NEUROSCIENCE

His brain, her brain?

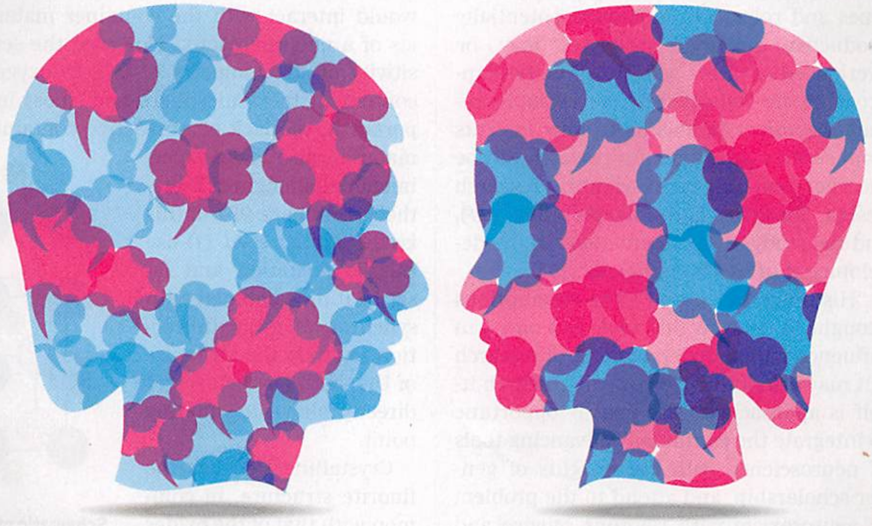
Research exploring sex differences in the human brain must overcome "neurosexist" interpretations

By **Cordelia Fine**

There is a long history of scientific inquiry about what role biological sex plays in differences between brain function in human males and females. Greater knowledge of the influence of biological sex on the human brain promises much-needed insights into brain function and especially dysfunctions that differentially affect the sexes (*1*). Certainly, advancing technologies and an increasing wealth of data (with more sophisticated analyses) should prompt robust future research—carefully conducted and well replicated—that can elucidate sex effects in the brain. However, this field of research has spurred an equally long history of debate as to whether inherent differences in brains of males and females predispose the sexes to stereotypical behaviors, or whether such claims reinforce and legitimate traditional gender stereotypes and roles in ways that are not scientifically justified—so-called neurosexism. Although this topic remains controversial, a commonly held belief is that the psyches of females and males are highly distinct. These differences are perceived as natural, fixed, and invariant across time and place (*2*), presumably due to unique female versus male brain circuitry that is largely fixed by a sexually differentiated genetic blueprint. A major challenge in the field is to crtically view previous experimental findings, as well as design future studies, outside the framework of this dichotomous model. Here, gender scholarship can hasten scientific progress by revealing the implicit assumptions that can give rise to inadvertent neurosexism.

Contemporary gender research, mainly across the disciplines of psychology and sociology, has overturned many old views of gendered behavior—traits (e.g., aggression), abilities (e.g., empathic accuracy), attitudes (e.g., sexual), interests (e.g., in science), and roles (e.g., caregiving)—as polarized and immutable (*3*). Rather, female-male distributions substantially overlap on the majority of gender characteristics (*3*, *4*). Moreover, these different feminine and masculine characteristics are only weakly intercorrelated, if at all. Thus, rather than falling neatly into masculine and feminine clusters, males and females possess a complex mosaic of both characteristics (*5*). And gendered behavior is mutable: Female-male differences and individual behavior vary across time, place, group, and context (*3*).

Also transformed is our understanding of brain development, with a growing appreciation that it is a dynamic developmental process that interacts with experience. Thus, nonhuman research demonstrates that biological sex interacts in complex ways with many other factors that influence brain development (*6*). For example, work on rats has shown that brief exposure to stress can reverse a sex difference in a hippocampal brain characteristic (the density of neuronal dendritic spines) in one region and create a sex difference in a second hippocampal region, while having no effect elsewhere (*7*). Sex influences therefore give rise not to distinctive male and female brains, but rather to unique mosaics of "male" and "female" characteristics (*6*).



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These research advances in behavior, neuroanatomy, and sexual differentiation of the brain indeed challenge "essentialist" assumptions of distinctive, fixed sex differences in behavior and brains. Nonetheless, research that examines the human brain can still sometimes be designed and reported in the context of this outdated model. For example, a recent study used diffusion tensor imaging technology to assess sex differences in neuronal connectivity in about 1000 children and young adults (*8*). The data indicated that on average there is greater connectivity within each hemisphere in males and greater connectivity between the hemispheres in females. Notably, the connectivity differences were of degree, not of kind. And in the larger sample from which the participants were a subset, the sexes showed highly similar performance on a battery of psychological measures (*9*). Yet the connectivity differences were speculated to underpin psychological differences between the sexes. Brain-behavior correlations were not explored, nor was theoretical or empirical attention given to the possible influence of gendered differences in male and female participants' past experiences (hobbies, sports participation, and subjects studied, for instance) on brain and behavior. Thus, neurosexist interpretation of research that is taken as scientific proof of "hardwired" sex differences can support old stereotypes, which can obscure the actual findings (*10*).

Research can be influenced by essentialist assumptions, albeit more implicitly. A review of all functional magnetic resonance imaging–based studies conducted in 2009 and 2010 on sex differences (*11*), for example, found that nearly three-quarters of the studies had fewer than 16 participants in each experimental cell. Although this would be unproblematic if brain function in females versus males were highly distinctive, the low reliability of small samples creates conditions for both false-negative and false-positive errors. More than two-thirds of the surveyed studies speculated on behavioral implications of reported sex differences in brain activations—most often either in the absence of data showing relevant behavioral differences between the sexes, or despite

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contradictory data. All the studies made single "snapshot" comparisons of the sexes, even though contemporary gender research indicates the importance of asking why, how, in whom, and when differences occur (*3*). Thus, the snapshot approach does not allow challenge to the notion of stable, universal sex differences in the brain.

Although the scientific and/or popular impact of most studies in this field may be modest, the overall outcome is a scientific literature that can be viewed as subtly biased toward a presentation of sex differences in the brain as more dichotomous, fixed, and functionally important in stereotype-consistent ways than is warranted (*11*). And while scientists have rallied to redress popular misrepresentations of their research (*12*), it is worth considering how research implicitly entrenched in essentialist assumptions may reinforce and legitimate traditional gender stereotypes and roles (*13*). Moreover, potentially productive research strategies may be overlooked or unnoticed. However, new approaches are indicated by, for example, recent recommendations as to how insights from contemporary gender research can be incorporated into neuroscientific research design, analysis, and interpretation (*14*), and the study of sex interactions in the development of psychopathology (*15*).

"His brain, her brain?" The assumptions brought to bear on this topic not only can influence public understanding of research but may also influence how the research itself is approached. The time is opportune to integrate the continually advancing tools of neuroscience with the insights of gender scholarship, and attend to the problem of neurosexism with rigorous science and discussion. ■

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NUCLEAR MATERIALS

Taking the measure of molten uranium oxide

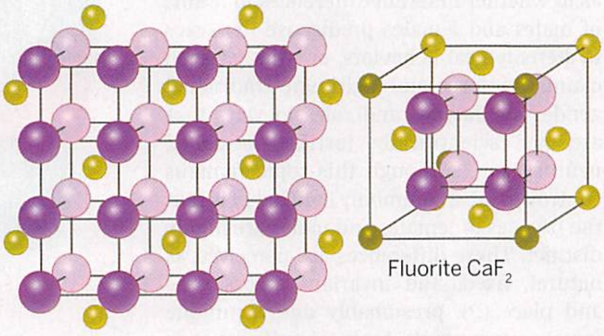
Levitated droplets of uranium oxide reveal a complex structure below and above the melting point

By **Alexandra Navrotsky**

Uranium dioxide (UO_2) occurs as the mineral uraninite and is the most common fuel in nuclear reactors. Its high melting point (near 3140 K) makes studying its properties near, at, and above this temperature difficult for both experimental and theoretical approaches, but understanding molten UO_2 is critical for understanding how the melt would interact with the container materials of a nuclear reactor. However, the sensitivity of stoichiometry of UO_2 to oxygen content in the atmosphere and, most importantly, the lack of unreactive container materials also make experiments challenging. Nonetheless, on page 984 of this issue, Skinner *et al.* (*1*) use sample levitation and laser heating combined with synchrotron x-ray diffraction to study the structure of UO_2 both just below and directly above its melting point.

Crystalline UO_2 has the fluorite structure, in common with that of the oxides of cerium, thorium, plutonium and, at high temperature, zirconium and hafnium (see the first figure). This cubic structure provides eightfold cation coordination (U^{4+}) and fourfold anion coordination (O^{2-}). There is only one type of cation site and one cation-anion bond length, but at temperatures near the melting point, many fluorite-type compounds undergo disordering in the anion sublattice in the solid state that can lead to high ionic conductivity, excess heat capacity, and changes in other properties.

Theory and experiment need to complement one another in benchmarking fundamental properties of refractory materials at high temperatures, but the number of physical observables that can be measured accurately above 2500 K is small. The properties of molten UO_2 and their relation to those of the solid are important for applications as well. Modeling of solid-liquid phase equilibria in UO_2-containing systems—for example, by standard CalPhaD formalisms (computer coupling of phase diagrams and thermochemistry)—requires knowledge of its melting thermodynamics and melt properties. The temperature dependence of density and heat capacity must also be estimated, both above and below the melting point (the latter in the supercooled liquid). Structural changes in the melt can profoundly affect these temperature-dependent properties.



Schematic of fluorite structure. UO_2 **and other actinide dioxides have the same structure as** CaF_2.

ILLUSTRATION: P. HUEY/*SCIENCE*

For predicting and understanding "fuel meltdown" and the formation of both small highly radioactive particles that could be easily transported in the atmosphere and corrosive bulk melts containing uranium (e.g., the Chernobyl "lavas") during a runaway loss-of-coolant nuclear accident (*2*, *3*), one must understand melt properties in multicomponent systems. Uranium oxide can mix in the molten state with several other components, including zirconium oxide from oxidized zircalloy cladding, iron oxide from steel, and calcium, aluminum, silicon, and other oxides from cement, concrete, and sand. The lowest-melting point mixtures (deep eutectics) and their crystallization, viscosity, rheology, thermal expansion, and thermal conductivity are all critically important parameters that are still poorly constrained. Melt structure is a major determinant of such properties. Understanding multicomponent systems starts

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