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TOXICOLOGICAL IMPLICATIONS OF EXTENDED SPACE FLIGHTS

Bernard Weiss, Ph.D. Mark Utell, M.D., and Paul Morrow, Ph.D.

Center for Space Environmental Health,
Environmental Health Sciences Center
University of Rochester
School of Medicine and Dentistry
Rochester, NY 14642, USA

ABSTRACT

The dominant reason for exposing humans to the risks of space flight is their ability to perform complex tasks and make complex decisions. To fulfill such a role, crews must be shielded against even incipient degradation of performance capacity. The space environment contains potential hazardsranging from microgravity to infectious microorganisms to chemical toxicants. An extensive literature indicates that incipient disruptions of function may occur at low levels of exposure to toxic agents and degrade performance. Such questions need to be pursued before irreversible decisions are made about space vehicle design.

INTRODUCTION

The space environment contains potential hazards ranging from microgravity to infectious organisms to chemical toxicants. Especially for toxicology, prolonged exposure to such an environment entails risks in a unique context that poses new sorts of questions.

One set of questions, often asked, reveals the way in which the criteria of toxicity need to be formulated. Are humans essential for space exploration? Do they need to be endangered by journeying to and living in that inimical environment? Can equivalent functions be fulfilled by machines? The question was cogently addressed by the noted test pilot, Scott Crossfield, 35 years ago. "Where else," he asked, "Could you find a 150-pound servomechanism that can be mass-produced by unskilled labor?"

The same retort applies today, even with the advances in technology, then unimaginable, that are now routine. We expose humans to the risks of space flight because of their ability to perform complex tasks and to make complex decisions. The human brain remains infinitely superior to computers in its ability to integrate information, to improvise responses, and to weigh the outcome of those actions. To fulfill such a role, and to protect that ability, crews must be shielded against even incipient degradation of performance capacity. Incipient is the key phrase, because it frames a novel structure for the enterprise we know as risk assessment.

Risk assessment is the process by which we identify potential hazards, correlate their probability or intensity with dose or exposure level, and finally estimate the magnitude of adverse effects in a setting that presents a particular set of exposure parameters. In its conventional guise, the process has been dominated by cancer. It typically embodies extrapolation from high experimental exposures to low environmental exposures and from a detectable incidence of tumors to a projected incidence of, say, 10-5 over a 70-year lifetime.

Space environments, in contrast, confront us not just with complex mixtures of chemicals, a risk assessment conundrum in itself, but with their toxic potential amplified by factors unique to space. The most gratifying aspect of risk assessment in the space environment is that its vistas can be limited in both duration and scope. We direct our attention, not to delayed or remote dangers, but to those elements posing imminent threats to mission integrity.

PERFORMANCE DIMENSIONS

Performance measures are increasingly recognized as among the most sensitive indicators of adverse health effects, especially in the work environment.[1] They serve a special role as monitors of environmental safety because, as these authors note, health is not simply the absence of disease, but the capacity for optimal function.

Performance is a global term, however. To appreciate how it might be affected by the space environment, we have to untangle its constitutents. One dimension of performance is physical capacity. Although we do not require space crews to be competitive athletes, we do demand a high level of fitness so that crew members can undertake stressful duties such as extra-vehicular activities, or have an adequate margin of dexterity, strength and endurance to respond to physically taxing emergencies such as fires. Physical capacity, however, cannot be measured in isolation, as by an acute test of strength, or by heart rate changes on a treadmill. The ingredient that some call motivation is equally critical and requires other approaches.

Another dimension to performance might be termed fluidity of judgment, or the ability to make crucial decisions when confronted with unexpected or unpracticed situations. It requires an aptitude for weaving together many strands of information and choosing an action suitable to the product. If any aspect of space flight is certain, it is that the unpredictable is even more likely to happen there than in our tamer terrestrial neighborhood.

Alertness and vigilance comprise a third dimension of performance. Critical signals, ranging in subtlety from programmed instrument queries to transient deviations in a control system to peculiar fluctuations in some indicator to odd behavior on the part of a crew member should trigger an appropriate response. It may lead to a series of decision steps, as noted above, or a sequence of probes to establish the cause, or a straightforward correction or intervention.

SOURCES OF IMPAIRED PERFORMANCE

The principal aim of maintaining environmental integrity is to insure optimal, not simply adequate, crew performance. In fact, performance should be the primary metric by which we measure integrity; but, in space, its definition vastly exceeds our customary prescriptions. Workplace exposure criteria, such as Threshold Limit Values, are based on individual chemicals or chemical groups and conventional 8-hour durations. Even under these circumstances, performance is accorded a central role. Note the definition of the Short-Term Exposure Limit given by the American Conference of Governmental Industrial Hygienists, the organization that pioneered the concept of Threshold Limit Values:

"The maximum concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from...narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency..."

Space environments multiply the sources of performance degradation, compared to the workplace setting, by orders of magnitude; at the same time, they exact far higher levels of performance from crew menbers. The potential sources of health hazards have been discussed in many publications. They include chemicals such as solvents and irritants, infectious microorganisms, potential antigens, particulates from numerous sources, including skin, inadvertant contaminants from food and water, and detritus from manufacturing processes. Microgravity and its impact pervades all the other, perhaps more tractable, challenges.

A useful source of information about the potential adverse effects of such exposures is the literature of behavioral toxicology and behavioral pharmacology. Behavioral toxicology evolved from concerns about the more subtle effects of exposure to environmental contaminants; it contrasts with traditional endpoints of toxicology, which emphasized tissue damage and death. Behavioral pharmacology, a predecessor of its toxicological counterpart, arose in response to the introduction of effective chemotherapy, the tranquilizers, for behavioral disorders. It stimulated a literature that encompassed not only therapeutic endpoints, but adverse effects as well. Many drugs, even those not designed to alter behavior, possess central nervous system actions that can impair functions such as automobile driving.

Workplace hazards represent a major theme in the research conducted by behavioral toxicologists. Volatile organic solvents occupy a major role in these efforts because they are clearly neurotoxic at higher levels. Some, in fact, such as trichlorethylene, have even been used as anesthetics. Most of this research has been fixed on chronic effects because of evidence pointing to deficits on psychological tests in workers exposed for many years. Acute or subchronic experimental studies would be more informative for our current purposes. First, they would be more representative of the conditions that arouse our concern; exposure standards for the space environment should derive primarily from their more immediate and short-term consequences than from the effects they might produce if extended over a working lifetime. Second, exposure conditions, such as ambient concentrations, can be specified and controlled, unlike the retrospective chronic studies that must rely on rather sketchy and often inaccurate exposure estimates. But such studies are less plentiful than chronic studies, partly because they require inhalation facilities that are relatively uncommon.

Even the best of the experimental studies offer rather sparse information useful to planning for space. The protocols are typically based on rather short exposure durations, rarely exceeding a few hours, or, at most, a full 8-hour workday. The space environment, however, delivers continuous exposures. The discipline of pharmacokinetics, which studies and constructs quantitative models of chemical uptake, distribution, metabolism, and excretion needs to target the problem of 24-hour exposures. Few facilities, however, such as the human exposure chamber located in the University of Rochester Medical Center, are available for the conduct of such research. In addition, most of the available performance data are based on batteries of relatively simple tests bearing little resemblance to the duties that flight crews are ultimately responsible for. The elements of most such batteries comprise cognitive function tests, psychomotor tests, and measures of mood. They are designed to survey a wide range of functions, and to serve as a tool for screening impaired workers, not to secure definitive information about any single dimension of performance.[2] Nor do they seek for complex dysfunctions such as impaired foresight or judgment. Nor are they suitable for tracing the kind of progessive decline in complex function that might ensue, say, from a slow solvent leak that remains undetected for several hours. For the tasks carried out by space crews, test batteries need to be amplified.

EXTANT DATA

Neurotoxicants

Anger[3] surveyed findings from the world literature reporting behavioral deficits allegedly due to chronic worksite exposures. The range of behavioral effects associated with exposure to volatile organic solvents appears in Table 1. Solvents of many kinds are combined in the table simply to demonstrate the scope of the results; no one disputes that different solvents (carbon disulfide, styrene, toluene, etc.) may produce different response contours. The table is useful for our purposes because it captures some of the functional deficits that excessive exposures to neurotoxicants might elicit. It is equally useful because of its omissions, which arise from the limited repertoire of those test batteries on which the findings are based. They include only superficially, if at all, the high-level functions, noted earlier, that space crew members will be required, at certain times, to display. Even these relatively simple tests argue that exposures insufficient to provoke overt signs of impairment may still handicap the individual's ability to perform optimally.

TABLE 1.

Functional Parameters Sensitive to Chronic Solvent Exposure

	Cognitive
Intelligence	
Memory	
Vigilance	
Acquisition	
Coding	
Concept Shifting	
Spatial Relations	
Categorization	
	Motor
Coordination	
Response Speed	
	Sensory
Color Vision	
	Personality
Mood Changes	

One component of the literature that merits attention by this audience is that portion derived from environmental conditions other than neurotoxicant exposure. Performance degradation by noise, vibration, physical work load, and to moderately elevated or reduced temperatures has also come under study (Gamberale et al, 1988). Aspects of this literature are discussed below.

Respiratory Infections

Infectious organisms introduced into the space environment by the crew itself, or from waste processing activities, or by intrinsic contamination, offer another set of hazards with the potential to impair performance. A series of studies, conducted in the late 1960s and early 1970s, directly addressed the kinds of deficits that might be elicited by mild infections. The investigators relied on what they called a synthetic work situation designed to mimic the kinds of tasks that air crew members might be called on to perform. Its components included vigilance, sensory-perceptual functions, arithmetic computations, information reception and transmission, and procedural functions such as interpersonal coordination.[4]

In reviewing these data, the investigators noted that infections with Pasturella tularensis, or Rabbit fever, reduced efficiency on this task by 6-8% for each 10F of fever. Illness produced by Phlebotomus infections (Sandfly fever) produced a fall of 3-6% per 10F rise in body temperature. They also observed marked individual differences in sensitivity, despite a subject population consisting of healthy young men, including flight crews and Air Force cadets. Performance decrements ranged from essentially zero to 20% for each 10F of fever.

More recent work,5 although based on much simpler test situations, supports the earlier data. These studies were conducted at the Medical Research Council's Common Cold Unit in the UK. In one experiment, a computerized 5-choice serial reaction time task served as the measure of performance. The subjects experiencing colds after challenge with a coronavirus responded at a significantly slower rate (about 14%) than the uninfected subjects. In a second experiment, volunteers were infected with respiratory synctial viruses and the course of infection monitored by both nasal washings and serum IgG levels. Those subjects who later developed colds responded about 4% more slowly, during the incubation period, than uninfected subjects or subjects who did not develop colds. On symptomatic days, subjects with colds and subclinical infections responded about 4% more slowly than uninfected volunteers. These are not massive deficits, but still notable given the relatively simple and undemanding nature of the task.

Pulmonary Function

Clinically defined pulmonary dysfunction, like other overt indications of disease, is not the primary question posed in space flight. Space crews must meet exacting criteria of health, and would be unlikely, even under extreme conditions, to evince marked reductions in physical capacity. The problem, again, is the possibility of performance below optimal standards.

Ozone provides some useful examples.[6] The available literature indicates that relatively low ambient levels of ozone, a deep lung irritant, induce performance changes in healthy subjects. One early epidemiological study indicated that high-school cross-country runners in the Los Angeles area declined from predicated optimal performance in direct relation to the measured oxidant level that day. Controlled experiments in laboratory settings report similar findings. Trained athletes, exercising while breathing low concentrations of ozone, often ceased performing even when lung function tests showed no abnormalities. The voluntary termination of the exercise routine seemed related more to motivational variables, such as aversive subjective effects, than to objective indices of capacity. Similar findings seem to emerge from the animal literature. Moreover, marked individual differences are seen in subjects participating in air pollutant experiments despite rigorous selection criteria. The presence of numerous sources of pulmonary irritants in the space environment, and the possibility of synergistic effects from mixtures of such agents, makes it mandatory that performance effects be thoroughly investigated.

Failure Modes

The emphasis on various kinds of performance variables noted above, and the sources of performance degradation already recognized, stem from the requirement to eliminate potential sources of performance failure. Human error accounts for the majority of aircraft accidents. At least 52 percent of significant event reports in nuclear power plants are attributable to performance failures. Catastrophic accidents, such as those at Chernobyl and Bhopal, are primarily the result of human rather than machine failures.

Furthermore, performance failures may not be apparent at first. Active failures, that is, errors and violations resulting in an immediate hazard, may be less threatening to mission integrity than latent failures; the latter comprise decisions or actions whose consequences may lie dormant for a considerable time or that emerge gradually and insidiously. Studies of the variables inducing performance degradation, particularly in response to low-level toxic exposures, deserve a higher priority in space research than accorded them in the past. Space vehicle design should succeed, not precede, the collection of this information.

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REFERENCES

[1]Gamberale, F. Use of behavioral performance tests in the assessment of solvent toxicity. Scand. J. Work Environ. Hlth. 11(Suppl. 1):65-74, 1985.

[2]Anger, W.K. Human neurobehavioral toxicity testing. In R.W. Russell, P.E. Flattau, and A.M. Pope (eds.) Behavioral Measures of Neurotoxicity. Washington, D.C.:National Academy Press, pp. 69-85, 1990.

[3]Anger, W.K. Worksite behavioral research: Results, sensitive methods, test batteries, and the transition from laboratory data to human health. Neurotoxicology 11:629-720, 1990.

[4]Morgan, B.B. and Alluisi, E.A. Synthetic work: Methodology for assessment of human performance. Percept. Mot. Skills 35:835-845, 1972.

[5]Smith, A.P., Tyrrell, D.A.J., Al-Nakib, W., Coyle, K.B., Donovan, C.B., Higgins, P.G., and Willman, J.S. Effects of experimentally induced respiratory virus infections and illness on psychomotor performance. Neuropsychobiology 18:144-148, 1987.

[6]Weiss, B. Behavior as an endpoint for inhaled toxicants. In R. McClelland and R. Henderson (eds.) Concepts in Inhalation Toxicology. Washington, D.C.:Hemisphere Publishing Co., pp. 493-513, 1988.