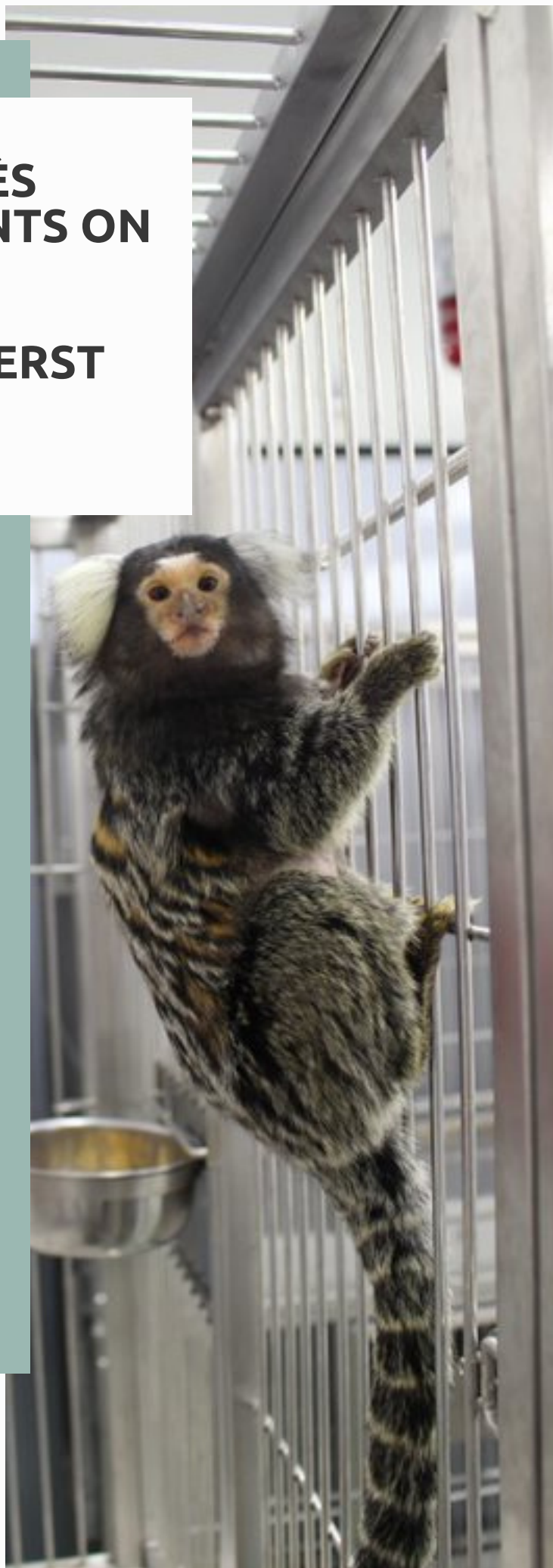


CRITICAL REVIEW: AGNÈS LACREUSE'S EXPERIMENTS ON MARMOSETS AT THE UNIVERSITY OF MASSACHUSETTS-AMHERST

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Agnès Lacreuse's experiments on marmoset monkeys, conducted at the University of Massachusetts-Amherst (UMass), cause irreversible harms to animals with no adequate scientific justification.



Executive Summary

- Marmoset monkeys in Lacreuse's laboratory are subjected to approximately eight years in a cage, during which they endure **multiple major surgeries, social isolation, sleep deprivation, fluid deprivation, harmful hormonal manipulations, and frequent lengthy restraint** before being killed and dissected.

- The interaction between age, hormones, genetics, reproductive history, general physical health, and mental health status on menopause-related symptoms in humans **is far too complex to be "simulated" in a laboratory in nonhuman primates.**

- **Marmosets do not experience menopause or the physiological symptoms it presents in humans.** Menopausal symptoms are induced in this laboratory through surgeries, pharmaceutical interventions, applications of heating pads, and noise-induced sleep deprivation.

- Critical differences between humans and marmosets in brain size and morphology, rates of development, hormone production and responsivity, neurodevelopment, neuroanatomy, and neurodegeneration make marmosets **a poor model for human menopause and its association with age-related cognitive decline and neurological disease in humans.**



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- Although Lacreuse cites the short life expectancy of marmosets to justify using them in aging experiments, their accelerated development makes them **inappropriate to study the much more protracted, hormone-sensitive, and age-related changes in the human brain.**

- Surgically induced, abrupt menopause in captive marmosets **cannot elucidate the complex genetic, environmental, or epigenetic factors known to influence the transient and protracted menopausal transition in humans.**

- The application of extraneous heat and noise-induced sleep deprivation are **not biological simulations of the hot flashes and sleep disturbance that plague women in perimenopause.**

- Marmosets in laboratories suffer from numerous **abnormal physiological systems and functions**, confounding all data coming from these experiments.

- It is specious to try to study the effects of age-related hormone changes and extraneous hormone manipulation in a species that **does not undergo age-related hormone changes and that is resistant to extraneous hormone manipulation.**

- There are **superior non-animal alternatives available** to study the role of menopause and age-related hormonal change on cognitive decline and neurodegeneration in humans.

Introduction

For the past 10 years, Lacreuse has been subjecting marmoset monkeys to years of captivity, multiple invasive surgeries, hormone manipulation, frequent restraint, fluid restriction, sleep deprivation, and batteries of fear- and stress-inducing tests—before killing and dissecting them. The purported purpose of these harmful and deadly experiments is to study the role of menopause and its associated disruptions in thermal regulation, sleep, and cognitive function in the increased risk of neurodegenerative diseases in women. However, as reviewed in detail below, marmosets are an exceptionally inappropriate species to study for this purpose. Inherent differences in sex hormone function, aging, and gene expression between marmosets and humans, critical differences in endocrine and neurological processes between the two species, and the profound impact of captivity on marmosets' physiological systems render data from these experiments irrelevant to humans.



To date, these experiments have cost taxpayers more than \$4 million without producing any meaningful data to inform new interventions, treatments, or cures for humans.

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Ethical Considerations

Brief overview

The experiments conducted by Lacreuse at UMass inflict irreversible harms on common marmosets—highly intelligent, sensitive monkeys, who, in nature, are profoundly social and bond in pairs and multi-generational families that stay united throughout their lifetimes. Marmosets are shipped to Lacreuse’s laboratory when they are approximately 2 years old. They are then held captive in indoor cages for up to eight years, during which they are denied any opportunity to see sunlight, climb trees, produce offspring, and enjoy family life. Instead, they languish in cages, enduring numerous invasive surgeries as well as stressful, painful, and fear-inducing daily procedures before being killed and dissected. This is in addition to the extensive, well-documented harms that afflict nonhuman primates—and common marmosets in particular—in a laboratory setting.

Lacreuse’s experiments induce irreversible harms

Marmosets in Lacreuse’s laboratory are subjected to multiple major surgeries. Female marmosets undergo ovariectomy surgery to have their uterus and ovaries removed. Male marmosets, typically used as a comparison group in this laboratory, are vasectomized and in some cases endure additional gonadectomy surgeries to remove their testes.



The experimenters drill burr holes into the marmosets’ skulls and screw electrodes directly into the bone.

Photo credit: Yun, J. W., Ahn, J. B., & Kang, B. C. (2015). Laboratory animal research, 31(4), 155–165.

Experimenters implant telemetry devices into both the male and female marmosets’ bodies, through which they monitor brain activity, heart rate, and temperature during sleep and cognitive testing. To implant these devices, experimenters drill burr holes into the marmosets’ skulls and screw electrodes directly into the bone. Experimenters make additional incisions in the marmosets’ necks and abdomens so that electromyography leads can be implanted.

In an attempt to induce human-like menopausal symptoms, the experimenters give the marmosets the drug letrozole to lower their estrogen levels even further than is caused by the surgery. Letrozole is an aromatase inhibitor used to lower non-ovarian produced estrogen. Typically used to keep estrogen levels low in post-menopausal women with a risk or history of estrogen (E+) sensitive breast cancers, the side effects in humans include hot flashes, joint pain, dizziness, nausea, weight gain, edema, diarrhea, cognitive difficulties, and fatigue.

In Lacreuse's approved protocols and funded grant applications, the majority of these side effects are omitted from the listed potential harms to the animals. Either Lacreuse is underestimating the effects of the drug or the marmosets are responding to it in a way that is dramatically different from humans.

Either of these possibilities is cause for concern.



The experimenters induce hot flashes by applying 120°F heating pads to the animals' bodies

Photo credit: Carl Fox

As the aforementioned hormone manipulation does not appear adequate to cause human-like sleep disturbances or thermal dysregulation (hot flashes) in the marmosets, the experimenters induce hot flashes by applying 120°F heating pads to the animals' bodies and mimic the sleep disruption observed in aging humans and women in menopause by subjecting them to audio stimuli at 60 to 90 decibels lasting for 6 minutes every 15 minutes throughout the night. By comparison, the noise that an average vacuum cleaner makes is at about 70 decibels. Lacreuse wakes up the marmosets 46 times per night, keeping them awake for a total of 276 minutes a night, three consecutive nights a week.

The marmosets are subjected to repeated blood, urine, and cerebrospinal fluid collections and frequent restraint. They are repeatedly anesthetized for procedures and are required to wear collars overnight to monitor their activity. To ensure cooperation on the multitude of cognitive tests the laboratory subjects them to, the marmosets are deprived of their most basic need—water—for hours on end. The marmosets also endure stressful social separation tasks that raise their cortisol levels and are forced to watch videos designed to be aversive. For awake neuroimaging, experimenters place the marmosets in movement-restricting jackets and helmets for hours at a time. When experiments are completed, the marmosets are perfused, killed, and dissected.



Photo obtained by PETA via FOIA

This is all in addition to the profound physiological and psychological harm caused by captivity and life in a laboratory setting.[1],[2] Primates experience increased stress from common laboratory procedures such as cage cleaning,[3] physical examination,[4] blood draws,[5] and restraint.[6],[7] Numerous studies have demonstrated that even minor changes in primates' captive environment, including temporary changes in cage size or location, increase stress levels. [8],[9] In fact, the mere physical presence of human experimenters and technicians increases stress in primates.[10],[11]

Primates in laboratories display aberrant immune-system functioning, including increased stress-related hormones, dysregulation of the hypothalamic-pituitary-adrenal axis, and depressed immune-system functioning.[12] Stress-induced immune dysregulation and systemic inflammation result in significant health consequences, including increased vulnerability to infection,[13] delayed wound healing and recovery from surgery,[14] and accelerated aging.[15] The lack of adequate mental and social stimulation in the laboratory, along with frequent subjection to common laboratory procedures, leads to chronic stress that negatively affects primates not only psychologically but also physiologically. Primates held captive in laboratories and subjected to experimental procedures exhibit signs of extreme distress, including pacing, rocking, head-twisting, and eating their own feces. Highly traumatized primates will bite their own flesh, pull out their own hair, and engage in other forms of severe self-mutilation.[16],[17], [18],[19]



Photo obtained by PETA via FOIA

Marmosets are particularly vulnerable

Marmosets in laboratories suffer from all the same effects of acute and chronic stress as other primates but also have several additional health concerns. For example, marmosets are extremely sensitive to physical restraint, and their response to restraint affects their heart and respiratory rates, temperature, and blood pressure.[20] Captive marmosets are prone to metabolic bone disease,[21] which results in bone lesions and fractures and may be the cause of the frequent oral disease, including tooth decay, in these animals. Experimenters currently believe this may be related to the higher vitamin D requirements of marmosets, differences in vitamin D metabolism in marmosets, or vitamin D deficiency caused by complete deprivation of sunlight in laboratory cages.[22] Marmosets in laboratories are also likely to suffer from secondary systemic amyloidosis[23] and insulin resistance.

At a recent National Academies of Sciences, Engineering, and Medicine workshop dedicated to discussing the care, use, and welfare of marmosets in biomedical experiments, experts drew the following conclusion:

[Marmosets] have unique requirements in terms of housing, feeding, social interactions, and other facets, many of which remain poorly understood. There is no standardized diet for captive marmosets, and there are few people who have expertise in working with them. Marmosets in captivity are susceptible to a range of diseases and are particularly prone to marmoset wasting syndrome, which is not one disease but a perplexing composite of multiple conditions and etiologies that could be due to poor nutrition, stress, infection, or a combination of these factors. Their breeding and parenting behavior is also poorly understood, and although marmosets are easier to handle than tamarins (as they tend to be less easily stressed and are more easily habituated to handling), their multiple births can lead to poor parenting performance.[24]



Photo obtained by PETA via FOIA

Participants of this workshop acknowledged that the welfare needs of marmosets are poorly understood. The current standards for their housing and enrichment do not meet their needs to forage, climb, and engage in problem-solving and complex social interactions.[25],[26] Perhaps even worse, experimenters do not know how to provide marmosets with a proper diet. Not surprisingly, this lack of understanding of even the most basic care causes the marmosets to experience a host of devastating and debilitating health conditions, including a condition referred to as marmoset wasting syndrome (MWS).



Photo credit: Carl Fox

Marmoset wasting syndrome causes weight loss, diarrhea, anemia, alopecia, weakness, intestinal inflammation, osteoporosis, paralysis, and death

MWS, also called chronic lymphocytic enteritis (CLE), is a systemic inflammatory disorder that leads to weight loss, diarrhea, anemia, alopecia, weakness, intestinal inflammation, osteoporosis, paralysis, and death.[27],[28] Efforts to curb the profound and deadly weight loss associated with improper nutrition have only caused additional health concerns. If they are not wasting away, marmosets in laboratories are becoming obese and suffering from health complications associated with that condition, including altered glucose metabolism, reduced insulin sensitivity, increased risk of heart disease and diabetes, and myriad metabolic dysfunctions.[29]

Effects of harm-induced altered physiology on data reliability

The cascade of negative effects on marmosets' health and well-being, caused by the acute and chronic stress of captivity, laboratory procedures, and improper diet, is reason enough not to proceed, but it is also important to consider the scientific ramifications of the numerous physical and psychological abnormalities these animals experience.

The uncontrolled and unmeasured immune system dysfunction and subsequent inflammation in these animals will confound any data being collected in this laboratory, as inflammation plays a crucial role in menopause symptomology[30] and most neurodegenerative and age-related conditions, including Alzheimer's disease.[31],[32],[33],[34] Stress is also known to impact marmosets' performance in a variety of cognitive tasks, and this varies across age and sex in this species.[35]



Photo obtained by PETA via FOIA

The altered insulin sensitivity seen in marmosets in laboratories is also cause for concern, as studies indicate that in humans, changes in insulin growth factor play a critical but complex role in mediating the effects of age-related estrogen and androgen reduction. Additionally, the impact of MWS/CLE on nutrient absorption makes medication dosing, especially oral dosing such as is used in Lacreuse's lab, particularly problematic.[36]

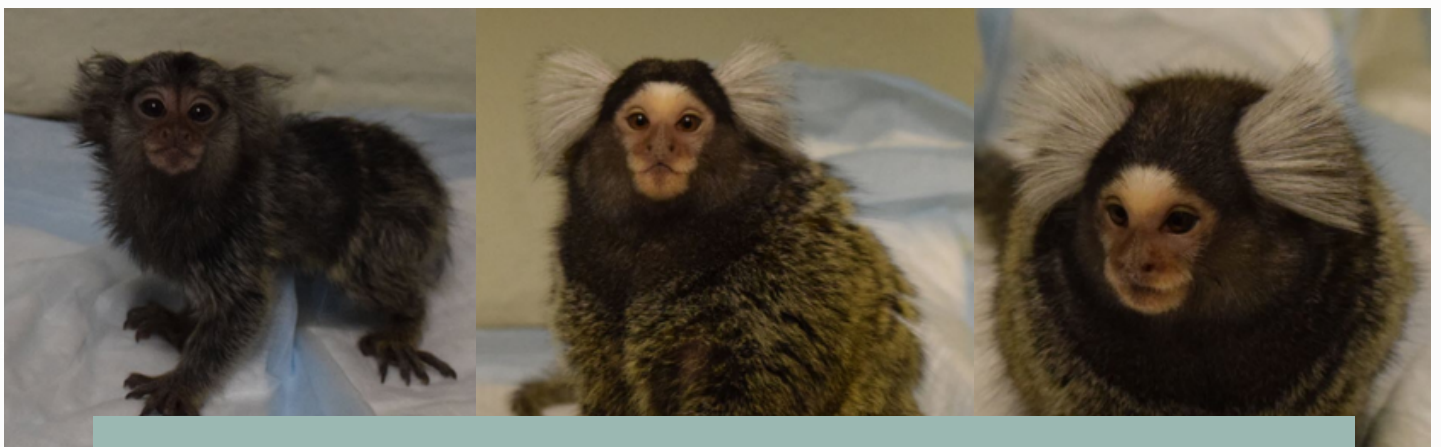
In summary, marmosets in laboratories suffer from numerous abnormal physiological systems and functions prior to any additional experimental manipulations. This impacts the scientific value of these experiments as well as the ethics of conducting them in the first place. Alarming, this information was omitted from Lacreuse's approved protocols and her funded National Institutes of Health grant applications, making it impossible for the reviewing bodies to conduct a true evaluation of the harms and benefits of these studies before approving them. These potential confounds are also excluded from Lacreuse's publications, compromising reviewers' ability to assess the scientific merit of the data being published.

Scientific Limitations

Brief overview

In humans, menopause, or the cessation of menses,[37] is preceded by a gradual decline in ovarian function that typically lasts between 4 and 8 years[38],[39] and involves multiple physiological systems. During this transitional process (often referred to as perimenopause), hormone levels begin to fluctuate and fall[40] and some women may begin to experience cognitive difficulties,[41],[42],[43] mood disturbances,[44],[45],[46] vasomotor symptoms (hot flashes and or night sweats),[47] irregular sleep patterns,[48],[49] bone loss,[50] and urogenital symptoms.[51] Age of onset, duration, symptomology, symptom frequency, and symptom severity vary considerably among individual women. [52],[53],[54] Additionally, there are complex interactions between age of onset,[55],[56],[57] diet,[58] body mass,[59],[60] exercise regimes,[61] medical history,[62] reproductive history,[63] genetics,[64] and cultural[65],[66] and environmental factors[67],[68],[69] that influence women's peri- and post-menopausal symptomatology and their subsequent risk for neurodegenerative or cardiovascular disease.[70]

As will be reviewed in more detail below, common marmosets are an exceptionally poor choice of species for the study of human menopause. In short, surgically induced, abrupt menopause in captive marmosets cannot mimic the complex genetic, environmental, or epigenetic factors known to influence the natural menopausal transition and its associated symptoms in humans. Critical differences between humans and marmosets in age-related changes in hormone production,[71] reproductive physiology,[72],[73] response to extraneous hormones, neurodevelopment,[74],[75] neuroanatomy,[76],[77] age-related neurodegeneration,[78],[79] and tau isoform expression[80] severely limit the likelihood that Lacreuse's experiments will advance our understanding of menopause and its association with age-related cognitive decline and neurological disease in humans.



Marmosets are an exceptionally poor choice of species for the study of human menopause

Marmosets are an inappropriate choice of species for the study of human menopause

Unlike humans and other primates, *common marmosets do not naturally undergo menopause*. Their estrogen levels do not gradually decrease with age. They display no evidence of reproductive senescence or hormone-mediated osteoporosis—even when they are well into their more advanced ages of 14 and 16 years.[81] In fact, throughout their lifetimes, marmosets have elevated concentrations of plasma estradiol[82] and progesterone[83] compared to humans and Old World primates. This is true for marmosets who are intact and for those who have had their ovaries surgically removed.[84] Additionally, marmosets *do not respond to circulating or extraneous hormones in the same way as humans and other primates*. Compared to humans and other primates, marmosets display what is referred to as “generalized steroid hormone resistance,”[85] i.e., relatively high levels of steroid hormones in circulation and relatively low response to exogenous steroids. And they exhibit target-tissue resistance to gonadal steroid hormones.[86]



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In short, Lacreuse has chosen to study the effects of age-related hormone changes and extraneous hormone manipulation on cognition and brain pathology in a species that does not undergo age-related hormone changes and that is resistant to extraneous hormone manipulations. In a futile attempt to circumvent marmosets' natural biological processes, Lacreuse surgically removes their ovaries. However, ***surgically induced menopause in marmosets is not comparable to the gradual menopausal transition experienced in women*** or even the abrupt drop in hormonal levels from surgical menopause in women.

Experimenters have been performing ovariectomies on sensitive marmosets for decades, and the data from these experiments is consistent and clear—ovariectomized (OVX) marmosets do not exhibit menopausal symptoms similar to those observed in human women. For example, OVX marmosets do not exhibit the changes in metabolism, body weight, body composition, bone density, energy expenditure, physical activity, fasting glucose, or glucose tolerance, or the measurable mood changes or cognitive impairments seen in peri- or post-menopausal women.[87],[88] More importantly, in regards to Lacreuse's experiments, ***OVX marmosets do not experience hot flashes, mood disorders, sleep disturbances, or cognitive impairments***.

The data from OVX marmosets, on the other hand, is in direct contrast with data from human women, for whom surgically induced menopause is associated with more severe symptoms and health risks than those observed in spontaneous gradual menopause.[89] For example, women who have had surgically induced menopause are shown to have significantly greater cognitive impairments than women who undergo non-surgical menopause.[90],[91] The earlier the surgical induction of menopause, the more rapid the cognitive decline, the higher the risk of dementia, and the closer to Alzheimer's disease the pathology.[92],[93] Induced menopause is associated with a higher risk for cardiovascular disease,[94],[95] slower gait speed,[96] decreased bone mineral density, and increased fracture risk[97] compared to natural spontaneous menopause.

Marmosets do not naturally undergo menopause



Photo credit: Carl Fox

Likely because of the lack of natural menopause in marmosets, their unhuman-like response to ovariectomy, and their inherent insensitivity to estrogen, generating the menopause symptoms that occur naturally in humans requires additional experimental manipulation in marmosets. For example, Lacreuse orally administers the drug letrozole, which in post-menopausal humans is known to cause hot flashes, joint pain, dizziness, nausea, weight gain, edema, diarrhea, cognitive difficulties, hypercholesterolemia, and extreme fatigue.[98],[99], [100] Presumably, if OVX marmosets dosed with letrozole were physiological similar to women in peri- or post-menopause, they would experience the vasomotor symptoms observed in those women. Not surprisingly, given the existing literature on and understanding of marmosets' unique endocrinology, this is not the case. Lacreuse still has to induce "hot flashes" in these marmosets using heating pads and thermal vests, and she is now inducing sleep fragmentation using thermal manipulations and frequent loud noises.

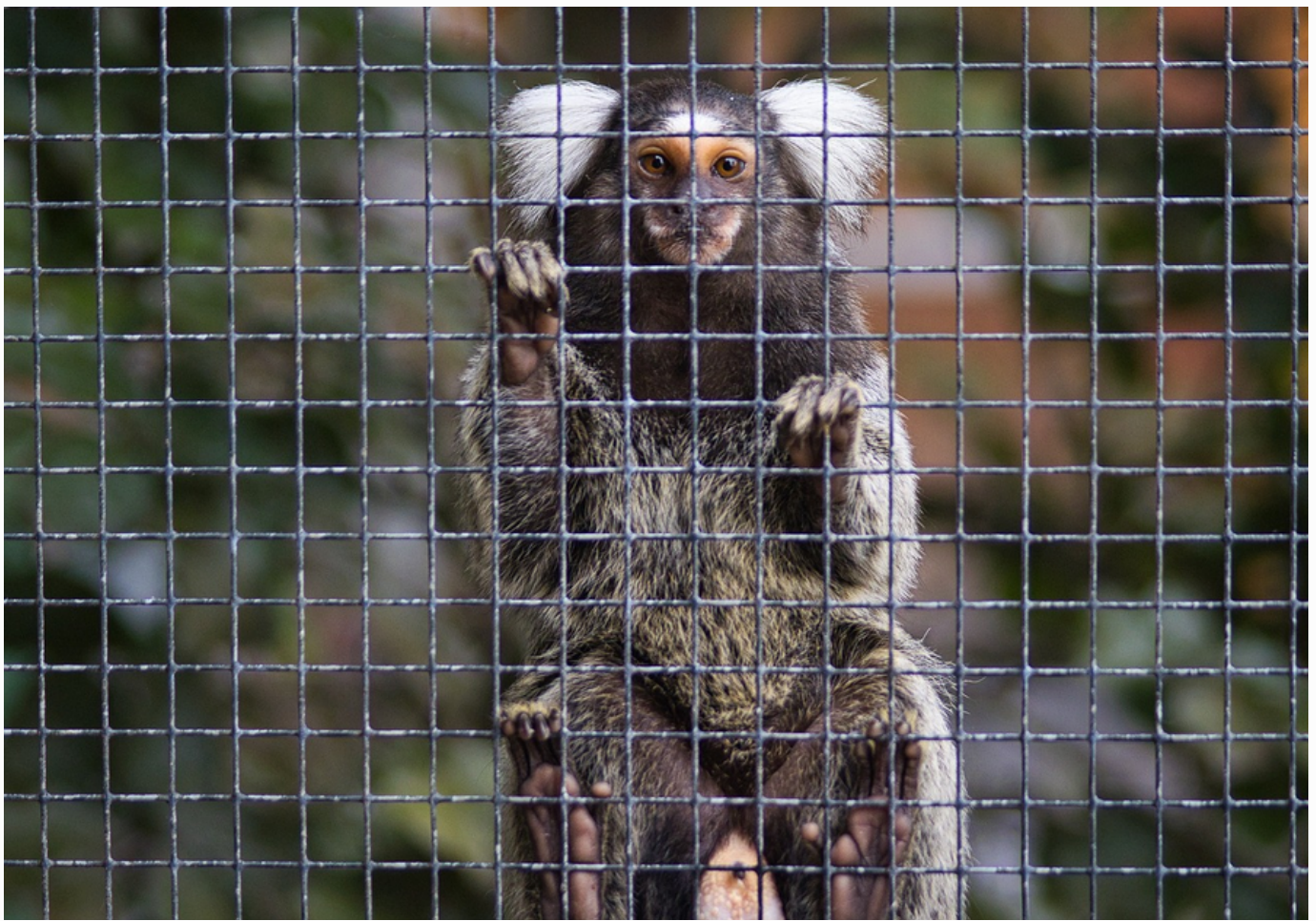


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Interestingly, none of Lacreuse's published studies to date compares menopause-like symptoms in OVX female marmosets to those in intact female marmosets. This seems a critical comparison to make when attempting to simulate human menopause via ovariectomy. The published data compare only OVX females to other OVX females on or off hormone replacement therapy,[101] intact males to intact females,[102] or OVX females to gonadectomized (GDX) males.[103],[104] In some instances, OVX marmosets whose baseline estrogen levels were considered too high were excluded from analysis,[105] or baseline estrogen level measurements themselves were thrown out and replaced with values the experimenters were comfortable with.[106]

In summary, surgically induced menopause is associated with increased symptomology in humans, but in hormone-insensitive marmosets, ovariectomies do not appear to create even the natural human menopause-like symptoms Lacreuse is interested in, such as hot flashes, cognitive impairments, and sleep disturbances. In other words, Lacreuse's own work does not indicate that marmosets exhibit human menopause-like symptoms even after surgical and pharmaceutical intervention, yet she continues to claim that these animals are a good model for studying human menopause.

OVX marmosets will not provide useful data on the effects of menopause on age-related changes in the brain and cognition in humans

Typically described as a type of “brain fog,” women in menopause describe particular difficulty with memory and lexical access, verbal fluency, as well as subtle difficulties with verbal and episodic memory, attention, and executive function.[107],[108] For most women, these cognitive symptoms are temporary and primarily associated with the perimenopausal stage, often dissipating after the menopausal transition is complete.[109],[110] This is important to note because there is no perimenopausal stage to evaluate in Lacreuse’s experiments. Marmosets’ ovarian-produced hormones are abruptly shut down surgically, preventing Lacreuse from studying the physiological mechanisms occurring during perimenopause that are likely involved in the cognitive symptoms women experience during this time.

In a recent review of the role of estrogen in cognitive aging, Russell *et al.* emphasized exactly the problem with using surgically induced menopause to model perimenopausal cognitive impairments:

[O]variectomy models the loss of E2 [estradiol], temporally this is markedly different from the changes that occur during natural menopause. In menopause, the less abrupt loss of E2 can produce cognitive deficits that continue to develop through later life. Furthermore, studies utilizing ovariectomy in young animals will produce a preclinical model that is inappropriate to interrogate the interaction between decreased estrogen, the aging brain, and cognitive dysfunction. The aging brain and associated cognitive dysfunction is developing concurrently with the menopausal transition in clinical populations. These age-related changes will not be occurring in the preclinical model.[111]

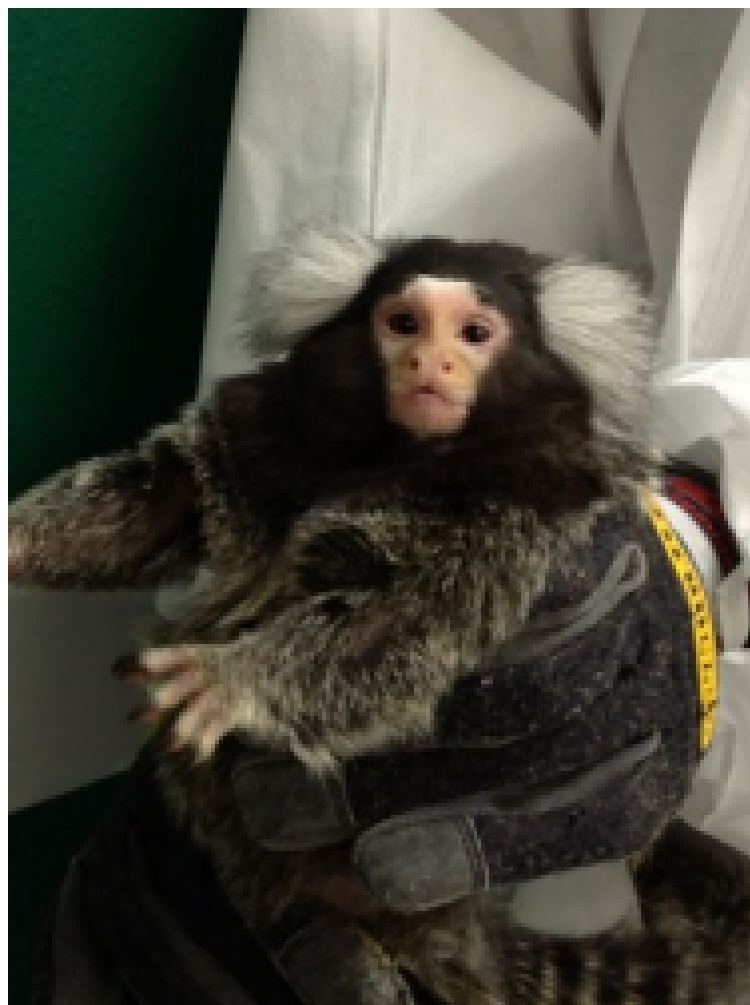


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In other words, in addition to the dramatically different effects experienced by marmosets with surgically induced menopause and women with induced or spontaneous menopause, the fact that Lacreuse's experiments forgo the entire "transitional" stage of menopause is particularly problematic for her cognitive assessments.

In humans, the effect of estrogen levels on menopause-related cognitive symptoms is very unclear—some studies show enhanced cognitive performance with increased plasma estradiol, whereas others do not. A large-scale study of more than 4,000 post-menopausal women failed to show any cognitive benefit from taking hormone replacement therapy.[112] Similarly, other contributing factors, such as body mass index (BMI) and overall health, are as predictive for cognitive difficulties as circulating estrogen levels.[113] Interestingly, some studies in humans indicate that menopausal women outperform age-matched men on memory tasks,[114] suggesting dropping estrogen levels may play less of a role in sex differences in cognitive decline than Lacreuse would have us believe. Most studies that find a cognitive benefit from hormone replacement therapy find them during the perimenopausal period, which Lacreuse cannot study in marmoset monkeys.



The fact that Lacreuse's experiments forgo the entire "transitional" stage of menopause is particularly problematic for her cognitive assessments.



Photos obtained by PETA via FOIA

Also critical to consider are the substantive differences between marmoset and human brain size, development, structure, and function. One of Lacreuse's purported goals is to investigate whether the hormonal changes that occur during menopause contribute to women's increased risk of neurodegenerative disease, with particular emphasis on Alzheimer's disease. While all primate brains share some degree of similarity, there are key differences in marmoset brain structure, function, and development that make any neurological findings from Lacreuse's studies highly unlikely to be applicable to humans. There are fundamental differences in gene expression and protein function in the brains of marmosets compared to humans.[115] There are differences in neurodevelopment[116], [117] and neuroanatomy,[118],[119] including in the timing, rate, and patterns of gray- and white-matter development across the animal's lifespan.[120-125] In marmosets, tau—a protein that makes up a major component of the neurofibrillary tangles in Alzheimer's disease—is actually much more similar to the protein found in rodents' brains than that found in humans.[126] Marmoset brains are also less sexually dimorphic than those of humans and other primates,[127] which will likely impact the applicability of any of Lacreuse's sex-related findings to humans. While marmosets exhibit some evidence of cognitive decline with age, they do not develop human-like Alzheimer's disease. In fact, Alzheimer's disease is a condition unique to humans that has never been successfully recapitulated in a non-human animal.[128-132]

Though Lacreuse cites the short life expectancy of marmosets to justify their use in aging experiments, their accelerated development makes them an inappropriate choice for studying the much more protracted and hormone-sensitive age-related changes in the human brain. In a recent (2019) review, biological anthropologist and Yerkes National Primate Research Center experimenter Todd Preuss writes:

The very small size of the marmoset brain makes it very likely that the functions of its cortical systems differ in important ways from those of larger-brained primates, if only because of the much more limited amount of neural machinery marmosets and other callitrichines have to work with. . . . Given the small size and rapid development of marmosets, it is tempting to view marmoset life history as a condensed version of that of longer-lived primates. Yet there is evidence primates vary in patterns of postnatal growth and development.....This difference, and the specializations of human development recognized by Bogin—namely, the addition of childhood and adolescent stages—imply differences in the hormonal control of development.[133]



Photo credit: Carl Fox

Humane, effective non-animal methods are available for the study of human menopause

The success rate for new treatments for age-related conditions in humans developed from preclinical animal experimentation is abysmal.[134-138] Lacreuse's ill-conceived marmoset experiments will be no exception. The complex interaction between age, hormones, genetics, diet, and pre-existing physical and mental health status on menopause and menopause-related symptoms in humans is far too complex to be "simulated" in a laboratory. It is absurd to try to do this in a species with such substantial differences in key physiological systems.

On the other hand, in vivo imaging of women at various stages of the menopausal transition, who are at risk for developing or living with various neurological disorders, [139],[140] postmortem analysis of brain tissues from patients,[141] and large-scale epidemiological studies[142],[143] are helping researchers understand the role of estrogen in various human diseases and behaviors.[144] Cutting-edge technology, including pluripotent stem cell models,[145],[146] three-dimensional cell-culture models,[147],[148] and organ-on-a-chip technologies[149],[150] are being used not only to serve as more accurate and detailed models of human neurodegenerative disease but also to test the effects of estrogen at the cellular level. [151],[152]



Photo credit: Wikimedia Commons

For example, the effects of estrogen on cognition,[152-155] brain structure and function,[156-159] mood,[160-162] hot flash frequency and severity,[163],[164] sleep disturbances,[165],[166] and risk for neurodegenerative diseases have all been successfully studied in human volunteers. Researchers studying human women have investigated whether hormone replacement therapy is associated with lower risk for the amyloid β -deposits associated with Alzheimer's disease,[167] and whether resveratrol, a phytoestrogen available in many foods, can ameliorate symptoms associated with menopause.[168],[169] A recent study of more than 2,500 post-menopausal women indicated that the degree of cognitive decline experienced was associated with corresponding depressive symptoms.[170] These studies with human volunteers are advancing our understanding of the complex interaction between genetics, [171] age of onset, baseline health,[172] and menopause symptomology and allowing researchers and physicians to calculate the risks and rewards of estrogen replacement for individual patients.[173-176]

These critical findings are not obtainable in animal models of menopause or human disease.

Conclusion

Marmoset monkeys have only recently come into favor as a model for human aging and age-related conditions and diseases. Chosen for their convenience, including their small size, fecundity, and short life expectancy, rather than their physiological proximity to humans, marmosets are being subjected to harmful experimental procedures in areas of research for which they are profoundly inappropriate. The evidence presented above clearly demonstrates that Lacreuse's experiments are an alarming example of this poorly thought-out research plan. It is abundantly clear that marmosets are not an appropriate model to advance our understanding of menopause, its associated symptoms in humans, or its potential role in neurodegenerative disease risk in women. The decision to choose a species that fares so terribly in a laboratory setting and does not experience a menopausal transition or its associated symptoms, is insensitive to extraneous hormone fluctuations, and does not develop Alzheimer's disease naturally to study how menopause and hormones influence the risk of neurodegenerative disease in humans is absurd. Worse, in their attempts to force marmosets to experience menopausal symptoms, the experimenters are conducting additional invasive procedures and inflicting increasingly greater harm on these vulnerable animals, all while moving further away from the phenomena that they are attempting to study. To spend taxpayer dollars on such ill-conceived experiments when there are non-animal alternatives is unnecessary and a flagrant misuse of the already sparse resources dedicated to women's health. Please discontinue your support of these valueless experiments on marmosets immediately.



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