The politics of plasticity: Sex and gender in the 21st century brain
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Chapter five

Women’s mental health and the therapeutic promise of brain sex

‘There is no female mind. The brain is not an organ of sex. Might as well speak of a female liver’
(Gilman 1898, 149)

‘every cell has a sex’
(Wizemann & Pardue 2001, 4)

Introduction

Mental disorders are considered ‘the core health challenge of the 21st century’ (Wittchen et al. 2011, 670). Together with neurological diseases, they are estimated to comprise more than 10% of the global disease burden in terms of DALYs (Disability-Adjusted Life Years), a number that is only expected to increase in the near future. Besides causing considerable human suffering, these diseases pose an increasingly large financial burden: the global cost of mental health conditions was estimated at $2.5 trillion USD in 2010, with a projected cost of $6.0 trillion by 2030 (Bloom et al. 2011). Confronted with these numbers, it is no wonder that many speak of mental illnesses as a widespread epidemic (e.g. Angell 2011). Underdiagnosis represents part the problem: according to the WHO, ‘Less than half of those who meet diagnostic criteria for psychological disorders are identified by doctors. Patients, too, appear reluctant to seek professional help. Only 2 in every 5 people experiencing a mood, anxiety or substance use disorder seeking assistance in the year of the onset of the disorder’ (“Gender and Women’s Mental Health”).

At other moments, this epidemic is portrayed as a largely fabricated effect of over-diagnosing and over-medicating health practices promoted by psychiatrists and the pharmaceutical industry. For example, when the American Psychiatric Association announced

45. Data from 2013, via http://vizhub.healthdata.org/gbd-compare/. The DALY is a metric that represents years of life lost due to disease, and is calculated as the sum of life years lost due to premature mortality and life years lost due to disability (see “Metrics”).
its most recent edition (2013) of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), Frances (who chaired the DSM-IV Task Force) wrote that the,

DSM-IV was an unwitting contributor to three false positive “epidemics.” Its publication coincided with high rates of attention deficit hyperactivity disorder, autistic disorder, and childhood bipolar disorders. Other factors contributed to these epidemics, particularly the ubiquitous marketing efforts of drug companies directed at doctors and the general public. … The proposals contained in the first draft of DSM-V could potentially set off at least eight new false positive epidemics of psychiatric disorder. In their efforts to innovate, the working groups could expand the territory of mental disorder and thin the ranks of the normal. (2010, c1168)

Rather than posing a contradiction, professionals considered under-recognition and over-recognition of mental disorders two sides of the same problem (PLOS Medicine Editors 2013). Both concerns point to the necessity of a better understanding of the nature and impact of mental disorders. Despite decades of research, major techno-scientific advances in genetics and neurobiology, and the development of a vast pharmaceutical market, most disorders remain poorly understood. Heterogeneous patient groups, high rates of comorbidity, and multifactorial aetologies render the diagnostic landscapes of clinical psychology and psychiatry highly complex, and limit our ability to recognise and treat (let alone prevent) mental disorders.

One recent strategy to grasp this problem better is to conceptualise mental disorders explicitly as brain diseases. The definitions of the disorders listed in the DSM-5 and similar diagnostic handbooks have been based on symptomatology, allowing clinicians to make diagnoses without having to speculate about specific causes. Whilst these categories are reliable for diagnostic purposes, they have proven of very limited value when it comes to identifying biomarkers for disease and to predicting treatment outcomes (Charney et al. 2002). In what Walter (2013) has identified as ‘the third wave of biological psychiatry’ (2), researchers and clinicians invest in genetic and neuroscientific studies of mental health in order to remedy this problem. When the DSM-5 was developed, attempts were made to reflect the insights coming from these research areas better, but it proved too soon to do so (Walter 2013). In response, the US National Institute of Mental Health distanced itself from the DSM and launched the Research Domain Criteria (RDoC) project, which aimed to create a new classification system based on neuroscientific insights (Insel 2013). Instead of studying experiences of anxiety, for example, this new approach would study fear circuits in the brain. A number of practical and
philosophical problems confront such a neuroscientific approach to psychiatry, which are beyond the scope of this chapter (see Kanaan & McGuire 2011; Kirmayer & Crafa 2014; Walter 2013). Extending my previous examinations of sex and gender, in this chapter I am specifically interested in the convergence of two strategies: the ‘neurofication’ of mental disorders and the focus on sex and gender as determinants of health.

From the moment mental disorders were first conceptualised, differences between men and women in terms of prevalence, age of onset, symptomatology, progress, and prognosis have been noted. An oft-cited statistic, for example, apprises that autism diagnoses in boys outpace diagnoses in girls fourfold (Fombonne 2009). Some evidence suggests that autism is expressed differently in girls than in boys (Thompson, Caruso & Ellerbeck 2003). Depression, on the other hand, remains twice as common in women than men, and its symptomatology also appears to vary with sex/gender (Nolen-Hoeksema 1990; Seedat et al. 2009).

Explanations for such differences often seek to distinguish ‘artefactual’ factors from ‘real’ factors (e.g. Parker & Brotchie 2010). ‘Artefactual’ factors include the possibility that a clinician does not recognise autism in girls due to its strong association with boys, or the possibility that depressed women may be more willing to seek help for depression than men (Giarelli et al. 2010; Wilhelm & Parker 1994). ‘Real’ determinants include sociocultural roles and norms, psychological attributes, and biological factors, each of which can influence the development of pathology in sex/gender-specific ways. Even though models have been proposed for many disorders that attempt to integrate these different factors, like diathesis-stress models that consider the interaction of predispositional vulnerability with stressful experiences (e.g. Hyde, Mezulis & Abramson 2008), the different factors are often studied in isolation. In recent decades, biological factors have received the most interest. This is part of a broader movement that promotes the assessment of sex as a biological variable in medical and basic research in the interest of women’s health. This movement emerged in the 1990s, and has come to dominate the landscape of gender-sensitive healthcare (Eckman 1998; Epstein 2007; Richardson 2013).

In this chapter, I examine how this biologisation of the women’s health movement, in conjunction with the biologisation of mental disorders in general, has imbued brain organisation theory with a significant therapeutic promise. After discussing the emergence and implications of the sex-based biology movement in more detail, I will examine how brain sex is used to explain sex/gender differences in the prevalence, course, and symptomatology of mental disorders. I will do so by considering past and present definitions and investigations of schizophrenia and autism. My concern here is twofold. First, I aim to highlight how brain sex,
understood as the result of pre-natal hormones exposure, reifies (sex/gender differences in) mental disorders and obscures the fact that not only the biological but also the social aspects of sex/gender have played an intimate role in definitions and redefinitions of these conditions. As such, a purely brain-based, sex-based approach obscures crucial information needed to understand the emergence of mental disorders. My second concern is how the brain-based, sex-based approach to mental disorders legitimises and expands the authority of brain organisation theory. Both issues point to the need for generating embodied, developmental models that consider the entanglement of sex and gender. I will then expand my discussion by considering not just how brains and brain health should be conceptualised but also what modes of subjectivities the very preoccupation with brains—hardwired or plastic—gives rise to. Using Rabinow’s (1996) concept of ‘biosociality’, Woodward’s (1999) notion of ‘statistical panic’, and Dubriwny’s (2012) view of the ‘vulnerable empowered woman’, I will examine how brain sex and brain plasticity are mobilised by women’s mental health organisations and brain health organisations in order to address and activate women. Together, these considerations suggest that envisioning a different future for the women’s health movement is at once a political, ontological, and epistemological challenge.

Mainstreaming sex as a biological variable

Current efforts to understand the nature of mental disorders by focussing on sex differences in the brain are part of a more general movement that promotes sex-based biological research in the interest of women’s health. As documented by Eckman (1998) and Epstein (2007), this movement emerged in the 1990s after the Society for Women’s Health Research (SWHR) started to campaign against women’s exclusion from medical research in the US. At the time, women were effectively excluded from medical studies after the US Food and Drug Administration (FDA) banned women of childbearing age from clinical trials in 1977 to protected them and their future children from exposure to potentially harmful drugs. In 1985, the Task Force on Women’s Health—an arm of the US Public Health Service—concluded that the FDA’s regulation threatened women’s health rather than protecting it, since drugs were approved for general use without prior testing on women. Under the influence of the SWHR’s

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46. This rule was introduced in the wake of several cases in which foetuses were severely harmed by pharmaceutical drugs. Among the drugs implicated were thalidomide, a tranquiliser widely prescribed off-label to pregnant women for morning sickness, resulted in birth defects throughout the 1950s and early 1960s, and DES, a synthetic oestrogen prescribed against birth complications from the late 1930s onwards, caused vaginal cancer and reproductive complications in daughters.
advocacy, the National Institute of Health (NIH) founded its Office of Research on Women’s Health, and strengthened its policies to encourage researchers to include women and to analyse data by sex; the FDA reversed its guideline excluding women in 1993. Eckman (1998) detailed that these developments profoundly changed the landscape of women’s health advocacy, as the notion of women’s health went mainstream and was extended beyond strictly reproductive and obstetric issues. Sex was mobilised as a crucial consideration for all aspects of health and disease: ‘biological sex, now understood as residing throughout a woman’s body, has been constructed as the difference that most determines women’s health’ (141).

In 1996, the SWHR requested the Institute of Medicine (IOM) to fund a Committee on Understanding the Biology of Sex and Gender Differences, which could validate the necessity of advancing research on sex differences in health and disease, referred to by the organisation as ‘sex-based biology’. This resulted in the landmark publication Exploring the Biological Contributions to Human Health: Does Sex Matter? (Wizemann & Pardue 2001). Evaluating scientific knowledge about the impact of sex on health and disease, this report answers the rhetorical question in its title with a resounding ‘yes’: sex ‘matters in ways that we did not expect. Undoubtedly, it also matters in ways that we have not begun to imagine’ (x). The report recommends that sex must be studied ‘from womb to tomb’ (5) ‘in all areas and at all levels of biomedical and health-related research’ (xix), because ‘every cell has a sex’ (4). In order to study sex properly, the report states, it must be separated from gender. The following definitions of sex and gender are recommended:

In the study of human subjects, the term sex should be used as a classification, generally as male or female, according to the reproductive organs and functions that derive from the chromosomal complement.

In the study of human subjects, the term gender should be used to refer to a person’s self-representation as male or female, or how that person is responded to by social institutions on the basis of the individual’s gender presentation.

In most studies of nonhuman animals the term sex should be used. (8)

Interestingly, the report takes note of two dissenting committee members:

Although such definitions [of sex and gender] are helpful, two committee members argued that they imply that the idea of biological difference suggests a predominance of physiology, with a subsequent fine-tuning by environment. Moreover, the two committee
members were concerned that dividing biological and environmental events into separate spheres could make researchers less likely to ask solid mechanistic questions about, for example, how diet and mechanical stress affect bone development. (18)

The report advises in particular that research on sex differences in brain organisation and function are expanded, and foregrounds brain organisation theory as a useful framework for doing so. Again, the report mentions two committee members who raise concerns about the advocated research directions:

Two members of the committee argued that continuing to use the phrase *organizational effect* as an explanation [of the development of particular behaviours] could preclude experiments that might reveal the actual mechanisms by which hormones, genes, and a variety of postnatal experiences produce the sex and gender differences of interest. Two members of the committee believed that reliance on analyses that divide variance into main effects and smaller contributing effects sidetracks other biologically appropriate analysis, such as pursuing developmental understanding of the emergence of cognitive skills. It also does not enable researchers to see how experience and biology work together to produce difference. (95)

Instead of brain organization theory, the two members wish to advance a developmental systems approach which ‘examines the mutual construction of cognition by physiology and by experience during key periods of development’ (95), which reflects the same approach that I advocate in the beginning of this thesis.

Epstein (2007) writes that this IOM report ‘conferred crucial legitimacy’ on the movement promoting sex-based biology (240). Unfortunately, it seems that the concerns of the two critical committee members have made no lasting impression on this movement. The interaction of sex and gender is often paid lip service, but very rarely pursued as a starting point for research. Instead, dividing sex and gender is widely promoted as best-practice. For example, the US NIH Office for Research on Women’s Health offers an online infographic entitled ‘how SEX and GENDER influence health and disease’. At the top, it states ‘While sex and gender are distinct concepts, their influence is inextricably linked.’ Nevertheless, the poster offers examples neatly classified into sex and gender influences. Amongst the phenomena labelled

‘sex’ is the fact that ‘Women are twice as likely as men to experience depression, with some women experiencing mood symptoms related to hormone changes during puberty, pregnancy, and perimenopause’. A ‘gender’ dimension of depression, according to the infographic, is that ‘Women are more likely to admit to negative mood states and to seek treatment for mental health issues’. Similarly, the website of the Sex and Gender Women’s Health Collaborative, an organisation co-founded by the SWHR, offers an infographic entitled ‘What a difference an “X” makes’. It lists examples of sex differences in health outcomes, including the female preponderance in depression, to which it adds that ‘Estrogen receptors may be associated with higher risk for major depressive disorder’. Here, the association between women and depression is entirely defined in biological terms: it is the ‘difference an “X” makes’. As a final example, the Canadian Institute for Gender and Health, on its webpage titled ‘Shaping Science for a Healthier World’, emphasises that sex and gender are ‘interrelated and potentially inseparable’, yet it recommends a dichotomised understanding of sex and gender as the best working-hypothesis: ‘While putting simple boxes around something as complex and interconnected as sex and gender is not easy, doing so helps researchers to apply the two concepts consistently and distinguish between the many different mechanisms through which sex and gender shape our lives’ (Canada 2016).

As I have argued in Chapters 1 and 2, studying sex as an independent, dichotomous variable in isolation from gender is a strategy rooted in biological determinism and essentialism. Such a method belies the fact that differences between males and females are typically small, with extensive between-group overlap and within-group variation, and that sex/gender interacts with other group characteristics. Moreover, differences between males and females emerge from interactions of biological and environmental factors, which should be specified if we wish to understand these differences. As Springer, Mager Stellman and Jordan-Young (2012) have written, ‘sex is not a biological mechanism and its use as a proxy for other measures does little to further the understanding of health-related research questions’ (1818). So even though the sex-based biology movement is often represented as continuous with the feminist women’s health movement from the 1970s and 1980s, it in fact disregards central feminist critiques that have examined the production of biomedical knowledge and the links between postulated

48. Another example of sex offered by the infographic is that ‘Women have less bone tissue than men and experience a rapid phase of bone loss due to hormonal changes at menopause.’ One is immediately reminded of Anne Fausto-Sterling’s treatment of osteoporosis in The Bare Bones of Sex (2005), in which she demonstrates that bone density is the result of multiple, dynamically interacting systems of physical and cultural factors. Indeed, for Fausto-Sterling, ‘osteoporosis is a condition that reveals all of the problems of defining sex apart from gender’ (1499).
bodily differences and social inequalities (Dubriwny 2012; Eckman 1998; Epstein 2007; Richardson 2013). Its preoccupation with—indeed, its celebration of—sex as a binary, biological variable has eclipsed considerations of the social and material conditions that shape individual women’s lives in various ways, and with that the intersections or interdependencies of sex/gender, race/ethnicity, social class, age, and other pertinent categories. ‘Lost from this new body of women’s health’, Eckman (1998) writes, ‘is the understanding, hard fought for by the women’s health movement, that women’s bodies are also sites of societal struggles’ (152). Leaving behind issues surrounding agency and empowerment, the new movement delegates women to ‘a subject position that feminist critics of science have roundly critiqued: women as research object, albeit an object with more than reproductive organs’ (150). As a result, as Epstein (2007) writes, ‘where the earlier groups often sought to “demedicalize” women’s experiences, the new advocacy, often led by women inside medicine and science, seeks to extend scientific scrutiny of their bodies’ (247, citing Ruzek and Becker 1999).

Despite critical responses from feminist scholars, the sex-based biology movement has come to determine the agenda of contemporary gender-sensitive healthcare. One of its latest successes is the NIH policy, announced in 2014, that obliges all NIH-funded investigators to include both male and female animals or tissues in their research and to include sex as a biological variable in their analyses. This policy aims to remedy the fact that even though the male-centred bias in clinical trials has diminished, biological research on non-human animals has continued to rely heavily on male animals and tissues, even in studies potentially relevant for diseases that affect women disproportionally (Lebron-Milad & Milad 2012; Beery & Zucker 2011). In their review, Zucker and Beery (2011) found that the largest disparities are in the fields of neuroscience and pharmacology, with ratios of studies using only male animals versus only female animals of 5.5:1 and 5:1, respectively. Two contradictory reasons appear to underlie this bias. The first is that sex matters a great deal: female animals are believed to introduce undesirable variability into a sample due to the oestrous cycle, making research bothersome (but see Mogil & Chanda 2005; Prendergast, Onishi & Zucker 2014). The second is that sex does not matter at all: results obtained with male animals and tissues are extrapolated to females without additional research. Both premises are disputed by the new NIH policy, which ‘require[s] applicants to report their plans for the balance of male and female cells and animals in preclinical studies in all future applications, unless sex-specific inclusion is unwarranted, based on rigorously defined exceptions’ (Clayton & Collins 2014, 283). By making mainstream the consideration of sex as a biological variable, the NIH aims to ‘[support] science that meets the highest standards of rigour’ (283). One area expected to benefit from this
intervention is neurological disease, like schizophrenia. ‘It is well known that many neurological conditions are sexually dimorphic’, Clayton and Collins write (283), which is reason to study sex differences at the most basic biological levels.

Whilst including female animals and cells in research is certainly a welcome and important move, obliging researchers to report sex differences runs into the problems stated above. It promotes the dominant view that sex is a straightforward, dichotomous variable that is best understood by focussing on its main effects, rather than on its interactions in specific mechanisms. This makes it likely ‘that one mistake, treating males as the norm, will be replaced with another; namely, treating males and females as two distinct entities’ (Fine et al. 2014, paragraph 2), and that the contingency of sex differences on factors like strain, age, or prior experience will be disregarded (Joel & Yankelevitch-Yahav 2014). In addition, it is likely to further entrench the authority of controversial theories like brain organisation theory, thereby perpetuating the popular idea that ‘men are from Mars, women are from Venus’. It is to the application of brain organisation theory as a crucial lens to understanding (sex/gender differences in) mental health and disease to which I now turn.

The therapeutic promise of brain sex

Together with the increasing neurofication of mental disorders, the movement advancing sex as a key biological variable in all medical and premedical research imbues brain organisation theory with a significant therapeutic promise. Understanding ‘normal’ or healthy sex differences in the brain is strongly promoted as relevant, if not crucial, to clinical psychology and psychiatry (e.g. Cahill 2006; Ruigrok et al. 2014; McCarthy et al. 2012). Autism and schizophrenia are commonly referred to as conditions that would be particularly amenable to this therapeutic promise of brain organisation theory. Autism, with its conspicuous preponderance in males, is popularly understood as the result of having an extreme male brain (Baron-Cohen 2002; Baron-Cohen & Hammer 1997). Schizophrenia, characterised by more subtle and lesser-known sex differences, has been linked to a reversal of ‘normal’ sexual differentiation (Gur et al. 2004).

In what follows, I will consider how in each of these cases, brain sex is invoked as a heuristic device that helps researchers to reduce heterogeneity within patient populations and to identify potential risk factors or mechanisms. I will place these theories in a historical perspective, since looking at the way by which these two disorders have been (re)defined in gendered terms over time better equips analysing the merits of contemporary brain sex
perspectives. I will argue brain sex is not an appropriate perspective for the elucidation of etiological pathways. Using brain sex to explain sex/gender differences in autism and schizophrenia obscures the potentially crucial influence of social factors in the development of pathology. Instead, an embodied model of development that takes into account the dynamic interaction of sex and gender is better suited to provide insight into the origin of sex differences in mental disorders, and to further our understanding of these disorders in general.

Schizophrenia

Schizophrenia originates from dementia praecox, a condition first described by Emil Kraepelin (1856–1926). Kraepelin revolutionised modern psychiatry by replacing symptomatology-based classifications of mental disorders with his clinical nosology. For him, mental disorders were discrete, physical diseases, and each would have a specific, organic cause. To identify the nature of these diseases, he argued, psychiatrists had to look beyond superficial symptoms and focus on course and prognosis instead (1896). Different diseases could involve similar symptoms, but they would each have a distinctive pattern.

Kraepelin defined dementia praecox in contrast to manic-depressive psychosis (1899). The manic-depressive psychosis replaced the older concepts of mania and melancholia, which were, at the time, already associated with femininity (Showalter 1985). Manic-depressive psychosis was defined in primarily emotional terms, whereas dementia praecox was associated with disturbed reasoning and thinking (Busfield 2002). Kraepelin noted that manic-depressive disorders affected women predominantly, whilst dementia praecox was somewhat more general in men, especially in certain subtypes and at younger ages (1919). Whereas male patients were characterised by an overall early onset,

the tendency of the female sex to attacks of dementia praecox, which on the average is somewhat less, experiences a certain increase in three different periods of life, before the fifteenth, between the twenty-fifth and thirty-fifth, and after the fortieth year. There will certainly be a temptation here to think of sexual development which is earlier in the woman, of the time of the work of reproduction and of the years of involution. (1919, 231)

On what grounds were these sex differences established? Were they indeed the logical outcome of sex differences in sexual development, or did perceptions of masculinity and femininity also factor into the definition of patient populations? Historian of science Lunbeck (1994) notes that
the emphasis Kraepelin placed on patterns, rather than on symptoms per se, meant that the diagnostic choice between dementia praecox or manic-depressive psychosis was partly determined by the clinician’s affective response to a patient. Manic-depressive patients were described as eliciting a friendly, amused response, whereas the dementia praecox patient was experienced as strange and repelling. This, she argues, ‘suggests that psychiatrists perceived something essentially male or female in the diseases themselves’, which was something ‘encoded into the very categories that ordered psychiatrists’ observations’ in the first place (148).

49. When a difficult choice had to be made between one and the other diagnosis, Lunbeck shows, men were twice as likely to be diagnosed with dementia praecox than women. For women, the diagnosis could hinge on whether their symptoms were seen as erotic (psychosis) or simply foolish (dementia praecox). This circularity between diagnosis and perceptions of masculinity, femininity, and sexuality might very well have played a role in Kraepelin’s observation that patients with late-onset dementia praecox are predominantly women: as a woman approached an age at which she was not longer considered desirable by her doctors, her chances of being diagnosed with dementia praecox rather than manic-depression would rise considerably. 50

In addition to the differences in prevalence and onset, Kraepelin also noted a sex difference in the ‘psychic peculiarities’ that dementia praecox patients exhibit from childhood onwards: male patients with dementia praecox tended to have been shy, quiet, and withdrawn, whereas female patients with the same disorder were reported to have been more irritable, excited, nervous, and wilful (136). This purported tendency towards gender nonconformity observed in dementia praecox patients became a phenomenon of great interest to psychiatrists, because it seemed to give them a clue about the possible causes of the disease. Physicians speculated about the possible role of endocrine disturbances, pointing out abnormal physical characteristics observed in psychotic patients. When theorising about the role of hormones, ‘physicians liberally mixed their assumptions about sex roles with their observations about hormonally based sex characteristics’ in order to draw the connections between hormonal functions, gender role, and mental disorder (Hirshbein 2010, 164).

49. The symptoms of the manic patient symbolised ‘an unbounded, out-of-control femininity’ (149) marked by a periodicity that ‘mimicked in a more marked form the natural periodicity of women’ (150); in contrast, the signs of dementia praecox resonated as ‘the extreme, pathological manifestations of men’s naturally more stable nature’ (Lunbeck 1994, 150).

50. Lunbeck recounts the story of a forty-year-old woman, singing and playing naked in her room after losing her lover, who was not perceived by her psychiatrist as displaying the erotic behaviour associated with mania: ‘[her] nudity had failed to attract’ (149).
Meanwhile, psychoanalysts attempted to link the disease to psychosexual development, drawing connections with homosexuality (see Rosario 2002). Hirshbein (2010) notes that psychiatrists in the late nineteenth and early twentieth century did acknowledge the fact that the male and female role placed different demands on men and women. However, traditional gender roles were deemed natural, unchanging and healthy. Problems were thought to arise not from the roles themselves but from the failure to perform them through ‘neglect or through too enthusiastic adherence’ (159). Deviation from general health norms and deviation from gender norms were thus deeply enmeshed: gender nonconformity (whether cause by hormonal disruptions or not) was understood as both the cause and the sign of mental breakdown (162). Solutions, however, were not sought in social reform but in the restoration of femininity to women, and of masculinity to men.

The Swiss psychiatrist Eugen Bleuler redefined dementia praecox in 1911 as ‘schizophrenia’ to signify that the splitting of psychic functions—and not dementia—was the primary characteristic of the disorder. Bleuler understood schizophrenia as a heterogeneous group of clinical presentations rather than one specific syndrome, which vastly expanded the diagnosis (Heckers 2011). With this new, broad definition, schizophrenia became one of the most important disorders after World War I instead of hysteria (Libbrecht 1994). Mitchell (2001) suggests that the ‘the massification of male hysteria’ during the war played a crucial role in this transition. The idea that men were collectively becoming hysterical (i.e. feminine) was ‘simply unpalatable to the medical community—or, more generally, to standard images of “maleness”’ (127). In response, enthusiasm about the diagnosis deteriorated in favour of schizophrenia.

By absorbing hysteria, schizophrenia gradually attracted more female patients, until they outnumbered male patients by the 1960s (Mitchell 2001, 125; see also Chesler 1972). Mitchell (2001) writes that the “‘neutered’ schizophrenic’ thus replaced the female hysteric as the model patient of psychiatry (126). Showalter, however, has argued that schizophrenia carried gender-specific meaning despite its equal distribution across men and women, and that it was therefore specifically the schizophrenic woman who succeeded the hysteric (1985, 203). Even though female patients were not greater in number than male patients, they were much more frequently selected for ‘cures’ like electroshock and lobotomy, which were used from the

51. Despite being influenced by psychoanalysis, Bleuler (and his student Carl Jung) rejected the belief espoused by Sigmund Freud and Karl Abraham that there was a psychosexual aetiology to dementia praecox. Like Kraepelin, he believed that schizophrenia was an organic disease. However, he did insist on studying the psychodynamics of individual patient’s experiences (Maatz, Hoff & Angst 2015).
late 1930s onwards (205-210). These debilitating treatments, Showalter shows, were deemed particularly suitable for women because their mental capacities would not need to be fully functional in their role as housewives. Thus, the expected treatability of patients was directly linked to the gender role that was expected of them.\footnote{52. In addition to these medical links between disease, treatment and femininity, Showalter identifies a genre of English women’s writings, chronicling women’s experiences with madness and institutionalisation between 1920 and the early 1960s. In these writings, populated by female schizophrenic protagonists, ‘schizophrenia became the bitter metaphor through which English women defined their cultural situation’ (210).}

Another link between women and schizophrenia, which developed in US-American psychiatry from the 1930s onwards, is the schizophrenogenic mother, who induces schizophrenia in her child. As Hartwell (1996) notes, the popularity of this figure constitutes a most peculiar moment in the history of schizophrenia, one that marked a time during which the disorder was not viewed in strictly biochemical terms. She traces the origin of this notion back to post-World War I United States, where gender relations had been uprooted by the war and women’s right to vote, and concerns over women’s femininity and men’s masculinity were met by the psychoanalysis movement with reaffirmations of a natural gender order (276). After World War II, the notion of the schizophrenogenic mother was widely adopted by US-American psychiatrists, who had begun to turn away from the Kraepelinian disease model under the influence of psychoanalysis, redefining disease and health as a continuum rather than a dichotomy and emphasising environmental rather than biological causes of dysfunction (Decker 2007).\footnote{53. At that time, Bleuler’s work on schizophrenia was translated in English for the first time. His psychodynamic approach and expansive definition resonated with US-American psychiatrists. With the emergence of this more dynamic view of schizophrenia, the sharp divide between schizophrenia and health became less unbridgeable. It started to seem possible to prevent at least a number of subtypes of schizophrenia by implementing early interventions, and thereby to reduce the number of institutionalised patients. This motivated the search for the schizophrenogenic mother.}

Hartwell describes the devastating double bind that this concept placed women in: mothers harbouring unfulfilled ambitions were deemed pathogenic, but so were mothers realising their ambitions by working outside of the home (1996, 280). As such, not only women’s behaviour, but their very desires became a source of danger: the only way to be a good mother was to make marriage and homemaking one’s genuine ambition. Again, we see the failure to live up to gender roles, and not gender roles themselves, as the source of mental disorder – only in this context, women risk not (just) their own health but also that of their child.\footnote{54. Interestingly, the studies of schizophrenogenic mothers Hartwell describes all focus on male patients.}

By the late 1960’s, when schizophrenia was shown to have a genetic component, antipsychotic drugs were on the market, social attitudes towards women were changing under the influence of the Women’s Movement, and the antipsychiatry movement challenged the
legitimacy of diagnoses, the ‘schizophrenogenic mother concept was no longer politically or intellectually consistent with the spirit of the times’ (Hartwell 1996, 288). Psychiatry reaffirmed a neo-Kraepelinian, biological medical model, marginalising psychoanalysis (Decker 2007, 245). Then in the 1970s, CT (computer assisted tomography) and MRI became available, and the first modern brain scan studies of schizophrenic patients appeared (Johnstone et al. 1976; Smith et al. 1984). Studies of possible social causes of schizophrenia disappeared from the US-American literature, and previous evidence of social risk factors was forgotten or renounced (Jarvis 2007). When the DSM-III was published in 1980, it specified much narrower criteria for schizophrenia than the DSM-II had listed, and put a greater emphasis on affective disorder as a differential diagnosis (Compton & Guze 1995). As a result, about half the patients who met DSM-II criteria for schizophrenia no longer met the DSM-III criteria, a large proportion of whom now qualified for affective disorders (Silverstein et al. 1982). Most of these patients were women, and as a result the male predominance in schizophrenia increased markedly (Aleman, Kahn & Selten 2003; Lewine, Burbach & Meltzer 1984; Westermeyer and Harrow 1984).

From this point onwards, schizophrenia has been studied mainly from genetic and neurobiological perspectives. Whereas Plum had dubbed schizophrenia the ‘graveyard of neuropathologists’ in 1972, by 1990 psychiatrists remarked that ‘To have forgotten that schizophrenia is a brain disease will go down as one of the great aberrations of twentieth century medicine’ (Ron & Harvey 1990). By that time, some brain abnormalities in schizophrenic patients had been established, but patient populations were still heterogeneous, and etiological factors remained elusive. Subtypes were proposed but failed to yield reliable subpopulations. Faced with these difficulties, some researchers focussed their attention on sex differences as a possible way of reducing heterogeneity and of identifying mechanisms through which schizophrenia develops. The hypothetical relationship between brain sex and schizophrenia

55. The validity of schizophrenia as a real disease was further questioned when, in the early 1970s, the psychologist David Rosenhan had a number of fake patients admitted in psychiatric hospitals. These actors told hospital staff they heard voices, and were all diagnosed with schizophrenia. Once admitted, the actors started acting normal and professed their health, yet they were detained and medicated for several weeks until they were released with the diagnosis ‘schizophrenia in remission’ (Rosenhan 1973).

56. During the 1990s, the first sex-based comparisons of neurobiological abnormalities in schizophrenia started to emerge. One of the most reliable brain abnormalities found in schizophrenic patients was a lateral ventricular enlargement (Chua & McKenna 1995). Subsequent studies of sex differences suggested that male patients were more prone to ventricular enlargement, but the overall evidence was inconsistent (Salem & Kring 1998). The corpus callosum, a popular brain sex difference at the time that has been debunked since (Fausto-Sterling 2000), was also investigated but also yielded inconsistent outcomes (Salem & Kring 1998). Despite these initial disappointments, researchers have remained convinced that sex differences in the brain are a crucial window onto the aetiology of schizophrenia (e.g. Castle 2000; Goldstein 2006).
was tightened by the growing belief that schizophrenia is a neurodevelopmental disorder, caused by subtle influences on brain development before or during birth, such as maternal influenza or obstetric complications (Harrison 1997, Marenco & Weinberger 2000). This led researchers to propose a close link between prenatal hormone exposure and sexual differentiation of the brain for the development of schizophrenia.

For example, after finding sex-by-group interaction effects on the volumes of a number of cortical brain regions (schizophrenic women exhibited a reduction in anterior cingulate volume compared to healthy women), Goldstein and colleagues suggested that ‘factors that contribute to producing normal sexual dimorphisms may be the same factors that modulate brain abnormalities in schizophrenia’ (2002, 161-62). They restrict their discussion of possible factors to genetic and hormonal effects during the foetal and early postnatal period and activational effects of circulating hormones later in life, not considering the possibility that gender-specific life experiences might also play a role in the relationships between sex, brain, and disease. The proposed link between sexual differentiation of the brain and development of schizophrenia therefore hinges implicitly on the assumption that sex differences in the brain are either present or pre-programmed at birth.

This assumption underlies other available studies of sex differences in the schizophrenic brain as well. Gur and colleagues (2004) found that the volumetric ratio of the orbitofrontal cortex to the amygdala (OAR) is typically higher in healthy women than in men, but that there is a significant sex-by-group interaction effect on this trait. For female patients, the OAR was lower than that of their healthy controls, and for male patients the OAR was higher than for healthy men. As such, the authors state that, ‘schizophrenia results in “feminizing” the men and “masculinizing” the women’ (615), but at different nodes. In women, the orbitofrontal cortex largely drove this difference; in men, the amygdala incited the effect. ‘Because the amygdala is formed early in neurodevelopment,’ the authors state, ‘reduced amygdala volume in men with schizophrenia might represent direct gene effect or an earlier neurodevelopmental insult’ (615).

However, studies with non-human animals have established that the amygdala shows considerable structural plasticity (see McEwen et al. 2012). More research needs to be done on the human amygdala, but there is already some evidence that amygdala volume in humans can be affected by (early) experiences, including maternal depression (Lupien et al. 2011). This challenges the assumption that any ‘abnormal’ sexual differentiation in schizophrenic patients necessarily emerges at the beginning of life.

Gur and colleagues link their observations in the brain to the idea that female patients exhibit more positive symptoms, whereas male patients exhibit more negative symptoms. This
sex difference in clinical presentation is widely espoused, yet meta-analyses show that this difference has not been replicated across studies.\[57\] Gur and colleagues, however, did find a higher rate of avolition (but not other negative symptoms) for men and more severe delusion (and a non-significant increase in hallucinations) for women. Higher OAR was associated with more severe symptoms for men, but with less severe symptoms for women. The authors conclude that the ‘masculinization’ of the brains of female patients and the ‘feminization’ of the brains of male patients constitutes a compensatory process in response to the disease process (515).

As an adaptation to the ‘schizophrenia as reduced sexual dimorphism’ hypothesis, Crespi and Badcock recently proposed a two-axis system to understand sex differences in schizophrenia as well as autism (2008). One axis is that of ‘normal’ sexual differentiation between male and female brains, the other is an axis of cognition determined by maternally or paternally expressed imprinted genes. They argue that autism involves a predominance of paternally expressed genes, which results in the underdevelopment of social cognition; whereas schizophrenia emerges from a predominance of maternally expressed genes, which leads to an overdevelopment of social cognition. As such, autism and schizophrenia are positioned on opposite ends of a cognitive continuum from mechanistic to mentalistic thinking. This axis, the authors argue, is partially but not wholly aligned with the male-female axis, which should explain the preponderance of males with autism and of females with positive-symptom schizophrenia. On this account, then, schizophrenia is the expression of an extremely maternal brain, which correlates with having a female brain. Again, this is a theory that represents the link between sex and schizophrenia as a purely biological and homogenous process (for other critiques, see Fitzgerald & Hawi 2008, Keller 2008, Langdon & Brock 2008).\[58\]

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57. Although no studies find the opposite effect, a range of studies have found no significant differences (see Ochoa et al. 2012, Falkenburg & Tracy 2014). The content of delusions and hallucinations does appear to differ between men and women, but this might be explained by gender-specific experiences of trauma (Falkenburg & Tracy 2014, 64). In the study by Goldstein and colleagues (2002), there were no significant sex differences in positive and negative symptom ratings (but a non-significant trend towards more formal thought disorder and more hallucinations, both positive symptoms, in the men, as well as a non-significant trend towards more paranoid subtypes in the women).

58. Besides research on structural brain differences in schizophrenia, cognitive performance in schizophrenic patients has also been investigated. The results of this research have been highly inconsistent, in part due to poor design and low generalisability (e.g. Krysta et al. 2013; Mendrek & Mancini-Marie 2015; Mosholam-Gateley et al. 2009). One of the most prominent researchers in this area is Mendrek, who in 2009 held a talk at the scientific day of the Chair on Sex, Gender and Mental Health of the Canadian Institute of Gender and Health entitled ‘Schizophrenia: Trapped in the brain of the wrong sex?’. Unlike what this intentionally provocative title suggests, Mendrek’s work makes clear that the evidence linking sex differences in the brain and prenatal hormone exposure to schizophrenia is inconsistent, and that the influence of sex on cognitive functioning and brain morphology in schizophrenia patients is not homogenous. That is, depending on the structure or function of interest, studies find similar, absent or opposite sex differences in schizophrenic samples compared to healthy controls (Guillem et al. 2009). Even though she takes the link between schizophrenia and in-utero sexual
Meanwhile, what happened to research on sociocultural risk factors? Even though research in this area has been deprioritised, evidence has been mounting that sociocultural factors can increase the risk of schizophrenia, sometimes in gender-specific ways. Work by Lewine, for example, has shown that femininity, independent from being female, is a predictor of neuropsychological functioning across a number of domains (Lewine 2004; Lewine, Thurston-Snoha and Ardery 2006). In another study, it was found that socioeconomic status correlates with more severe symptoms in men, but with less severe symptoms in women, pointing to the role of class- and gender-specific social expectations placed on susceptible individuals (Parrott & Lewine 2005). Other preliminary evidence points to the possibility that positive and negative gender-related experiences, like sexual abuse, social support or caregiving responsibilities, affect the development of schizophrenia (reviewed in Falkenburg & Tracy 2014).

Gender is not the only social category of relevance, however. There is evidence that ethnic minorities are more vulnerable to schizophrenia. In particular, migrants and their children are at elevated risks up to five times higher than in native-born populations (reviewed in Selten, Cantor-Graae & Kahn 2007). Recent incidence studies suggest that black male migrants in particular are at high risk of developing schizophrenia due to their minority position. A study of very-late onset schizophrenia-like psychosis (SLP) in African- and Caribbean-born elders in London, for example, found a strongly increased risk in this group (Mitter et al. 2005). This risk was disproportionately greater in men, which was attributed to their greater social isolation. In addition, the age of onset for SLP was notably lowered in the migrant women compared to British-born women, an affect possibly mediated by an overall increase in mortality in female migrants. Overall, sex differences in risk and age of onset for SLP that were observed in the British-born population disappeared in the migrant group.\(^{59}\) The observation that migration differentiation of the brain very seriously, she has also stressed the entanglement of sex and gender and called for more research on the role of gender socialisation (Mendrek & Mancini-Marie 2015).

In addition, researchers have studied the role of hormones. Some evidence has emerged that oestrogen can act as a protective factor against schizophrenia in a number of ways, for example by lowering the risk of birth complications (Häfner 2003, Olsen et al. 2008). Endogenous oestrogen appears to be correlated with less severe symptoms in both men and women, and adjunctive oestrogen seems to alleviate symptoms somewhat (Da Silva & Ravindran 2015). However, the evidence is inconsistent and a number of studies have failed to replicate findings of lower circulating oestrogen levels in schizophrenic patients compared to controls (although no study reports to have found higher levels, see Da Silva & Ravindran 2015).

59. The interaction of gender and ethnicity not only affects an individual’s exposure to risk factors but also medical perceptions of what and who should count as schizophrenic—two related, but distinct phenomena. As Metzl (2010) shows in his book on race and schizophrenia, the disorder was described specifically as an expression of angry black masculinity in the 1960s and 1970s, coinciding with the Civil Rights Movement. His analysis shows that this connection between black masculinity and schizophrenia was forged by anxieties over racial power relations. Indeed, the history of schizophrenia is as racialised as it is gendered.
elevates the risk of schizophrenia (and might therefore correlate with ethnicity) was already made in a number of studies in the early twentieth century, but research on this topic was largely abandoned once it had been suggested that causality had to be understood in the opposite direction (i.e. schizophrenia increases chance of migration, see Selten & Cantor-Graae 2004). From the 1980s onwards, while US-American psychiatry turned towards neurobiological models, European researchers started looking into the effects of migration once more (Selten, Cantor-Graae & Kahn 2007, Jarvis 2007). Unfortunately, it is still eclipsed by the dominant tripartite frame of genetics, neurology, and endocrinology, especially in US-American research (Nasser, Walders & Jenkins 2002, Jarvis 2007).

The overview of the history of schizophrenia I have provided here is but a crude representation of a long and complicated history, but it should suffice to demonstrate the extent to which schizophrenia has been defined, contested, and redefined in gendered terms. Not only have restrictive gender roles caused men and women to develop gender-specific dysfunctions, but perceptions of ideal femininity and masculinity have affected how patient populations are defined, how patients are selected for treatment, and how research questions about the aetiology of the disease are formulated. Such biases have not been restricted to biological approaches; as the notion of the schizophrenogenic mother shows, accounts of social causation are just as amenable to sexist perceptions as biological explanations. Nevertheless, the greatest concern that I currently deduce is posed by the neurobiological approach that mobilises brain sex theory as a tool to understand schizophrenia. This strategy takes sex differences in the prevalence, age of onset, and symptomatology of schizophrenia for granted (even though they are to this day subject of debate, see Eranti, MacCabe, Bundy & Murray 2013; Ochoa et al. 2012), and assumes that these differences can be fully explained by genetic, hormonal, and/or neurological mechanisms. In addition, it assumes that sex differences in the healthy brain are well-understood and uncontroversial, and that they are hardwired. These assumptions justify each other: naturalising sex/gender differences in the brain encourages the naturalisation of sex/gender differences in schizophrenia, and vice-versa. Consequently, not only is ‘normal’ sexual differentiation of the brain used to understand how schizophrenia develops; sex/gender differences in schizophrenia are also mobilised as an argument to justify

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60. One important issue that I have not addressed here for the sake of brevity is the historical association between schizophrenia and gender identity. Elements of gender dysphoria in patients diagnosed with schizophrenia have been described since transsexualism was first considered as a psychiatric diagnosis (Hoenig & Kenna 1974), with some reports describing schizophrenic patients misdiagnosed as transsexual (e.g. Campo et al. 2001). It cannot be estimated how many transgender people have been misdiagnosed as schizophrenic throughout history. To this day, evidence of comorbidity between schizophrenia and gender dysphoria is contested, and the implications of a possible link unclear (Rajkumar 2014).
and promote more basic research on sex differences in the brain (e.g. Bao & Swaab 2010; Cahill 2006; Cosgrove, Mazure & Staley 2007; McCarthy et al. 2012). The problem is therefore not only that the deprioritisation of social factors stands in the way of fully understanding the nature of schizophrenia, but also that it legitimises a problematic understanding of sex differences in the brain.

In the end, what is required for a better understanding of schizophrenia is more integrative research that allows us to understand the interaction of vulnerabilities that may arise at very early stages of development (which may or may not be distributed unevenly in relation to sex) with relevant environmental influences (which may or may not be distributed unevenly in relation to gender and its intersecting categories). To achieve such an integration, a diathesis-stress model of schizophrenia has been developed from the 1980s onwards (Neuchterlein & Dawson 1986; Walker & Diforio 1997). This dual-risk model proposes that stressors act on existing biological vulnerabilities through specific neurobiological mechanisms. As Jones and Fernyhough (2007) have argued, one limitation to the model has been ‘the assumption that psychosocial stressors, a notoriously subjective concept, form a homogeneous category with similar physiological effects’ (1172). This highlights the necessity of studying physiological processes in context, an altogether more appropriate and promising research direction than brain organisation theory provides.

**Autism**

Like schizophrenia, autism has proven to be a heterogeneous category with heterogeneous aetiology. Previous editions of the DSM delineated subtypes, but research has not been able to link these to specific causes or pathways. In the DSM-5, the single umbrella term ‘autism spectrum disorder’ has replaced the subtypes. And like schizophrenia, autism has been studied mostly in relation to genetic, hormonal, and neurobiological factors, with a starring role for hardwired sex differences in the brain.

When Bleuler (1911) redefined dementia praecox as ‘schizophrenia’, he specified four core symptoms: abnormal associations, abnormal affect, ambivalence, and autism. He defined autism as an active withdrawal from the outer world in favour of the object of inner life, and used the term as an alternative to Freud’s notion of autoeroticism (Bleuler 1911, 1951; Dalzell 2007). In 1943, US child psychiatrist Leo Kanner had reported on 11 children displaying ‘extreme autism, obsessiveness, stereotype and echolalia’ (248). Kanner argued that these symptoms are very similar to childhood schizophrenia, but also different in that the children have these symptoms from birth onwards, and display ‘an excellent, purposeful, and
“intelligent” relation to objects’ (249). Kanner therefore maintained that he had observed a distinct syndrome. When considering the aetiology, he offered his observation that the parents of his subject group were cold, ‘strongly occupied with abstractions of a scientific, literary, or artistic nature’, and prone to unhappy marriages (Ibid.). However, Kanner argued in the end, since these children appear to be affected from birth onwards, it would be better to ‘assume that these children have come into the world with innate inability to form the usual, biologically provided affective contact with people, just as other children come into the world with innate physical or intellectual handicaps’ (Ibid.). At the same time, the Viennese psychiatrist Hans Asperger reported similar cases in Austria. Like Kanner, he argued that these cases represented a distinct childhood disorder, which he labelled ‘autistic psychopathy’ (1944).

This disorder, he observes, is characterised by ‘severe and characteristic difficulties of social integration’, which is sometimes compensated by ‘a high level of original thought and experience’ which can ‘lead to exceptional achievements in later life’ (37).

Gillis-Buck and Richardson note that observations of male prevalence shaped the diagnosis of autism from these early beginnings onwards (2014). Both Kanner and Asperger observed that their childhood syndromes affected boys much more often than girls. When medical professionals debated whether or not Kanner’s ‘early infantile autism’ should indeed be distinguished from childhood schizophrenia, ‘Sex difference was part of this debate, with the male prevalence of autism cited as evidence for two discrete disorders’ (4). ‘Infantile autism’ was eventually included in the DSM-III in 1980. In 1994, ‘Asperger’s disorder’ was added, creating a spectrum of autism from low to high functioning, before the DSM-5 merged them under the single header ‘Autistic Spectrum Disorder’ in 2013.

These developments, Gillis-Buck and Richardson argue, have contributed to the current success of the ‘extreme male brain’ (EMB) theory of autism, which has been proposed by Baron-Cohen (Baron-Cohen & Hammer 1997, Baron-Cohen 2002). According to this view, sex differences in human cognition and emotion can be understood as a continuum with ‘empathizing’ on one end and ‘systemizing’ on the other. The ‘essential difference’ between male and female brains is that male brains are wired for systemising, whereas the female brain is predisposed towards empathising. These differences are supposedly hardwired from birth onwards. Baron-Cohen (2002) proposes that autism is the expression of an extremely masculinised brain: superior at systemising, yet very poor when it comes to empathising. This

61. Nevertheless, the concept of the ‘refrigerator mother’ would persist; see Nadesan (2005).
62. For a discussion of the differences between Kanner’s ‘early infantile autism’ and Asperger’s ‘autistic psychopathy’, see Van Krevelen (1971).
theory has received critique from a wide range of writers, including autistic bloggers, autism researchers, philosophers of mind, and gender scholars, who have argued that the extreme male brain hypothesis simplifies and misrepresents the nature of autism and that it relies on an outdated, unsupported notion of hardwired brain sex (e.g. Rogers 2003; Levy 2004; Bumiller 2008; Cohen-Rottenberg 2009; Fine 2011; Grossi & Fine 2012; Krahn & Fenton 2012; Sample 2012). To put it shortly, in Baron-Cohen’s work, autism is used to provide a rationale for brain sex as much as brain sex is used to provide a rationale for autism. Nevertheless, the EMB theory has become very influential.

Gillis-Buck and Richardson (2014) write that a male prevalence of 4:1 in autism is ubiquitously cited in research in service of constructing a ‘biomedical platform’ for basic sex-difference research. Analysing recent grant-funded research, they show that researchers have increasingly made their genetic, hormonal, or neurological research relevant to autism by citing this statistic, which enables them to profit from the large amount of funding available for autism research. However, they argue that this statistic is ‘empirically underdetermined’ (17). The male prevalence is significantly smaller in individuals with intellectual disabilities, and research on girls with autism is generally lacking. Similar to the neuroscientific studies of schizophrenia discussed above, studies citing the 4:1 statistic assume that the male prevalence in a relatively small subset of the autistic population ‘carries insight into the general aetiology of the condition’ and that ‘current diagnosis rates of males and females reflect organic facts about autism and not gender stereotypes in diagnostic practices’ (8). Consequently, they argue, the preoccupation with the 4:1 statistic provides a platform for brain sex studies and also marginalises a large (and arguably the most vulnerable) part of the population with autism, does little to encourage research on autism in girls, and entrenches the harmful gender stereotype that male brains are wired for systemising cognition.

In a recent paper, Mottron and colleagues (2015) proposed an alternative to the EMB theory: the enhanced plasticity hypothesis. Building on recent work that suggests that aberrant plasticity underlies autism, Mottron has proposed a ‘Trigger-Threshold-Target’ model in which genetic mutations or environmental insults increase synaptic plasticity (Mottron et al. 2014). Depending on the individual’s unique threshold, this induces functional reallocations that result in mild or severe disabilities. According to Mottron, autism affects males more often and in different ways, because males and females display different plastic reactions in response to the same event, and because males’ overall threshold for a plastic reaction is lower (2015). The authors link these sex differences back to genetically and hormonally regulated prenatal and early postnatal development. While the enhanced plasticity hypothesis proposes a more
complex account of autistic development than the EMB theory, it also relies solely on a notion of congenital sex differences in the brain (specifically, sex differences in plasticity) to explain the male preponderance of autism. Whilst this makes autism more amenable to early intervention, it does not take into account the possibility that the sex disparity in autism itself may be, at least partly, contingent on environmental influences.

Against this common view that males must be inherently more vulnerable to autism and that socialisation does not play a significant role in the male preponderance, Cheslack-Postava and Rebecca Jordan-Young (2012) have argued that ‘considering how social as well as biological forces might be acting to cause observed disparity may provide new insights into its etiology’ (1668). Taking the entanglement of sex and gender as their starting point, the authors propose a gendered embodiment model of autism spectrum disorders, in which gender is understood as a ‘pervasive developmental environment’ (2012). This model traces the developmental trajectories through which children with initial vulnerabilities, ‘any of which might be differentially distributed by (genetic) sex, nor not’ (1669), interact with gendered social processes (e.g. in the parent-infant interaction). As such, it opens up for investigation a realm of questions that is typically ignored in the research literature on autism.63

**Statistical panic: the female brain at risk**

My discussion of schizophrenia and autism has made clear that male-female differences in health outcomes are not clear-cut, and not necessarily reducible to biological causes. Nevertheless, the movement for sex-linked biology foregrounds sex as a biological variable as one of the main determinants of health. Epstein (2007) writes that this salience of sex as a medical category has not merely grown out of objective scientific observations, but has specific historical and ideological roots. He points out that socioeconomic status is one of the best predictors of health outcomes, yet it is not nearly awarded the same significance as sex is. The implications of such visibilities and invisibilities go beyond the realm of medical practice: ‘if social class were incorporated as a standard signifier, the political effects might be significant: because social class is not seen as a biological category, to call attention to differential health outcomes by class is to call attention to the effects of social inequality on health’ (144). The

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63. Again, I have left aside the issue of gender identity. Recent studies have suggested a link between autism and gender dysphoria, but the available evidence is limited and the implications of such a link unclear (Van der Miesen, Hurley & de Vries 2016; Van Schalkwyk, Klingensmith & Volkmar 2015).
current focus on sex, as separate from gender, has the opposite effect: it shifts the attention away from social inequalities by attributing risk to immutable individual characteristics.

Following Epstein (2007), I consider sex, as it is currently mobilised as a prominent medical category, as a ‘biosocial’ category. Biosociality a concept formulated by Rabinow (1996), who builds on Foucault’s notion of ‘biopower’ (1976) to give an account of the emergence of new identities and affiliations under the influence of the life sciences. Sex—as the sex-based biology movement defines it—is a biosocial category, because its emergence as a medical classification has transformed the way women’s bodies and their health are understood (from reproductive organs to sex in every cell, including the brain), thereby forming a new basis for affiliations between women (sharing susceptibilities for specific diseases). This process has been about inclusion as much as it has been about exclusion, as it gave rise to a normative view of ‘the’ woman, thus marginalising the needs of women who fall outside of this norm (Eckman 1998; Dubriwny 2012). Further, this transformation involved not only scientific processes but also ethical struggles, as knowing women’s physiological makeup has been equated with acknowledging women’s fundamental human rights; yet, at the same time, as discussed above, many aspects of women’s health have been depoliticised.

Considering sex as a medical category in terms of biosociality suggests that the sex-based biology movement has not only increased medico-scientific objectification, inspection, and intervention regarding women’s bodies but also arguably changed women’s self-perception, affiliation, and conduct. At stake in challenging the contemporary discourse surrounding women’s health is thus not just what bodies/brains are but also what kinds of subject positions the very preoccupation with neurobiology brings about. This much was already suggested in my discussion of the sex-based biology movement at the beginning of this chapter, and I wish to develop this direction further before closing this chapter. I will, therefore, briefly examine the modes of subjectification to which consumer-oriented advocacy for women’s mental and brain health gives rise. In particular, I am interested in the role of the statistic. Above, I discussed the observation from Gillis-Buck and Richardson (2014) that statistics expressing sex/gender disparities in pathology are mobilised to create a biomedical platform for basic sex difference research. What kind of work do these statistics perform when they are used to address and activate women as health consumers and (prospective) patients?

Consumer-oriented messages from the sex-based biology movement often rely on statistics to inspire concern. Take for example, the website of the Women’s Brain Health
Initiative (WBHI), which is based in Toronto and has a branch in Florida. The aims of the WBHI include raising funds for research on female physiology in the interest of reducing age-related brain disorders, to educate women about the risks that affect them, and to inform women about the ways in which they can ‘detect, prevent, and manage [their] brain health’. The site offers many informative articles with news about women’s brain health, as well as numerous tips on how women can adjust their lifestyles to ward off age-related decline. These tips revolve mostly around eating healthy and staying physically, mentally, and socially active (adjustments, the Initiative posits, that owe their efficacy to the phenomenon of brain plasticity). The WBHI homepage greets its visitors with the message that ‘70% of Alzheimer’s sufferers will be women’, and that ‘all of your female employees are at risk’ of age-related brain disease. In the ‘about’ section, the website states that ‘It was frightening to learn that women suffer from depression, stroke and dementia twice as much as men and an astounding 70% of new Alzheimer’s patients will be women’.

The prominence of such statistics expresses something fundamental about how risk, health and disease are conceptualised in daily life. As Greco (1993) has written over two decades ago, disease is no longer commonly understood as an interruption of a healthy state but rather as continuous with a person’s normal life (359). Rather than causes, this conceptualisation of health and pathology focuses on ‘a personal susceptibility which is logically prior to cause’ (359). To live, then, ‘is already and ever-increasingly to be at-risk’, and ‘to “prevent” becomes already to “cure” something’ (360). As a result, individuals are continuously compelled to work on their health. The website of the US Office for Women’s Health (OWH) expresses this conceptualisation of health, illness, and risk bluntly: ‘You don’t automatically have good mental health just because you don’t have mental health illness. You have to work to keep your mind healthy’. No longer directly connected to environmental or individual causes, risk can no longer be bodily experienced: ‘Neither health nor illnesses are states of being: they are states of knowledge; they are epistemic’ (Dumit 2012, 13). Hence, the requirement of the statistic, a crucial tool to calculate one’s risk and act accordingly.

To further understand the work that statistics expressing health disparities do in this context, it is useful to consider them in relation to Woodward’s (1999) discussion of ‘statistical panic’. Woodward writes that the statistic is a language that pervades our culture, ‘one that continuously offers itself up as a way of understanding our lives and the world and condenses itself into a single figure’ (178). Constituting ‘a discourse of probability’ (179), the language

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64. See http://womensbrainhealth.org/.
of statistics is fully detached from the material body; it tells nothing of the present except the risk we are currently at: ‘I have an eighty percent chance… you have a ten percent risk… … We are at risk, it seems, of anything and everything’ (179). The ubiquity of risk, Woodward contends, engenders ‘a structure of postmodern feeling that oscillates between urgency and boredom’ (193). That is, the constant confrontation with impending doom inspires both panic and cynicism. So for movements like the women’s health movement, statistics are a critical tool, but are insufficient alone:

In part the challenge for those activists is to convince others to understand the urgency implied in the tedious, quantitative language of the statistic. … Much public policy depends on mobilizing statistical panic … Statistical panic: fatally, we feel that a certain statistic, which is in fact based on an aggregate and is only a measure of probability, actually represents our very future. (185)

One way of making sure women experience health statistics as urgent and personal is to appeal to their gendered responsibilities. The WBHI website features a glossy online magazine entitled *Mind over Matter* (MOM), offering ‘insights into the latest research findings to combat brain ageing diseases and the tools you need to stay brain healthy longer’. The opening article, entitled ‘Good, better, best’, features Dr Brown, who discusses women’s priorities: ‘women taking care of themselves is not being selfish, it’s being selfless. It will ensure they stay healthy and able to take care of the people in their lives. The whole concept of creating time for yourself, making yourself a priority, is important not just for you but for your whole family’ (8). Other resources on women’s mental and neurological health likewise address women explicitly as caretakers. The US Office on Women’s Health (OWH), for example, explains the importance of women protecting their own mental health by monitoring and adjusting their nutrition, exercise, sleep and stress levels by stating that ‘Your health is very important. you will not have a healthy body if you don’t also take care of your mind. People depend on you’ (US 2010). Similarly, the consumer guide *Women’s Mental Health: What it Means to You* (US 2009), published by the Women’s Mental Health Initiative (WMHI, overseen by the OWH), writes that ‘Other people depend on you and your well-being. Your mental health affects how you act with family and friends. It affects your work. Taking care of your mental health is important to

the people around you’ (2). Whereas these resources acknowledge the fact that women’s gender role exposes them to stressors, they simultaneously urge women to stay healthy by carefully managing their lifestyle in order to optimally perform their gender role. As such, the visibility of women’s specific health needs is won at the price of de-politicisation: their health is addressed, but valued explicitly in relation to traditional feminine values. The desirability or necessity of those values is not put in question.

This consumer-oriented material on women’s mental and brain health, then, gives rise to a female identity that Dubriwny (2012), in her analysis of today’s dominant women’s health discourse, has called ‘the vulnerable empowered woman’. This identity, Dubriwny argues throughout her book, is shaped by postfeminist and neoliberal ideologies and thereby ‘disarticulated’ from feminist politics (13). These ideologies govern the women’s health discourse ‘through a larger rhetoric of risk in which women are represented as part of an inherently at-risk group that must engage in a constant monitoring and management of risk’ (Ibid.). Within this discourse, women’s purported empowerment is merely the freedom to shop amongst a limited offering of lifestyle advices and treatments.

Both biological determinism and plasticity-based arguments play a role in the emergence of the vulnerable empowered women. Research programs linking gender disparities in health to sex differences in the brain—understood as hardwired and dichotomous—give rise to a perception of risk as unequally distributed across male and female brains. Similarly, by offering up statistics that indicate gender disparities rather the percentage of women that actually develop a disease like Alzheimer’s, organisations like the WBHI implicate all women as a single group defined by a shared, inherent susceptibility of the female brain. This susceptibility places women in ‘a state that at some inevitable future time will be fulfilled as a state of disease or health’ (Woodward 1999, 196). The constitution of ‘women’ as a biosocial category thus takes place in reference to the notion of the female brain. However, the notion of biosociality also points to forms of authority and truth claims that compel individuals to work on themselves in the interest of their health. Crucially, a woman’s risk of actually developing a disease is not 100%, and therefore not fully determined by the sex of her brain. This state of uncertainty, communicated to her in the language of the statistic (in reference to her responsibilities as a woman to induce a sense of alarm), is what should compel her to monitor and manage her life in order to minimise her risk. And just as brain sex appears to be the material referent for the abstract statistics of susceptibility (‘the female brain has a 60% chance of…’), so brain plasticity appears as the material ground for the purported risk-lowering effects
nature does not define the disorders designated by our current diagnostic labels, all of which were devised by committees of clinicians who were voting on the symptoms. …
While genes cut across the current diagnostic labels, neuroimaging often helps us to subdivide groups. By studying patterns of brain activity at rest or with activation, we can begin to let the brain tell us the different forms of mood, anxiety, or psychotic disorders. (2012)

There is a suggestion in this comment that neuroscience can ‘carve nature at its joints’. This same suggestion is at work in studies that use brain sex to elucidate the nature of psychiatric disorders. In these studies, the reification of brain sex and of brain diseases go hand in hand. Following Haraway (1988) and Barad (2007), I consider scientific practices to be a fundamental part of what they aim to measure. That is, the boundaries between male and female, healthy and pathological, and nature and nurture are not materialised in brains and then ‘discovered’ in scientific practices. Rather, they materialise, or are enacted, in the relationship between brains, scanners, observers, and the technosocial conditions in which these and other relevant actors are embedded (including the gendered history of mental health described in this chapter). This is not to say that disorders are not real, or not biological. They are, but in a different sense than suggested by Insel’s words. That is, they are relational and cannot be understood in isolation from the ‘apparatus of bodily production’ (Haraway 1988: 595) that maps them.

At stake in this discussion is not just the question what women’s brains are but also the question of what kinds of subject positions the very preoccupation with brains brings about. As Thornton (2011a) has written, life is not medicalised so much because individuals are ‘brainwashed to accept pharmaceutical remedies for common distress’ but rather because ‘they are conditioned to understand life as a calculable project that they are responsible for assessing and quantifying through neurobiological lenses’ (113). Plasticity-based arguments that insist on the entanglement of nature and culture may be used as a tool to bring back into view the social factors shaping women’s bodies and their health, and thereby contribute to the re-politicisation of women’s health. Yet, at the same time, plasticity-based visions of the subject contribute to the individualisation of risk and health management precisely by rendering risk a non-deterministic and manageable phenomenon that may be targeted at the level of the individual body. That is, in popular brain-based discourses, plastic brain anatomy does not equal destiny, but it does figure as the point where all risk factors can be translated into a common brain-based language, and therefore functions as the appropriate target of intervention. As a result, a reconsideration of what bodies are and how knowledge about bodies is produced in a biomedical context should not take place without a simultaneous consideration of who can and
must be responsible for these bodies. In other words, envisioning an alternative future for women’s health advocacy is an ‘ethico-onto-epistemological’ challenge (Barad 2007, 185).