Le differenze di genere in psicogeriatria

Angelo Bianchetti
Many physicians currently in practice trained in the ‘70s and ‘80s, and at that time, women’s health was not on the agenda. A woman was viewed as just a little man with a uterus.
Lawrence Henry "Larry" Summers
(New Haven, 30 novembre 1954)
Segretario al Tesoro degli Stati Uniti per l'ultimo anno e mezzo della presidenza Clinton e rettore dell'Università Harvard dal 2001 al 2006.

Lawrence Summers suggested that innate differences in the build of the male and female brain might be one factor underlying the relative scarcity of women in science. (2005)

Lawrence Summers resigned yesterday as president of Harvard University after a relatively brief and turbulent tenure of five year (NYT, February 22, 2006)
International Society of Gender Medicine

The International Society of Gender Medicine (IGM) is an umbrella organisation for associations of gender medicine worldwide. It was founded during the 1st World Congress on Gender-Specific Medicine in Berlin 2006. IGM is an international, multidisciplinary, scientific organisation, bringing together experts on gender medicine for professional exchange and collaboration.

Aims:

To establish and promote gender medicine by

- Position papers and guidelines
- Distribution of results
- Organisation of congresses
- Implementation into medical education

During the 2nd International Congress of Gender Medicine 2007, in Vienna, Austria, 2nd - 3rd June, 2007, we had a chance to discuss the future structure, the organisation, and the preliminary board of the IGM.
Società Italiana per la Salute e la Medicina di Genere

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Università di Bari
Roma, April 24-26 2009
Salone delle Fontane

3rd World Congress on Gender-Specific Medicine and Ageing
Brain, Mind and the Gender Impact

DEADLINES

submission of symposia proposals
December 15th, 2008

abstract submission
January 15th, 2009

special price for registration fees
March 1st, 2009

Download here the Preliminary Program updated to September 18th, 2008

(pdf 585 kb)
The article summarized the current knowledge on the topic:

- different mating behaviours in male and female rats
- evidence indicating how sex hormones influence these behaviours
- only one brain region, the hypothalamus, known to be a crucial regulator of hormone action
- ‘sex differences in the brain’ came to refer exclusively to sex behaviours, sex hormones and the hypothalamus.
Sex and brain: some common misconceptions

- sex influences are small and unreliable
- average differences between the sexes result from a few extreme cases in a distribution
- the differences within a sex are much more substantial than those between the sexes (sex influences can therefore be dismissed as trivial)
- all sex differences, once established, can be completely explained by the action of sex hormones (oestrogen)
- if no sex difference exists in a particular behaviour, it can be assumed that the neural substrates underlying that behaviour are identical for both sexes

Why sex matters for neuroscience

*Nature Reviews Neuroscience*, 2006
The authors examined the neural correlates of retrieval of emotional, autobiographical memories in men and women.

Memory performance did not differ between the sexes, nor did the degree of emotion induced by retrieval.

However, brain regions associated with retrieval in the two sexes differed significantly.

Isomorphic performance between the sexes does not necessitate isomorphic neural mechanisms.

Neural sex differences can, in some cases, create behavioural sex differences, but might, in other cases, prevent them (when, for instance, they would be maladaptive) by compensating for sex differences in other physiological conditions, such as sex hormone levels.

Box 2 | **Evolutionary explanations for sex differences in the brain**

What evolutionary explanations might be offered to account for widespread sex influences on brain function? In some cases, they seem obvious. For example, Kazuhito Tomizawa and his colleagues\textsuperscript{91} recently found that oxytocin, a hormone that is necessary for mammalian labour and lactation, improves both spatial memory and memory-related neurochemistry in the hippocampus of female mice that have had litters. The improved spatial memory has clear advantages, allowing a mother to wander further afield to find and recall locations of food and water and thereby better ensure the development and survival of her offspring.

In more general terms, the best developed idea concerns sexual selection, a concept originally proposed by Charles Darwin and developed more recently by David Geary\textsuperscript{92}. Sexual selection refers to the competition for mates that occurs both within and between sexes. Extensive evidence from many species makes it clear that males and females have evolved different behavioural strategies to optimize their chances of successful mating. Females tend to compete with other females more subtly, in ways that may depend more heavily on the processing of finer details; for example, of social cues. Such evolutionary accounts may help to explain the heightened recall of detailed information in females found in several studies of human memory so far\textsuperscript{93}.

Regardless of the ultimate evolutionary explanations, it seems incontrovertible that males and females evolved under some similar, and some very different pressures. We should therefore expect a priori that their brain organization will be both similar in some respects, and markedly different in others. This is precisely the situation suggested by the sex difference literature.
An illustration of sex differences in the size of various human brain regions.
Goldstein et al. measured the volume of 45 brain structures taken from MRI scans in a sample of male (n = 27) and female (n = 21) subjects. As shown here, significant differences between the sexes were detected in widespread brain regions. The authors also found that the size of the sex differences were related to the presence of sex steroid receptors in homologous brain regions during critical developmental periods, as determined in animal studies, suggesting that sex differences in the adult stem from sex hormone influences on brain development.

Neuroscientists are uncovering anatomical, chemical and functional differences between the brains of men and women.

These variations occur throughout the brain, in regions involved in language, memory, emotion, vision, hearing and navigation.

Researchers are working to determine how these sex-based variations relate to differences in male and female cognition and behavior. Their discoveries could point the way to sex-specific therapies for men and women with neurological conditions such as schizophrenia, depression, addiction and post-traumatic stress disorder.
The implications of sex influences for understanding and treating disease states are considerable. Many CNS-related disorders show sex differences in their incidence and/or nature. These diseases include, but are not limited to, Alzheimer’s disease (AD), PTSD and other anxiety disorders, schizophrenia, stroke, multiple sclerosis, autism, addiction, fibromyalgia, attention deficit disorder, irritable bowel syndrome, Tourette’s syndrome and eating disorders.

The mere existence of sex differences in the incidence and/or nature of a disorder requires us to examine sex influences in both our basic and clinical research to fully understand, and treat, the disorder.
Gender Differences in Dementia Risk Factors

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ABSTRACT

Background: With the aging of the population, dementia has become an important health concern in most countries. There is a growing body of literature on the importance of cardiovascular risk factors in the development of Alzheimer’s disease (AD), vascular dementia, and mixed dementia (AD with cerebrovascular disease).

Objective: This article reviews the role of major risk factors in dementia between both sexes.

Methods: The MEDLINE, PubMed, and HealthSTAR databases were searched between 1966 and January 2007 for English-language articles on the risk factors for dementia.

Results: The distribution and prevalence of major risk factors between the sexes and age groups are varied. Female sex has been associated with increased risk of the development of AD. In women aged >75 years, rates of hypertension, hyperlipidemia, and diabetes are higher than in similarly aged men. Apolipoprotein E ε 4 genotype status appears to have a greater deleterious effect on gross hippocampal pathology and memory performance in women compared with men. Midlife hypertension and hypercholesterolemia in both sexes predict a higher risk of developing AD in later life. Diabetes is increasing in frequency to a greater extent in women than in men, and is associated with a substantial risk for cognitive impairment. Dementia in women (probably) and in men (possibly) is influenced by obesity in the middle of life.

Conclusions: It remains critical that large prospective clinical trials be designed to assess the effect of optimum management of vascular risk factors on cognitive functioning and dementia as the primary outcome, and include women and men in numbers adequate for assessment of gender effects.

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KCI License Number: R0783413286
Genetic variation in PCDH11X is associated with susceptibility to late-onset Alzheimer's disease. Carrasquillo MM et al.

By analyzing late-onset Alzheimer's disease (LOAD) in a genome-wide association study (313,504 SNPs, three series, 844 cases and 1,255 controls) and evaluating the 25 SNPs with the most significant allelic association in four additional series (1,547 cases and 1,209 controls), we identified a SNP (rs5984894) on Xq21.3 in PCDH11X that is strongly associated with LOAD in individuals of European descent from the United States.

Analysis of rs5984894 by multivariable logistic regression adjusted for sex gave global P values of $5.7 \times 10^{-5}$ in stage 1, $4.8 \times 10^{-6}$ in stage 2 and $3.9 \times 10^{-12}$ in the combined data.

Odds ratios were 1.75 (95% CI = 1.42-2.16) for female homozygotes ($P = 2.0 \times 10^{-7}$) and 1.26 (95% CI = 1.05-1.51) for female heterozygotes ($P = 0.01$) compared to female noncarriers. For male hemizygotes ($P = 0.07$) compared to male noncarriers, the odds ratio was 1.18 (95% CI = 0.99-1.41).
Sex Differences in the Clinical Manifestations of Alzheimer Disease Pathology

Lisa L. Barnes, PhD; Robert S. Wilson, PhD; Julia L. Bienias, ScD; Julie A. Schneider, MD; Denis A. Evans, MD; David A. Bennett, MD

Context: Sex differences in risk of clinically diagnosed Alzheimer disease (AD) have been studied extensively, but little is known about the relation of the pathologic indices of AD to the clinical manifestations of the disease in men compared with women.

Objective: To test whether the relation of AD pathology to the clinical manifestations of the disease differs in men and women.

Design: Longitudinal, clinicopathologic cohort study.

Participants and Setting: Analyses were conducted on 141 older Catholic clergy members who underwent detailed annual clinical evaluations and brain autopsy at death. The number of neuritic plaques, diffuse plaques, and neurofibrillary tangles in a 1-mm² area sampled from 4 cortical regions was counted, and a global measure of AD pathology (range, 0-2.98 U) and specific measures of each pathology were derived.

Main Outcome Measures: Clinical diagnosis of probable AD and level of global cognitive function at the last evaluation before death.

Results: Women had more global AD pathology than did men ($P = .04$), due primarily to more neurofibrillary tangles ($P = .02$). At the last evaluation before death, 57 persons met clinical criteria for probable AD (34 [60%] of them women). In logistic regression models, sex was not related to odds of clinical AD (odds ratio [OR], 1.35; 95% confidence interval [CI], 0.56-3.25), but the relation of global AD pathology to clinical diagnosis differed for men and women. Each additional unit of AD pathology was associated with a nearly 3-fold increase in the odds of clinical AD in men (OR, 2.82; 95% CI, 1.03-7.65) compared with a more than 20-fold increase in the odds of clinical AD in women (OR, 22.67; 95% CI, 5.11-100.53). Results were unchanged after controlling for potential confounders or using level of cognition as the outcome.

Conclusion: These data suggest that AD pathology is more likely to be clinically expressed as dementia in women than in men.

Arch Gen Psychiatry. 2005;62:685-691
Figure 1. Probability of clinically diagnosed Alzheimer disease (AD) proximate to death as a function of level of global AD pathology (A), neuritic plaques (B), diffuse plaques (C), and neurofibrillary tangles (D) in men (solid line) and women (dashed line). See the "Neuropathological Evaluation" subsection of the "Methods" section for an explanation of the scoring.

Figure 2. Level of global cognitive function proximate to death as a function of global Alzheimer disease (AD) pathology in men (solid line) and women (dashed line). See the "Neuropathological Evaluation" subsection of the "Methods" section for an explanation of the global AD pathology scoring. For global cognitive function, higher scores indicate better function.
Gender Differences in Caregiver Stressors, Social Resources, and Health: An Updated Meta-Analysis

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\textsuperscript{2}School of Medicine and Dentistry, University of Rochester, New York.

This meta-analysis integrates results from 229 studies on gender differences in caregiver psychological and physical health, caregiving stressors, and social resources. Contrary to common perceptions, gender differences in caregiving variables were small to very small. Women had higher levels of burden and depression, and lower levels of subjective well-being and physical health. They reported that their care recipient had more behavioral problems; they provided more caregiving hours, helped with more caregiving tasks, and assisted with more personal care. Women and men did not differ in the use of informal and formal support. Statistically controlling for gender differences in stressors and resources reduced the size of gender differences in depression and physical health to levels that have been observed in noncaregiving samples. The results support stress-and-coping theories on gender differences in caregiving.
Gender Differences in Depression and Response to Psychotropic Medication

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ABSTRACT

Background: In the United States, depression is approximately twice as common among women as among men, across all age groups.

Objective: This review examines gender differences in the epidemiology and clinical presentation of depression, and explores whether women respond differently than men to antidepressant medications.

Methods: This is a selective review focusing on current issues in the management of depression, with particular attention to gender differences in the epidemiology, diagnosis, and treatment of the disease.

Results: Women are more likely than men to have atypical symptoms of depression (eg, hypersomnia, hyperphagia), to have comorbid anxiety disorders, and to attempt suicide. Women are also more likely to have seasonal affective disorder. Mood and anxiety symptoms that seem to be related to the menstrual cycle do not often represent genuine premenstrual dysphoria, but when premenstrual dysphoric disorder does occur, its impact on quality of life is similar to that of major depressive disorder. There is ongoing controversy about whether men and women respond equally well to antidepressant medications, and preliminary evidence suggests that selective serotonin reuptake inhibitors (SSRIs) are more effective in the presence of estrogen. Depression affects about 10% of pregnant women. Antidepressant medication should be considered during pregnancy if depression is moderate or severe, or if withdrawal of maintenance medication is likely to result in recurrent depression. The potential benefits of using antidepressant medications in a pregnant or breastfeeding woman should be balanced against the potential risks to the newborn. Because of the risk of neonatal withdrawal syndrome, SSRIs should be used at the lowest effective dose during the third trimester of pregnancy and should be tapered before delivery.

Conclusions: Continuing research is needed to determine how gender influences the risk, clinical presentation, and response to treatment of depression. Exploration of sex differences in animals and humans should aid in efforts to treat depression as an organic disorder rather than a psychological maladaptation. (Gend Med. 2006;3:93–109) Copyright © 2006 Excerpta Medica, Inc.)