Report of the NASA Space Radiation ad hoc Expert Panel on CNS Risks.

K. Held, A. Koretsky, R. Meyn, M. Robbins, R. Nowakowski, W. Schimmerling, G. Beven, M. Barratt, R. Tanzi, F. Cucinotta, A. Hein, F. Sulzman, W. J. Koroshetz

Human missions outside of the earth's electromagnetic field will expose astronauts to energetic protons and high energy (E), heavy charged (Z) particle radiation denoted as HZE particles. Current technologies are incapable of shielding these particles which makes assessing their health effects, particularly on the central nervous system (CNS), an important goal. However, limited knowledge exists to estimate the clinical relevance of such effects. The National Aeronautics and Space Administration (NASA)-funded studies of animals exposed to high energy particles have demonstrated that some brain alterations can occur at total exposures that fall within the range of a prolonged human mission to outer space. These experiments raise the question of whether deep space radiation might cause changes in cognition that could affect astronaut performance during a long mission, as well as whether radiation exposure may increase the risk of accelerated onset of Alzheimer's disease, Parkinson's disease, cerebrovascular disease, or other neurodegenerative diseases.

Studies to date have examined a wide spectrum of behavioral, pathologic, and physiologic changes in irradiated animals exposed to a variety of heavy ions at different energies and fluences. The experiments have been conducted for different purposes and by different groups and, thus, are not easily comparable. For these reasons, it is difficult to know whether they are tracking a common effect, whether the effects seen have been replicated, or whether they can be extrapolated to the human condition. Although these studies do not clear concerns for either short term effects on cognition or long term delayed risk of accelerated neurodegeneration, neither do the studies establish a definitive, clinically significant brain effect of high energy radiation within the expected range of exposure.

The panel identified a number of limitations in the evidence presented on CNS space radiation risk that need to be addressed to enable a more definitive determination of the CNS risk related to radiation exposure. To address these limitations, the panel made the following recommendations for future studies. 1) Identify quantifiable endpoints for the assessment of cellular, molecular, physiological, and behavioral changes and standardize these endpoints among research groups. 2) Conduct more functional assays, to determine how radiation affects cell physiologic activity. 3) In addition to long term time points, include acute time points that will inform astronaut risk for cognitive dysfunction during space flight. 4) Create a limited and standardized set of HZE exposures to allow comparison and replication of data among research groups. 5) Promote tissue/sample sharing between CNS and carcinogenesis studies. 6) Continue primarily using rodent models, including studies of Alzheimer's disease (AD) and other neurodegenerative risks, with a long term goal of moving to a non-human primate (NHP) to assess cognitive risk to humans. Because of the current gaps in our understanding of the causes of neurodegenerative disease, even with these changes, the panel felt that a true estimate of the risk of accelerated neurodegenerative disease due to space radiation will be difficult to establish in the near time. However, a predictive risk model that estimates those acute exposures which have a reasonable likelihood of causing acute or subacute neurological impairment was considered feasible.

In considering a long term research strategy to quantitatively assess CNS risk from space radiation exposure, the panel recommended a 4-step process. 1) Definitively establish those pathological processes and behavioral correlates triggered by single dose high energy radiation in rodents. 2) Test the impact of chronic, fractionated exposures as compared to single dose high energy radiation at discrete and limited energies, doses, and time points. 3) Determine whether robust effects demonstrated in rodents are seen in the NHP. 4) Develop a set of experiments to test whether CNS effects suggested by work at the NASA Space Radiation Laboratory (NSRL) are indeed seen after exposure in deep space. This may include animal experiments but should certainly include a well-thought out evaluation of astronauts during and immediately after return from the first deep space missions.

Overall, the panel recommends that NASA adopt a more integrated research approach. The CNS space radiation research to date has been highly correlative and discovery-driven. This approach has helped lay a strong foundation of knowledge. In addition to further early stage discovery research, there is now a need, and the knowledge base, to mount a more coordinated research approach. For instance, NASA should consider developing a standardized set of radiation procedures at NSRL (i.e., exposures with standard range of fluency, energies, particles, and exposure timelines) that most closely represent the astronaut's exposure in deep space and establish those durations of deep space flight that would not be expected to pose short term safety concerns to the astronaut. NASA could achieve this integrated research approach with more NASA Specialized Centers of Research (NSCOR) on mission-critical topics. This strategy would ensure that NASA's human research program in CNS radiation risk makes tangible steps towards quantifying the CNS risk by 2020.