

# 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

Helen Cohen, Professor, Department of Otolaryngology, Baylor College of Medicine

# Neuroscience Working Group Members and Affiliations



- **Co-Chairs:**
  - **Millard F. Reschke, PhD**, Chief of Neuroscience, NASA Johnson Space Center
  - **Helen S. Cohen, EdD**, Professor, Baylor College of Medicine
- **Jody M. Cerisano, BS**, Wyle Science, Technology & Engineering Group
- **Janine Clayton, PhD**, National Institutes of Health
- **Ronita Cromwell, PhD**, USRA, NASA Johnson Space Center
- **Richard Danielson, PhD**, USRA, NASA, Baylor College of Medicine
- **Emma Hwang, PhD**, Wyle Science, Technology & Engineering Group
- **Candace Tingen, PhD**, National Institutes of Health
- **Ex-Officio members:**
  - **John R. Allen, PhD**, NASA Headquarters
  - **David L. Tomko, PhD**, NASA Headquarters

# 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 Russian Space Agency have had little interest in exploring sensory differences between men and women during space flight.
  - Women do differ from men in most sensory systems, neural anatomy and functional responses operationally on Earth.
- **General differences known about sexual dimorphism in the brain**
  - Known sex differences include in gross anatomy, differentiation and development of neurons, neurochemical pathways, and responses to stress or other environmental cues.<sup>1</sup>
  - Some central nervous system-related disorders that show sex differences: Alzheimer's disease, addiction, attention deficit disorder, autism, fibromyalgia, irritable bowel syndrome, multiple sclerosis, post traumatic stress disorder (PTSD), other anxiety disorders, schizophrenia, stroke, Tourette's syndrome and eating disorders.<sup>2-4</sup>

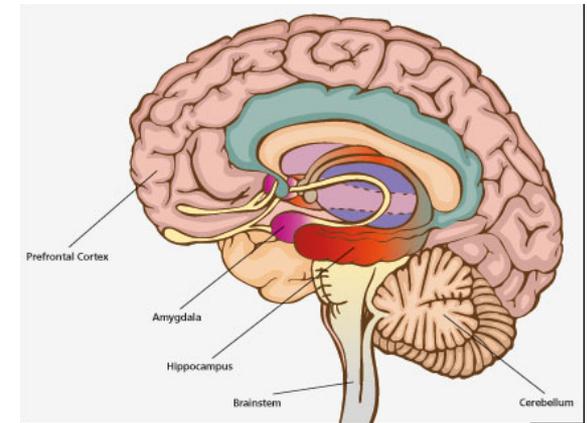
# Neuroscience in Space: Are there Neurosensory Differences Based on Sex and Gender



- **Specific Neurological and Sensory Differences**

- **Gross Neurological Anatomy:**

- The hippocampus is larger in women.
- The amygdala is larger in men. These areas are important for memory and emotion processing.<sup>5</sup>
- Ratios of grey to white matter in the cortex also differ between men and women.<sup>6</sup>



(uvamagazine.org)

- **Effects of Stress:**

- In rats and monkeys, chronic stress causes more damage to the hippocampus in males than females. This susceptibility to chronic stress may have a role in PTSD and clinical depression.<sup>7</sup>
- Brief exposures to stressful learning situations increase the density of dendritic spines in male rats, but decreases spine density in female rats.
- In Pavlovian conditioning stress enhances performance in males rodents, but impairs it in female rodents.<sup>8</sup> The differential effects of stress in humans is not yet known.

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- **Specific Neurological and Sensory Differences**
  - **Memory Processing:**
    - Preferential involvement of the left amygdala in memory for emotional material (generally visual images) in women, but
    - preferential involvement of the right amygdala in memory for the same material in men.<sup>9-11</sup> This ‘women left, men right’ laterality 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.
  - **Neuronal Cell Death:**
    - Female neurons more often die through classical, caspase-dependent apoptosis;
    - male neurons die more often through caspase-independent, apoptosis initiating factor-mediated cell death. This difference could potentially be important in treatment of neurodegenerative disorders and stroke.<sup>12</sup>

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- **Specific Neurological and Sensory Differences**
  - **Opioid Receptor Binding:** Different levels of opioid receptor binding in some brain regions, including the amygdala and thalamus. Possible mechanism for sex differences in response to pain analgesics.<sup>14</sup>
  - **Somatosensation:** Minimal information on the sex differences. Generally, women are more sensitive (over the entire body) to touch, and pressure. Women are more sensitive to temperature differences; men score better on tasks of object or position recognition.
  - **Pain:** Reporting of pain and pain sensation is rife with bias (social, gender, ethnicity, culture, etc.), but generally women seem to have greater sensitivity to pain.<sup>23</sup>

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- **Specific Neurological and Sensory Differences**
  - **Spatial Task Performance:** Well-known sex differences in many kinds of spatial orientation.<sup>18-19</sup> Differences may be biological as well as environmental (e.g., toys given to boys versus girls) but training for attention to cues can decrease these sex differences.<sup>20</sup>
  - **Spatial Navigation:** Sex differences in spatial navigation tests may be due to differences in the way the tasks are approached.
    - Women employ a strategy based on memory
    - Males use spatial relations
    - Many visual and spatial tests may be biased in their design, allowing the male approach to score as better performing.<sup>28</sup>

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- **Specific Neurological and Sensory Differences**

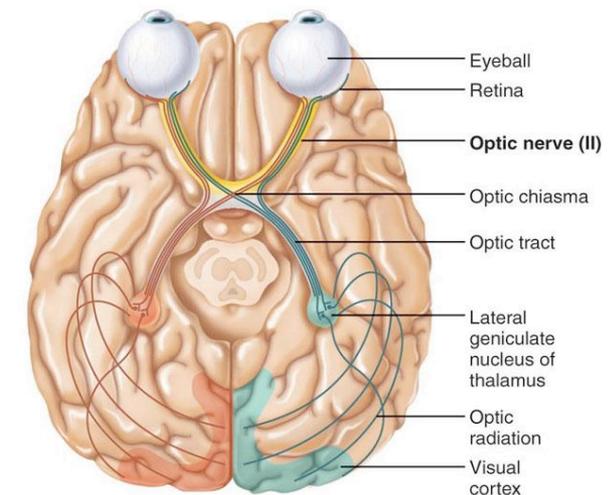
- **Vision Processing:**

- Males have significantly greater sensitivity for fine detail and rapidly moving stimuli.
- Females have better color discrimination (e.g. more males have color blindness).<sup>21-22</sup>

- **Visual Performance:**

- Women perform better on visual tracking tasks during louder acoustic noise; men's performance is not enhanced by sound. The disparity might be linked to thalamic control of sensory gating.<sup>29</sup>
- Many differences in visual task performance are likely linked to biological factors rather than social conditioning; some can be seen in infants as young as 4 months old.<sup>30</sup>

## The Optic Nerves -II



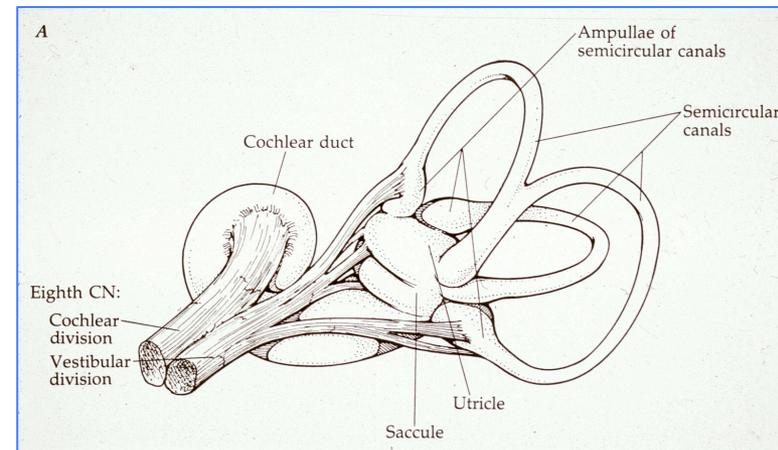
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# Neuroscience in Space: Are there Neurosensory Differences Based on Sex and Gender



- **Specific Neurological and Sensory Differences**

- **Vestibular System:** The sensory system with receptors in the inner ear that detect head movement. Central pathways generate the vestibulo-ocular reflex for stable gaze, and contribute to balance and spatial orientation.
- **Vestibular System Gross Anatomy:** Women have fewer myelinated axons in the vestibular nerve than men, which may help explain the female bias of many vestibular disorders, such as vertigo.<sup>15</sup> In males, the otoliths, utricle, saccule and superior semi-circular canals are significantly larger than in females.<sup>16</sup>
- **Vestibular Nucleus and Hormones:** The estrus/menstrual cycle may influence the medial vestibular nucleus synaptic transmission and plasticity, with the levels of circulating  $17\beta$  Estradiol being the main factor in these differences.<sup>17</sup>



Martin JH. Neuroanatomy text and atlas. Elsevier. NY. 1989.

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



- **Specific Neurological and Sensory Differences**

- **Vestibular:** Vestibular responses include:

- Postural responses
    - Locomotion
    - Vision
    - Motion sickness
    - Spatial orientation
    - Changes in postural muscles



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- Computerized posture testing, a required medical test, suggests no post-flight differences between male and female crewmembers when adjusted for height.

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



- **Specific Neurological and Sensory Differences**
  - **Motion Sickness – Laboratory Testing:**
    - Research in the Johnson Space Center Neurosciences Laboratory has subjected approximately 100 subjects to a variety of motion sickness tests (Coriolis Sickness Susceptibility [CSSI], sudden stop, off-vertical rotation, parabolic flight etc.). Men and women did not differ in susceptibility, nor did testing during any phase of the menstrual cycle for women have an effect. Responses to particular tests were variable. For example, some individuals became nauseous during a CSSI test but not during the off-vertical axis rotation test.

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- **Specific Neurological and Sensory Differences**

- **Motion Sickness – Space Flight:**

- Incidence of Motion Sickness obtained from post flight debriefs of long duration ISS (32 Male; 10 Female) and short duration Shuttle (564 Male; 100 Female) astronauts show:
      - On average, female crewmembers who flew on both the ISS and Shuttle reported both Space Motion Sickness (SMS) and Entry Motion Sickness (EMS) symptoms more frequently than male crewmembers.
      - Exception: male crewmembers on the ISS reported a higher incidence of EMS than females after returning from a long duration space flight.

ISS	Males (32)	Females (10)
% with SMS	38%	50%
% with EMS	47%	40%

Shuttle	Males (564)	Females (100)
% with SMS	64%	75%
% with EMS	32% (3% no data)	50% (3% no data)

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



- **Specific Neurological and Sensory Differences**

- **Postural Ataxia – Space Flight:**

- On average, female crewmembers that flew on both the ISS and Shuttle reported post flight vestibular instability symptoms (**feeling abnormally heavy, clumsiness, vertigo, persisting sensation after-effects, having difficulty walking a straight line**) more frequently than male crewmembers.

ISS	Males (32)	Females (10)
% Postflt Ataxia	59% (16% no data)	50% (10% no data)

Shuttle	Males (564)	Females (100)
% Postflt Ataxia	90% (6% no data)	94% (5% no data)

- Total subject numbers include reflights.
      - All responses were subjective and reported to a Flight Surgeon as part of a standard post flight medical debrief (debrief did not always specify symptoms, only if one or more were present).
      - Data collection not well controlled.
      - Note many fewer female crew members

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



- **Specific Neurological and Sensory Differences**

- **Hearing / Auditory Function:**

- Epidemiological studies show: <sup>24-27</sup>

- Hearing sensitivity declines more than twice as fast in men as in women at most ages and frequencies.
- Hearing levels and longitudinal patterns of change are highly variable, even in this highly selected group (due most likely to occupational noise exposure).
- Greater high frequency hearing loss is seen in the left ear (when compared to the right ear).

- **Otoacoustic Emissions:**

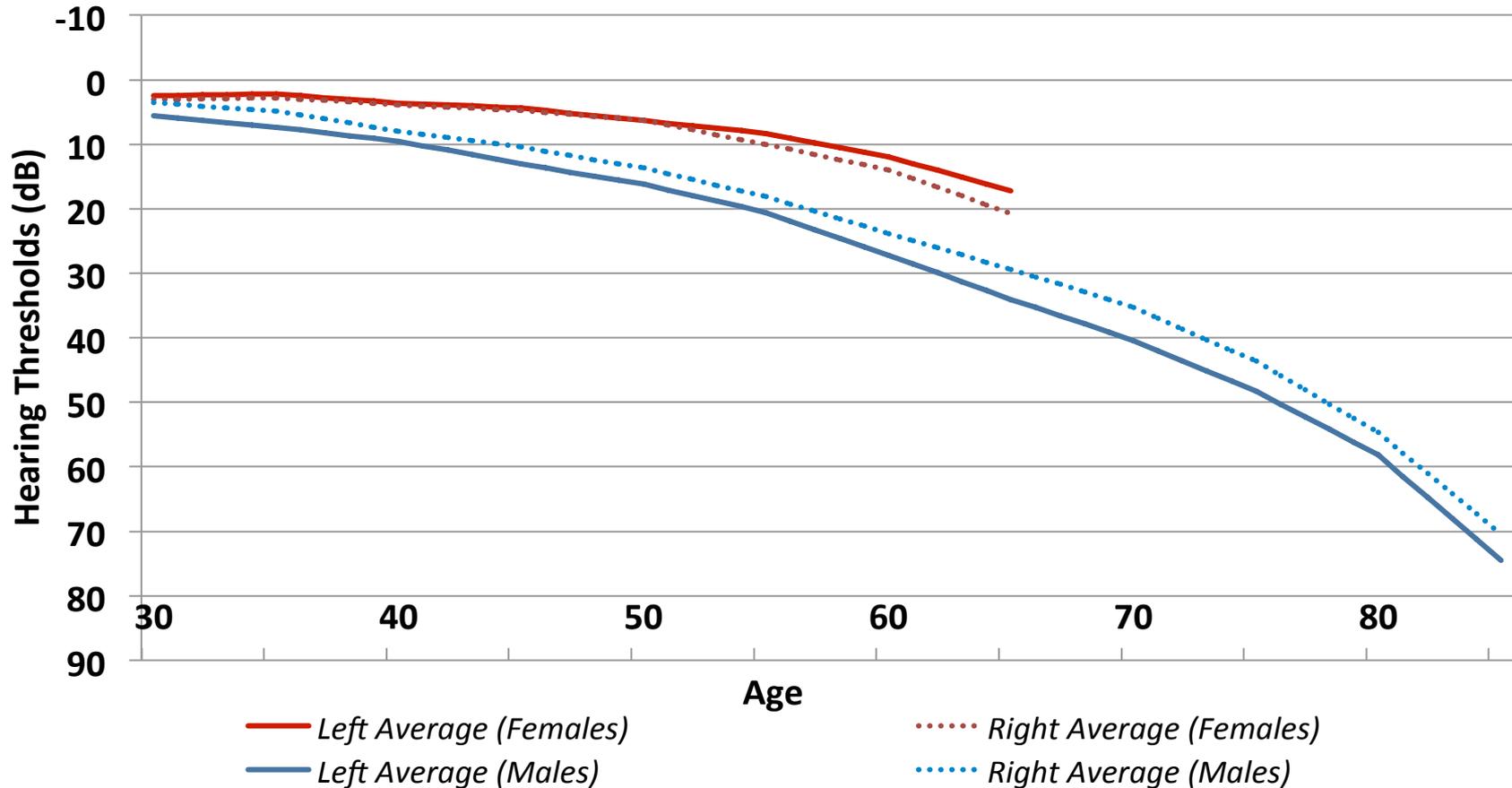
- Test of sounds emitted by the ear. Differ between the sexes, louder and more frequent in females than males.<sup>13</sup>

- Post flight, however, no significant differences in rate of difference are found between male and female astronauts on any measures.

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



## Hearing Trends, Male vs. Female Astronauts, by Age and Ear, Averaging Audiometric Thresholds at 2k, 3k, 4k Hz



\*Graphics prepared by Richard Danielson, Ph.D., USRA / Baylor College of Medicine from NASA's Life-time Surveillance of Astronaut Health (LSAH) population.

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



Questions- Are the neurosensory differences:

- Evident in- or post flight?
- Modified/magnified by space flight?
- Evident in existing countermeasures (primarily drugs and preadaptation)?
- A benefit?
- A functional risk?

Answers:

- We do not know.
- To find the answers, fly more women.
- Address the gender discrepancy through NASA risk management to enhance funding opportunities. This is necessary for interplanetary travel with women as crew members.

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