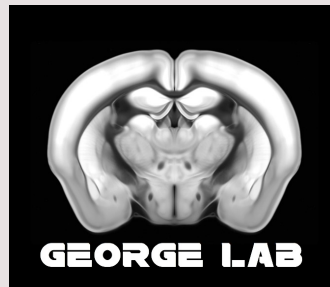


The history of sex differences in preclinical and clinical research

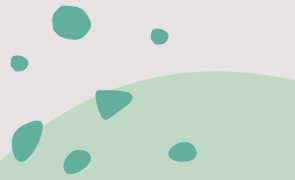
Elizabeth A. Sneddon-Yeppez, Ph.D.
Department of Psychiatry



My path to neuroscience



Systems Neuroscience and Behavior Lab



Today's agenda

Discuss the history of women in research

- Why were women excluded to begin with?
- Historical examples of how/why this is a problem

Focus on sex biases in neuroscience research

Progress that has been made

What's next?

Sex vs. gender

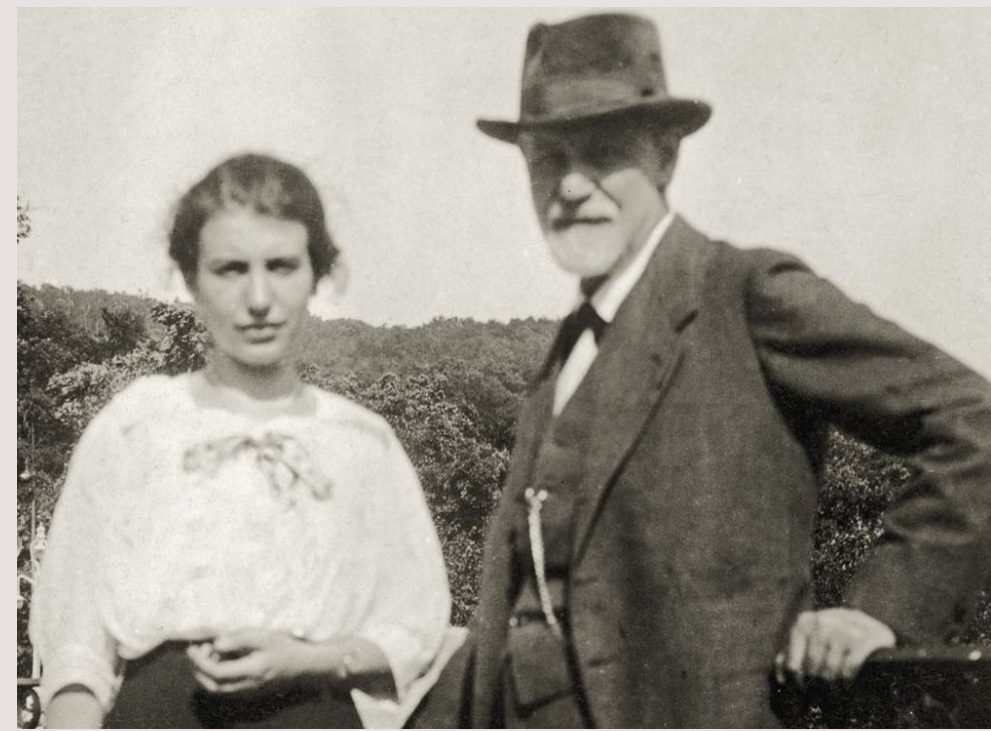
Sex

- A **biological category** based on reproductive, anatomical, and genetic characteristics, generally defined as male, female, and intersex.
- Sex is used when describing anatomical, chromosomal, hormonal, cellular, and basic biological phenomena.

Gender

- **Socially constructed** roles, behaviors, activities, and/or attributes that a given society associates with being a woman, man, girl, or boy, as well as relationships with each other.
- As a social construct, gender **varies from society to society** and **can change** over time.

Why do you think women have been understudied in neuroscience research?

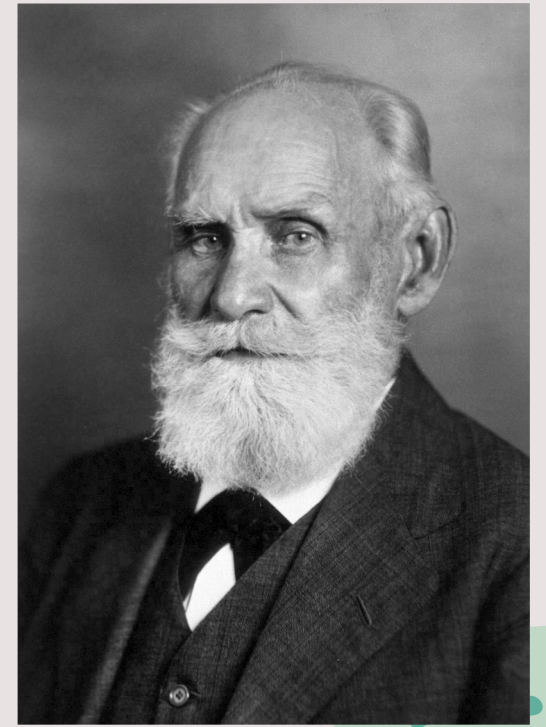


Anna Freud

Sigmund Freud



Burrhus Frederic Skinner



Ivan Pavlov

Why do you think women have been understudied in neuroscience research?



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Why do you think women have been understudied in neuroscience research?

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Neuroscientists

From sources across the web



Antonio Damasio



Adele Diamond



Joseph E. LeDoux



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Brenda Milner



Fred Gage



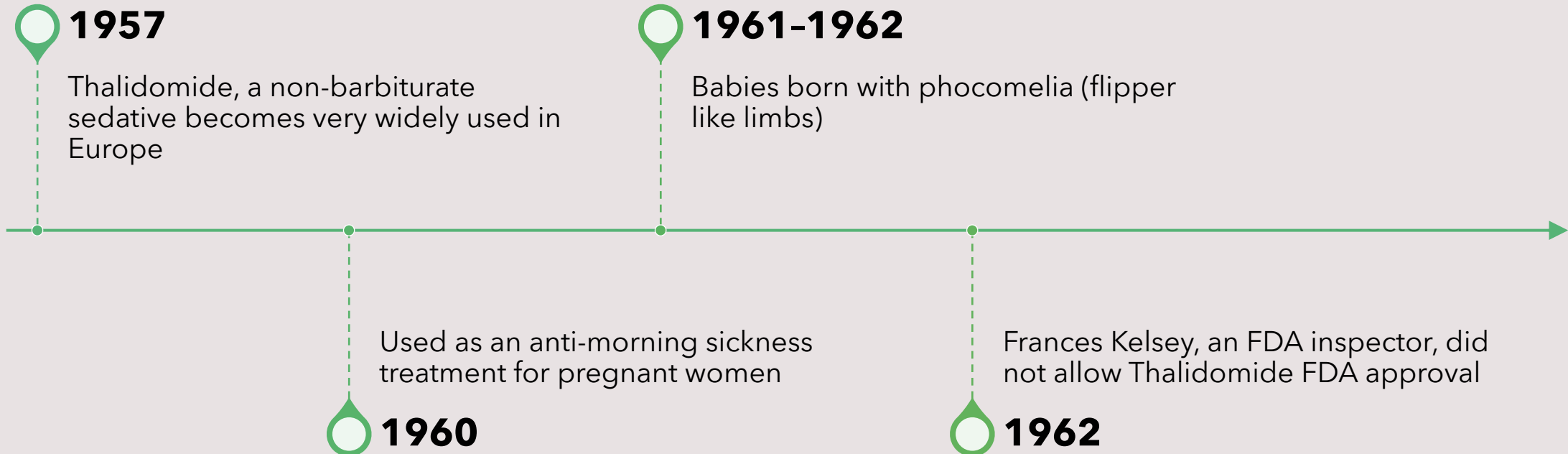
Suzana Herculano-Houzel



Michael Merzenich

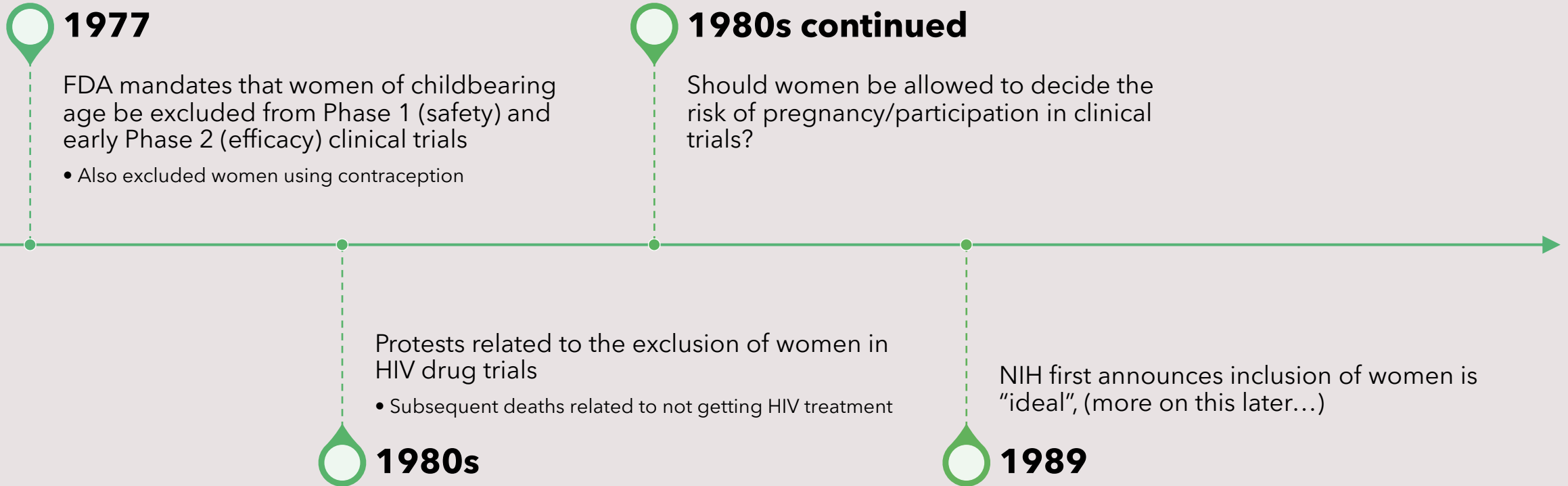


Beginning of Female Exclusion: Thalidomide



This reinforced concerns about use of women in clinical trials

Consequences of thalidomide



New Drug: Zolpidem Tartrate (Ambien)



2005-2011

Extended acting versions of the drug remarketed for insomnia

2013

FDA requires new prescribing practices related to Ambien

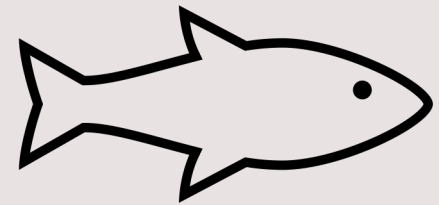
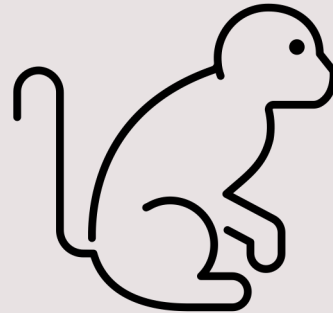
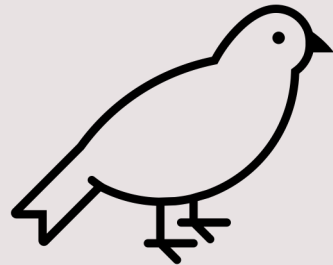
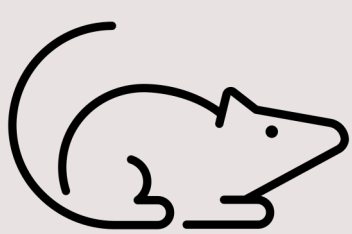
- ½ the dose required for men
- Starts a "trend," for more female inclusion in research

2011

Extended acting versions found to be substantially more potent in females the morning after taking the drug

- Strongly linked to increase car rate accidents

Let's shift our focus to preclinical research



Preclinical research: connects the basic science of disease with human medicine. During this stage, scientists develop model interventions to further understand the basis of a disease or disorder and find ways to treat it.

Main rationale for excluding women and nonhuman female subjects from research

Bias.

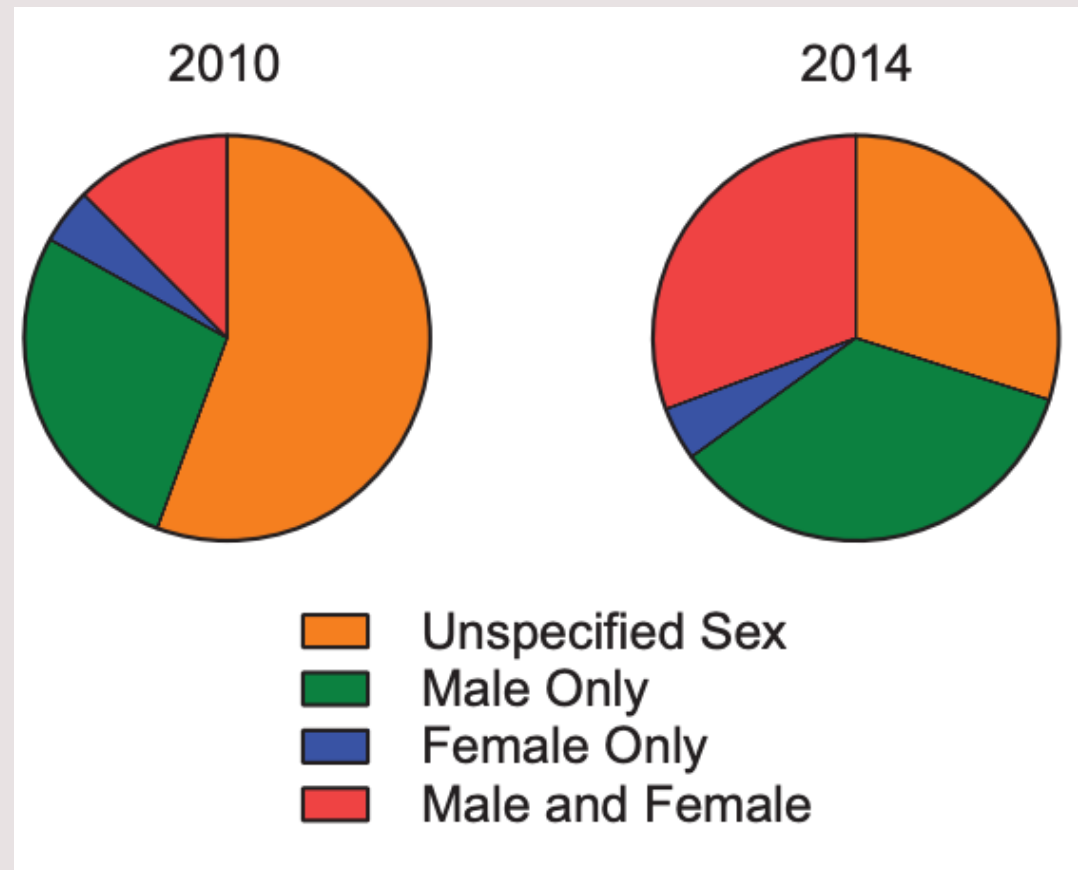
Women are constantly called “**hormonal**” or “**emotional**”.

Due to female hormones and the menstrual cycle, females have been categorized as more “**variable**” than males.

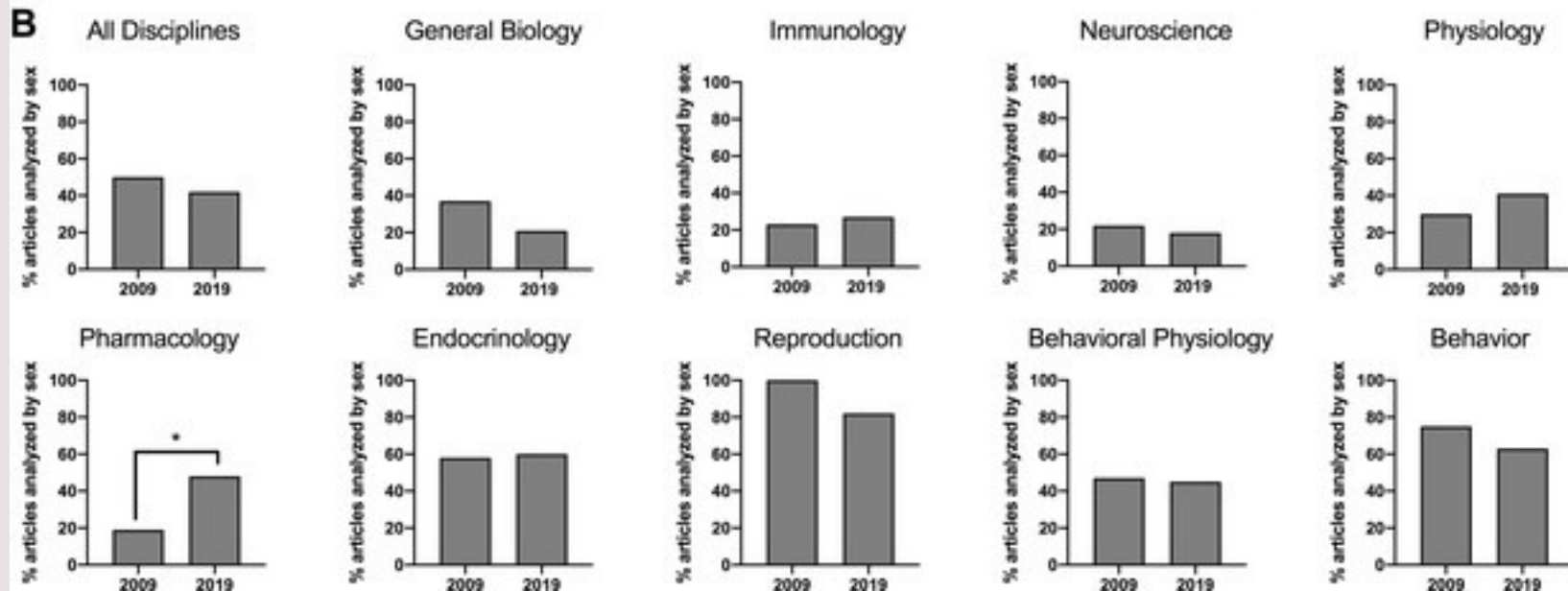
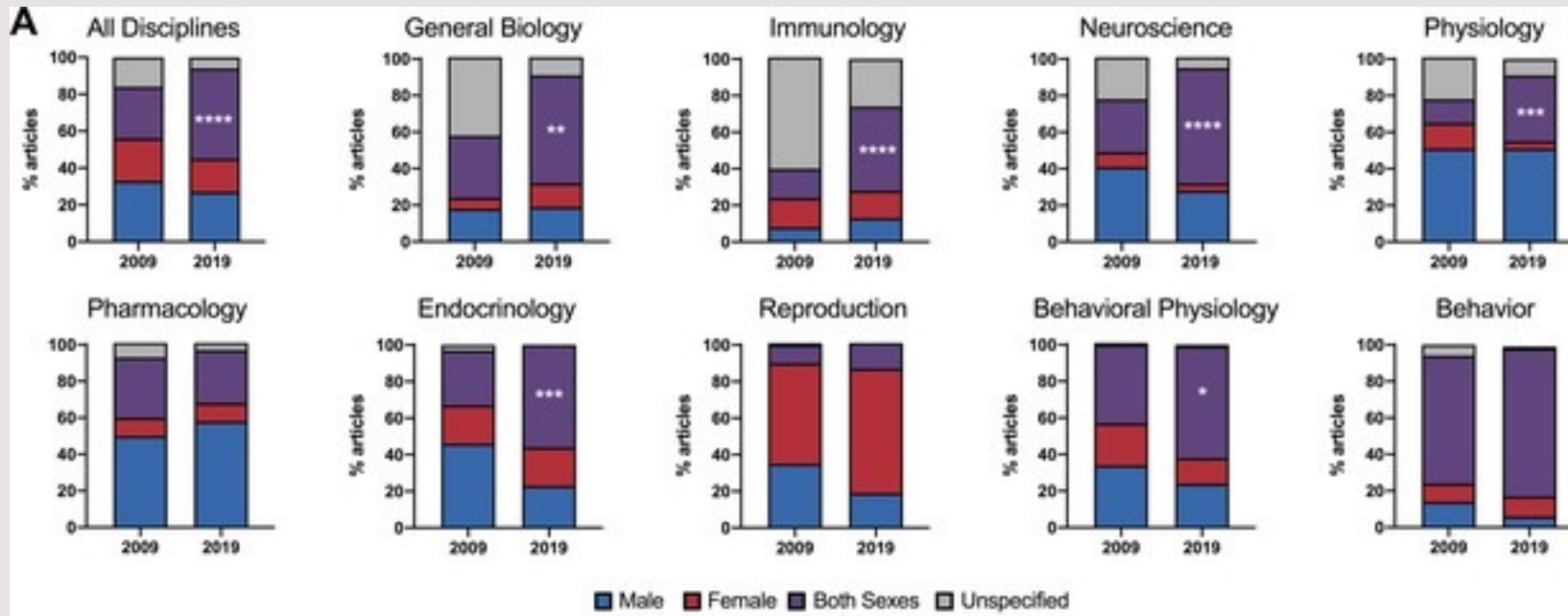
A recent meta-analysis showed that physiological, cellular, hormonal, and behavioral measures are **equally variable** in males and females with males sometimes showing more variability than females!

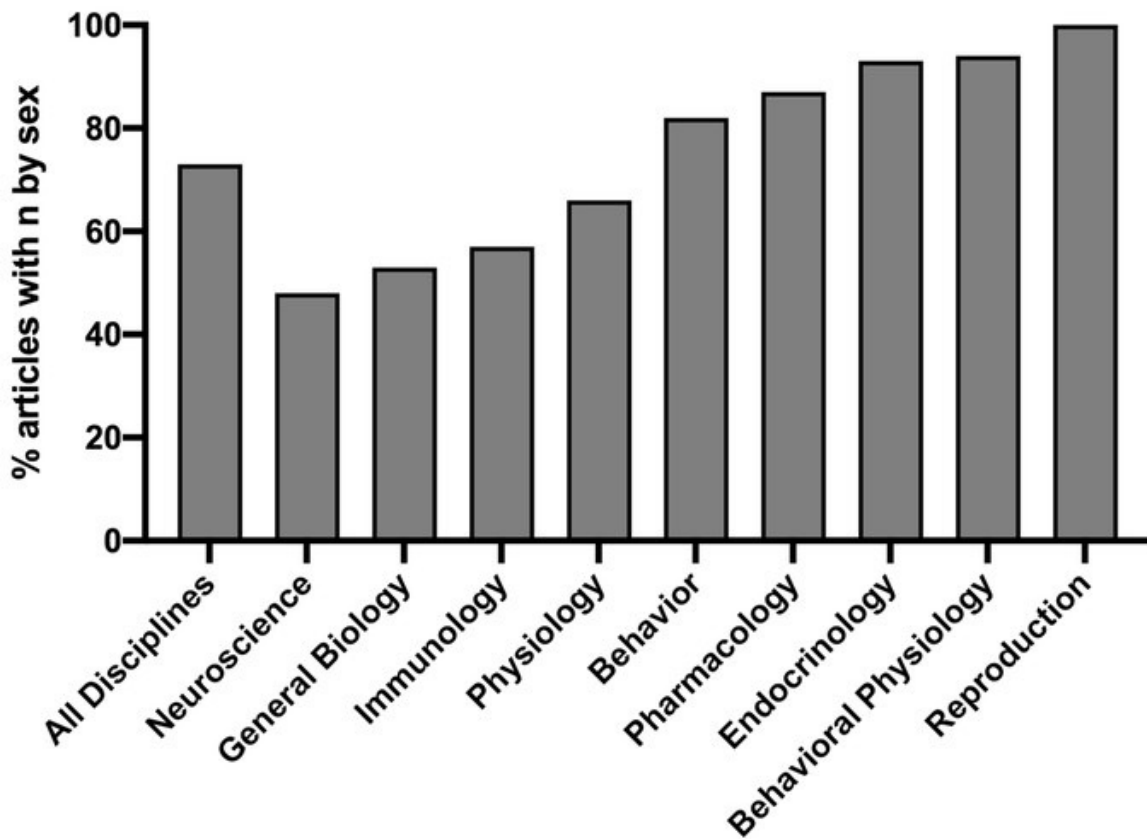
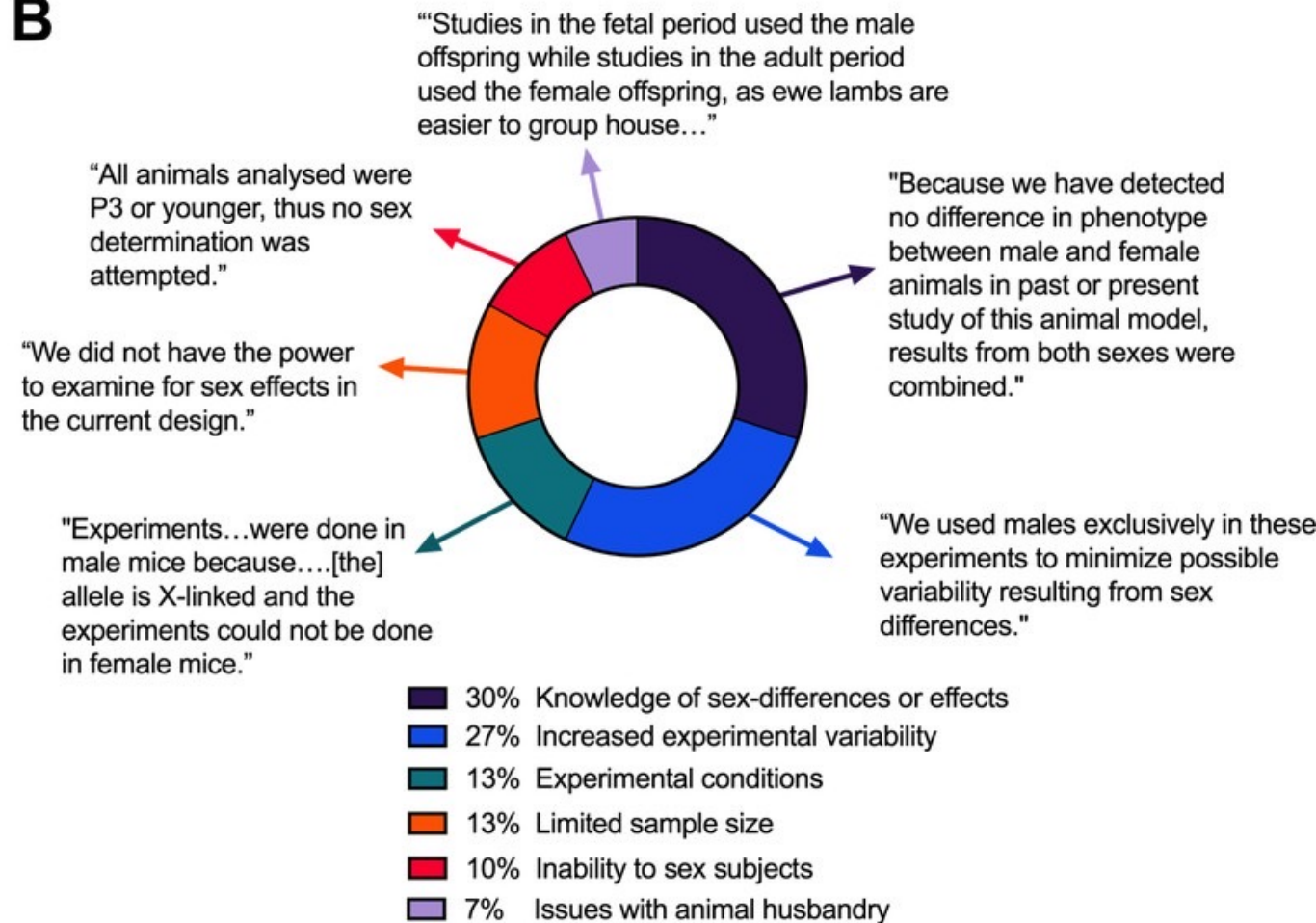


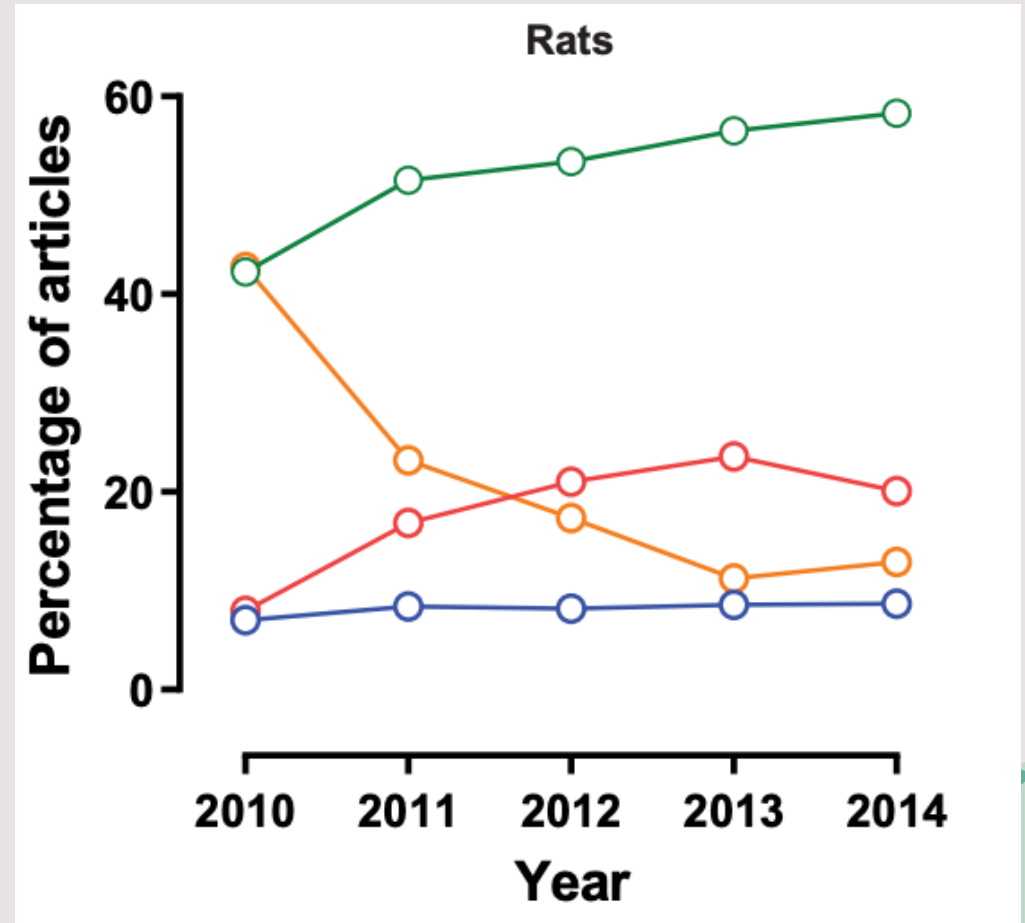
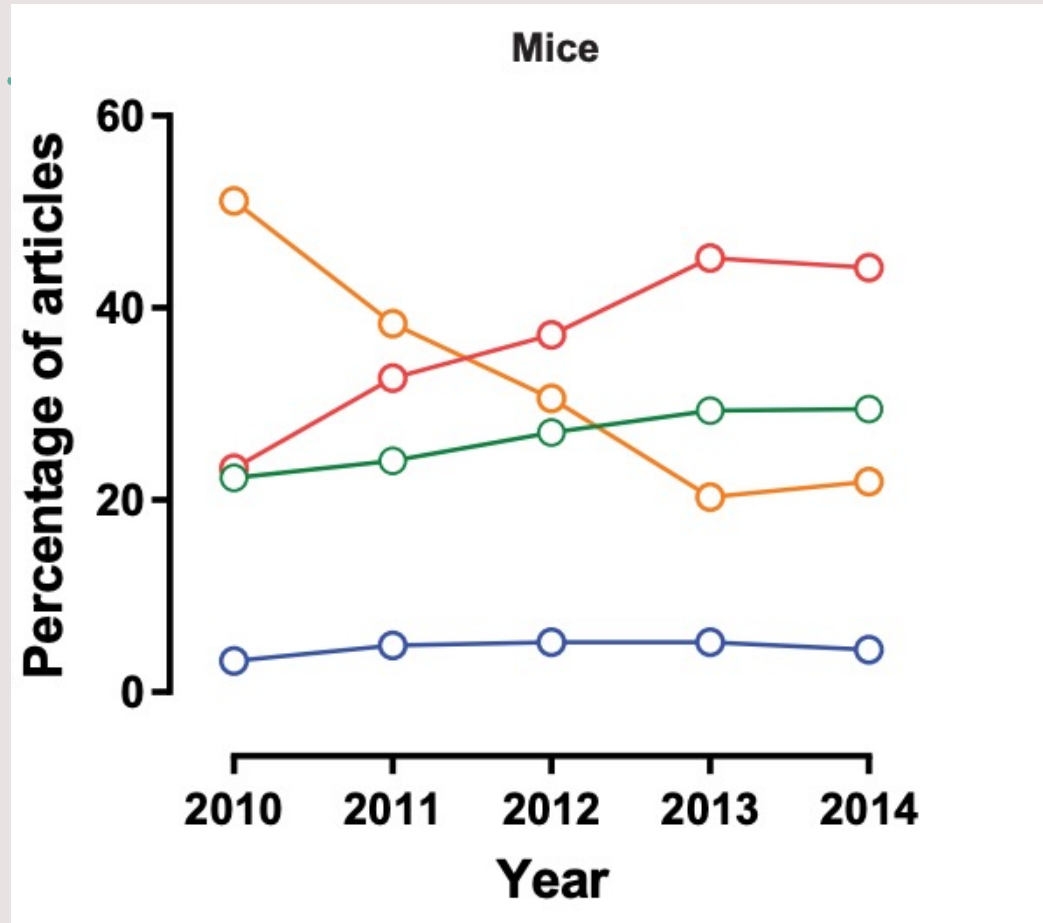
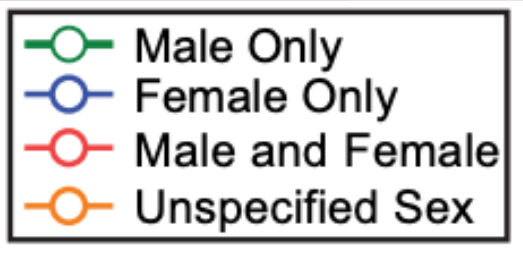
Female subjects are underrepresented in neuroscience research



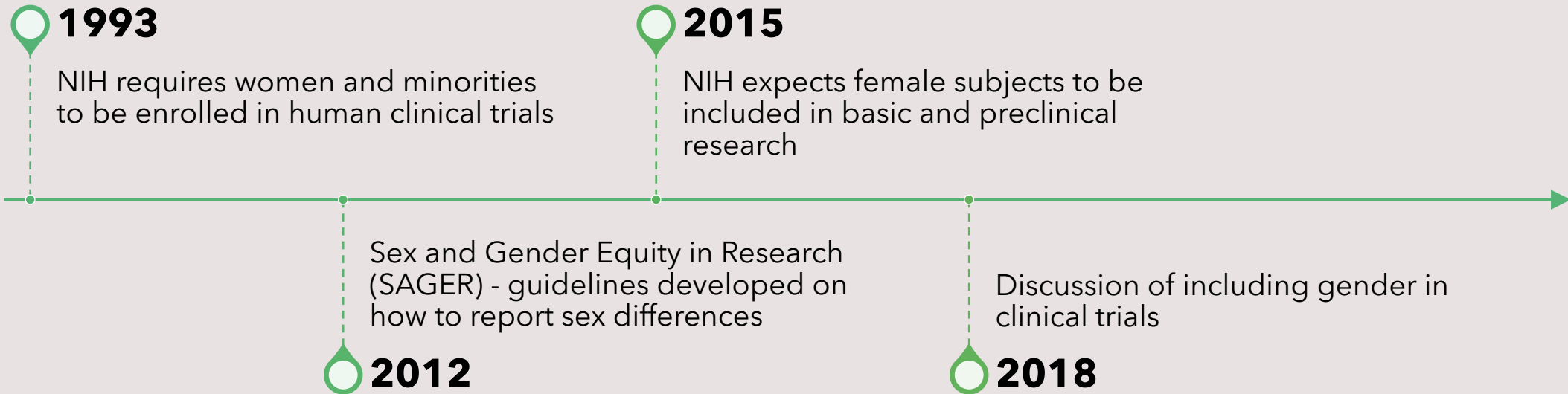
Changes in the trend



A**B**



Sex as a biological variable (SABV)



The 4 Cs of Studying Sex to Strengthen Science



Consider

Design studies that take sex into account, or explain why it isn't incorporated



Collect

Tabulate sex-based data



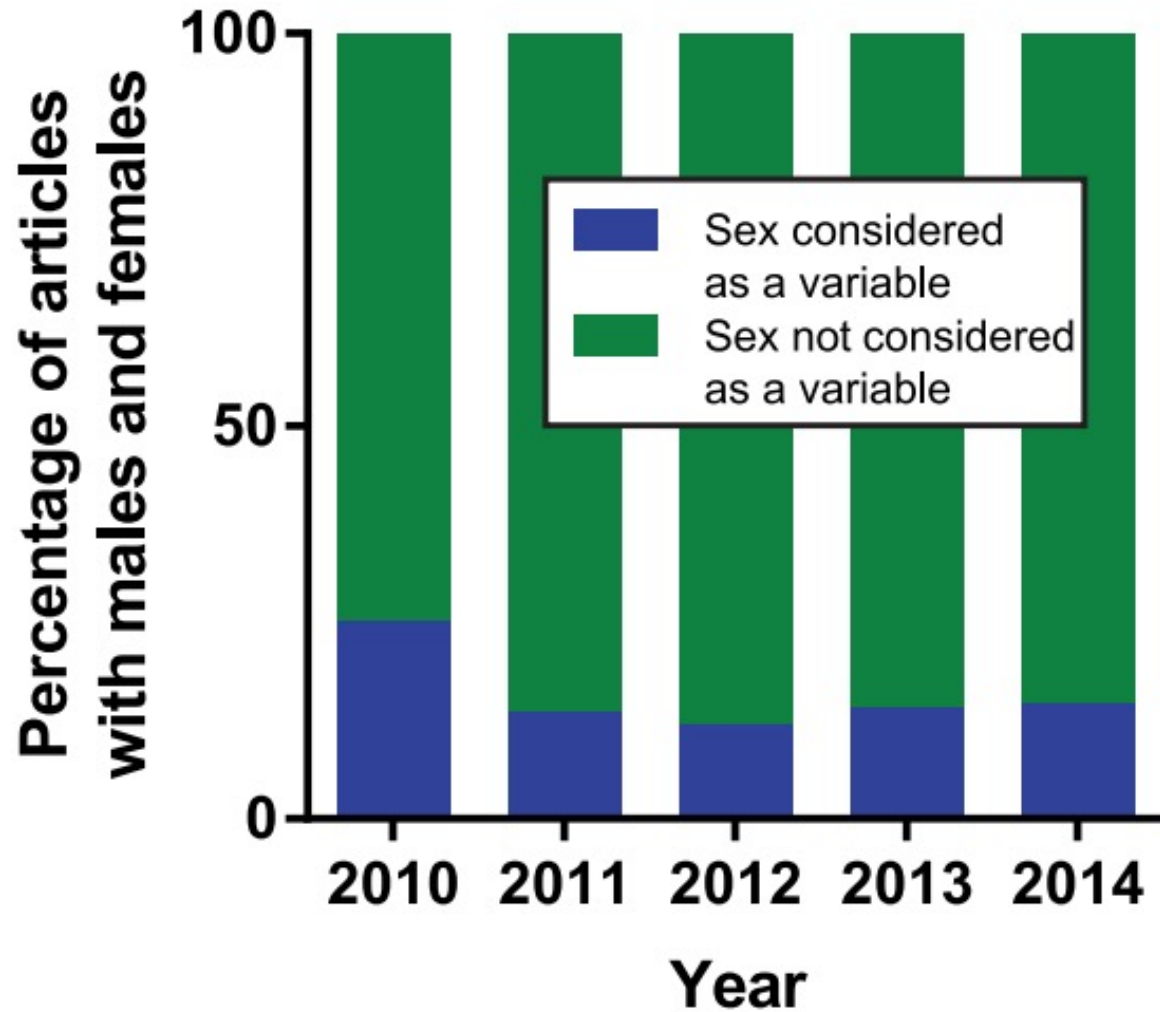
Characterize

Analyze sex-based data



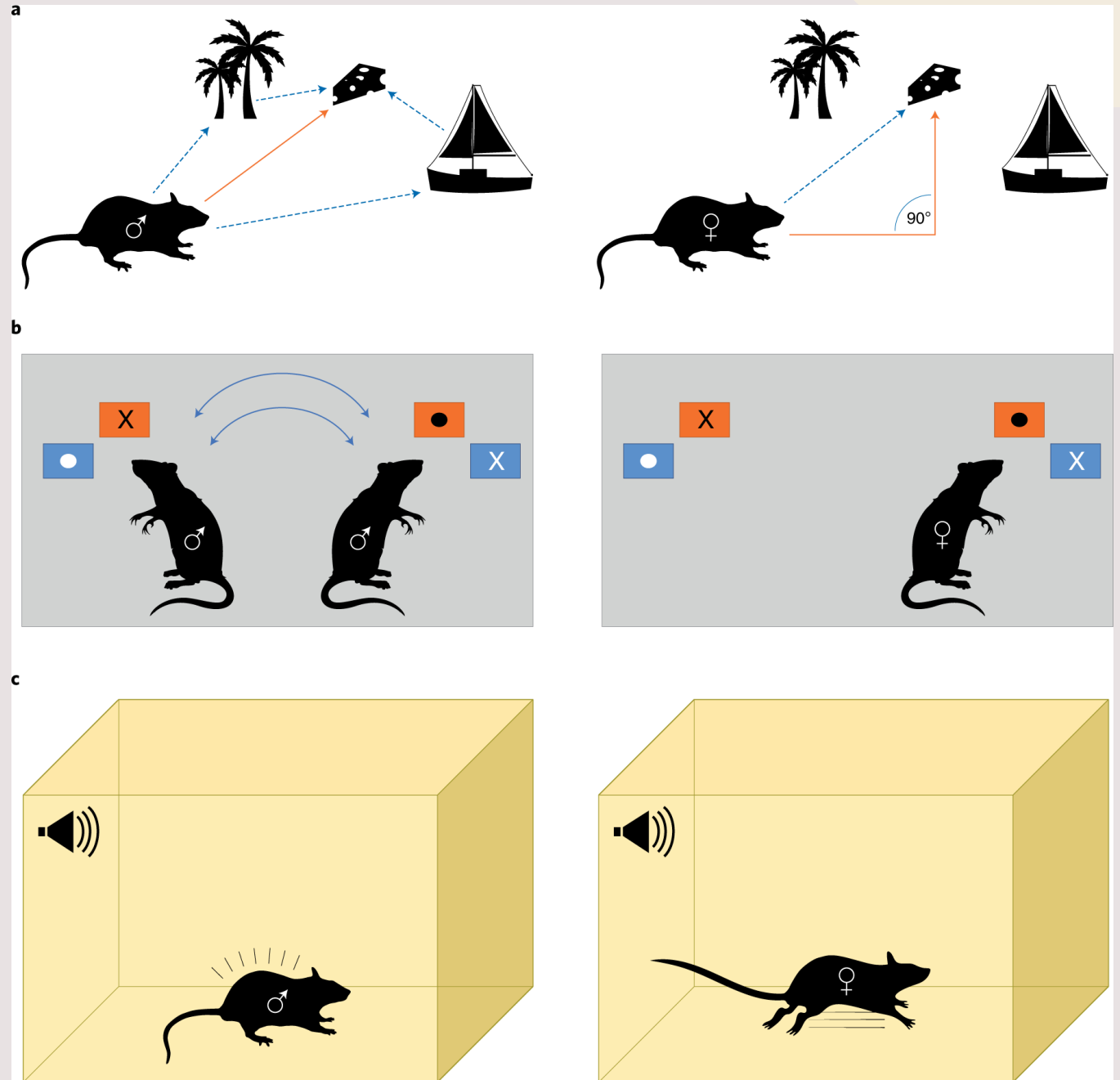
Communicate

Report and publish sex-based data

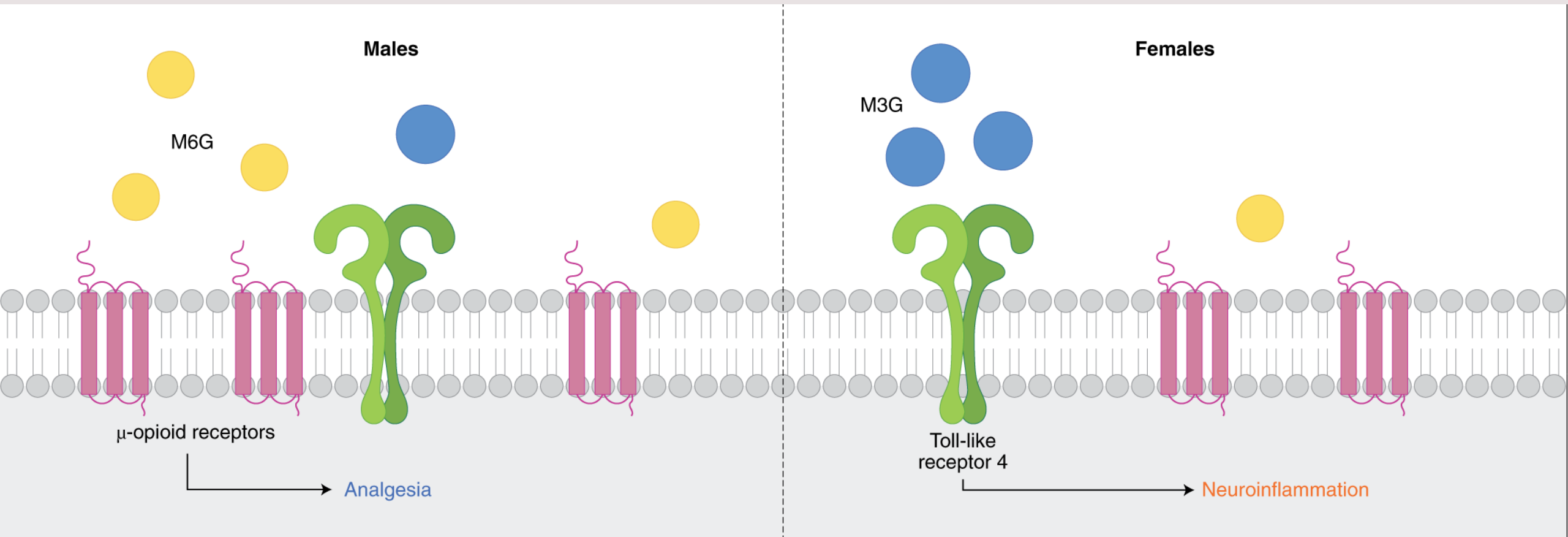


Why may it be an issue that sex is not considered as a variable?

What have we learned from including both sexes in preclinical studies?



What have we learned from including both sexes in studies?





World Health Organization

Women and health Key facts

Women live longer than men around the world
74.2 years
69.8 years
Global life expectancy

Every day, approximately **830** women die from preventable causes related to pregnancy and childbirth
Especially young adolescents and women older than **35**

Noncommunicable diseases are the **biggest killers** of women globally
Among women of all ages, groups and countries

Female health workers comprise **70%** of the health workforce worldwide
Yet half of women's contributions to global health are in the form of unpaid care

Cardiovascular disease is the **top cause** of women's death

Unipolar depression is **twice** as common in women

Globally, **1 in 3** women are likely to experience **physical or sexual violence**
This has a profound impact on women's physical, sexual, reproductive and mental health

Women represent a **majority** of people living with **HIV**
Particularly young women aged **15-24**

What progress has been made?



What still needs to be done?

Continue to research males and females in preclinical and clinical research!

Develop research questions focused on women's health.

Try to eliminate any biases when conducting research.

What still needs to be done?

Research focus: gender minorities

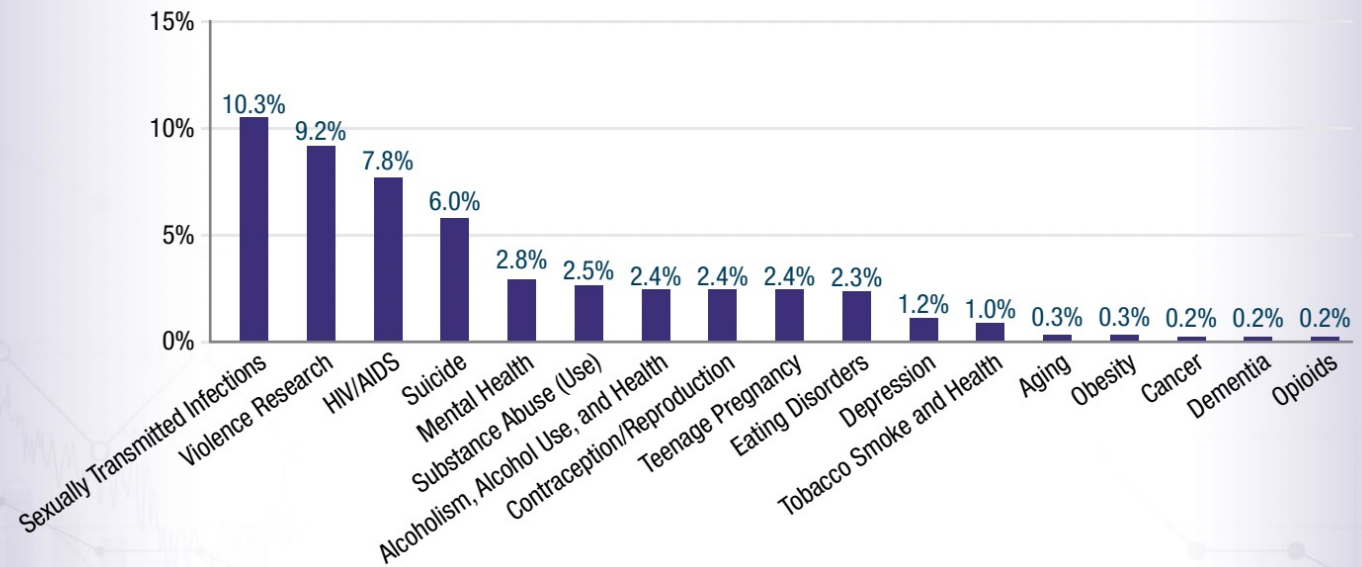
2010

NIH began to systematically examine the state of lesbian, gay, bisexual, and transgender (LGBT) health

NIH strategic plan on the health and wellbeing of sexual and gender minorities

2016 - 2020

Figure 7. FY 2020, SGM Projects as a Percentage of All NIH Projects, by Selected Research, Condition, and Disease Categories (N = 500)



Questions?

Contact info.:



easneddon@health.ucsd.edu



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