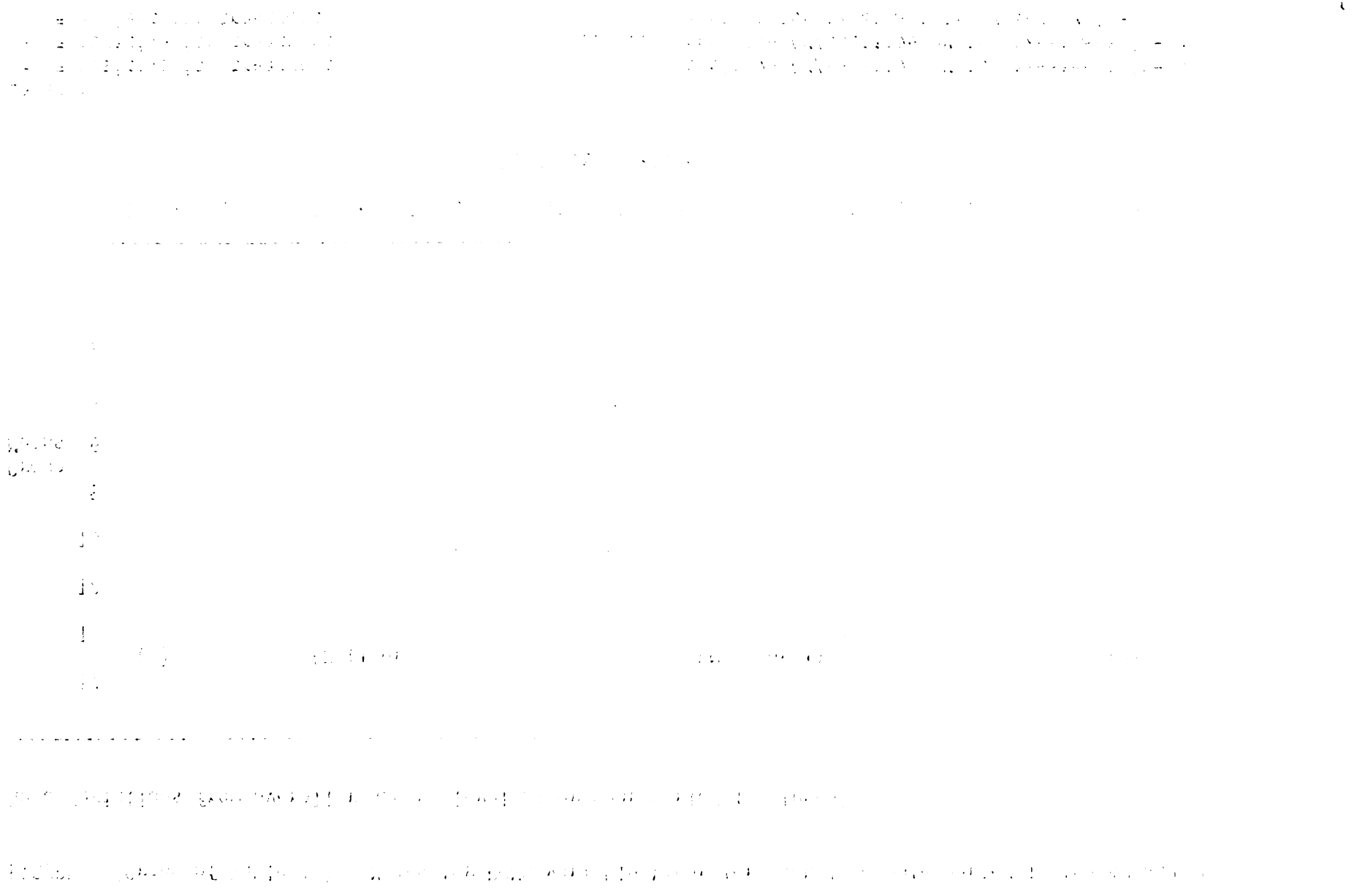
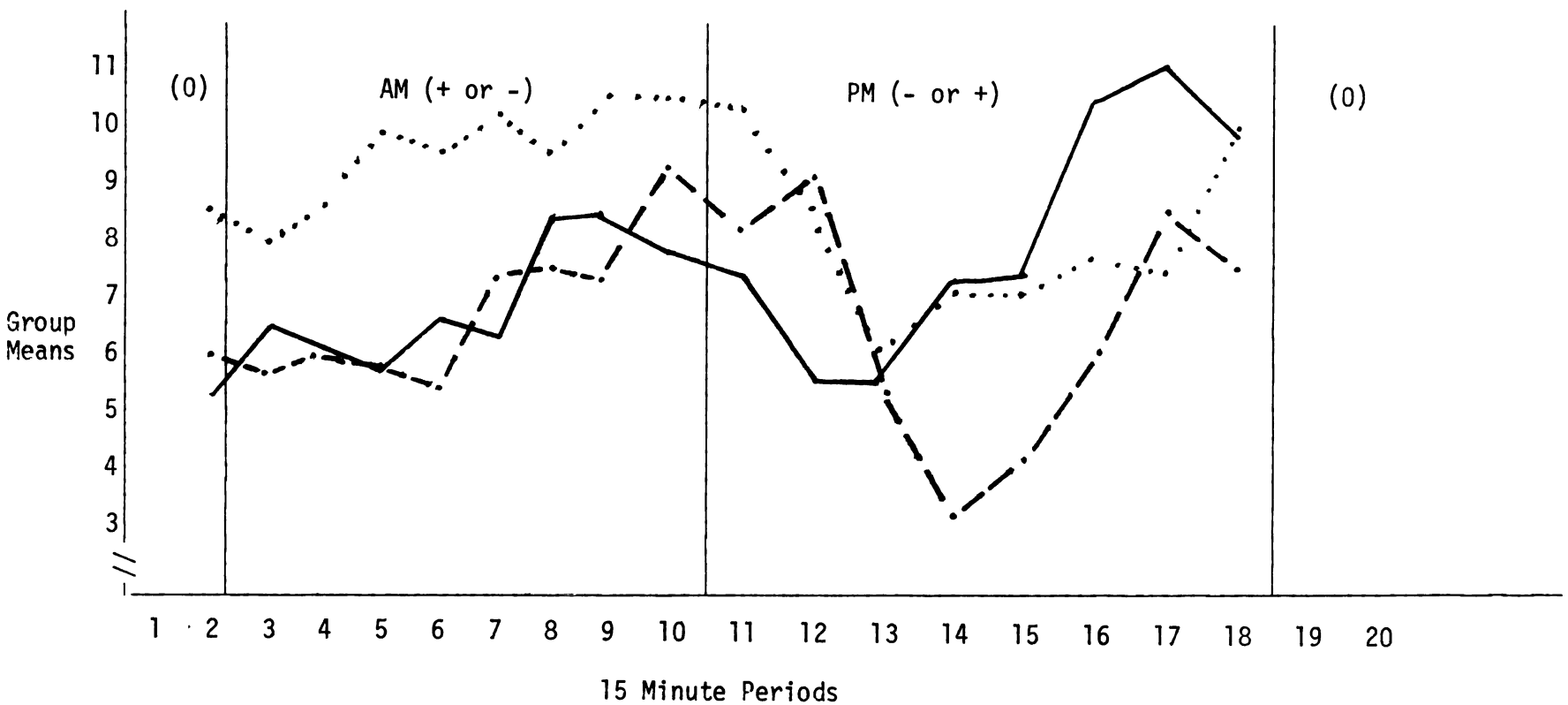


Figure 3 (Graph of Table 11): Means for POMS variable Fatigue-Inertia for each 15 minute period in the AM and

FIGURE 3 (Graph of Table 11): Means for POMS variable Fatigue-Inertia for each 15 minute period in the AM and PM

Note deviations from overall response level at or near period 12 (lunch).

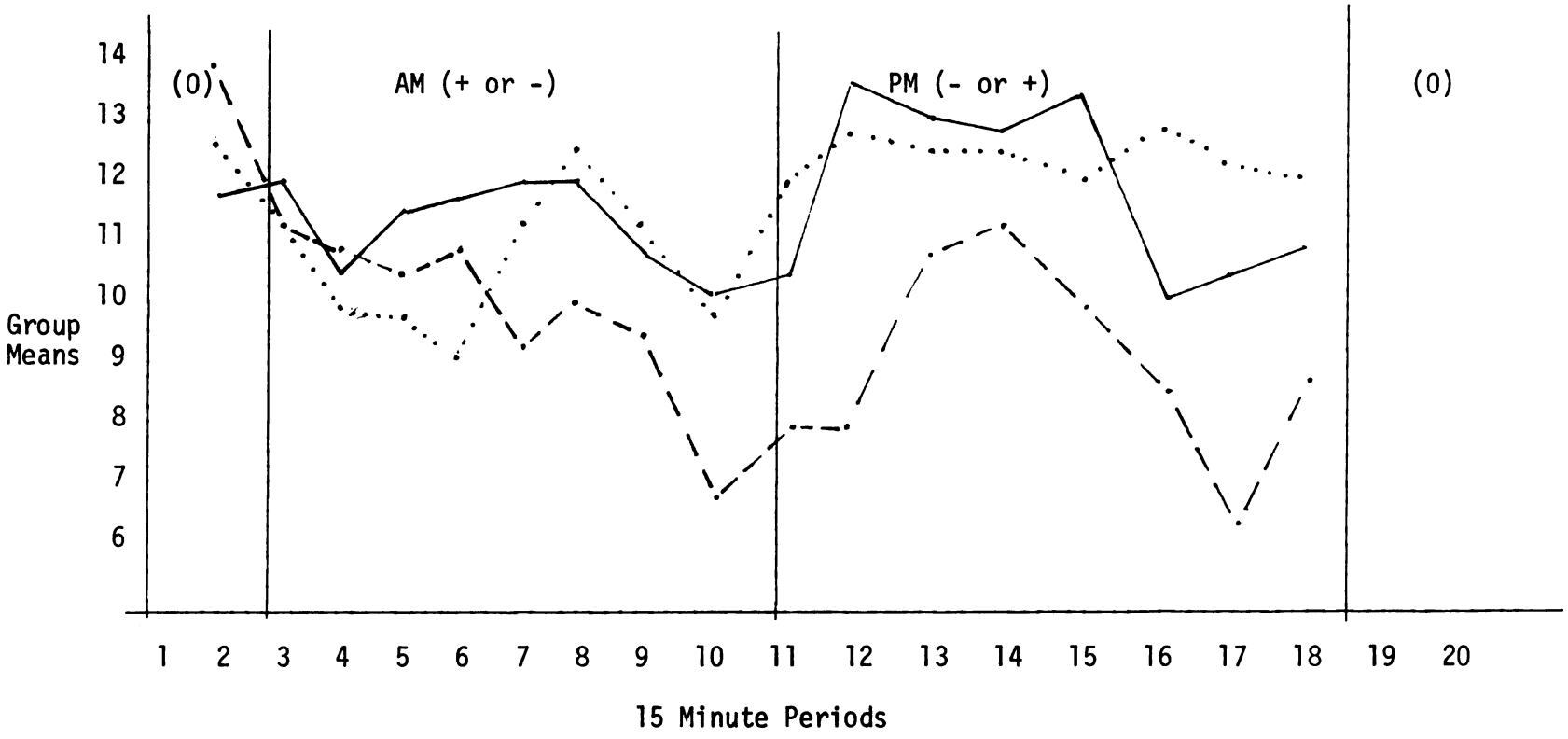


Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

——— = positive AM/negative PM ion treatment (N=13)
..... = negative AM/positive PM ion treatment (N=13)
.— — = ambient ion treatment in AM and PM (N=7)

FIGURE 4 (Graph of Table 13): Means for POMS variable Friendliness for each 15 minute period in the AM and PM

Note deviations from overall response level at or near period 12 (lunch).



Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

——— = positive AM/ negative PM ion treatment (N=13)
..... = negative AM/ positive PM ion treatment (N=13)
.— — = ambient ion treatment in AM and PM (N=7)

means among groups, and between pooled treatment groups vs control groups, for AM and PM separately.

There were seven psychological variables indexed by the POMS tests: Tension-Anxiety (T); Depression-Dejection (D); Anger-Hostility (A); Vigor (V); Fatigue-Inertia (F); Confusion-Bewilderment (C); and Friendliness (Fr). The basic data are the means for each group (positive, negative or control) for pre-treatment period 2 and treatment periods 3 to 10 (AM) and 11 to 18 (PM) for each dependent variable (see Tables 7 through 13). There were few missing data: one subject failed to complete a POMS test for period 9 and another subject overlooked some POMS items for period 11. These missing data were filled in by taking the raw score from the subjects' previous period for each psychological variable. Thus, if the subject had a score of 10 for period 8, a 10 was also used for the missing period 9 in calculating the group mean.

There were three biochemical variables analyzed: urine volume (VOL), concentration of 5HIAA in the urine (CONC) and amount of 5HIAA in the urine (AMT). The basic data for the biochemical variables are the means for each group (positive, negative or control) for pre-treatment period 2 and treatment periods 3 to 10 (AM) and 11 to 18 (PM) for each dependent variable (see Tables 14 through 16). There were numerous missing data for the CONC and AMT variables. Therefore, for all of the analyses, except those using group means, the data were collapsed for paired treatment periods. Thus, data from periods 3 and/or 4 were averaged for analyses and so forth on through periods 17 and 18, creating four group means for the AM analyses and four group means for the PM

TABLE 7: Means (± S.D.) for POMS variable Tension-Anxiety for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	7.38		7.08		5.00	
3	7.69	6.75	8.46	4.48	5.14	3.67
4	6.77	7.52	9.46	6.01	5.43	4.43
5	7.38	8.32	8.92	5.47	5.29	4.27
6	6.38	7.12	10.00	7.77	3.57	2.99
7	7.46	5.04	8.08	5.51	5.86	6.31
8	5.85	4.06	6.31	4.68	3.43	1.72
9	6.62	4.63	5.54	4.01	4.14	3.08
10	6.23	4.27	6.46	4.41	6.14	5.87
PM						
11	6.77	4.76	6.46	5.29	5.57	4.83
12	6.62	4.37	5.69	4.52	5.86	5.61
13	6.62	3.82	6.62	6.23	5.43	3.15
14	7.46	5.32	6.08	5.56	3.00	1.15
15	8.23	5.61	5.69	4.85	4.71	2.75
16	8.38	5.25	7.23	6.65	4.43	1.99
17	7.23	3.85	7.31	6.88	5.71	3.30
18	7.92	4.92	8.00	7.87	5.71	3.68

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 8: Means (± S.D.) for POMS variable Depression-Dejection for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	4.00		8.15		1.14	
3	5.00	6.16	7.54	7.55	1.57	0.79
4	3.38	4.44	7.54	8.18	2.57	2.44
5	4.31	6.43	9.23	10.93	2.29	1.80
6	4.38	6.37	9.92	9.33	1.86	1.35
7	5.00	6.32	8.15	7.53	5.29	7.99
8	5.08	7.42	6.85	6.18	1.57	1.81
9	6.77	8.23	6.92	5.57	1.86	2.27
10	5.31	4.79	6.85	6.34	4.86	6.34
PM						
11	6.77	6.85	6.62	9.06	3.57	4.16
12	6.77	6.30	5.00	6.88	4.29	5.28
13	6.38	5.17	5.31	8.93	2.29	2.36
14	6.31	6.22	6.62	10.86	1.86	2.27
15	7.77	6.43	6.38	9.17	2.14	1.86
16	7.31	6.18	6.46	8.05	2.43	2.30
17	7.31	6.20	6.38	7.61	2.71	2.29
18	10.15	9.80	6.54	11.19	2.43	2.94

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 9: Means (± S.D.) for POMS variable Anger-Hostility for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	6.46		5.00		1.57	
3	5.31	9.02	8.00	7.12	2.86	2.85
4	5.15	9.14	6.54	6.62	2.43	2.51
5	5.69	9.04	7.54	10.30	1.57	2.07
6	5.00	8.15	7.69	9.94	2.71	2.75
7	5.31	8.16	6.08	4.54	4.29	6.34
8	5.08	6.63	3.69	4.25	1.29	2.56
9	4.85	6.52	3.62	3.95	1.71	3.25
10	6.69	9.69	4.77	5.13	3.29	4.27
PM						
11	5.00	6.00	6.54	10.38	3.14	3.98
12	4.85	4.02	4.62	7.51	3.14	4.41
13	4.69	5.42	7.15	10.53	1.71	1.70
14	3.92	4.42	5.92	9.34	0.86	1.46
15	4.62	4.25	6.69	10.80	0.86	1.46
16	3.92	4.59	7.46	10.79	1.57	1.72
17	4.77	4.46	7.15	9.63	3.86	4.02
18	5.92	4.91	8.00	12.83	2.00	1.53

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 10: Means (± S.D.) for POMS variable Vigor for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	10.77		10.46		8.57	
3	9.31	6.71	9.00	5.20	6.57	4.72
4	9.69	7.19	8.62	5.01	7.86	4.95
5	10.31	6.73	8.69	5.84	5.86	2.85
6	11.31	7.43	8.54	5.44	6.43	7.46
7	11.00	5.99	9.38	5.58	4.00	3.46
8	9.85	6.48	10.15	6.23	5.57	4.86
9	9.00	5.85	10.08	6.46	2.86	2.34
10	9.54	7.08	9.00	5.32	2.29	2.81
PM						
11	10.46	5.50	10.08	4.68	4.14	4.18
12	12.62	6.61	13.77	5.36	4.29	4.86
13	11.85	3.69	14.31	6.52	7.86	6.52
14	10.85	4.71	12.23	7.72	8.14	5.96
15	12.15	6.18	13.54	6.89	7.14	6.91
16	17.15	20.11	11.08	6.36	6.29	4.92
17	11.08	6.42	8.08	6.69	3.29	3.20
18	8.69	5.63	10.46	6.31	5.71	6.50

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 11: Means (± S.D.) for POMS variable Fatigue-Inertia for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	5.31		8.54		6.00	
3	6.54	5.17	8.00	5.60	5.57	5.83
4	6.00	5.24	8.62	7.32	6.00	4.80
5	5.77	3.90	10.00	6.42	5.71	4.46
6	6.92	5.11	9.77	5.99	5.29	3.95
7	6.31	5.68	10.31	6.79	7.14	3.02
8	8.54	7.30	9.85	7.51	7.43	4.04
9	8.54	6.94	10.62	8.99	7.14	4.38
10	7.92	5.69	10.46	8.02	9.14	3.13
PM						
11	10.15	7.03	7.38	7.05	8.14	4.67
12	8.69	7.92	5.69	7.04	9.14	5.43
13	6.15	4.69	5.69	8.73	5.29	4.82
14	7.15	5.55	7.31	9.00	3.14	3.80
15	7.15	5.97	7.38	8.00	4.43	2.99
16	7.92	4.89	10.38	7.78	6.14	4.10
17	7.77	6.26	11.00	8.59	8.57	3.21
18	10.00	7.59	9.92	8.50	7.57	4.89

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 12: Means (± S.D.) for POMS variable Confusion-Bewilderment for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	8.54		7.62		4.14	
3	8.62	4.27	8.15	5.13	4.29	1.38
4	7.46	3.20	8.54	4.91	4.57	1.40
5	7.62	5.12	8.85	5.84	4.57	1.27
6	7.15	3.74	8.23	4.49	3.71	2.14
7	7.69	4.84	7.77	4.13	4.57	2.82
8	8.31	4.37	6.46	3.86	3.71	1.70
9	8.92	5.45	7.31	4.29	4.71	1.70
10	7.77	4.46	7.69	3.75	6.00	2.58
PM						
11	6.77	3.39	7.15	4.60	4.57	1.40
12	7.15	3.95	5.08	4.35	4.71	1.89
13	5.54	4.59	5.85	4.85	3.71	1.50
14	6.92	4.37	7.00	5.26	3.71	1.80
15	6.77	4.85	7.77	6.19	3.86	2.27
16	8.23	5.60	9.08	5.96	4.14	1.46
17	7.08	4.75	9.08	6.25	4.86	1.46
18	8.38	4.46	8.54	7.37	4.86	1.68

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 13: Means (± S.D.) for POMS variable Friendliness for each 15 minute period in the AM and PM

	+ (N = 13)		- (N = 13)		0 (N = 7)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	11.77		12.54		13.86	
3	11.85	5.67	11.00	3.29	11.00	5.77
4	10.31	5.60	9.69	4.48	10.71	4.89
5	11.08	5.14	9.62	5.41	10.14	3.89
6	11.38	5.49	8.92	4.97	10.71	5.12
7	11.62	4.68	10.77	3.63	9.00	6.68
8	11.62	5.36	12.31	4.40	9.86	5.46
9	10.69	5.30	11.08	5.31	9.14	5.55
10	10.23	5.57	9.92	4.29	6.86	4.22
PM						
11	11.85	3.74	10.77	5.10	7.86	4.81
12	12.38	5.33	13.62	4.31	7.86	5.37
13	12.23	4.49	12.85	4.69	10.71	5.28
14	12.23	4.09	12.46	4.39	11.29	1.80
15	11.77	5.88	13.08	3.07	9.86	4.88
16	12.62	6.19	10.00	3.98	8.29	3.25
17	12.15	5.40	10.31	5.74	6.29	3.99
18	11.69	5.84	10.54	4.37	8.86	4.71

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 14: Means (± S.D.) for Urine Volume for each 15 minute period in the AM and PM (ml)

	+ (N = 13)		- (N = 10)		0 (N = 5)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
3	55.65	96.21	42.65	48.87	11.60	10.83
4	35.92	46.97	48.51	63.60	21.80	10.92
5	59.15	58.55	55.00	83.17	41.80	36.44
6	51.15	53.84	70.55	88.35	67.60	66.72
7	53.12	83.74	56.80	63.58	77.40	65.73
8	52.54	51.91	67.00	73.95	99.60	91.71
9	62.54	86.50	63.15	68.80	42.40	43.70
10	59.42	57.45	53.55	53.86	64.80	57.77
PM	(N = 10)		(N = 13)		(N = 5)	
11	48.50	41.95	53.69	51.47	70.80	58.85
12	42.65	44.31	50.15	48.86	96.60	97.03
13	30.55	21.18	51.31	45.65	109.20	89.41
14	19.15	22.59	21.69	15.67	101.60	119.27
15	33.10	24.90	36.23	38.58	117.20	120.40
16	48.80	55.16	44.69	56.08	106.80	133.08
17	45.25	49.77	40.12	42.69	56.20	46.84
18	58.65	59.49	44.62	50.69	63.60	62.64

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 15: Means (± S.D.) for Concentration of 5HIAA in urine for each 30 minute period in the AM and PM (μg/ml)

	+ (N = 8)		- (N = 6)		0 (N = 3)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
2 (covariate)	3.11		3.69		3.09	
3-4	2.15	1.81	3.26	2.55	4.06	2.73
5-6	1.47	1.58	1.97	1.93	2.86	2.52
7-8	1.59	1.29	1.43	1.38	2.58	2.12
9-10	1.26	0.95	1.19	0.97	3.02	2.59
PM	(N = 5)		(N = 8)		(N = 2)	
11-12	1.02	0.85	1.10	1.06	3.02	1.38
13-14	1.41	1.09	1.58	1.25	3.01	3.61
15-16	1.77	1.09	2.82	2.48	2.20	2.75
17-18	2.35	1.54	2.24	2.27	1.80	2.26

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 16: Means (± S.D.) for Amount of 5HIAA in urine for each 30 minute period in the AM and PM (μg)

	+ (N = 8)		- (N = 6)		0 (N = 3)	
Period	Mean	S.D.	Mean	S.D.	Mean	S.D.
AM						
3-4	56.82	25.60	37.83	26.12	109.27	79.21
5-6	41.68	34.30	28.17	10.44	68.56	44.98
7-8	42.55	23.16	20.26	10.35	52.63	7.57
9-10	33.95	12.91	25.10	7.46	66.13	62.75
PM	(N = 5)		(N = 8)		(N = 2)	
11-12	22.58	8.80	33.09	15.58	40.29	10.84
13-14	25.64	8.61	33.30	14.63	70.13	64.44
15-16	30.46	13.22	39.15	13.62	58.30	46.55
17-18	35.20	19.22	35.15	15.39	32.76	25.73

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

analyses. Subjects who did not have at least one data point for the combined periods were dropped from the entire analysis of that dependent measure.

Visual inspection of the pre-treatment scores for several of the variables showed initial differences among the groups. For some variables, this proved to be significant. Therefore analyses of covariance (ANCOVA), using the pre-treatment period 2 as the covariate, were performed on all of these dependent variables (BMDP IV, 1977), and analyses of variance (ANOVA) were performed when the covariate (period 2) was not significantly associated with the rest of the scores. Separate ANCOVAs or ANOVAs were performed on all of the dependent measures for AM and PM group means in order to determine the effects of ion-treatment. There were two planned contrasts. They compared: 1) the combined group means for positive and negative air ions to the control group mean ([+]/[-] vs [0]); and 2) the positive ion group mean to the negative ion group mean ([+] vs [-]).

Several variables seemed to change over the course of the experimental session. To examine these changes a 2 x 8 repeated measures ANOVA program, with Period as the repeated measure, was written and used to examine time trends and Group x Time linear trend interactions (Bostrum, 1977). ANCOVAs were not required because these time analyses would not be affected by the pre-treatment group differences described above. The computer program had the capacity to analyze time trends by using several higher order mathematical models, e.g. quadratic com-

ponents, but the linear model provided a consistently good fit to the data, so only slope components were reported.

The Time and Group x Time linear interactions repeated ANOVAs assess:

1) the slope component of the time analysis;

2) parallel changes in means over time; (is the difference between means constant at each period)

3) differences of slopes across the three experimental groups;

4) differences for the slope of (+/-) vs the slope of (0); and

5) differences for the slope of (+) vs the slope of (-).

The Group x Time repeated measure ANOVAs described above were used to indicate the presence of Time or Group x Time interaction effects. However these analyses could not be used to specifically identify the group for which a significant effect was found. For instance, a significant Group x Time effect in the Group x Time ANOVA indicates only that the slope of the (+), (-) and/or (0) groups differ. The analysis does not signify for which group(s) the slope was significantly different. Therefore, a program for repeated measures ANOVAs by Group was written and used to refine the Group x Time analyses (Bostrum, 1977). By examining each set of group means separately for within-group changes over time, the group(s) for which the effect was significant could be identified.

It was reasoned that ion-treatment may induce changes in response variability which would be reflected in the other analyses' variance

components, but not specifically tested. Therefore, the F_{max} statistic was used to test differences in variability across the experimental groups (Winer, 1970). The Dixon method for determining outlying samples was used to test whether significant differences in variability indicated by the F_{max} test were the result of excessive variability in just a few subjects' responses (Dixon, 1953).

A summary list of the analyses performed on each dependent variable follows:

1) Analysis of covariance (ANCOVA) or analysis of variance (ANOVA) on the AM and PM group means.

2) Repeated measures ANOVA for Time and Group x Time linear trend interactions on the AM and PM data.

3) Repeated measures ANOVA for Time by Group (+), (-) or (0) on the AM and PM data.

4) Comparisons of time variance across (+), (-) and (0) groups for AM and PM data (F_{max} test).

V. RESULTS

MAIN ISSUES

1) Effects of Positive and Negative Air Ions on Mood

The results of the ANCOVAs comparing group means for all measures in the AM and PM periods are shown in Table 3a. In the AM the treatment groups were shown to be different than the control groups for the POMS indicators Vigor ($P = 0.037$) and Friendliness ($P = 0.046$). These differences between the treated and control groups were enhanced for the PM (Vigor, $P = 0.004$; Friendliness, $P = 0.004$). The control groups reported less Vigor and Friendliness than the treatment groups for the AM and PM (see Table 3b). None of the POMS variables indicated a difference between the two treatment groups ([+] vs [-]) in the AM or PM.

The results of the repeated measure ANOVAs for Time (and Group x Time interactions) for all measures in the AM and PM periods are shown in Table 4. In the AM the POMS mood variable Fatigue showed a positive linear trend ($P = 0.025$): all groups showed a slight increase in the amount of Fatigue reported. The control group reported the greatest increase in Fatigue (see Table 11). In the PM the POMS mood variable Fatigue showed a time trend which was not linear ($P = 0.050$): the positive and ambient groups remained essentially unchanged and the negative group reported a slight increase in the amount of Fatigue reported (see Table 11). Also in the PM, the POMS mood variable Confusion showed a positive linear time trend ($P = 0.036$): all groups

TABLE 3a: Main Effects Analysis

Summary of significant ($P < 0.05$) mood and urine ANCOVA and ANOVA effects for treatment and control group means in the AM and PM

	Mood							Urine		
AM	T	D	A	V	F	C	Fr	Vol*	Conc	Amt*
Group (+, -, 0)										.029
(+/-) vs (0)				.037			.046			.021
(+) vs (-)										
PM										
Group (+, -, 0)										
(+/-) vs (0)				.004			.004	.026		
(+) vs (-)										

*ANOVAs

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 3b: POMS Mood Analysis

Raw and adjusted group means (± S.D.) for analyses of covariance in the AM and PM

Dependent Variable	$\bar{X}$'s ± S.D.			ANCOVA Adjusted Group $\bar{X}$'s		
	+ (N = 13)	- (N = 13)	0 (N = 7)	+	-	0
AM						
Tension-Anxiety	6.80 (5.98)	7.90 (5.44)	4.88 (4.12)	6.40	7.70	5.99
Depression-Dejection	4.90 (6.22)	7.88 (7.68)	2.73 (3.94)	5.71	5.44	5.76
Anger-Hostility	5.38 (7.97)	5.99 (6.86)	2.52 (3.46)	4.23	5.88	4.87
Vigor	10.00 (6.51)	9.18 (5.49)	5.18 (4.56)	9.70	9.04	6.01
Fatigue-Inertia	7.07 (5.61)	9.70 (6.96)	6.68 (4.18)	8.16	8.30	7.24
Confusion-Bewilderment	7.94 (4.37)	7.88 (4.50)	4.52 (1.94)	7.27	7.68	6.12
Friendliness	11.10 (5.20)	10.41 (4.49)	9.68 (5.08)	11.63	10.40	8.71
PM						
Tension-Anxiety	7.40 (4.66)	6.63 (5.92)	5.05 (3.46)	7.26	6.35	5.85
Depression-Dejection	7.34 (6.63)	6.16 (8.78)	2.81 (3.03)	4.80	7.00	5.89
Anger-Hostility	4.71 (4.67)	6.69 (10.01)	2.14 (2.84)	4.59	5.37	4.83
Vigor	11.85 (8.84)	11.69 (6.48)	5.86 (5.43)	11.76	11.50	6.39
Fatigue-Inertia	8.13 (6.26)	8.10 (8.07)	6.55 (4.51)	6.94	9.02	7.03
Confusion-Bewilderment	7.11 (4.46)	7.44 (5.66)	4.30 (1.66)	6.90	6.73	6.00
Friendliness	12.11 (5.02)	11.70 (4.56)	8.88 (4.41)	12.10	12.07	8.21

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

TABLE 4: Time and Group x Time Analysis

Summary of significant ($P < 0.05$) mood and urine repeated measure ANOVAs for treatment and control group means in the AM and PM

	Mood							Urine		
AM	T	D	A	V	F	C	Fr	Vol	Conc	Amt
TIME									.011	.017
Slope Component					.025				.006	.015
GROUP x TIME										
Differences in slopes:										
(+) (-) (0)				.005			.026			
Slope (+/-) vs slope (0)				.002			.014			
Slope (+) vs slope (-)										
PM										
TIME					.050				.003	
Slope component						.036			.020	
GROUP x TIME									.032	.016
Differences in slopes:										
(+) (-) (0)										.021
Slope (+/-) vs slope (0)									.022	.021
Slope (+) vs slope (-)										

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

showed a slight increase in the amount of Confusion reported (see Table 12).

The results of the repeated measure ANOVAs for Group x Time interactions for all measures in the AM and PM periods are shown in Table 4. In the AM the POMS mood variables Vigor and Friendliness showed a significant Group x Time linear trend interaction ($P = 0.005$; $P = 0.026$). The interaction was shown to be the result of differences in slope between the treatment vs the control groups for the two variables ($P = 0.002$; $P = 0.014$). Repeated measure ANOVAs by group showed no linear trend for the positive or negative treatment groups for either Vigor or Friendliness, and a significant negative trend for the control groups ($P = 0.033$; $P = 0.043$). Thus, the interaction effects can be seen to be the result of reports of less Vigor and Friendliness by the control group (see Tables 10 and 13). The effects on Vigor and Friendliness were not observed in the PM: the control group which showed a negative linear trend in the AM remained down in the PM. However, the treatment vs control differences in group means observed for Vigor and Friendliness in the AM were, it was noted, enhanced in the PM: the control subjects reported less Vigor and Friendliness in the PM ($P = 0.004$; $P = 0.004$).

2) Effects of Positive and Negative Air Ions on Urinary 5HIAA and Volume

Analyses of covariance were not required to examine the Volume (VOL) and Amount (AMT) variables because the covariate (period 2) was

not significantly associated with the AM or PM means for these two dependent variables. The results of the ANOVAs comparing group means for all measures in the AM and PM periods are shown in Table 3a. In the AM, a group effect was found for the variable AMT ($P = 0.029$). This result was shown to be due to differences between the treatment vs the control groups: the AMT of urinary 5HIAA was higher in the control subjects' urine ($P = 0.021$, see Tables 3a and 3c). The treatment vs control group differences were not found in the PM urines. However, a significant PM difference between treatment vs control groups was shown for the variable VOL: the VOL of urine was higher in the control subjects ($P = 0.026$, see Tables 3a and 3c).*

The results of the repeated measure ANOVAs for Time (and Group x Time interactions) for all measures in the AM and PM periods are shown in Table 4. In the AM the urine variables CONC and AMT showed negative linear time trends ($P = 0.006$; $P = 0.015$): all groups showed a decrease in the CONC and AMT of urinary 5HIAA (see Tables 15 and 16). In the PM the urine variable CONC showed a time trend ($P = 0.003$) which was shown to be primarily linear ($P = 0.020$): the treatment groups each showed

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*The variable Amount (AMT) is a product of Concentration (CONC) and Volume (VOL). The mathematical function dictates that if, for instance, AMT were held constant, and VOL increased, CONC must decrease. These relationships hold for any given subject's data. The group data, as evident in Tables 14 to 16, fail to meet the demands of the equation. The primary reason for the discrepancies is due to the missing data for the variables CONC and AMT. Whereas N = 13 for the variable VOL in the AM positive treatment group, the Ns for CONC and AMT equalled only 8. The numbers for the group data cannot be compared directly because the data are comprised of different groups of subject samples: a relatively intact set of data for VOL, but not for CONC and AMT.

TABLE 3c: Urine Volume, 5HIAA Concentration and 5HIAA Amount Analysis

Raw and adjusted group means (± S.D.) for analysis of variance or covariance in the AM and PM*

Dependent Variable	$\bar{X}$'s ± S.D.			ANCOVA Adjusted Group $\bar{X}$'s		
	+	-	0	+	-	0
AM						
Volume (ml)	53.69 (67.22)	57.15 (66.64)	53.38 (56.88)	--	--	--
N =	13	10	5			
Concentration (µg)	1.67 (0.98)	1.98 (0.99)	2.43 (0.98)	1.78	1.82	2.55
N =	7	6	2			
Amount (µg)	43.75 (25.35)	27.84 (15.83)	74.15 (47.62)	--	--	--
N =	8	6	2			
PM						
Volume (ml)	40.83 (44.77)	42.81 (42.13)	90.25 (89.52)	--	--	--
N =	10	13	5			
Concentration (µg)	1.50 (1.15)	2.18 (1.15)	0.62 (1.14)	1.38	2.26	0.71
N =	6	7	2			
Amount (µg)	28.47 (13.06)	35.17 (14.31)	50.37 (35.51)	--	--	--
N =	5	8	2			

*Subjects with missing data for period 2 or who did not have at least one data point for combined periods were dropped from the AM and/or PM analyses.

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

an increase in the CONC of urinary 5HIAA and the control group showed a decrease (see Table 15).

The results of the repeated measure ANOVAs for Group x Time interactions for all measures in the AM and PM periods are shown in Table 4. In the AM no interactions are revealed for any of the urine dependent variables. In the PM, CONC and AMT show significant Group x Time interactions ($P = 0.032$; $P = 0.016$). The interaction was shown to be the result of differences in slope between the treatment vs control groups for each variable ($P = 0.022$; $P = 0.021$). Repeated measure ANOVAs by group for CONC showed positive linear trends for the positive and negative treatment groups ($P = 0.013$; $P = 0.066$), and no linear trend for the control group. Repeated measure ANOVAs by group for AMT showed no significant linear trends for any of the groups: the treatment vs control group contrast for slopes was, however, significant. For both variables, CONC and AMT, the treatment groups each showed an increase over time and the control group showed a decrease (see Tables 15 and 16).

The results of the F_{max} tests comparing mean sum square (MSS) within-subject variances for all measures in the AM and PM periods are shown in Table 5. In the AM, the F_{max} test revealed a significant difference in variance for the POMS variable Anger ($P = 0.010$). The negative group showed the highest variability levels, and the positive and ambient groups were nearly the same. In the PM, the F_{max} test revealed significant differences in variability for the POMS variables

TABLE 5: F_{max} Test Scores

Comparing mean sum square (MSS) within-subject variances for mood and urine variables in the AM and PM

	Mood*							
	AM				PM			
Scale	+	-	0	F_{max}	+	-	0	F_{max}
Tension-Anxiety	5.60	34.21	7.45	6.11	6.68	8.90	6.65	1.34
Depression-Dejection	12.30	17.38	15.49	1.41	19.93	5.24	4.61	4.32
Anger-Hostility	4.46	40.95	6.94	9.18*	5.25	14.22	8.78	2.71
Vigor	8.57	5.25	26.43	5.03	78.58	60.22	23.10	3.40
Fatigue-Inertia	16.27	11.09	11.62	1.47	25.80	56.08	32.26	2.17
Confusion-Bewilderment	4.83	7.34	3.59	2.04	10.44	27.99	1.77	15.81*
Friendliness	5.05	15.08	12.85	2.99	1.34	26.93	19.28	20.10*
	Urine†							
	+	-	0	F_{max}	+	-	0	F_{max}
Volume	870.33	878.82	4316.71	4.96	1568.87	1388.92	2697.39	1.94
Concentration	1.14	5.12	1.26	4.49	4.52	1.60	0.74	6.11
Amount	726.54	329.85	1194.89	3.62	153.11	63.18	576.62	9.13

*$P < 0.01$, $F < 7.4$ with 3, 10 df (10 df is harmonic mean of subjects/experimental group: N = 13 [+], 13 [-], 7 [0]).

†$P < 0.01$, $F < 37$ with 3, 4 df (4 df is harmonic mean of subjects/experimental group: N = 5 [+], 8 [-], 2 [0]).

Legend:
(+) = positive ion treatment
(-) = negative ion treatment
(0) = ambient ion treatment

Confusion and Friendliness (P = 0.010; P = 0.010). The negative group showed the highest variability levels. The positive group showed more variability than the ambient group for Confusion and less variability than the ambient group for Friendliness. The negative group showed the highest variability levels for the three POMS variables for which significant F_{max} ratios were found. There were no significant differences in variability for any of the urine variables in the AM or PM F_{max} analyses.

The results of the Dixon (1953) test for determining outlying samples were not significant for AM Anger, PM Confusion or PM Friendliness, indicating that the differences in variability revealed by the F_{max} test were not the result of excessive variability in just a few subjects' responses. The significant within-subject F_{max} test for Friendliness in the PM does not bear on analyses comparing group means, where a significant effect on Friendliness in the PM was reported (see Table 3a). The relevant F_{max} test for the between-subjects error term (group means ANCOVA) was not significant for Friendliness in the PM.

SUB-ISSUES

1) Charge specificity of ion effects: do positive and negative ions have different effects? The planned contrast between treatment groups ([+] vs [-]) for the dependent variables shows that positive and negative air ions do not differ significantly on the dependent measures assessed (see Table 3a). There may be differences between positive and negative air ions' influences on response variability, but the evidence is presently weak (see Table 5).

2) Time-course: when are the effects of air ions large enough to be detected? Planned contrasts for treatment vs control group means at each AM period (3 to 10) were computed for the variables Vigor and Friendliness (these were the dependent mood measures for which significant ion effects were found; see Table 3a). The effects of air ions on Vigor were large enough to be detected by period 7, or 60 to 75 minutes after continuous ion exposure began ($P = 0.006$). The effects of air ions on Friendliness did not approach significance until period 10 ($P = 0.097$). The effects on Friendliness may be construed to be weaker, or as having a longer latency. The results of the ANCOVAs suggest a weaker ion effect on Friendliness (see Table 3a).

3) Subject selection: are individuals with self-reported mood lability, "weather-sensitivity" and/or minor health problems different than individuals comprising a "normative" college sample on certain personality dimensions? Comparisons of raw CPI means between the experimental subjects (N = 22*) and normative samples for college males (N = 3,103) revealed significant differences for 13 of the 18 standard scales (see Table 6). Subjects with self-reported mood lability, "weather-sensitivity" and/or minor health problems scored significantly lower for most CPI scales for which there were significant differences in the means: sociability ($P = 0.05$); sense of well-being ($P = 0.001$); responsibility ($P = 0.001$); socialization ($P = 0.001$); self-control ($P = 0.001$); tolerance ($P = 0.001$); good impression ($P = 0.001$); communality

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*Eleven subjects were tested before the CPI questionnaires were available.

TABLE 6: Subject Selection: Results of California Psychological Inventory (CPI)

Comparisons of raw CPI means (± S.D.) between experimental subjects and normative samples for college males (from Gough, 1975)

	Experimental Subjects (N = 22)		Normative Sample (N = 3103)			
Scale	Mean	S.D.	Mean	S.D.	t	P <
Dominance	27.7	4.4	28.0	6.0	-0.23	-
Capacity for Status	20.7	3.3	21.6	3.7	-1.14	-
Sociability	23.4	5.2	25.7	4.8	-2.24	0.050
Social Presence	37.7	5.4	36.4	5.8	1.05	-
Self-acceptance	23.9	4.1	22.2	3.9	2.04	0.050
Sense of Well-being	31.1	6.2	36.8	4.3	-6.17	0.001
Responsibility	23.9	4.9	32.8	4.0	-10.38	0.001
Socialization	29.5	5.4	39.7	4.8	-9.92	0.001
Self-control	20.6	9.1	29.7	7.1	-5.98	0.001
Tolerance	19.0	5.0	24.6	4.1	-6.37	0.001
Good Impression	13.3	5.9	17.7	5.7	-3.61	0.001
Communality	23.3	4.3	25.8	1.99	-6.06	0.001
Achievement via Conformance	23.5	5.1	28.3	4.1	-5.46	0.001
Achievement via Independence	20.1	3.7	21.5	3.8	-1.72	0.100
Intellectual Efficiency	36.5	4.5	40.7	4.8	-4.09	0.001
Psychological-Mindedness	11.1	3.2	10.8	2.8	0.50	-
Flexibility	13.6	4.4	11.3	3.7	2.90	0.010
Femininity	17.5	3.2	23.2	3.3	-8.07	0.001

(P = 0.001); achievement via conformance (P = 0.001); intellectual efficiency (P = 0.001); and femininity (P = 0.001). On two scales, self-acceptance and flexibility, the mean scores for the experimental subjects were significantly higher than were the normative sample means (P = 0.05; P = 0.001).

Comparisons between treatment ([+]/[-], N = 18) and control ([0], N = 4) subjects' CPI scores revealed no significant differences, except for the communality scale (P = 0.02).

VI. DISCUSSION AND CONCLUSION

Sulman et al. (1970; 1975) have reported extensively on correlations between Sharav-induced changes in 5HT and mood in human subjects. Gilbert (1973) and Olivereau (1971) have investigated the mechanism(s) of action of air ions at biochemical, tissue and behavioral levels of system organization in rodents. This study examined the effects of air ions: 1) at biochemical and psychological levels of system organization; 2) under controlled laboratory conditions; 3) using standard psychological tests (POMS and CPI); 4) in humans. It was shown that air ions can influence 5HT and mood and that these effects were not charge related.

MAIN ISSUES

The results of POMS tests show that the treatment groups' mood remained relatively stable across time, while the controls reported feeling less Vigor and Friendliness. These data can be interpreted as support for: 1) theories that air ions have a "normalizing" influence on physiological systems (Schulz, 1965); or 2) reports that air ions make people "feel better." That is, while the control subjects reported a change in affective state, increasing dysphoria, the treatment subjects' reports remained stable. No significant ion effects were found for the other mood measures: Tension-Anxiety; Depression-Dejection; Anger-Hostility; Fatigue-Inertia; or Confusion-Bewilderment. Other researchers

have reported effects on indices of negative mood which were not found here (Charry, 1976; Rim, 1977). The two positive mood variables, Vigor and Friendliness, were the only mood indicators to show air ion effects.

Quantitative urinalyses show treated groups excreted less 5HIAA than control groups. The result is opposite to the increase in 5HIAA predicted by the serotonin hypothesis. Considerable documentation exists to support the serotonin hypothesis at the tracheal tissue level of system organization. However, as it is currently stated, the serotonin hypothesis cannot account for the outcome of decreased total urinary 5HIAA in intact humans.

The 5HIAA data reported show that air ions can affect 5HT. Whether the effects of 5HT were related to the effects on mood is not known. However, future studies may be able to show the degree to which the changes in 5HT and mood are related if experimental factors that contribute to variability can be systematically reduced. These factors include subject variables such as ion-sensitivity, age and perhaps gender.

The results show another effect of air ions on urine measures: treatment group volumes were less than control volumes in the PM. In different studies, Olivereau (1971) reported that 20,000 positive ions/cc decreased urine volume, 20,000 and 50,000 negative ions/cc increased urine volumes, but 150,000 negative ions/cc did not influence it. In this study positive or negative ions (ca 100,000 ions/cc) decreased urine volume.

Ad lib liquids were available throughout the experiment and their consumption by the subjects was not monitored. We cannot tell whether the ions affected diuresis per se or whether ions made the treated groups less thirsty as compared to controls. However, Olivereau (1971) reported that in rats, negative ions produced a mild polydypsea and that positive ions produced a clear adipsea. The changes in "behavior of thirst" appeared 24 hours after the changes in diuresis and Olivereau suggested that the initial effect of ions on diuresis modified the thirst responses. For humans, a simple question, "Did you feel thirsty?" could resolve this particular issue. Drinking might also be monitored or controlled.

SUB-ISSUES

1) Do Positive and Negative Air Ions Have Different Effects?

Positive and negative air ion effects on the dependent measures did not differ except for effects on variability of a few indices (see Table 5). Negative ions tended to produce increased variability, sometimes by a factor of X20. No interpretation of the significantly increased variability of the negative ion groups for the three significant mood measures is offered.

It has been suggested that somehow air ions reduce the variability of responses, whether they increase or decrease overall levels of activation (Rosenberg, 1972). If this were true, control groups might be expected to show more response variability than ion-treated groups.

While there were a few instances of significance (three out of 14 mood measures and one out of six urine measures), only one was among the control group. Therefore, the results of the F_{max} test in this study did not support the conclusion that air ions reduce the variability of responses.

Although there are many reports of charge-specific effects, numerous researchers have reported similar effects of positive and negative ions in various organisms and at all levels of biological system organization studied: anti-bacterial action (Fuerst, 1955; Kingdon, 1960; Kreuger et al., 1957; Phillips et al., 1964; Pratt and Barnard, 1960; Tchijevsky, 1933); seedling growth (Krueger et al., 1962a); gross motor activity (Bachman et al., 1966); brain 5HT (Krueger and Kotaka, 1969).

According to Rivolier et al. (1975) and Vasiliev (1951), "ion overload" may account for many experimental outcomes where charge related differences in response are not found. It should be noted that Sulman, who studies the effects of ion densities found in nature, does report charge-related differences in responses. As mentioned in Chapter III (Issues), most investigators choose ion doses on the basis of maximum generator capacity; the assumption being that a stronger stimulus will maximize the probability of subject response. In this study, ion concentrations well beyond those found in nature (ca 100,000 ions/cc) were used. While subject responses to air ions were obtained, the responses were not differentiated on the basis of charge: ions of either polarity stabilized positive affect and decreased urinary 5HIAA relative to controls.

The assumption that "more (ions) is better" may have obscured any test of whether positive and negative ions have different effects.

Sensory cues can probably account for other instances when charge-related differences between positive and negative ions are not found. Both positive and negative air ions may provide cues in modalities for which their influence has not been systematically studied. For instance, Winsor and Beckett (1958) reported that the inhalation of air ions may alter skin temperature. Ions have been reported to influence EEG rhythms, heart rate, blood pressure and respiratory rates; and the Russians have developed hypotheses about cutaneous reception of air ions. The production of ozone as a by-product of positive and/or negative ion generators could provide olfactory cues for exposed subjects. Even though the ion generator used in this study produced less than 0.002 ppm of ozone, this concentration may not be below the threshold sensitivity for olfaction.* Thus, the treatment group subjects may have used olfactory cues to detect the presence of the ionized stimuli.

The "sensory cue hypothesis" does not explain why treated subjects reported "feeling better" relative to controls, unless it is supposed that the treated subjects "reasoned" that, "I feel different. It must be due to the ions, and since ions are supposed to make you feel good, I must feel good." Though subjects in this study gave no consistent reports in post-treatment interviews about their attendance to feelings

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*The presence of ozone can be detected by olfaction in concentrations as low as several parts per hundred million by volume (Kirk and Othner, 1967).

not listed in the POMS tests, there is no reason to assume that all of their responses to the experimental situation were at the conscious level.

2) Time-course of Ion-related Events

It was stated in Chapter III (Rationale) that information is needed on the time-course of ion-related events. Latencies reported for air ion effects are said to range from two minutes for the remediation of hay fever symptoms (Winsor and Beckett, 1958) to years for inducing some aspects of the Adrenal Deficiency Syndrome (Sulman et al., 1970). The results of this study show that the effects of air ions on Vigor were large enough to be detected 60 to 75 minutes after continuous exposure began. The latencies for detection of this and other dependent measure effects can be expected to vary under differing conditions of ion-density, measurement and subject sample. However, these data do suggest that exposure periods of about one hour are sufficient to induce ion effects, some of which can be indexed by changes in mood and urinary 5HIAA content.

Along with a discussion of latency, the distinction between primary causes and secondary ion effects was noted to be an important issue. The results of this study show that air ions have biochemical and psychological effects, but one influence was not established as causal over the other. Few investigators consider the issues of causality in studying bio-psychological and psychophysiological effects. The oversight is particularly limiting in those disciplines where processes at

two or more levels of system organization are studied concurrently. Kuhn (1962) has discussed the implicit acceptance of a given perspective in the sciences. For instance, a current paradigm is that biochemical events are causal agents for psychological phenomena. Studies which suggest that a given behavior or affective state may precede what was considered to be its biochemical cause (Bridger, 1978; Levine et al., 1978) contradict the reigning paradigm and are therefore slow to be assimilated into the scientific stream of knowledge.

The distinction between primary causes and secondary effects was brought up to establish the necessity of consideration of this issue. Advances in research require an awareness of alternative theoretical perspectives. New concepts of the relationships among air ions, mood and 5HT should include the possibility that the mood effect causes the 5HT effect.

3) Subject Selection

In Chapter III (Rationale) it was reasoned that if subjects could be selected for sensitivity, ion effects would be more pronounced. Subjects were thus selected for self-reported mood lability, "weather-sensitivity" and/or minor health problems (Charry, 1976; Frey, 1961; Sulman et al., 1970). Although an "ion effect" was observed in this study, it cannot be determined if the selective screening of subjects contributed to the results: no subjects supposed not to be especially "sensitive" were tested.

The CPI data do show that the sample tested is not representative of the population at large (see Table 6). Therefore attempts to gen-

eralize or replicate this work should take note of the special sample. However, now that an ion effect has been demonstrated, future investigations can undertake a direct study of selection criteria: the magnitude of the ion effect can be compared among subjects designated as high or low on several screening criteria, including the personality measures identified here.

CONCLUSION

It can be concluded from the data reported in this dissertation that air ions have bio-psychological influences: they have effects on 5HT and mood in men. Whether the biochemical and psychological effects were related to one another is not known.

Progress was made in resolving the methodological issues of ion generation and subject response indicators noted to be important in Chapter 1. The ions generated by corona discharge were measured and consistently observed to have mobilities characteristic of small air ions. Small air ions are the molecules demonstrated to have biological activity. The ion densities achieved in the subject room were monitored and noted to be stable within 15% of mean levels during the five hour exposure periods. The mood variables Vigor and Friendliness were shown to indicate the effects of air ions where treated subjects reported stable affect relative to controls who reported less Vigor and Friendliness over time. The urine variables VOL and 5HIAA AMT indicated differences between treated and control subjects' responses to air ions.

Quantification of subject dose of air ions remains a problem. A resolution of this issue is necessary for the accurate determination of dose response data.

The results of this dissertation should encourage future studies in air ion research on the general issues of: 1) lack of models; 2) health; and 3) environmental influences. Today, it is well established that air ions have biological activity and their depletion from the atmosphere can therefore be considered to have biological consequences.

Studies are now underway to help resolve the issue of lack of specificity of the serotonin hypothesis. Attempts are being made to replicate findings that positive air ions increase, and negative ions decrease, the 5HT content of in vitro blood. If the results of these experiments are encouraging, in vivo blood studies will be pursued. Among the questions of interest will be: does tolerance develop after "frequent" or prolonged ion exposure; and at what levels of system organization are the changes manifest?

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APPENDIX A: Profile of Mood States (POMS) test

NAME _____ DATE _____

Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE space to the answer to the right which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.

IDENTIFICATION

The numbers refer to these phrases.
0 = Not at all
1 = A little
2 = Moderately
3 = Quite a bit
4 = Extremely

	0 NOT AT ALL	1 A LITTLE	2 MODERATELY	3 QUITE A BIT	4 EXTREMELY
1. Friendly	0	1	2	3	4
2. Tense	0	1	2	3	4
3. Angry	0	1	2	3	4
4. Worn out	0	1	2	3	4
21. Hopeless	0	1	2	3	4
22. Relaxed	0	1	2	3	4
23. Unworthy	0	1	2	3	4
24. Spiteful	0	1	2	3	4
25. Sympathetic	0	1	2	3	4
26. Uneasy	0	1	2	3	4
27. Restless	0	1	2	3	4
28. Unable to concentrate	0	1	2	3	4
45. Desperate	0	1	2	3	4
46. Sluggish	0	1	2	3	4
47. Rebellious	0	1	2	3	4
48. Helpless	0	1	2	3	4
49. Weary	0	1	2	3	4
50. Bewildered	0	1	2	3	4
51. Alert	0	1	2	3	4
52. Deceived	0	1	2	3	4

NOTE: The publisher of the POMS adheres to the general policy that, due to their restricted nature, psychological tests not be bound with theses and dissertations. For this reason the test is not shown in its entirety.

APPENDIX B: Example Page from California Psychological Inventory (CPI) Test

1. I enjoy social gatherings just to be with people.
2. The only interesting part of the newspaper is the "funnies."
3. I looked up to my father as an ideal man.
4. A person needs to "show off" a little now and then.
5. Our thinking would be a lot better off if we would just forget about words like "probably," "approximately," and "perhaps."
6. I have a very strong desire to be a success in the world.
7. When in a group of people I usually do what the others want rather than make suggestions.
8. I liked "Alice in Wonderland" by Lewis Carroll.
9. I usually go to the movies more than once a week.
10. Some people exaggerate their troubles in order to get sympathy.
11. People can pretty easily change me even though I thought that my mind was already made up on a subject.
12. I often feel that I made a wrong choice in my occupation.
13. I am very slow in making up my mind.
14. I always follow the rule: business before pleasure.
15. Several times a week I feel as if something dreadful is about to happen.
16. There's no use in doing things for people; you only find that you get it in the neck in the long run.
17. I would like to be a journalist.
18. A person who doesn't vote is not a good citizen.
19. I think I would like the work of a building contractor.
20. I have had very peculiar and strange experiences.
21. My daily life is full of things that keep me interested.
22. When a person "pads" his income tax report so as to get out of some of his taxes, it is just as bad as stealing money from the government.
23. In most ways the poor man is better off than the rich man.
24. I always like to keep my things neat and tidy and in good order.
25. Clever, sarcastic people make me feel very uncomfortable.
26. It's a good thing to know people in the right places so you can get traffic tags, and such things, taken care of.
27. It makes me feel like a failure when I hear of the success of someone I know well.
28. I think I would like the work of a dress designer.
29. I am often said to be hotheaded.
30. I gossip a little at times.
31. I doubt whether I would make a good leader.
32. I tend to be on my guard with people who are somewhat more friendly than I had expected.
33. Usually I would prefer to work with women.
34. There are a few people who just cannot be trusted.
35. I become quite irritated when I see someone spit on the sidewalk.
36. When I was going to school I played hooky quite often.
37. I have very few fears compared to my friends.
38. It is hard for me to start a conversation with strangers.
39. I must admit that I enjoy playing practical jokes on people.
40. I get very nervous if I think that someone is watching me.
41. For most questions there is just one right answer, once a person is able to get all the facts.

APPENDIX C: Advertisement Appearing in San Francisco Bay Area Publications for Recruiting Experimental Subjects

MEN WANTED FOR AIR IONIZATION STUDY. Ages 18-29. UC Med Ctr. Phone 681-8080 x425

APPENDIX D: Summary Pages of 135-item Health Questionnaire Used to Review Experimental Subjects' Health History

IDENTIFICATION DATA Fill in the following information. PLEASE PRINT.

Name _____ Date _____ #_____

Address _____ Date of birth _____ ___Male ___Female

_____ ___Married ___Separated ___Divorced ___Widowed ___Single

Home telephone _____ Education: ___years Elementary ___years High School

(area code) ___years College, Technical, Business, etc.

Business telephone _____ Occupation _____

(area code)

FAMILY HISTORY Please follow the instructions given for each heading outlined below.

FAMILY
Print the names of your relatives, living or dead, in the list below. If there is not enough space, place an (X) here: ☐

YEAR OF BIRTH HEALTH STATUS
Give the year of birth for all your relatives listed at the left and mark an (X) to indicate whether their health is good or poor.

ILLNESSES
Place an (X) in the appropriate column for any illnesses that you or the relatives listed at the left have now or have had.

DEATHS
If a relative you have listed has died, write the cause of death and the age at death in the columns below.

	Year of Birth	Good	Poor	Allergies or Asthma	Anemia	Bleeding Tendencies	Cancer or Tumor	Diabetes	Epilepsy	Glaucoma	Gout	Heart Trouble	High Blood Pressure	Kidney or Bladder Trouble	Nervous Breakdown	Rheumatism or Arthritis	Stomach or Duodenal Ulcer	Stroke	Tuberculosis	Cause of Death	Age
Father:																					
Mother:																					
Brothers or Sisters:																					
Spouse:																					
Children:																					
Grandparents (Mark an (X) for illnesses only.)																					
YOUR ILLNESSES Start here →																					

Give your age at onset for any of the following illnesses you have now or have had.

Age	Age	Age	Age	Age
____eczema	____eye disease	____neuralgia or neuritis	____measles	____rheumatic fever
____hives or rashes	____hemorrhoids	____pancreatitis	____mononucleosis	____venereal disease
____bronchitis	____hernia	____thyroid disease	____mumps	____yellow jaundice
____diverticulosis	____liver disease	____chicken pox	____nervous exhaustion	____other_____
____emphysema	____malaria	____German measles	____polio	____ _____

Have you ever been turned down for life insurance, military service or employment because of health problems? ..... ____Yes ____No

Have you been hospitalized more than three times? ..... ____Yes ____No

Give the following information for the last three times you have been hospitalized starting with the most recent. (Women: Do not list normal pregnancies.)

	HOSPITALIZATION (1)	HOSPITALIZATION (2)	HOSPITALIZATION (3)
Type of operation or illness:			
Month and year hospitalized:			
Name of hospital:			
City and State			

Place an (X) next to any of the following tests or immunizations you have had and if you can, give the year you last had them.

(X)	(Year)	TESTS	(X)	(Year)	IMMUNIZATIONS
___	_____	chest x-ray	___	_____	smallpox
___	_____	kidney x-ray	___	_____	tetanus
___	_____	G.I. series	___	_____	polio
___	_____	colon x-ray	___	_____	typhoid
___	_____	gallbladder x-ray	___	_____	flu
___	_____	electrocardiogram	___	_____	mumps
___	_____	T.B. test	___	_____	measles
___	_____	other x-rays	___	_____	other

Place an (X) in the appropriate column for any medicines you use or are allergic to.

(Use)	(Allergic to)	MEDICINES
___	___	aspirin
___	___	penicillin
___	___	sulfa
___	___	codeine
___	___	Demerol
___	___	antibiotics
___	___	laxatives or sedatives
___	___	other

CONTINUE TO NEXT PAGE

APPENDIX E: Human Subjects Consent Form

Submitted for approval to the University of California San Francisco Committee on Human Research

ic _____ Date _____ Patient I.D. _____

tor's notes _____

_____

_____

_____

1. HEAD and NECK
___ frequent headaches
___ neck pains
___ neck lumps or swelling

2. EYES
___ wears glasses
___ blurry vision
___ eyesight worsening
___ sees double
___ sees halos
___ eye pains or itching
___ watering eyes
___ eye trouble

3. EARS
___ hearing difficulties
___ earaches
___ running ears
___ buzzing in ears
___ motion sickness

4. MOUTH
___ dental problems
___ swellings on gums or jaws
___ sore tongue
___ taste changes

5. NOSE and THROAT
___ congested nose
___ running nose
___ sneezing spells
___ headcolds
___ nose bleeds
___ sore throat
___ enlarged tonsils
___ hoarse voice

6. RESPIRATORY
___ wheezes or gasps
___ coughing spells
___ coughs up phlegm
___ coughed up blood
___ chest colds
___ excessive sweating

7. CARDIOVASCULAR
___ high blood pressure
___ racing heart
___ chest pains
___ dizzy spells
___ shortness of breath
___ swollen feet or ankles
___ leg cramps
___ hot flashes
___ heart murmur

8. DIGESTIVE
heartburn ___
bloated stomach ___
belching ___
stomach pains ___
nausea ___
vomited blood ___
difficulty swallowing ___
constipation ___
loose bowels ___
black stools ___
grey stools ___
pain in rectum ___
rectal bleeding ___

9. URINARY
night frequency ___
day frequency ___
wets pants or bed ___
burning on urination ___
brown, black or bloody urine ___
difficulty starting urine ___
urgency ___

10. MALE GENITAL
weak urine stream ___
prostate trouble ___
burning or discharge ___
lumps on testicles ___
painful testicles ___

11. FEMALE GENITAL
menstrual trouble ___
breakthrough bleeding ___
heavy bleeding ___
premenstrual tension ___
birth control pill ___
lumps in breasts ___
vaginal discharge ___
PAP smear _____
last period _____

12. PREGNANCIES
gravida _____
miscarriages _____
stillbirths _____
premature births _____
para _____
cesareans _____
abortion ___

13. MUSCULOSKELETAL
___ aching muscles or joints
___ swollen joints
___ back or shoulder pains
___ painful feet
___ handicapped

14. SKIN
___ skin problems
___ itching or burning skin
___ bleeds easily
___ bruises easily

15. NEUROLOGICAL
___ faintness
___ numbness
___ convulsions
___ change in handwriting
___ trembles

16. MOOD
___ nervous with strangers
___ difficulty making decisions
___ lack of concentration or memory
___ lonely or depressed
___ cries often
___ hopeless outlook
___ difficulty relaxing
___ worries a lot
___ frightening dreams or thoughts
___ shy or sensitive
___ dislikes criticism
___ loses temper
___ annoyed by little things
___ work or family problems
___ sexual difficulties
___ considered suicide
___ desired psychiatric help

17. GENERAL
___ weight changes
___ tends to be hot or cold
___ loss of interest in eating
___ always hungry
___ armpits or groin swelling
___ fatigue
___ sleeping difficulties
___ lack of exercise
___ smokes
___ drinks alcohol daily
___ heavy coffee or tea drinker
___ marijuana
___ heroin, LSD, similar drugs
___ bites nails

cial problems or symptoms: _____

_____

_____

_____

_____

_____

_____

University of California, San Francisco: Consent to Act as Research Subject

---

) I hereby agree to have Sheelah Sigel perform the following procedures on me for experimental purposes:

A. Expose me to different types of air molecules; the same kind encountered in the natural environment. The amount I shall receive may vary above and below that which I may experience in everyday living, but it is not expected to produce any extreme changes in me.

B. Collection of all urine at 15 minute intervals during the course of the study.

C. Fill out a psychological questionnaire every 15 minutes.

) These procedures will be done at the United States Public Health Service Hospital Bldg. #18 at 15th and Lake Streets and will take 5½ hours.

) The purpose of performing these procedures is to study the effects of certain types of air on some of my biochemical and psychological processes.

) I understand that the procedures described in paragraph 1 involve the following risks and/or discomforts:

A) There may be some inconveninece to collecting urine samples at 15 minute intervals. In order to remain well hydrated (have enough water for urine formation) I understand I must consume about a quart of liquids during the study.

B) Some people are affected adversely by changes in the weather. I understand that this procedure may mimic some of these changes and that I may therefore experience some of the minor irritations reported by some weather-sensitives.

C) I understand some boredom or fatigue may be experienced by remaining in a small room for 5½ hours during which time I may engage in only limited activities, but I realize other people have done similar experiments without difficulty. No risk other than minor discomfort would be anticipated. However, I understand that if I become distressed I may withdraw at any time.

D) I understand these air treatments may have immediate effects on me ranging from some elevation of mood to some discomfort, or nothing at all.

) I understand that there will be no direct benefit to me from participation in this study. The research may help many branches of science and medicine by providing insight into some bioclimatological (environmental) phenomena to which organisms may be sensitive. In addition, this research may be applied as a therapeutic treatment to some individuals suffering from a wide range of illnesses.

) The information in this consent form was explained to me by Sheelah Sigel. I understand that she will answer any questions I may have concerning this investigation. If I have any questions I may contact her at 626-3131.

) I understand the payment for my participation is at the rate of 2.50/hour.

Signature:_____

Date: _____

APPENDIX F: Breakfast Menu for Subjects

INSTRUCTIONS FOR THE EXPERIMENTAL DAY. DO NOT MAIL THESE BACK. THEY ARE YOURS.

---

1) Please eat the following for breakfast:

   A) One or two slices of plain white bread. May be toasted. Grape or apple jelly OK.

   B) A dry cereal without fruit or nuts with a non-dairy creamer, e.g. Mocha Mix.

   C) An apple is optional.

DO NOT use any of the following foods in any form:

   A) Milk or dairy products (cheese, yogurt, butter, etc.)

   B) Caffeine (coffee or tea, etc.)

   C) High protein food or vitamins (eggs, meat, etc.)

   D) Citrus fruits (oranges, grapefruit, etc.)

   E) Bananas, apricots, pineapple.

These foods may interfere with some of the biochemical agents we are measuring.

APPENDIX G: Modified Profile of Mood States (POMS) Test

NOON

NAME _____ DATE _____

Below is a list of words that describe feelings people have. Read each one carefully. Then fill in ONE circle next to the word that best describes HOW YOU FEEL RIGHT NOW, that is, at the present moment.

NOW

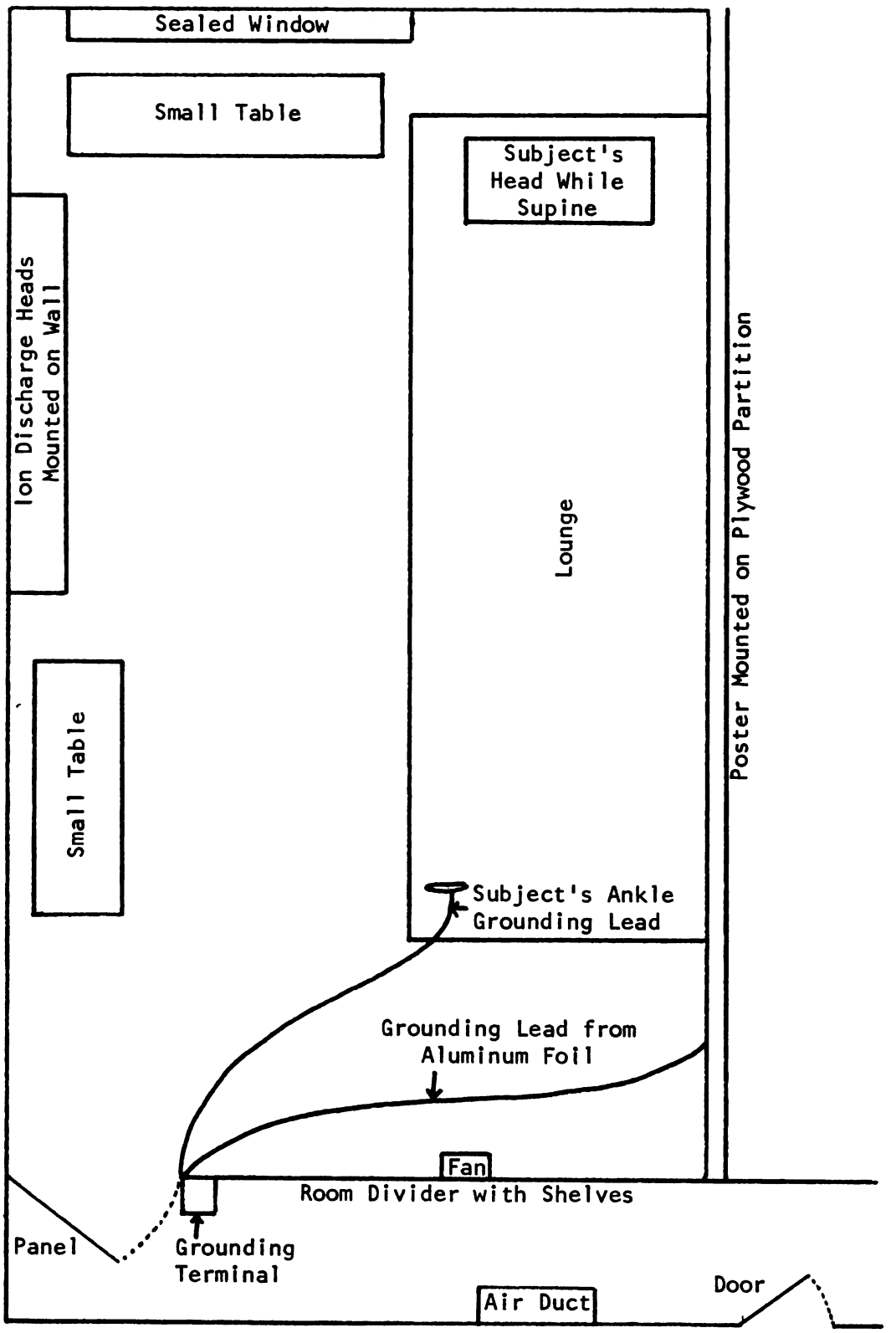
IDENTIFICATION

The numbers refer to these phrases.
0 = Not at all
1 = A little
2 = Moderately
3 = Quite a bit
4 = Extremely

	0 NOT AT ALL	1 A LITTLE	2 MODERATELY	3 QUITE A BIT	4 EXTREMELY
1. Friendly	0	1	2	3	4
2. Tense	0	1	2	3	4
3. Angry	0	1	2	3	4
4. Worn out	0	1	2	3	4
21. Hopeless	0	1	2	3	4
22. Relaxed	0	1	2	3	4
23. Unworthy	0	1	2	3	4
24. Spiteful	0	1	2	3	4
25. Sympathetic	0	1	2	3	4
26. Uneasy	0	1	2	3	4
27. Restless	0	1	2	3	4
28. Unable to concentrate	0	1	2	3	4
45. Desperate	0	1	2	3	4
46. Sluggish	0	1	2	3	4
47. Rebellious	0	1	2	3	4
48. Helpless	0	1	2	3	4
49. Weary	0	1	2	3	4
50. Bewildered	0	1	2	3	4
51. Alert	0	1	2	3	4
52. Deceived	0	1	2	3	4

NOTE: The publisher of the POMS adheres to the general policy that, due to their restricted nature, psychological tests not be bound with theses and dissertations. For this reason the test is not shown in its entirety.

APPENDIX H: Schematic of Ion-treatment Room


Sealed Window
Small Table
Subject's Head While Supine
Ion Discharge Heads Mounted on Wall
Lounge
Poster Mounted on Plywood Partition
Small Table
Subject's Ankle Grounding Lead
Grounding Lead from Aluminum Foil
Fan
Room Divider with Shelves
Panel
Grounding Terminal
Air Duct
Door

APPENDIX I: Derivation of Equation for Determining Concentration of 5HIAA in Urine

$$\Delta A = A - B = \kappa I C_u \qquad \text{Equation (1)}$$

$$\Delta C = C - B = \kappa I (C_u + \alpha) \qquad \text{Equation (2)}$$

Where:
A = fluorescence of tube A
B = fluorescence of tube B
C = fluorescence of tube C
κ is a proportionality constant relating net fluorescence to concentration
I is an inhibition resulting from the urine
α is the additional concentration of 5HIAA in tube C
C_u is the concentration of 5HIAA in the final assay mixture (total volume, 3.4 ml)

From (1): $\kappa I = \Delta A / C_u$

Substituting in (2): $\Delta C = \Delta A / C_u \times (C_u + \alpha)$

Therefore:

$$C_u \Delta C = \Delta A C_u + \Delta A \alpha$$

$$C_u (\Delta C - \Delta A) = \alpha \Delta A$$

$$C_u = \alpha \Delta A / (\Delta C - \Delta A)$$

From the protocol used, the following value arises:

$$\alpha = 1(0.1)/3.4 = 0.0294 \ \mu g/ml$$

The concentration of 5HIAA in the final assay medium is thus:

$$C_u = \alpha \Delta A / (\Delta C - \Delta A) = C_o V_u (8.5/10) \times 1/4 \times 1/3.4 \qquad \text{Equation (3)}$$

Where:

$$C_o = 1/V_u \times 1(0.1)/3.4 \times 3.4/1 \times 4/1 \times 10/8.5 \times \Delta A/(\Delta C - \Delta A)$$

$$= 0.4706/V_u \times \Delta A/(\Delta C - \Delta A) \qquad \text{Equation (4)}$$

This calculation was programmed on an HP65 calculator; which also calculated a recovery for each urine:

$$\text{Recovery} = (\Delta C - \Delta A)/\Delta F_{st}$$

Where:
ΔF_{st} = net fluorescence of tube C of the standard run

Note: Equation (4) includes the correction for recovery