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RADIATION: BEHAVIORAL IMPLICATIONS IN SPACE*

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SUMMARY

Since future space missions are likely to be beyond Earth's protective atmosphere, a potentially significant hazard is radiation. The following behavioral situations are addressed in this paper: (1) space radiations are more effective at disrupting behavior; (2) task demands can aggravate the radiation-disruption; (3) efforts to mitigate disruption with drugs or shielding are not satisfactory and the drugs can be behaviorally toxic; and (4) space- and radiation-induced emesis combined may be synergistic. Thus, future space travel will be a demanding, exciting time for behavioral toxicologists, and while the circumstances may seem insurmountable at first, creative application of scientific expertise should illicit solutions, similar to demanding situations confronted before.

Key words: Space; Radiation; Toxicity; Behavior; Performance

INTRODUCTION

The manned orbital space platform, extended space missions to Mars, and working colonies on the Moon will permanently establish our presence in space. These missions are projected to occur by the turn of the century. Since they will often be beyond Earth's protective atmosphere radiation is a serious concern [1,2]; this can come from radiation trapped in Earth's atmosphere, solar or galactic sources [3]. Depending on the flight path and spacecraft design, each source can contribute considerably to the total radiation effect during a mission. The major sources of radiation during near-Earth missions are proton and electron fluxes captured by Earth's geomagnetic fields creating a zone of increased radiation, or a radiation belt [3]. The major radiation hazard during polar orbits beyond Earth's protective atmosphere or on interplanetary flights will come from solar

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flares or explosions of supernovae, which produce mainly protons. α-particles, and particles of high charge and energy (HZE). Other sources of space radiation are those created on Earth, i.e., reactors used for power and from atmospheric testing of nuclear devices. In these cases, γ- and neutron radiation are the main products.

Biological research on the behavioral effects of radiation suggests some concerns for astronauts in space. Because radiation is added to other space problems, the behavioral toxicologist (radiobiologist) will address a plethora of scientifically interesting problems. They include (but are not limited to) weightlessness, bone demineralization, cardiovascular deconditioning, motion sickness, and psychophysiological and psychosocial stress [1—6]. Since the human component is crucial in the space program, the effects of radiation alone or combined with other stressors on behavior are critical concerns. This paper discusses radiation-induced behavioral situations that may exist in space and therefore are relevant to the space program. The findings are based on animal research. The topics discussed are: (a) radiation-induced performance decrement; (b) factors producing performance decrement; (c) radiation quality; (d) chemical radioprotection; and (e) physical shielding.

RADIATION-INDUCED PERFORMANCE DECREMENT

Rapidly delivered ionizing radiation disrupts animal behavior measured in a variety of tasks. Performance decrement (PD) is assumed to also occur in man [7,8]. The possible radiation-induced disruption is early transient incapacitation, early PD, or simply a statistically significant PD following exposure. Early transient incapacitation is an abrupt performance cessation that can occur 5—15 min post exposure and that can last for at least 5—15 min. Early PD is the less severe, time-related variant of early transient incapacitation, also temporary in nature. These 2 early behavioral responses may be produced uniquely by radiation [7]. In this paper, PD includes all forms of disruption that can occur within 60 min post-radiation.

FACTORS PRODUCING PD

In the future, when astronauts are in space in greater numbers and for longer durations, they will be exposed to increased low-level radiation and the chance of exposure to high-level radiation from solar flares (solar proton events) will be higher [3]. Thus, a major concern is how exposure to the increased radiation will affect functional ability. This section considers some behavior-related radiation issues that may exist in space.

When PD from radiation was initially reported in monkeys 3 decades ago, disruption occurred only at very high doses above 50 Gy [9—11], well in excess of the 6-Gy $LD_{50/30}$ [12]. Since death occurs very soon after exposure at these dose levels, PD would have been of little concern to space radiobiology. The dose levels that produced PD at that time were probably high because the behaviors studied were relatively simple and/or undemanding, and thus they were resistant to radiation [13]. The PD effect-

level (ED_{50}) was reduced to 15 Gy more recently when more complex visual discrimination performance was required [13]. When the visual discrimination performance was made more demanding by reducing response time from 5.0 to 0.7 s, the ED_{50} for PD was reduced even lower to 7 Gy [14].

Research with a delayed match-to-sample task further addresses the issue of task complexity [13,15,16]. In this test of cognition and memory, monkeys were irradiated at dose rates of 0.3, 0.8, and 1.8 Gy/min, for a total dose of 10.0 Gy. Eighty-one percent of the subjects experienced PD at the highest dose rate (1.8 Gy/min). Only 7% of the subjects experienced PD at the lowest dose rate (0.3 Gy/min), which means that dose rate is a significant factor in performance ability. More important, when PD occurred, since both behavior and blood pressure started to decline at less than the total dose, it was suggested that the ED_{50} for PD may be as low as 3 Gy. Since the delayed match-to-sample task is probably the most complex task of those discussed, the 3-Gy dose to produce PD is probably reasonable. The 3-Gy dose is relevant in space because this magnitude of radiation has been recorded during unmanned flights after solar proton events (SPEs) [3].

Related research shows how radiation effectiveness can be altered by task demands. This work [17] compared physically demanding and undemanding tasks. Monkeys performed either a physically demanding activity wheel task or a physically undemanding visual discrimination task. It was concluded that physically demanding performance generally was affected sooner and at lower radiation doses than was physically undemanding performance.

The key issue here for space is that radiation-induced PD is related to a number of factors like task complexity, task demands, dose and/or dose rate, and that as these factors increase, the dose-to-effect decreases. In addition, if these factors are combined or additional space insults are involved (like motion sickness, nausea, or cardiovascular deconditioning), the synergistic effect of the stressors may reduce the radiation-effect level even more.

The foregoing indicates that significantly increasing the task complexity decreases the dose to produce PD. However, the 3-Gy ED_{50} is still high. Further increasing task complexity no doubt will further decrease the dose-to-effect, but other research indicates that the effect level probably is lower, without increasing complexity. This research comes from 2 areas. The first involves the conditioned taste aversion (CTA) paradigm, which is believed to be related to emesis [18]. A CTA develops to a novel tasting solution that is normally preferred by an animal (i.e., sucrose-flavored water), when ingestion of the novel solution is paired with irradiation. The results indicate that CTA's are possibly with doses as low as 25 rads (0.25 Gy) and they can be reliably obtained at 0.5 Gy. The second area of research involves sodium uptake in the brain [19]. These results demonstrate an inhibitory effect of radiation on the voltage-sensitive sodium channels in brain synaptosomes at doses as low as 0.1 Gy. Producing this inhibition means that the brain is working below optimum, which might translate into reduced functional ability. Thus, both the CTA and sodium channel work suggest that meaningful behavioral and/or CNS changes may occur at doses considerably less than the 3 Gy reported for PD.

Another study is relevant here, in which behavioral manipulation was shown to affect lethality [20]. In this study, the $LD_{50/30}$ was compared for resting and non-resting rats. The $LD_{50/30}$ was 9.5 Gy for resting rats, but for rats performing a motor performance task (non-resting condition), it was 8.0 Gy. This 1.5-Gy difference is significant and indicates that the type of behavior required not only can affect a performance end point, (i.e. ED_{50}), but it also can affect the $LD_{50/30}$ end point.

RADIATION QUALITY

In space, astronauts will be confronted with a number of radiation qualities [2,3]. Proton radiation probably will be the most common, and electron radiation the next most common. Bremsstrahlung radiation from the interaction of particulate radiation with the spacecraft will also exist, as well as HZE particles. The concern is how these radiations may affect man and whether they are equally effective. Some studies [7,8] compared the PD-producing ability of bremsstrahlung, electron, γ-, and neutron radiations in rats performing a motor performance test, the accelerod. A dose-response relationship for PD was found for all radiations. Electron radiation disrupted performance at significantly lower doses than did the others i.e., a 25% lower dose than bremsstrahlung, 31% lower than γ-, and 42% lower than neutron. Bremsstrahlung was the next most effective, disrupting at 9% and 18% less than γ- and neutron radiations, respectively.

Related research has also reported that different qualities of radiation are not equally effective at disrupting behavior. For instance, Hunt [21] found that electron radiation produces PD at significantly lower doses than do γ-photons in rats performing an avoidance task. Other investigators [22,23] have shown that γ- radiation produces PD in monkeys and pigs at significantly lower levels than do neutrons. All of the radiation quality work indicates that neutrons are the least effective at disrupting behavior, while they are the most effective for lethality [7].

Although the rat/accelerod findings suggest that electron and bremsstrahlung radiations may be of greatest behavioral concern in space, this must be qualified. In these studies, the PD ED_{50}s were high, ranging from 61 Gy (electron) to 98 Gy (neutron) [7,13]. These doses are much higher than those likely to be found in space, unless anonymously large SPEs occur [2,3]. Also, these dose levels are probably higher than those necessary to produce PD in humans. As stated above, the monkey PD ED_{50} is 9 Gy for a mixed γ/neutron field [14], and it may be as low as 3 Gy for γ-radiation alone [15,16], which is probably a reasonable estimate for people. However, the main point of the accelerod data is the relative effectiveness, not the absolute ED_{50}s; that is, electron radiation affected accelerod performance at doses 25%–40% lower than did the other radiations. In addition, since the rat data indicate that electrons produce PD at a dose 31% lower than γ-photons, the 3-Gy ED_{50} speculated for PD in the monkey with γ-radiation may be as low as 2 Gy with electron radiation.

At the present time, no behavioral information exists about the effects of

proton or HZE radiation. In general, protons are supposed to resemble γ-, electron, and bremsstrahlung radiations [12]. However, PD findings indicate that electron radiation was effective at much lower doses, so it is difficult to speculate about the behavioral consequences of protons, the most common radiation in space. HZE radiation presents some unique problems, even though it is not extensive in space [3]. For instance, unlike other radiations [24], HZE radiation is little affected by shielding. Also, HZE radiation can penetrate tissue creating microlesions, which may be of special significance if the path involves the eye and/or a critical area of the central nervous system (CNS). Thus, because of the uncertainties about proton and HZE radiation, the CNS and behavioral effects of these radiations should be understood better, before man regularly participates in outer space.

ATTENUATION OF PD

The effects of radiation on behavior and the factors that can alter these effects are discussed above. The next section deals with ways to attenuate these behavioral effects. Topics discussed are chemical radioprotectants to attenuate PD, behavioral toxicity of radioprotectants, physical shielding to attenuate PD, radiation-induced emesis, and emesis produced by radiation and motion combined, which has possible implications to space motion sickness.

CATEGORIES OF CHEMICAL BEHAVIORAL RADIOPROTECTORS

Three categories of behavioral radioprotectors (BR) that might be used in space are considered [20]. The first category is direct attenuation, since the radioprotector is meant to act directly on correlated physiological responses in order to block PD. Direct BR studies were done with blood pressure stabilizers to attenuate hypotension and anti-histamines to attenuate histamine, which also can produce hypotension. A study [25] to diminish hypotension with the blood pressure stabilizer norepinephrine did not attenuate PD. This finding implies that although the correlated drop of blood pressure and PD is enticing, the association is not as direct as it seems, and a cause-effect relationship must be sought elsewhere [20]. Studies to block PD with an anti-histamine were done with monkeys and rats [26,27]. Chlorpheniramine attenuated PD up to 30 min post-irradiation, but after that time, monkey performance was the same as the radiation-only subjects, i.e., severely degraded [26]. More recent [28] work was done in monkeys with the anti-histamine disodium cromoglycate. Disodium cromoglycate maintained hypothalamic blood flow in non-performing monkeys significantly above controls. Since disodium cromoglycate maintained blood flow, it is speculated that it may do the same for PD. Thus, future disodium cromoglycate work is planned with performing monkeys.

The second BR category involves drugs that offer protection from lethality. Since these radioprotectants were not developed to attenuate PD, they are incidental attenuators [20]. Studies [29,30] were done with WR-1607

and WR-2721. WR-1607 offered protection for PD in monkeys up to 30 min after irradiation, but emesis was noted in all monkeys 8–10 min after WR-1607 injection. Attenuation from PD for 30 min seems to be a common denominator already noted with chlorpheniramine. However, to be an acceptable agent for use in space, the final BR should protect performance beyond 30 min and it can not have behavioral side effects like emesis.

Considerable research [20] was done assessing the ability of WR-2721 (ethiofos) to attenuate PD, for it is the leading radioprotectant for lethality. Ethiofos also was assessed for its behavioral toxicity. In all testing, ethiofos was behaviorally toxic alone, and it aggravated rather than attenuated PD. Thus, although ethiofos is effective on lethality, it is not effective on behavior. Weiss et al. [31] reported that ethiofos combined with selenium increases the dose level at which ethiofos is lethal (reduced toxicity) and increases its effectiveness as a radioprotectant for lethality. Behavioral testing with selenium indicated that the selenium/ethiofos/radiation condition shows slightly more PD than does the ethiofos/radiation condition [20,32,33]. Other research [34] at this Institute has shown that biological response modifiers attenuate radiation-induced lethality. Behavioral work is in progress to determine if biological response modifiers can also attenuate PD.

Besides the behavioral toxicity of ethiofos and the negative synergy of ethiofos and radiation combined, WR-2721 has another negative aspect for man in space, i.e. it produces hypocalcemia [2]. Hypocalcemia is potentially serious because weightlessness in space also decreases calcium by bone dimineralization. Consequently, the calcium losses superimposed on each other and the behavioral effects of ethiofos will require careful consideration before using WR-2721 in a space-radiation emergency.

Another consequence of exposure to radiation is nausea and/or vomiting, which may be a factor in producing PD [35]. The third BR category involves anti-emetics, which block these gastrointestinal effects. Considerable research on anti-emetics has been done with cancer patients treated with radiation, but in these cases, there was little concern for adverse effects on behavior. However, current requirements include functional well-being after anti-emetic treatment [2]. Dubois [36a] tested metoclopromide, dazopride and zacopride to determine their ability to block emesis in monkeys postirradiation. Dubois et al. [37] found that all drugs are effective anti-emetics, but only zacopride is free of behavioral side effects. Metoclopromide disrupts motor behavior and dazopride produces drowsiness. Since the behavioral assessments were based on casual observations, future work is planned to formally determine if zacopride causes behavioral toxicity.

In space, crews will also be faced with emesis caused by motion [2,38]. It has been suggested that more than 60% of all space travelers will be affected by motion sickness for 2 or 3 days. Even beyond the adaptation time, emesis thresholds in space may be permanently lowered. A study [39] was done in monkeys to test for synergy between radiation and motion. This study reported that the emesis ED_{50} was 4.5 Gy for radiation alone and 2.6 Gy for radiation and motion combined. Thus, the combined stressors significantly

reduced the ED_{50} for emesis, suggesting that in future space travel where radiation may be more pervasive, man will be more susceptible to emesis.

The increased susceptibility also indicates that effective anti-emetics will be needed, but the situation is not as simple as it appears. Because the mechanisms of effect for emesis produced by radiation and motion are different, combined drug treatments will be needed [38]. In addition, combined drug treatments may be necessary for radiation-induced emesis alone, since it is controlled both humorally and neuronally [35]. This paper has already shown that behavioral toxicity can occur with single-drug regimens and that combined regimens may increase the potential for toxicity. This all implies increased potential for compromising space crews, at least temporarily, with anti-emetic compounds [20].

SHIELDING

Physical shielding [2,3] is another way to protect people from radiation in space. A number of radiation studies [13] were done in which lead shielding was investigated to determine if it can attenuate PD. This behavioral work was done with monkeys or pigs, and it involved head shielding (body exposed) or body shielding (head exposed). Two of the studies [40,41] suggested that protection from PD might be offered by head shielding. However, 3 studies [42–44] did not show any benefit for shielding the head or the body. The behavior/shielding issue may be unresolved at this time, because in addition to different animal models, a variety of criteria, tasks, doses, and dose rates were used. Thus, before man becomes a regular participant in space, the issue of shielding for PD should be resolved.

CONCLUSIONS

Radiation in space will be at acceptable working limits in low-Earth or equatorial orbits. In low-Earth orbit, areas known to have high levels of geomagnetically trapped radiation can be avoided, while in equatorial orbit, Earth's atmosphere extends out considerably like a protective shield. But avoidance is not possible in polar orbits, in which Earth's atmosphere is very limited, and in high-Earth orbit or on interplanetary missions, in which atmospheric protection does not exist. In these instances, astronauts will be confronted with either unpredictable SPE's or cosmic/galactic radiation. The severity of the hazard will increase in direct proportion to duration of the flight, especially on interplanetary missions. With this in mind, the following are some behavioral/radiation considerations that should be taken into consideration prior to future extended space missions:

(1) Performance decrement may occur at radiation doses well below the $LD_{50/30}$, and if the radiation is combined with other insults and/or stressors, the ED_{50} for radiation may be even lower.
(2) Effects of radiation on the central nervous system or with an indirect measure of emesis (conditioned taste aversion) may occur as low as 0.1 –0.25 Gy.

(3) Radiation effects on performance decrement depend on task complexity, dose, dose rate, and radiation quality.
(4) Information is needed on the behavioral effects of HZE radiation because of its lesion-making ability, and on proton radiation because it is commonly found in space.
(5) Non-toxic radioprotectors of behavior are needed.
(6) The best shielding array for behavior needs to be determined.

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