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COMMENTARY

Your Brain on Mars

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Our recent report published in *Science Advances* entitled ''What happens to your brain on the way to Mars'' highlights certain adverse neurocognitive effects resulting from charged particle exposures (*1*). These findings have attracted considerable attention. For this reason, we would like to emphasize some of the critical findings along with the caveats, and put them into context in terms of implications for astronaut health, the space program and some future priority areas of research. While responding to multiple media organizations, invariably the first question I was asked was whether this is a ''show stopper'' for the space program, to which my response was ''of course not''. Our observations simply describe another risk encountered when traveling into the foreign environment of space, a risk that we need to understand more completely as NASA prepares for deep space travel.

One thing is certain: NASA's planned mission to Mars will unavoidably expose astronauts to the charged particles found in galactic cosmic rays (GCR). These particles cannot be shielded against and thus, will traverse the hull of a spacecraft and the body of an astronaut (*2, 3*). This is not to say that ongoing work by NASA to improve shielding will not provide benefits. Our study has documented an unprecedented sensitivity of mature neurons in the rodent brain when exposed to ^{16}O and ^{48}Ti charged particles. Mice exposed to space-relevant fluences (5 and 30 cGy) of charged particles developed significant behavioral impairments 6 weeks after irradiation. Cortical- and hippocampal-based deficits were linked to major structural alterations to neurons in the prelimbic layer of the medial prefrontal cortex (mPFC), a region of the brain known to be important for learning and memory. Charged particle exposure caused significant and persistent reductions in dendritic arborization and spine densities along with alterations in synaptic integrity, findings that corroborate past work with lower LET radiation modalities (*4, 5*). These changes are responsible for disrupting the connectivity of the brain and altering cognition. Collectively, these changes point to a marked sensitivity of the mature rodent brain to very low doses of space radiation and to a heightened risk to astronauts for developing radiation-induced cognitive deficits during prolonged exposure to the deep-space radiation environment (*1*).

By necessity, the doses used in our study were delivered in a matter of seconds to minutes, but approximate the doses an astronaut might receive over the course of one month (*6*). For this reason, it is difficult to extrapolate our findings to situations where protracted charged particle exposures would transpire over the course of several years. However, traditional dose-rate effects are not likely to play a significant role due to infrequent particle traversals (i.e., low doses), the high LET of charged particles, as well as the post-mitotic and differentiated state of the vast majority of neurons (*7*). Whether or not the brain mounts a compensatory response over the duration of deep-space flight is another matter, and without additional data it remains difficult to speculate on whether such a compensatory response would ameliorate or exacerbate potentially adverse behavioral outcomes.

Here on Earth, ground-based studies at the NASA Space Radiation Laboratory at Brookhaven National Laboratory (BNL) face certain practical limitations with regards to accurately simulating the GCR dose rate and spectrum encountered in space (*8*). The knowledgeable physicists at BNL are developing mixed beam fields using multiple ion types for more accurate exposure scenarios (*8*). Future work will focus more heavily on the use of these mixed beams as efforts continue to provide more realistic terrestrial simulations of the space radiation environment.

So where does this leave us? NASA continues to fund a number of skilled researchers investigating multiple acute and late effects in the central nervous system (CNS). Cognition is a multifaceted end point involving a wide range of signaling pathways that dictate the excitatory and inhibitory tone of the brain. Radiation disrupts this balance and the result is a perturbation of neurotransmission that could manifest as performance decrements in space, or longer term loss of cognitive capabilities. Our findings provide one piece to this complex puzzle, and have now linked structural and functional decrements in the CNS after

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exposure to space-relevant fluences. The persistence of the adverse CNS effects adds an element of concern, since we have no evidence that the structural changes measured in neurons ever resolves, and no evidence that human neurons would be any less susceptible to the types of changes found in rodents.

How best to translate our rodent findings to human behavioral scenarios in space remains challenging, as does determining precisely what types of decrements astronauts might experience during deep-space travel. Much of that will depend on specific situations and scenarios encountered and how the astronauts can respond to unexpected events under almost complete autonomy from Earth. While some may consider these findings controversial or inconclusive it remains difficult to dismiss these data sets and their potential implications for the space program. Suffice to say that NASA-funded research has now uncovered a mechanism leading to charged particle-induced cognitive impairment and only continued research will uncover the extent that this may ultimately prove problematic. Should these observations prevent us from going into space? My response is an emphatic ‘‘no’’. The effect of space radiation exposure on cognition is just another problem that NASA needs to take into account as they assess the overall risks associated with deep space travel.

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