# 2013 DECADAL STUDY

## The Impact of Sex & Gender on Adaptation to Space

A Joint Study by the National Aeronautics and Space Administration and the National Space Biomedical Research Institute

# Neurovestibular Workgroup

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# Neuroscience in Space: Are there Neurosensory Differences Based on Sex and Gender

- **NASA, Neuroscience and the Question of Sex and Gender**
  - Historically, NASA and the RSA have had little interest in exploring sensory differences between men and women during space flight.
  - From a Neuroscience perspective women do differ from men in most sensory systems, neural anatomy and functional responses operationally on Earth.

- **General Differences**
  - Extensive sex differences exist in the brain, including in gross anatomy, differentiation and development of neurons, neurochemical pathways, and responses to stress or other environmental cues. [1]
  - Additionally, many central nervous system-related disorders show sex differences in their incidence and/or nature. These diseases include, but are not limited to, Alzheimer's disease (AD), PTSD and other anxiety disorders, schizophrenia, stroke, multiple sclerosis, autism, addiction, fibromyalgia, attention deficit disorder, irritable bowel syndrome, Tourette's syndrome and eating disorders [2-4]

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- **Specific Neurological and Sensory Differences**
  - **Gross neurological anatomy**: The hippocampus is larger in women than in men, while the amygdala is significantly larger in men than in women when adjusted for total brain size; these areas are important for memory and emotion processing, respectively.[5] Ratios of grey to white matter also differ significantly between the sexes in diverse regions of the human cortex[6]
  - **Effects of Stress:** 1) In both rats and monkeys, chronic stress causes damage to the hippocampus in males, but does so far less, if at all, in female. The susceptibility of hippocampal cells to chronic stress has been suggested to have a role in two debilitating disorders — post-traumatic stress disorder (PTSD) and clinical depression[7]. Both disorders disproportionately affect women. 2) A brief exposure to a stressful learning situation increases the density of dendritic spines in male rats, but decreases spine density in female rats. Similarly opposing effects of stress are found in Pavlovian conditioning performance in males and females; stress enhances performance in males, but impairs it in females. [8]

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- **Specific Neurological and Sensory Differences**
  - **Memory Processing:** Studies consistently indicate a preferential involvement of the left amygdala in memory for emotional material (generally visual images) in women, but a preferential involvement of the right amygdala in memory for the same material in men[9-11]This laterality, 'women left, men right', mirrors what is seen at rest, indicating that the response to emotional stimulation stems from a baseline that is already differentially 'tilted' between the sexes at baseline.

  - **Neuronal Cell Death:** Neuronal cell death pathways differ between males and females: Female neurons more often die through classical, caspase-dependent apoptosis, while male cells die more often use caspase-independent, apoptosis initiating factor (AIF)-mediated cell death. This could potentially be important in treatment development for neurodegenerative disorders or injures following stroke.[12]

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- **Specific Neurological and Sensory Differences**
  - **Otoacoustic emissions:** differ reliably between the sexes, being both louder and more frequent in female than male adults, children and infants[13]
  - **Opioid receptor binding**: There are significantly different levels of opioid receptor binding in several brain regions in men versus women, including the amygdala and thalamus, which can lead to sex differences in response to pain analgesics.[14]
  - **Vestibular System Gross Anatomy**: Women have a lower total number of myelinated axons in the vestibular nerve than men, which may help explain the female bias of many vestibular disorders, such as vertigo. [15] In males, the otoliths, utricle, saccule and superior semi-circular canals are significantly larger than in females.[16]
  - **Vestibular Nucleus and Hormones:** There is some evidence that the estrus/menstrual cycle may influence the medial vestibular nucleus synaptic transmission and plasticity, with the levels of circulating 17β Estradiol being the main factor in these differences. [17]

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- **Specific Neurological Differences**
  - **Spatial Task Performance**: Sex differences exist in circular vection (orientation within a spinning environment), field dependence (perceiving orientation based only on visual cues), perception of veridical vertical with body tilt (correctly identifying the true vertical to the ground when the body is tilted), and perception of the morphological horizon.[18-19] These differences have been partially assigned to biological differences in the vestibular system, including the difference in otolith size, but there is some evidence that cognitive training regarding attention to cues can decrease these sex differences.[20]

  - **Vision Processing:** Males have significantly greater sensitivity for fine detail and for rapidly moving stimuli, while females exhibit better color discrimination.[21-22]

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- **Specific Neurological and Sensory Differences**

  - **Somatosensation**: Compared with the other senses there is little information on the sex differences associated with tactile sensation. On average, women are more sensitive (over the entire body) to touch, and pressure. Women appear to be more sensitive to temperature differences while men score better than women on a verity of haptic tasks (object or position recognition involving touch and proprioception).

  - **Pain:** We believe that reporting of pain and pain sensation is rife with any number of bias (social, gender, ethnicity, culture, tec.), but on average women do appear to show a greater sensitivity to pain than men (probably due to biological mechanisms, as well as psychological and psychosocial factors).

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- **Specific Neurological and Sensory Differences**
  - **Vestibular**: Although not entirely proper, it is convenient to lump vestibular responses between men and women in to those categories of responses that require vestibular input:
    - Postural Responses
    - Locomotion
    - Vision
    - Motion Sickness
    - Spatial Orientation
    - Changes in Postural Muscles

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- **Specific Neurological and Sensory Differences**
  - **Motion Sickness – Laboratory Testing:**
    - Common belief is that women are more susceptible to motion sickness. Again, both social and research design have, we believe contributed to this bias. Research in the Johnson Space Center Neurosciences Laboratory has subjected approximately 100 subjects to a variety of motion sickness tests (CSSI, sudden stop, off vertical rotation etc.) There was no difference in susceptibility between men and women, nor did testing during any phase of the menstrual cycle have an effect.

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- **Specific Neurological and Sensory Differences**
  - **Motion Sickness – Space Flight:**

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- Questions- are these differences:
  - Evident in- or postflight?
  - Modified/magnified by space flight?
  - Evident in existing countermeasures (primarily drugs and preadaptation?
  - A benefit?
  - A functional risk?
- Answers:
  - We do not know.
  - Fly more women.
  - Define appropriate risk scenario to enhance funding opportunities.