

# WOMEN'S HEALTH *In Focus* AT NIH

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## Sex Differences in Neurological Health Conditions



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## Director's Corner

Janine Austin Clayton, M.D., FARVO  
Director, NIH Office of Research on Women's Health  
NIH Associate Director for Research on Women's Health

On International Women's Day, March 8, 2023, the Economist Impact organization released a white paper titled [Sex, Gender and the Brain: Towards an Inclusive Research Agenda](#). This report, commissioned by the [Women's Brain Project](#), explores how females have often been excluded from brain disease studies to the detriment of the research and the health of women. The white paper makes a strong case for increased investment in sex- and gender-inclusive brain research—both to improve public health and to mitigate the economic burdens, lost productivity, and social costs associated with brain diseases, such as multiple sclerosis, stroke, Parkinson's disease, Alzheimer's disease, and migraine.

In this issue of In Focus, we explore these and other issues relevant to neuroscientific research. Our feature story discusses sex differences in neurological conditions involving glia, historically understudied cells in the central and peripheral nervous systems. An editorial considers the ways pregnancy, delivery, lactation, and caregiving alter the maternal brain. Additional articles examine the negligible effects of estrous on the behavior of experimental animals, studies on migraine, and career-oriented news and findings from the field of neuroscience.

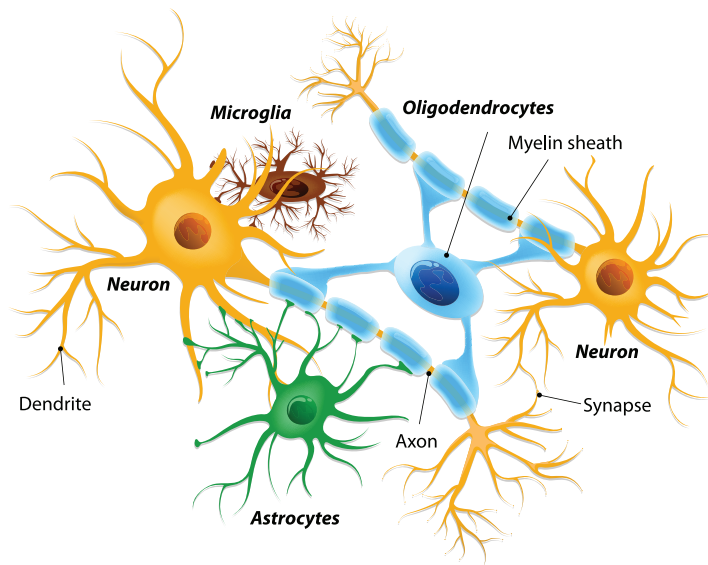
This issue also announces the establishment of a new division of ORWH, the Office of Autoimmune Disease Research (OADR-ORWH). Currently, about 8% of the U.S. population has an autoimmune condition, and the majority of these individuals are women. Last year, Congress allocated funds to ORWH to establish the new office, which will complement the efforts of NIH institutes, centers, and offices and of other organizations in studying autoimmune diseases, addressing gaps in the current understanding of these conditions, and improving treatment. Please see the article on p.14 as well as the next issue of In Focus for more information on OADR-ORWH.

If you find this issue of In Focus interesting and informative, please share it with your colleagues. You can subscribe by clicking the link on the front or back cover.

Janine Austin Clayton, M.D., FARVO  
Director, NIH Office of Research on Women's Health  
NIH Associate Director for Research on Women's Health

# Sex Differences in Neurological Health Conditions with Glial Cell Involvement

Historically, neuroscience has focused on—as the name suggests—neurons, the brain cells that send and receive electrical signals and constitute about 15% of the brain's volume. Involved in multiple aspects of human development, health, and disease, neurons function as a network of electrical circuits (Fig. 1). A neuron releases a neurotransmitter (e.g., acetylcholine or norepinephrine) from a nerve fiber, called an axon, into the synapse, the gap between the signaling neuron and a receiving—or postsynaptic—neuron. The dendrite, a fiber on the postsynaptic neuron, detects the neurotransmitter, decreasing the voltage in the postsynaptic neuron. When the voltage lowers sufficiently, the receiving neuron releases neurotransmitters from its own axon to the next neuron in the circuit. Many observers have compared the brain to a computer consisting of neuronal electrical circuits, with individual neurons serving as microprocessors. This analogy, however useful, overlooks the involvement of glial cells, or glia, the other 85% of the brain, what neuroscientist [R. Douglas Fields, Ph.D.](#), of the *Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)* calls “the other brain.”<sup>1</sup>



**Figure 1.** Diagram of neurons and glial cells.

Many early neuroscientists thought that neuroglia—literally “nerve glue”—were little more than support structures, with possible roles as insulators, housekeeping cells, or nutritional support for the neurons. Scientists now understand that glia communicate with one another chemically through calcium signals and other biochemical means, rather than electrically like neurons. Recent research has explored the importance of glial cells in brain development, learning and memory, and regulating neuronal activity. Many studies have also identified glial involvement in various diseases and health conditions.

Scientists have identified four major types of glia: astrocytes, oligodendrocytes, and microglia in the central nervous system (Fig. 1) and Schwann cells in peripheral nerves. Astrocytes provide structural and energy support for neurons, clear neurotransmitters from synapses, reprocess neurotransmitters to maintain the

## STAFF

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balance of ions in the synaptic gap, control synapses by adjusting the strength of neuronal connections in learning processes, “eavesdrop” on neuronal communications, send information to other astrocytes via calcium ions, form scars after brain injuries, and serve an immune function by detecting bacteria and viruses in the brain. Oligodendrocytes have long arms that form insulating sheaths of myelin around axons in the brain and spinal cord. Oligodendrocytes “listen” to axonal activity and interact closely with neurons. Microglia serve as the brain’s primary immune system, communicate with other microglia biochemically, and may function to “unplug” some neuronal connections. Schwann cells attach to axons in the peripheral nerves and form insulating sheaths of myelin around them. Schwann cells also listen to the information passed between peripheral nerve neurons—much as oligodendrocytes do in the central nervous system. Other types of Schwann cells have different functions, such as nonmyelinating Schwann cells, which protect fragile axons, and perisynaptic Schwann cells, which control the flow of information from nerves to muscles. Schwann cells also change structure and undergo cell division in response to injury. Other types of glial cells—including radial glia, NG2 glia, and others—have been identified elsewhere and show potential as therapeutic targets.

In addition to the roles mentioned above, glial cells build the fetal brain, direct the growth of the developing nervous system, repair the nervous system after many types of injury, provide energy to the neurons, supply substrates for neurotransmitters, organize neurons and synapses into functional groups, generate new neurons, communicate with the vascular and immune systems, control the speed of information through neuronal lines of communication, and perform a host of other functions.

## Economist Impact Reports on Sex, Gender, and the Brain

A recent report titled [Sex, Gender and the Brain: Towards an Inclusive Research Agenda](#), commissioned by the [Women’s Brain Project](#) and written by the [Economist Impact](#) organization, explores sex differences in brain health and disease and how, historically, brain disease research and treatment have relied on male-dominated data. Economist Impact researchers interviewed eight health and policy experts in compiling the report, including ORWH Director Janine A. Clayton, M.D., FARVO. *Sex, Gender and the Brain* explores not only the poorer brain health outcomes for women resulting from these historical trends but their wider economic consequences as well. The report makes a strong case for increasing investment in sex- and gender-inclusive brain research, as the burden of brain disease is not solely a public health issue but an economic one, involving caregiving costs, difficulty maintaining employment and income for patients and family caregivers, poor educational attainment, and other pecuniary factors.

*Sex, Gender and the Brain* features thorough discussions of how sex and gender differences have been identified in multiple sclerosis, stroke, Parkinson’s disease, Alzheimer’s disease, and migraine; how most brain diseases are more prevalent in women than men; how sex and gender differences may affect disease outcomes; how brain diseases have become increasingly prevalent in our aging global population; and how we can address the sex and gender imbalances in brain research.

Despite these many important glial functions, “research on the other brain is one hundred years behind research on the neuronal brain,” according to Dr. Fields.<sup>1</sup> Studying glia proved challenging for early neuroscientists, who developed methods of staining and microscopically visualizing neurons but found glial cells more difficult to study.

Contemporary neuroscientists have come to understand that just as glia participate in brain development, learning, memory, and other healthy brain functions, so too these cells participate in many neurological diseases and conditions. Interestingly, researchers have also identified sex differences in the prevalence, severity, disease progression, and outcomes of many of the health conditions with glial involvement. Within the past 10 years, innovative research has begun to elucidate some of the connections between glia and sex differences in these neurological conditions. This article

will describe observed sex differences in these conditions and explore how glial cells are or may be involved. (For more information on the agenda for sex differences in brain research, see *Economist Impact Reports on Sex, Gender, and the Brain*.)

## Sex-Specific Glial Mechanisms in Chronic Pain

Although both sexes can develop long-lasting pain conditions and experience pain hypersensitization after injury or surgery, data demonstrate that women are more susceptible to chronic pain. Migraines, debilitating vascular headaches, affect women three times more often than men.<sup>2</sup> Fibromyalgia, a condition involving widespread musculoskeletal pain and other symptoms, may result from dysfunction in the way the brain and spinal cord process both painful and nonpainful signals.<sup>3</sup> As many as 90% of diagnoses of fibromyalgia are in women, who tend

to have more severe and longer-lasting symptoms than men.<sup>4</sup> Women are also more likely to develop autoimmune conditions such as rheumatoid arthritis, which can cause debilitating pain. Women tend to experience an earlier age of onset of rheumatoid arthritis and have greater symptom severity than men.<sup>5</sup>

Pain, of course, has a protective function. It helps us avoid injury by prompting us, often involuntarily, to withdraw from potentially damaging stimuli—by dropping a hot pan, for example. However, neuropathic pain, which is often chronic and can occur after damage to the nervous system, is a disease condition that has no protective role. Although glia play no part in transmitting normal pain signals, recent research has implicated glial cells in chronic neuropathic pain conditions—for example, those emerging after injury or surgery.



**Jeffrey Mogil, Ph.D.**

[Jeffrey Mogil, Ph.D.](#), Professor and E. P. Taylor Chair in Pain Studies at [McGill University](#), studies the neurological mechanisms underlying pain, its perception, and its inhibition. “In chronic pain research, there are two separate questions that need to be answered about sex differences: One, why do women have more chronic pain, and two, what are the sex differences in the mechanisms underlying pain conditions in the first place?” says Dr. Mogil. “There are many hypotheses and answers as to why women have more pain, and they involve biology, gender role expectations, pain experiences like childbirth, and other factors,” he explains. Much of Dr. Mogil’s research has focused on the second question and has explored sex differences

in neurological and immunological pain mechanisms. He says, “There’s an increasing amount of evidence that the neurocircuitry of pain is radically different in males and females, involving completely different genes, pathways, and molecules. It’s much different than anyone would have guessed 20 years ago—even 10 years ago.”

A seminal study<sup>6</sup> by Dr. Mogil’s lab identified sex-specific mechanisms in a mouse model of chronic pain hypersensitivity. “In male mice, microglial signaling is required for hypersensitization,” says Dr. Mogil. “If you get rid of the microglia with a toxin or block them at one of several points along the circuit pathway, you interrupt chronic pain—but only in male mice.” Although female mice have the same microglia, the same experimental procedures have no effect in the female animals. “Interestingly enough, the pain sensitization still occurs in female mice, but the microglia have nothing to do with it,” he says. “Female sensitization involves different cells. We have hypothesized that T cells, rather than microglia, contribute to sensitization in female mice.”

Additional studies by Dr. Mogil’s lab and other research teams also suggest that glial-neuronal circuits operate differently in males and females. For instance, a more recent study<sup>7</sup> by the Mogil lab identified another sex-specific glial-neuronal pain circuit. In an animal model of long-lasting neuropathic pain, Dr. Mogil and colleagues showed that starting 4 months after a nerve injury, cellular senescence (i.e., a cessation of cellular division) occurs in microglia in the spinal cord, resulting in chronic pain. He says, “The senescence results from a telomere length reduction” (i.e., a shortening of the repetitive DNA sequences at the end of a chromosome). “Presumably, the injury causes the change in telomere length, which causes cellular senescence in the microglia, which in turn maintains the pain,” Dr. Mogil explains. “If you block this

senescence mechanism, you block the pain completely—but only in male mice.” The study showed that male mice with chronic pain also had shorter lifespans. Female mice with the same injury did not experience the telomere length reduction, cell senescence, long-lasting chronic pain, or increased mortality. “It’s an interesting story because when it comes to pain, in most ways, females have it worse,” Dr. Mogil adds.

These types of studies impart many lessons. First, the development of glia-targeting drugs holds great potential for the treatment of neuropathic pain, perhaps with sex-specific medications. Current drug therapies often prove ineffective in treating chronic pain conditions, as they do not address the roles of glial cells in pain processes.<sup>1</sup> Glia-targeting alternatives to opioid medications might alleviate neuropathic pain while avoiding the cognitive effects and addictive potential of opioid pain medications. For instance, medications targeting those astrocytes and microglia that release neuroexcitatory substances potentially contributing to migraine hold great potential for future treatment.<sup>1,8</sup> Second, these studies demonstrate the importance of considering sex as a biological variable (SABV) in biomedical research as articulated in [NIH’s SABV policy](#). Dr. Mogil’s article on the sex differences in glial-neuronal circuitry in pain hypersensitization states, “This sexual dimorphism suggests that male mice cannot be used as proxies for females in pain research.”<sup>6</sup> Clearly, robust pain research and the development of future pain treatments rely on experimental designs, data analyses, drug development processes, and clinical trials that consider SABV.

## Glia in Multiple Sclerosis

Multiple sclerosis (MS), the most common disabling neurological disease in young adults,<sup>9</sup> is an autoimmune disease that affects the oligodendrocytes. In patients with

MS, the immune system attacks the oligodendrocytes' myelin sheaths, which insulate axons, in the central nervous system. The lack of insulation leads to leakages and blockages in the flow of electrical impulses, which in turn results in vision problems, muscle weakness, numbness, and functional impairment at early stages and potentially more severe symptoms such as mood and cognitive effects or paralysis at later stages.<sup>9</sup> The onset of MS typically occurs between 20 and 40 years of age, and like many autoimmune diseases, MS has a strong female predominance (i.e., 3 in 4 individuals with MS are women).<sup>10</sup> Similar but less common disorders, such as neuromyelitis optica (also known as Devic disease), acute disseminated encephalomyelitis, and transverse myelitis, can also cause or result from damage to these myelin sheaths.

Although there is no cure for MS, several treatments—including corticosteroids, plasmapheresis, and oral, injected, or infused medications—can delay disease progression and prolong periods between relapses.<sup>9</sup> Developing new MS drugs that target glial cells represents a promising avenue of research.<sup>1</sup> The National Institute of Neurological Disorders and Stroke ([NINDS](#)) and ORWH's newly established Office of Autoimmune Disease Research (OADR-ORWH; see p. 14 and this [webpage](#) for more information) support research on MS.

## Glia in Neurodegenerative Diseases

Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease all involve the death of neurons, but glial dysfunction also plays a role in these and other neurodegenerative diseases. Neurons rely on the function of healthy astrocytes for electrical power, for clearing neurotransmitters from the synapse, and for responding to distress by releasing growth factors and stimulating the birth of new neurons.<sup>1</sup> Dysfunction in these

glial processes can lead to the neuronal death observed in neurodegenerative diseases. Interestingly, researchers have identified sex and age differences in the prevalence, onset, and symptom severity of many neurodegenerative diseases.

*Alzheimer's Disease.* Of the 6.2 million Americans age 65 or older with Alzheimer's disease, almost two-thirds are women.<sup>11</sup> Although advanced age is the greatest risk factor, women's longevity does not entirely account for the female predominance of the disease.<sup>11</sup> Researchers have hypothesized that we may find an explanation for this sex difference in the senile plaques associated with Alzheimer's disease.<sup>11,12</sup> In patients with this condition, neurons suffer damage in the cerebral cortex, hippocampus, and amygdala, regions associated with thinking, memory, and emotion, respectively. Senile plaques—accumulations of amyloid proteins—surround and “choke” the neurons in these brain areas. These amyloid deposits may serve to entrap viruses as part of the brain's immune response to infection.<sup>12</sup> Indeed, researchers have found pneumonia bacteria in the brains of many patients with Alzheimer's disease.<sup>1</sup> Once amyloid plaques form, microglia, the soldiers of the brain's immune system, and astrocytes accumulate around these plaques to attempt to clear them.<sup>1</sup> However, with the inflammation associated with the condition, glial cells have a diminished capacity to clear amyloid and thus resort to releasing neurotoxic factors to kill the damaged neurons.<sup>1</sup> According to this hypothesis, women, who mount stronger immune responses to infection, may form more amyloid plaques and thus have a greater risk for Alzheimer's disease than men.<sup>11</sup>

*ALS.* Also known as Lou Gehrig's disease, ALS is a progressive neurological disease affecting motor neuron cells in the brain and spinal cord that affect muscle movement and thus walking, breathing, talking, chewing, and other bodily

movements. ALS typically manifests in people between 55 and 75 years of age, and men under the age of 65 are slightly more likely than similarly aged women to develop the disease. Although ALS can affect people of all races and ethnicities, non-Hispanic White people are more susceptible. Some evidence suggests that military veterans are also more likely to develop ALS, possibly because of environmental exposures. Mutations in over a dozen genes have been linked to familial ALS, but only 5–10% of patients with ALS have a family history of the heritable form of the disease. There is no cure for this fatal disease.<sup>13</sup> Although research has firmly established that ALS stems from the death of motor neurons, researchers have shown that astrocytes with a defective *SOD1* gene release an as-yet-unidentified substance that selectively kills motor neurons.<sup>1</sup>

*Parkinson's Disease.* Data on Parkinson's disease point to significant sex differences, with men at twice the risk of developing the disease as women but with women experiencing more rapid disease progression and a higher mortality rate.<sup>14</sup> Parkinson's disease results from the death of neurons in a region of the brain called the substantia nigra. However, as in other neurodegenerative diseases, astrocytes may be involved in the death of those neurons. Evidence suggests that astrocytes, prompted by exposure to damaging chemicals (perhaps from environmental exposures), produce neurotoxins that kill the neurons in the substantia nigra, resulting in loss of fine muscle control. Administration of L-dopa, the current treatment standard, mitigates the tremors and motor control problems associated with the disease by substituting for endogenous dopamine in the brain. Novel interventions targeting the astrocytes could leverage astrocytes' natural neuroprotective function or prevent the production of neurotoxins.<sup>1</sup>

*Huntington's Disease.* This rare heritable disease causes brain cells to degenerate, resulting in functional and cognitive

problems as well as comorbid psychiatric disorders such as depression. Medications can manage some of the symptoms but do not prevent the associated physical and mental decline. A longitudinal study of over 8,000 patients with Huntington's disease found that women have more severe motor, cognitive, and depressive symptoms than men.<sup>15</sup> Recent research has revealed dysfunctions in both astrocytes and oligodendrocytes in Huntington's disease.<sup>16</sup> These glial cells fail to perform their normal functions of maintaining the health of neurons and regulating the chemical signals between them, resulting in poor communication between neurons and eventual cell death.

## Glia in Depression and Schizophrenia

Significant sex differences exist in the prevalence and severity of depression and schizophrenia. Women are almost twice as likely as men to receive a depression diagnosis,<sup>17</sup> and men with schizophrenia tend to have an earlier age of onset, more severe symptoms, poorer social function, and a greater likelihood of co-occurring substance use than women.<sup>18</sup>

Research has implicated poorly functioning glial cells in some of the biological mechanisms underlying these diseases. Patients with chronic depression, schizophrenia, and other mental illnesses lose brain mass—primarily oligodendrocytes and astrocytes.<sup>1</sup> Those with bipolar disorder have fewer glia in the brain regions responsible for mood than individuals who do not have the disorder.<sup>19</sup> Other studies have identified abnormal genes involved in regulating oligodendrocytes and forming myelin, as well as abnormalities in glial progenitor cells, in patients with these illnesses.<sup>20,21</sup>

Depression, schizophrenia, and other mental illnesses stem, at least in part, from problems with synaptic transmission. Often, such problems result from the failure of glial cells to clear

neurotransmitters from the synapse or to maintain an appropriate balance of neurotransmitters between neurons.<sup>1</sup> Imbalances of neurotransmitters such as serotonin, glutamate, and dopamine are characteristic of these psychiatric diseases. Many common medications for these illnesses—such as Prozac, Lexapro, and Zoloft—restore the balance of neurotransmitters in the synaptic cleft and thereby help to normalize synaptic function.<sup>1</sup>

While these drugs can be highly effective in mitigating symptoms for many patients, the development of new medicines and treatments targeting the glial cells themselves, rather than the neurotransmitters they regulate, holds promise for expanding the pharmaceutical options for treating psychiatric disorders. Dr. Fields speculates, "Almost certainly some of the drugs used now to treat mental disorders—including ADHD [attention-deficit/hyperactivity disorder], mania, depression, anxiety, and schizophrenia—act in part through their effects on glia."<sup>1</sup> Future research, informed by the sex differences observed with these diseases, may expand and strengthen the psychopharmaceutical arsenal.

## Glial Cancers: Gliomas and Glioblastomas

Researchers have reported and continue to investigate sex differences in many brain cancers. Studies have demonstrated that men are more likely than women to develop low- and high-grade gliomas, cancers of the glial cells. Glioblastomas are aggressive, high-grade brain cancers, representing 51% of brain cancers diagnosed in adults.<sup>1,22</sup> Evidence suggests that women may respond better than men to standard glioblastoma therapies,<sup>22,23</sup> but a body of innovative research over the past few years suggests that sex-specific therapies for low-grade gliomas and glioblastomas could improve outcomes for both sexes.



**Sadhana Jackson, M.D.**

Neuro-oncologist [Sadhana Jackson, M.D.](#), of NINDS and NCI explains that there are many biological mechanisms behind the sex differences identified in these brain cancers. "One recent glioblastoma study<sup>23</sup> detailed sex-based molecular differences related to the cell cycle and integrin signaling pathways," Dr. Jackson says. "Another study<sup>24</sup> on the glioblastoma microenvironment identified sex differences in the function of myeloid-derived suppressor cells, which are immune cells that help to identify and kill tumor cells." Additionally, future therapies for brain cancer might also leverage microglia's natural capacity to home in on brain tumors to deliver genes that can kill tumors or chemicals that can combat them.<sup>1</sup> According to Dr. Jackson, such findings suggest the need for more sex-specific treatment options. "Different chemotherapy or tumor microenvironment changes could help target diseased glial cells, which have unique sex-based molecular profiles, which may ultimately aid in halting overall disease progression," she says. "My own research focuses on the communication between malignant glioma cells in the restrictive environment of the blood-brain barrier, which limits how, when, and what therapy gets to the brain and brain tumors," Dr. Jackson says. "Regulation of the blood-brain barrier among glioma cells may involve sex differences, but no studies have been performed to date to evaluate such dynamic changes. These findings could help to optimize sex-specific treatments additionally."

Recent and proposed studies on gliomas that incorporate consideration of SABV hold promise for improving treatment and outcomes.

## The Future of Research on Glia

If, as Dr. Fields suggests, research on glia is 100 years behind that on neurons, then many still-unexplored avenues of glial cell research could improve human health. In addition to their involvement in the disease states discussed above, glia also play roles in infectious diseases such as Creutzfeldt-Jakob disease and AIDS. For example, when HIV is present in the brain, it infects glia rather than neurons. Researchers have also shown that glia play roles in hearing loss, ADHD, pathological lying, tone-deafness, autism, and addiction.<sup>1</sup> Future research on glial cells may lead to new treatments for these diseases and conditions.

Recently, researchers have discovered populations of glia residing in major organs of animals, and evidence suggests that analogous cells also exist in the human body and may play important roles in health and disease.<sup>25</sup> Researchers have shown that glia in the hearts of zebra fish regulate heart rate.<sup>26</sup> Glia in the spleens of mice reside between nerve cells and immune cells, suggesting an important role in stress responses.<sup>27</sup> Glia identified in the lungs of mice play an unknown but crucial role, perhaps one involving oxygen exchange,

as mice experimentally deprived of lung glia die.<sup>28</sup> As the blood-brain barrier complicates drug delivery to neurons and glia in the brain, some researchers have speculated about the potential of targeting the more accessible glial cells in these organs with current or novel medications. NIH will continue to support research on “the other brain”—glial cells—to turn scientific discoveries into better health for all.

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# MATERNAL HEALTH

## Pregnancy Changes the Maternal Brain



David Thomas, Ph.D.



Eric Sarlin, M.A., M.Ed.

Pregnant individuals undergo dramatic physiological and hormonal changes that serve primarily to create an environment conducive to fetal development and to prompt maternal bonding and caregiving behaviors. Incidental and sometimes unexpected outcomes may result from these changes as well. Pregnant people may experience fluid retention; physiological changes to the breasts and cervix; changes in sight, taste, and smell; increased hair and nail growth or hair loss; hyperpigmentation of some areas of the skin; changes in circulation, respiration, and metabolism; and profound changes in mood, behavior, and even the physiology of the brain. During birth, the postpartum period, and lactation, additional maternal brain remodeling may result in structural changes in some brain regions and increased neuronal size in others. Many of these and other changes may last throughout the mother’s life.<sup>1</sup>



Scientists and clinicians—as well as family members, friends, and new mothers themselves—have long observed behavioral changes associated with pregnancy and the postpartum period. However, only recently have researchers connected these new behaviors to changes in the prefrontal cortex, midbrain, and parietal lobes.<sup>2</sup> Increased production of estrogen, progesterone, and other hormones throughout pregnancy and postpartum concentrates gray matter and increases activity in brain regions associated with empathy, social interaction, and anxiety, resulting in maternal bonding, protectiveness, and often frequent worries about the baby.<sup>2</sup> In the months after delivery, activity in the amygdala increases. Researchers have connected this activity with hypersensitivity to the baby's needs.<sup>2</sup> Attending to the baby or even just staring at the newborn activates the reward centers of a mother's brain. The process creates a positive feedback loop of care and reward that some scientists have compared to obsessive-compulsive behavior.<sup>2</sup> In short, maternal neurological changes are associated with attentiveness and caregiving behaviors.

Oxytocin, a hormone synthesized in the hypothalamus, plays a role in pregnancy, delivery, lactation, and caregiving.<sup>2,3</sup> During pregnancy, astrocytes (a type of glial cell in the brain; see feature story, p. 3) withdraw from neurons and dendrites that make oxytocin, thereby increasing production.<sup>3</sup> Oxytocin prompts uterine contractions, stimulates milk release, and contributes to maternal bonding with the baby. Breastfeeding increases oxytocin production, and research has shown that breastfeeding mothers show a greater level of brain response to their babies' cries than mothers who bottle-feed.<sup>2</sup> In experiments, neutralizing oxytocin in rat mothers inhibits maternal behaviors,<sup>4</sup> and injecting oxytocin into virgin female rats prompts them to care for mouse pups placed in their cages.<sup>5</sup>

Approximately 20% of new mothers in the United States experience mental health issues, such as depression or anxiety,<sup>2,6</sup> and about 1 in 6 women experience postpartum depression.<sup>2</sup> Researchers have studied the brain and continue to do so to identify neuroimmune markers and hormones that may constitute risk factors or potential therapeutic targets for perinatal and postpartum depression.<sup>6</sup> For instance, clinicians often treat postpartum depression with brexanolone, a medicinal form of allopregnanolone, a naturally occurring neurosteroid converted from progesterone. Clinical use of brexanolone, the first treatment approved for postpartum depression and an important scientific advancement for women's health, resulted from NIH basic science research. Damage to the amygdala, a part of the brain associated with attentiveness to a baby's needs, has been associated with higher levels of depression in mothers.<sup>2</sup> Websites created and managed by the [U.S. Department of Health & Human Services](#)

include many resources and more information on perinatal depression (e.g., [Perinatal Depression](#) and [CDC Activities—Depression Among Women](#)).

Pregnancy, birth, and lactation result in a host of additional neurological changes. For instance, studies have shown consistently that pregnancy reduces pain. Basic animal research studies dating back to 1980 have identified increased acute pain tolerance during pregnancy.<sup>7</sup> In human studies, researchers also have found that pregnant women and postpartum women have had higher thresholds for experimenter-induced pain.<sup>8,9</sup> Many studies have found that pregnancy diminishes prepregnancy pain associated with temporomandibular disorders, headache/migraine, rheumatoid arthritis, and other conditions.<sup>10–14</sup> However, individuals from different racial and ethnic groups may experience different degrees of pregnancy-associated analgesia, and non-Hispanic Black individuals may experience little or no pain relief during pregnancy.<sup>15</sup> Other research links pregnancy and the postpartum period with memory changes. Memory changes and an inability to concentrate may stem from new mothers' sleep deprivation, stress, and hormonal and neurological changes. Although the scientific evidence for this condition remains inconclusive, recent research has linked factors regulating gene expression in learning and memory with the maternal experience in a mouse model.<sup>6</sup>

ORWH and NIH as a whole remain committed to investigating these and other aspects of maternal psychology, physiology, and wellness and to improving health and treatment for all pregnant people. For more information on maternal health and NIH's efforts to mitigate maternal morbidity and mortality, please visit the [NIH Maternal Morbidity & Mortality Web Portal](#), which contains information for researchers, clinicians, policymakers, mothers, mothers-to-be, and the general public.

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## Study Shows Estrous Cycle Negligibly Affects Behavior, Supporting Inclusion of Both Sexes in Biobehavioral Research

(Original article by [Levy et al. 2023. Curr. Biol. PMID: 36889318.](#))

A recent study by [Dana Rubi Levy, Ph.D.](#), [Rebecca M. Shansky, Ph.D.](#), [Sandeep Robert Datta, M.D., Ph.D.](#), and colleagues suggests that both male and female mice have highly individualized patterns of exploratory behavior, that the spontaneous behavior of the male mice varies more than that of the females, and that estrous state negligibly affects behavior in female mice.

The mouse estrous cycle is short and typically repeats every 4 to 5 days. The investigators, seeking to uncover the contribution of internal states to behavioral patterns, observed the behavior of genetically identical, similarly housed female and male mice as they explored a small, open circular chamber. Researchers tracked the estrous state of the female mice in daily sessions over 15 consecutive days. A validated machine learning algorithm analyzed video recordings of the mice and quantified behaviors such as running, rearing up, and grooming. The data indicated that mice have highly individualized behavior patterns. Surprisingly, estrous state, although known to play a role in the neural circuits involved in action selection and movement, had a negligible effect on behavior overall. The investigators concluded that differences in the individual animals' experiences, gene expression, and development had greater influence on their behavior than the estrous cycle.

These findings support the basis of the [NIH Policy on Sex as a Biological Variable](#) and the notion that both males and females should be included in biobehavioral studies. Historically, the flawed assumption that the estrous cycle induces variability in female data

and thus a confounding variable in studies has justified the exclusion of females from many biomedical and biobehavioral experiments. The current findings suggest that anticipated estrous cycle variability should not exclude females from research. In fact, this study demonstrates how inclusion of both males and females improves scientific rigor. Including animals of both sexes enabled the investigators to validate this animal model, to identify that behavioral sex differences exist, and to demonstrate that estrous state does not affect exploratory behavior in females.

## Researchers Investigate Migraine in Women

(Original articles by [Arab et al. 2022. Br. J. Nutr. PMID: 34763733](#) and [Ibrahimi et al. 2022. Neurology PMID: 35985832.](#))

Migraine affects women disproportionately, and [data show](#) that 1 in 5 women suffer from migraine syndrome (as opposed to only 1 in 16 men and 1 in 11 children). A recent study by [Aman Arab, Ph.D.](#), [Gholamreza Askari, M.D., Ph.D.](#), and colleagues explored the connections between diet and quality of life and migraine outcomes in women ages 20–50. A randomized controlled trial enrolled 102 women with migraine and compared the outcomes of study participants who ate the DASH (Dietary Approaches to Stop Hypertension) diet with the outcomes of control group participants given usual dietary instructions. (See [this webpage](#) from the [National Lung, Heart, and Blood Institute](#) for more information on the DASH diet.) The researchers observed decreases in the frequency, duration, and severity of migraine in those assigned to the DASH group compared with the control group. The participants on the DASH diet also reported less depression, but both

groups experienced similar outcomes in regard to quality of life and anxiety. The researchers conclude that the DASH diet may improve the clinical symptoms and mental health outcomes associated with migraine in reproductive-age women.

In another study, NIH-funded researchers [Khatera Ibrahimi, M.D.](#), [Tobias Kurth, M.D., Sc.D.](#), and colleagues investigated the association between migraine, which physicians consider a neurovascular disorder, and increased risk for cardiovascular disease (CVD) events. Analyzing data from a cohort of almost 28,000 women health professionals participating in the [Women's Health Study](#), the researchers indexed Framingham risk scores (FRS), which gauge the likelihood of coronary heart disease over the next 10 years, with study participants' self-reported histories of migraine. None of the women had a history of CVD or major diseases at baseline. Results suggest a complex relationship between CVD risk and migraine history. Study participants with midrange FRS were less likely to report having migraine at the start of the study or at the 5-year follow-up than those with the lowest-range FRS. However, participants in the highest three FRS ranges and thus at greatest risk for CVD events were more likely to report having a history of migraine but no active migraine (defined as having had a migraine attack in the previous year) at baseline or at the 5-year follow-up. The researchers conclude with a few hypotheses to explain their findings, including (1) that possible vessel stiffness both prevents headache and increases risk of CVD events in some patients and (2) that FRS may not serve as an accurate indicator of vascular health in patients with migraine. The investigators suggest considering migraine history when studying associations with the vascular system and state that a healthy vascular system (i.e., low FRS) may be associated with active migraine status or new-onset migraine.

## FEATURED RESEARCH AND PERSPECTIVES

## Researchers Share Their Experiences in “Stories of Women in Neuroscience”

(Original article by [Sibener et al. 2022](#). [J. Neurosci. PMID: 35705494](#).)

The Stories of Women in Neuroscience ([Stories of WiN](#)) project relates the professional and educational experiences of researchers in the discipline. The project aims to increase the visibility of these important and often-underrecognized scholars and to encourage aspiring young women to pursue careers in neuroscience.

In a recent article, [Leslie J. Sibener](#), [Nancy Padilla-Coreano, Ph.D.](#), and colleagues review many of the gender disparities in neuroscience (e.g., faculty appointments, tenure, citation), identify the common themes that emerged from the Stories of WiN profiles of over 70 researchers, and make policy recommendations to improve entry, advancement, retention, and recognition of women in neuroscience.

Overall, the women’s stories emphasized the importance of positive research experiences early in their educational and professional journeys, of managing work–life balance and self-doubt, and of resisting traditional roles of a scientific and academic system established primarily by White men. The authors of the article recommend increasing entry into the field by providing paid research opportunities for undergraduates and others, incentivizing good mentorship, establishing family-friendly policies for researchers, and recognizing women neuroscientists equitably for their professional and academic accomplishments.

## Neuroscience Journal Recognizes Four Pioneering Women Scientists

(Review article by [Yevo and Maffei. 2022](#). [Front. Integr. Neurosci. PMID: 35153689](#).)

*Frontiers in Integrative Neuroscience* recently published a review article by [Arianna Maffei, Ph.D.](#), and [Priscilla Yevo](#) recognizing the underappreciated work of four women who have made groundbreaking contributions to neuroscience.

[Sandhya Koushika, Ph.D.](#), of the [Tata Institute of Fundamental Research](#), studies axonal transport, a cellular process vital to the function and survival of neurons. She developed a system for live-imaging the movement of proteins from synapses in the roundworm *Caenorhabditis elegans* and other animals. Her research may help to elucidate neurodegenerative processes in diseases such as amyotrophic lateral sclerosis (ALS).

[Eve Marder, Ph.D.](#), the Victor and Gwendolyn Beinfeld Professor of Neuroscience at [Brandeis University](#), discovered that neural circuits can alter their output in response to different neuromodulators, a finding that disproved the previously accepted notion that neural circuits are hardwired to produce only specific, predictable patterns. Her work with crustaceans’ stomatogastric nervous systems, which are small networks of 30 neurons, revolutionized the way neuroscientists understand neural circuits and their behavior.

[Mary Jeanne Kreek, M.D.](#), formerly a professor and head of the Laboratory on the Biology of Addictive Diseases at [The Rockefeller University](#) and a senior attending physician at [The Rockefeller University Hospital](#), was a physician-scientist who developed methadone maintenance therapy for treating heroin

addiction. Her research characterized heroin addiction as a disease and helped shape the contemporary medical understanding of substance use disorder as a neurological disease rather than a criminal behavior. Dr. Kreek also studied how drugs of abuse alter brain function and identified genes associated with a predisposition to substance use disorders.

[Yasmin Hurd, Ph.D.](#), the Ward-Coleman Chair of Translational Neuroscience and the Director of the Addiction Institute at the [Icahn School of Medicine at Mount Sinai](#), studies substance use disorders and uses multidisciplinary approaches with animal and human models to elucidate the complex neurobiological mechanisms underlying addiction. Her work has expanded the scientific understanding of cannabis exposure on the brain, particularly on the transgenerational effects of cannabis use during pregnancy and associated behavioral and cognitive impairments in the offspring. Dr. Hurd also researches cannabidiol (CBD) as a potential treatment for opioid use disorder.

ORWH also recognizes these brilliant, groundbreaking scientists and thanks *Frontiers in Integrative Neuroscience* for highlighting their work.

## Researchers Identify Factors Influencing Neuroscientists’ Career Choices

(Original article by [Ullrich et al. 2021](#). [eNeuro. PMID: 34039650](#).)

A survey research study of almost 1,500 Ph.D. neuroscientists (54% women, 16% underrepresented racial and ethnic groups) paints a nuanced picture of career preferences, interests, and goals within the field. Although many studies of scientific careers begin with the assumption that all trainees and graduate students aspire to a research faculty position, the work of NIH’s

[Lauren E. Ullrich, Ph.D.](#), [John R. Ogawa, Ph.D.](#), and [Michelle D. Jones-London, Ph.D.](#), suggests that career choices in neuroscience stem from multiple evolving factors.

The researchers found that interest in research faculty careers wanes in all neuroscience graduate students over time, a trend even more pronounced in women and those from historically underrepresented racial and ethnic groups. Social identity; individual preferences; graduate school and postdoc experiences, including the influence of advisors; perceived incongruence between academic culture

and the values of other communities; and other factors function to shape the career paths, preferences, and goals of individual neuroscientists. For instance, the women surveyed expressed less interest in academic research careers as they began their Ph.D. programs, and their interest decreased over time. Women expressed correspondingly greater interest in scientific positions not involving research (e.g., teaching) at the start of their Ph.D. training, and this interest increased over time compared with men's interest. Many women responding to the survey listed a desire for work-life and work-family balance as a primary reason for choosing a career

other than one as a research faculty member. The researchers also found that advisors heavily influenced career interests, either positively by providing guidance and networking opportunities or negatively by discouraging mentees. Having a sense of belonging within academic and laboratory settings was a strong predictor of career interest, and individuals from minoritized groups, particularly women, were less likely to report this sense of belonging. The researchers conclude their analysis by calling for changes in the systemic structures and mentorship practices that affect neuroscientists' career choices.

## SCIENTIST SPOTLIGHT



**Guillermina Lozano, Ph.D.**

Geneticist [Guillermina "Gigi" Lozano, Ph.D.](#), earned an undergraduate degree in biology and mathematics at [The University of Texas Rio Grande Valley](#), did her graduate work at [Rutgers University](#) and the University of Medicine and Dentistry of New Jersey, and completed a postdoctoral fellowship at [Princeton University](#). Dr. Lozano currently serves as Professor and Chair of the Department of

Genetics at [The University of Texas MD Anderson Cancer Center](#). She is a member of the [National Academy of Sciences](#), the [National Academy of Medicine](#), and the [American Academy of Arts and Sciences](#). In December 2022, Dr. Lozano delivered a lecture titled "[Mutant p53 Activities in Mouse Tumor Models](#)" as part of the [NIH Director's Wednesday Afternoon Lecture Series](#) (WALS).

### **What are your primary areas of research?**

My lab studies the p53 tumor suppressor that prevents the formation of cancers in humans. We are interested in understanding how p53 prevents normal cells from proliferating uncontrollably. DNA damage, hypoxia, and other cellular stresses activate p53 to eliminate or repair cells with damaged DNA, but p53 mutations interfere with this process. Such mutations are common in patients with cancer, and we want to understand how p53 missense mutations drive tumor initiation, progression, and metastasis.

My lab developed mouse models to study the p53 tumor suppressor pathway. We determined the physiological relevance of proteins that inhibit normal p53 activity. These proteins are expressed at high levels in many cancers *without* p53 mutations and represent another mechanism for eliminating normal p53 function. Other models inherit germline mutations in which the whole mouse has the p53 mutation, similar to human Li-Fraumeni syndrome, a rare disorder that increases cancer risk. This model enables us to study what happens in every cell type of the mouse. Our newer mouse models, which I discussed in [the WALS lecture](#), are somatic models that enable us to make point mutations in particular tissue types, like the breast epithelium, to study tumor initiation, progression, and metastases. This new model was more difficult to develop but better emulates the types of human cancers we need to study and treat.

Finally, I have become interested in translating some of our findings into clinical practice. I am collaborating with physicians and clinician-scientists to determine whether the presence of mutant p53 is required for continued tumor growth. We have devised studies to remove the mutant p53 and observe tumor regression in some breast cancer models. A Phase I clinical trial at multiple institutions is testing dosage, toxicity, and other features of a drug that converts a specific p53 missense mutation to a wild-type (i.e., normal) conformation.

### **Which accomplishments are you proudest of?**

Soon after scientists discovered that p53 was a tumor suppressor and that many cancers had p53 mutations,

I studied the sequence of the protein to try to determine its mechanism of tumor suppression. I learned that p53 was a transcription factor—that is, a protein that prevents cancer by activating hundreds of genes to produce messenger RNA that subsequently make other proteins that kill cells or stop cells from proliferating. This was an exciting discovery early in my career.

Also, the mouse models that we developed demonstrate a dramatic difference in tumors with and without a p53 missense mutation. p53 missense mutations lead to more aggressive metastatic cancers. We need to develop different ways of treating patients with those kinds of mutations.

### **What are some of the biggest challenges you have faced as a scientist?**

Postgraduate and postdoc experiences do not teach you how to run a lab. Figuring that out was a big learning curve for me,

and in our society, running a lab may be harder for women. It is trial and error, and I made a lot of mistakes, particularly in making hiring decisions and managing people. Now there are more women in science and more sources of information and guidance for those starting their own labs. The MD Anderson Cancer Center now has a great mentoring program to guide faculty through these hurdles.

Having a child while managing a full-time research career was also a challenge. Day care options are few at medical centers. Fortunately, my husband contributed equally to raising our daughter.

### **What advice do you give to young scientists?**

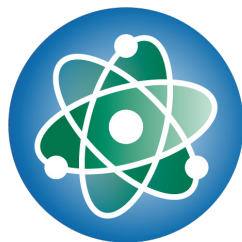
Being a scientist is hard, but discovering something new is so rewarding and absolutely thrilling. Do not give up.

## INSTITUTIONAL SPOTLIGHT

### **WISELI, a University of Wisconsin–Madison Institute, Advances Faculty Gender Equity**

NIH selected the Women in Science and Engineering Leadership Institute ([WISELI](#)) of the University of Wisconsin–Madison ([UW-Madison](#)) for the [NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science](#) in 2021. This award recognized institutions whose biomedical and behavioral science departments, centers, or divisions had achieved sustained improvement in gender diversity.

Established in 2002, WISELI represents the cornerstone of a 5-year [National Science Foundation ADVANCE award](#) to UW-Madison. WISELI has advanced gender equity in science, technology, engineering, mathematics, and medicine (STEMM) by using UW-Madison as a “living laboratory” to study gender equity, diversity, and campus climate; implement evidence-based interventions; and measure success. WISELI has consistently taken a systems approach, with multilevel interventions



# WISELI

that address institutional, interpersonal, and internalized barriers to the advancement of women and members of other groups underrepresented in STEMM. WISELI initiatives educate faculty members about the impact of unconscious or implicit bias on individual judgments and institutional processes and, most importantly, suggest evidence-based strategies for minimizing the influence of such bias.

WISELI interventions have included [Searching for Excellence & Diversity: Workshops for Faculty Search Committees](#), [Breaking the Bias Habit](#) workshops, and the Bias Reduction in

Medicine ([BRIM](#)) initiative, all of which were tested in controlled studies and found to be effective pro-diversity interventions. WISELI’s [Study of Faculty Worklife at UW-Madison](#), a longitudinal survey of the workplace climate, tracks the effectiveness of WISELI’s efforts over time and demonstrates climate improvements in those departments participating in WISELI initiatives compared with nonparticipating departments.

ORWH thanks UW-Madison for developing these interventions, congratulates WISELI on winning the award, and recommends WISELI programs to all STEMM departments.

## IN CASE YOU MISSED IT

### NSF Report Characterizes Diversity Within STEM in the United States

[Diversity and STEM: Women, Minorities, and Persons with Disabilities](#), a recent report from the National Science Foundation's (NSF) National Center for Science and Engineering Statistics (NCSES), presents demographic data on employment and education in science, technology, engineering, and mathematics (STEM). The report indicates that over the past decade, more women and individuals from minoritized racial and ethnic populations are working in STEM and earning degrees in engineering and science than in previous years. However, these groups, along with those with disabilities, remain underrepresented in STEM fields in relation to the U.S. population. Other key findings in the report indicate that (1) although women earn half of bachelor's and associate degrees in science and engineering, they represent only about a third of the STEM workforce and earn less than men in these fields; (2) similarly, in STEM fields, Latino, Black, and American Indian/Alaska Native workers earn less than

White and Asian workers; and (3) in 2021, 21% of workers with one or more disabilities were working in STEM, where they represented 3% of the workforce. You can read the complete report [here](#).

### Research Publication Disparities Related to Race, Ethnicity, and Gender Begin in Medical School

[Recent study results published in JAMA Network Open](#) show that women, Black, and Hispanic medical students publish less frequently than Asian and male medical students. This finding emerged from analysis of data on over 30,000 medical students matriculating in 2014 and 2015. The researchers speculate that disparities in research publication rates may stem from poor mentorship, negative stereotypes, and devaluation of research ideas from women and those in minoritized populations. Racial, ethnic, and gender disparities in publication and other areas persist throughout all career stages for physician-scientists.

## NOTEWORTHY

### ORWH to Lead New Office of Autoimmune Disease Research

In 2022, the U.S. Congress directed NIH to establish an Office of Autoimmune Disease Research (OADR-ORWH) within ORWH and allocated \$10 million in the fiscal year 2023 omnibus appropriations bill to fund its development. In establishing OADR-ORWH, ORWH is working with NIH leadership; other NIH institutes, centers, and offices (ICOs); researchers; clinicians; patient advocacy groups; and the public to ensure that plans for the new office synergize with other NIH efforts, observe congressional directives, address gaps in autoimmune disease research, and serve patients with autoimmune disorders. As part of this development process, ORWH will form the NIH-wide Coordinating Committee on Autoimmune Disease Research to address omnibus priorities, such as analyzing the landscape of research on autoimmune diseases, identifying emerging areas of innovation and research opportunity,

and developing an autoimmune disease-related strategic research plan for OADR-ORWH and all ICOs. Future research supported by OADR-ORWH will likely investigate genetics, environmental exposures, biomarkers, sex influences, co-occurring autoimmune diseases, therapeutic targets, animal models, systems biology, and translational research. The next issue of *In Focus* will provide more details on OADR-ORWH research and the health issues it will address.

Autoimmune diseases include more than 80 acute and chronic illnesses that are often disabling, such as multiple sclerosis, rheumatoid arthritis, fibromyalgia, and type 1 diabetes. Approximately 8% of the U.S. population has an autoimmune disease, and women constitute nearly 80% of this group. Autoimmune diseases represent a leading cause of death for young and middle-aged women, but individuals of any age, sex, or gender can develop these diseases.

### Women's Health Research Day Commemorates NIH SABV Policy, ORWH Director Clayton Honored

Women's Health Research Day commemorates the implementation of the NIH Policy on Sex as a Biological Variable (SABV) and raises awareness of the necessity of including male and female animals and cells in biomedical research as well as the historical underrepresentation of women in clinical trials. On January 25, Friends of ORWH (FORWH) celebrated this year's Women's Health Research Day with a reception at the [Rayburn House Office Building](#) for leaders in health care and biomedical research as well as representatives from several congressional offices. FORWH honored ORWH Director Janine A. Clayton, M.D., FARVO, for developing the NIH SABV policy and for her many contributions to women's health. The



Society for Women’s Health Research ([SWHR](#)) and the American Medical Women’s Association ([AMWA](#)) helped organize the event.

## Stat Editorial Calls for Prioritizing Women’s Health

In a [recent editorial](#) published on the health news website [Stat](#), Michelle Carnahan, President of the digital pharmacy Thirty Madison and former executive at pharmaceutical companies Sanofi and Eli Lilly, calls for making 2023 a year for prioritizing women’s health. Ms. Carnahan states that 2023 could represent a pivotal year for women’s health, given events such as the overturning of *Roe v. Wade* and increased awareness of systemic shortcomings in women’s health care made plain by the COVID-19 pandemic. Ms. Carnahan calls for expanding maternal, reproductive, and mental health care as well as normalizing women’s aging and menopause.

## ORWH Continues “Diverse Voices” Lecture Series on Intersectionality and the Health of Women

ORWH’s “Diverse Voices: Intersectionality and the Health of Women” lecture series amplifies research that incorporates an intersectional framework and addresses a breadth of topics relevant to the health of women. Recent lectures examined issues of intersectionality and equity in cancer treatment and mental health care.

On January 26, [Laura Fejerman, Ph.D., M.Sc.](#), a Professor in the Department of

Public Health Sciences at the University of California, Davis, and [Scarlett Lin Gomez, Ph.D., M.P.H.](#), a Professor and the Vice Chair for Faculty Development in the Department of Epidemiology and Biostatistics at the University of California, San Francisco, presented “Cancer Disparities: Methods and Measurement of Racial and Ethnic Diversity.” Drs. Fejerman and Gomez discussed the relationship between genetic ancestry and breast cancer risk in Hispanic/Latina women as well as research on cancer in Asian American, Native Hawaiian, and Pacific Islander populations that focuses on approaches beyond racial and ethnic categories and seeks a better understanding of cancer patterns, risk, and prognostic factors in distinct groups. A recording of this session is available [here](#).

On March 23, [Melissa DuPont-Reyes, Ph.D., M.P.H.](#), and [Janet M. Turan, Ph.D., M.P.H.](#), delivered a lecture titled “Intersectional Stigma and Mental Health.” Dr. DuPont-Reyes, an Assistant Professor at the Mailman School of Public Health of Columbia University, discussed using an intersectional lens to examine mental health in adolescents. Dr. Turan, a Professor in the Department of Health Policy and Organization at the University of Alabama at Birmingham, explained her analytical approach for measuring intersectional stigma. Both speakers described how considerations of intersectionality can enhance our understanding of the interaction between stigmatized mental health disorders and multiple marginalized identities and can inform advocacy health care and research interventions

that expand our capacity to address intersectional stigma and social context. A recording of these presentations is available [here](#).

## ORWH Hosts Maternal Health and Pregnancy Workshop for IMPROVE Researchers and Clinicians

Researchers and clinicians supported by the NIH IMPROVE ([Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone](#)) initiative met on March 9 to share their work and progress to date. Workshop participants shared research findings and lessons learned from their IMPROVE projects; identified common themes, knowledge gaps, and research opportunities; and clarified the needs of pregnant people and postpartum individuals to reduce preventable causes of morbidity and mortality. A recording of the workshop is available [here](#).

The NIH-wide IMPROVE initiative uses an integrated approach to understand biological, behavioral, sociocultural, and structural factors contributing to maternal mortality and severe maternal morbidity by building an evidence base for improved care and outcomes in specific populations and regions of the country. IMPROVE addresses geographical disparities and social determinants of health, including educational attainment, racism, and socioeconomic status. In fiscal years 2020 and 2021, NIH awarded over \$20 million to support 58 projects through the IMPROVE initiative to enhance our understanding of and develop mitigation strategies for the leading causes of



# NOTEWORTHY

pregnancy-related and pregnancy-associated morbidity and mortality. Congress has allocated \$30 million annually, beginning in fiscal year 2022, to support [IMPROVE efforts](#).

## WHAM Events Celebrate 30<sup>th</sup> Anniversary of NIH Revitalization Act, Promote Women's Health

The Women's Health Access Matters (WHAM) organization hosted [a series of panel discussions and other events](#) over the first half of 2023 to "increase

awareness about women's health research and drive change with the goal of accelerating investment in sex-based research." These events also recognized the 30<sup>th</sup> anniversary of the NIH Revitalization Act, a law that mandated that NIH-funded clinical trials and research include women and individuals from racial and ethnic minority groups. The first virtual event, "30 Years Later: How 1993 Shaped Women's Health," took place on January 19 and featured a panel discussion with ORWH Director Janine A. Clayton, M.D., FARVO, and other

health and policy leaders. Other virtual WHAM discussions in this series included "Women's Heart Health" on February 9, "Autoimmune Disease" on March 9, "Our Brains/Ourselves" on April 13, and "Cancer in Women" on May 18. A final in-person roundtable concluded the series on June 13 and included discussion from some of the original legislators and policymakers responsible for the NIH Revitalization Act of 1993 as well as current officials dedicated to women's health, business leaders, investors, advocates, economists, and academics.

## UPCOMING EVENTS

### Diverse Voices: Intersectional Approaches to Substance Use and Misuse

July 27, 2023

3:00 p.m. – 4:00 p.m. EDT

### Diverse Voices: Social Determinants and Uptake of Infectious Disease Control Measures

September 28, 2023

3:00 p.m. – 4:00 p.m. EDT

### 59th Meeting of the Advisory Committee on Research on Women's Health

October 18, 2023

8:00 a.m. – 5:00 p.m. EDT

### Specialized Centers of Research Excellence on Sex Differences (SCORE) 2023 Annual Meeting Keynote Address

November 3, 2023

10:00 a.m. – 11:00 a.m. EDT

### Building Interdisciplinary Research Careers in Women's Health (BIRCWH) 2023 Annual Meeting

December 5, 2023

8:00 a.m. – 5:00 p.m. EST

For up-to-date information, visit [www.nih.gov/women](http://www.nih.gov/women).

## FUNDING OPPORTUNITIES

### Understanding Chronic Conditions Understudied Among Women (R21 Clinical Trial Optional) ([RFA-OD-23-013](#))

### Understanding Chronic Conditions Understudied Among Women (R01 Clinical Trial Optional) ([RFA-OD-23-014](#))

## NIH Office of Research on Women's Health (ORWH)

6707 Democracy Boulevard, Suite 400  
Bethesda, MD 20817  
Phone: 301-402-1770

[ORWHinfo@mail.nih.gov](mailto:ORWHinfo@mail.nih.gov)  
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